

## Redacted Data Submitted by the Primary Manufacturer and Other Interested Parties for Xarelto

Below are redacted versions of the data submitted by the Primary Manufacturer and other interested parties in response to the Negotiation Program information collection request.<sup>1</sup> These redacted data have been redacted consistent with the confidentiality standards described in section 40.2 of the revised guidance and do not contain proprietary information, protected health information (PHI)/personally identifiable information (PII), or other information that is protected from disclosure under applicable law.

Respondents were permitted to include citations and attachments (hereinafter, collectively called “supplemental materials”) within their submissions for certain questions specified in the information collection request; therefore, you may observe that the number and order of any supplemental materials included as part of each response below will vary.

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<sup>1</sup> The Negotiation Program information collection request is available on the Office of Management and Budget’s (OMB’s) website at the following link: [https://www.reginfo.gov/public/do/PRAViewICR?ref\\_nbr=202306-0938-013](https://www.reginfo.gov/public/do/PRAViewICR?ref_nbr=202306-0938-013) and described in section 50 of revised guidance.

Section 1194(e)(1) Data Factors
<b>IPAY Year:</b> 2026
<b>Manufacturer:</b> Janssen Pharmaceuticals, Inc.
<b>Drug:</b> Xarelto (Rivaroxaban)
<p><b>Background:</b> For the first year of the Medicare Drug Price Negotiation Program (“the Negotiation Program”), CMS selected 10 Part D high expenditure, single source drugs for negotiation. Section 1194(e) of the Act requires Centers for Medicare &amp; Medicaid Services (CMS) to consider two sets of factors as the basis for determining the offer and counteroffer throughout the negotiation process: (1) certain data that must be submitted by the manufacturer of each drug selected for negotiation and (2) evidence about alternative treatments, as available, with respect to each selected drug and therapeutic alternative(s) for each selected drug. After entering into an agreement under the Negotiation Program with CMS and in accordance with section 1193(a)(4) of the Act, the Primary Manufacturer of each selected drug submitted to CMS the following information with respect to a selected drug: information that CMS required to carry out negotiation, including but not limited to the factors listed in section 1194(e)(1) of the Act. For IPAY 2026, the Primary Manufacturer of each selected drug were tasked to provide the following data factors for each of its selected drug(s), which were specifically:</p> <ul style="list-style-type: none"> <li>C: Research and Development Costs and Recoupment,</li> <li>D: Current Unit Costs of Production and Distribution,</li> <li>E: Prior Federal Financial Support,</li> <li>F: Patents, Exclusivities, and Approvals, and</li> <li>G: Market Data and Revenue and Sales Volume Data.</li> </ul> <p>The Primary Manufacturer is responsible for aggregating and reporting all necessary data on its selected drug(s) from other parties, as applicable.</p> <p><b>Disclaimers:</b> With the exclusion of publicly available data, all manufacturer submitted data is considered proprietary and confidential. The data contained in this document are solely those of the authors and do not necessarily reflect the views or policies of CMS. The authors assume responsibility for the accuracy and completeness of the information contained in this document.</p>

**Note:** Primary Manufacturers submitted required data in the Health Plan Management System (HPMS). Please note that the format of manufacturer responses is dependent on the data element requested. For example, some requested responses are “yes or no”, while other response options in HPMS provided a drop-down menu. However, some responses could be more complex and subjective, such as dollar



amounts, cost per unit, etc. For many questions, the ICR instructs the manufacturer to include an explanation. In some instances, an explanation is required and in other instances, the ICR directs the user to include an explanation “as necessary.” CMS instructs manufacturers to indicate “n/a” if they choose not to include an explanation in this case.

C. Research and Development Cost							
<b>Description:</b> Section C contains five questions, related to different types of R&D costs incurred by the Primary Manufacturer, including acquisition costs. Each of these questions required the Primary Manufacturer to report, as applicable: (1) dollar amounts for R&D costs, which must be reported in the numerical response field and (2) explanations of how those costs were calculated in the free response field. Section C also contains one question about the Primary Manufacturer’s global and U.S. total lifetime net revenue for the selected drug. This question required the Primary Manufacturer to report, as applicable: (1) the dollar amount for global, total lifetime net revenue, which must be reported in the numerical response field, (2) an explanation of how this amount was calculated in the free response field, (3) the dollar amount for U.S. lifetime net revenue, which must be reported in the numerical response field, and (4) an explanation of how this amount was calculated in the free response field.							
Primary Manufacturer Acquisition Costs of the Selected Drug	Total Acquisition Costs for the Selected Drug	Basic Pre-Clinical Research for All Approved Indications of the Selected Drug	Post-IND Costs for All Approved Indications of the Selected Drug	Costs of Failed or Abandoned Products Related to the Selected Drug	Direct Costs of Other R&D for the Selected Drug Not Accounted for Above	Global Total Lifetime Net Revenue for the Selected Drug	U.S. Total Lifetime Net Revenue for the Selected Drug

**Explanations:**

Explanation of Allocation of Total Acquisition Costs for the Selected Drug

Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

Please note that the adjusted data elements as of December 22, 2023 are in response to the email from CMS IRA Rebate and Negotiation <IRAREbateandNegotiation@cms.hhs.gov> with the subject “RE: Janssen Pharms section 1194(e)(1) Xarelto Data Submission Follow-up” received on December 14, 2023 – and includes the requested adjustments to Topic (5), Topic (6), and Topic (7).

The following free text was entered as part of our original HPMS submission for these data elements, and the previously referenced email provides context regarding the requested data element adjustments.

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“Primary Manufacturer Acquisition Costs of the Selected Drug” include upfront payment to Bayer Healthcare AG (“Bayer”) [REDACTED]

[REDACTED]

Annual Spend by Year is broken out below in USD, inclusive of Cost of Capital adjustments:

[REDACTED]

Annual Spend by Year is broken out below in USD, excluding the Cost of Capital adjustments:

[REDACTED]

It should be noted that responses to Section C do not represent the full cost incurred by Janssen for XARELTO. This does not include full investment, and excludes R&D overhead, Cost of Goods sold over the life of the product, ongoing Operating expenses such as Sales & Marketing, as well as Infrastructure Overhead.

[REDACTED]

Explanation of Basic Pre-Clinical Research Costs

Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

“Basic Pre-Clinical Research for All Approved Indications of the Selected Drug” is not being submitted as this activity took place prior to Janssen/Bayer collaboration which began in 2005, Post IND. Original IND Filed May 29, 2002 by Bayer.

Explanation of Post-IND Costs

Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

[REDACTED]

[REDACTED] These direct costs include global clinical operations, product development and supply, quantitative sciences, and other direct functional costs to support approved XARELTO indications. The approved indications did not receive early approvals. [REDACTED]

[REDACTED]



Annual Spend by Year is broken out below in USD, inclusive of Cost of Capital adjustments:

[REDACTED]

Annual Spend by Year is broken out below in USD, excluding the Cost of Capital adjustments:

[REDACTED]

[REDACTED]

Explanation of Costs on Allowable Failed or Abandoned Products Related to the Selected Drug

Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

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The following free text was entered as part of our original HPMS submission for these data elements, and the previously referenced email provides context regarding the requested data element adjustments.

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[REDACTED]

Abandoned and failed program total includes Xarelto Acute Coronary Syndrome (ACS) which was a positive study that was approved in Europe but rejected by the US FDA, XARELTO Congestive Heart Failure, XARELTO Embolic Stroke Undetermined Source, XARELTO VTP in Cancer (CASSINI), XARELTO ACS Dual Therapy, and XARELTO PREVENT study which looked at a subset of medically ill patients with COVID.

[REDACTED]

[REDACTED]

[REDACTED]

Annual Spend by Year is broken out below in USD, inclusive of Cost of Capital adjustments:

[REDACTED]

Annual Spend by Year is broken out below in USD, excluding the Cost of Capital adjustments:

[REDACTED]

[REDACTED]

#### Explanation of Costs of Other R&D

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Please note that the adjusted data elements as of December 22, 2023 are in response to the email from CMS IRA Rebate and Negotiation <IRAREbateandNegotiation@cms.hhs.gov> with the subject “RE: Janssen Pharms section 1194(e)(1) Xarelto Data Submission Follow-up” received on December 14, 2023 – and includes the requested adjustments to Topic (5), Topic (6), and Topic (7).

The following free text was entered as part of our original HPMS submission for these data elements, and the previously referenced email

provides context regarding the requested data element adjustments.

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“Direct Costs of Other R&D for the Selected Drug Not Accounted for Above” includes life cycle management studies, pharmacovigilance expenses, and medical affairs programs inclusive of investigator-initiated studies, registries, and publications consistent with the ICR. Total also includes the Janssen contribution to Portola for a FXA inhibitor reversal agent, Andexanet Alfa (ANDEXXA).

[REDACTED]

[REDACTED]

Annual Spend by Year is broken out below in USD, inclusive of Cost of Capital adjustments:

[REDACTED]

Annual Spend by Year is broken out below in USD, excluding the Cost of Capital adjustments:

[REDACTED]

[REDACTED]

Explanation of Global Lifetime Net Revenue



Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

“Global and U.S. Total Lifetime Net Revenue for the Selected Drug” is inclusive of the dates ranging from 2011-2023. These figures conform with GAAP Accounting Standard Certification (ASC) 830 for translating foreign currencies and are consistent with External disclosures.

For XARELTO, U.S. and Worldwide are the same figures due to the fact that Janssen as the Primary Manufacturer only recognizes sales in the U.S. based on a licensing agreement.

Third Party Royalties are deducted from externally reported Net Trade Sales as per the ICR guidance.

In the case of both license agreements the royalties are paid to the licensors [REDACTED]. [REDACTED]. Third party royalties are included in the P&L of Janssen Pharmaceuticals, Inc. as a part of Cost of Goods Sold (OCNIS - Other Costs Not In Standard). Third Party Royalty figures conform with GAAP Accounting Standard Certification (ASC) 830 for translating foreign currencies and are consistent with External disclosures.

### Explanation of U.S. Lifetime Net Revenue

Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

“Global and U.S. Total Lifetime Net Revenue for the Selected Drug” is inclusive of the dates ranging from 2011-2023 and was derived from our enterprise reporting system (BRAVO). These figures conform with GAAP Accounting Standard Certification (ASC) 830 for translating foreign currencies and are consistent with External disclosures.

For XARELTO, U.S. and Worldwide are the same figures due to the fact that Janssen as the Primary Manufacturer only recognizes sales in the U.S. based on a licensing agreement.

Third Party Royalties are deducted from externally reported Net Trade Sales as per the ICR guidance. These royalties are paid to two licensors. The first is to Bayer Healthcare AG under the 2005 Collaborative Development and License Agreement between Ortho-McNeil Pharmaceutical

Inc. (later renamed Janssen Pharmaceuticals, Inc.) and Bayer. Royalties have been paid to Bayer upon the first commercial sale of XARELTO. Royalties are calculated on a tiered rate basis based on annual Net Sales in the US of XARELTO.

. Third party royalties are included in the P&L of Janssen Pharmaceuticals, Inc. as a part of Cost of Goods Sold (OCNIS - Other Costs Not In Standard). Third Party Royalty figures conform with GAAP Accounting Standard Certification (ASC) 830 for translating foreign currencies and are consistent with External disclosures.

D. Current Unit Costs of Production and Distribution				
<b>Background:</b> Manufacturers were required to report production and distribution unit costs separately for each NDC-11 of the selected drug, including any NDC-11 of the selected drug marketed by a Secondary Manufacturer. A free response field was provided to explain the methodology for calculating the amount reported.				
NDC-11	Average Per Unit Production Cost	Average Per Unit Distribution Costs	Indicate Unit Used	Total Unit Volume
50458-0580-10			EA	
50458-0580-30			EA	
50458-0579-10			EA	
50458-0579-30			EA	
50458-0579-90			EA	
50458-0578-10			EA	
50458-0578-30			EA	
50458-0578-90			EA	
50458-0577-10			EA	
50458-0577-18			EA	

#### D. Current Unit Costs of Production and Distribution

**Background:** Manufacturers were required to report production and distribution unit costs separately for each NDC-11 of the selected drug, including any NDC-11 of the selected drug marketed by a Secondary Manufacturer. A free response field was provided to explain the methodology for calculating the amount reported.

NDC-11	Average Per Unit Production Cost	Average Per Unit Distribution Costs	Indicate Unit Used	Total Unit Volume
50458-0577-60			EA	
50458-0584-51			EA	
50458-0580-90			EA	
50458-0579-89			EA	
50458-0575-01			ML	
50458-0578-14			EA	
50458-0580-07			EA	
50458-0577-14			EA	
50458-0578-07			EA	
50458-0579-07			EA	
50458-0579-99			EA	
50458-0584-52			EA	
55154-1422-00			EA	
55154-1424-00			EA	
55154-1423-08			EA	
50458-0577-01			EA	
50458-0578-01			EA	
50458-0579-01			EA	
50458-0580-01			EA	
55154-1424-08			EA	



**Explanations:** Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

Please note that the adjusted data elements as of December 22, 2023 are in response to the email from CMS IRA Rebate and Negotiation <IRAREbateandNegotiation@cms.hhs.gov> with the subject “RE: Janssen Pharms section 1194(e)(1) Xarelto Data Submission Follow-up” received on December 14, 2023 – and includes the requested adjustments to Topic (5), Topic (6), and Topic (7).

The following free text was entered as part of our original HPMS submission for these data elements, and the previously referenced email provides context regarding the requested data element adjustments.

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Thirty-six NDC-11s for “XARELTO” are included in the “Selected Drug List for Initial Price Applicability Year (IPAY) 2026”.

Consistent with CMS guidance, this submission reflects information on NDC-11s of the selected drug marketed by the Primary Manufacturer (Janssen Pharmaceuticals, Inc. or “JPI”) and any Secondary Manufacturer.

CMS has prepopulated Section A to include NDC-11s for XARELTO that include NDC-11s for XARELTO distributed by entities that do not meet the definition of “Secondary Manufacturer” because they are not listed in the XARELTO NDA and do not market XARELTO pursuant to an agreement with a Johnson & Johnson company. These NDC-11s are: One for Aphena Pharma Solutions -Tennessee, LLC (71610-0690-42), four for A-S Medication Solutions (50090-3625-00, 50090-3639-00, 50090-4468-00, 50090-4469-00), and one for Avera McKennan Hospital (69189-0578-01).

The NDC under Avera (69189-0578-01) was discontinued, and, after reasonable investigations, the following NDCs under A-S Medication Solutions do not appear to have ever been in use (i.e., 50090-3625-00, 50090-3639-00, 50090-4468-00, and 50090-4469-00).

Seven NDC-11s are sample NDCs under JPI labeler 50458: 50458-0577-14, 50458-0578-07, 50458-0578-14, 50458-0579-07, 50458-0579-99, 50458-0580-07, 50458-0584-52; Rows were added to – “enter “0” in the total unit volume field and left blank for other calculated fields.”

Four NDC-11s are inner NDCs under JPI labeler 50458: 50458-0577-01, 50458-0578-01, 50458-0579-01, 50458-0580-01: Rows were added to – “enter “0” in the total unit volume field and left blank for other calculated fields.”

Four NDC- 11s [55154-1422-00, 55154-1423-08, 55154-1424-08, and 55154-1424-00 discontinued] for Xarelto are repackaged by Cardinal Health LLC 107 (“Cardinal”) [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

It should be noted that responses to Section D do not represent the full costs incurred on XARELTO. The production and distribution costs do not include full investment, and exclude Corporate overhead, continued R&D investments in innovation, as well as ongoing Operating expenses such as Sales & Marketing, as well as Infrastructure Overhead. The costs reported also exclude third party royalties for XARELTO, which are another cost that should be considered in determining cost of production and distribution of XARELTO.

E. Federal Financial Support				
<b>Description:</b> This section pertains to all prior federal financial support provided by federal agencies or federally supported grants or contracts that contributed to direct costs for the basic pre-clinical research and clinical trials phase of research and development for FDA-approved indications of the selected drug to the Primary Manufacturer only. It also pertains to prior federal financial support received for indirect costs of developing the selected drug.				
Total Federal Financial Support	Federal Financial Support	Type of Agreement	Federal Agency(ies) Participating in Agreement	Nature of Agreement
[REDACTED]	(refer to Explanations)	OTH	Other	

**Explanations:** Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

“Federal Funding Support Amount” provided in question number 9 is comprised entirely of IRC 41, credit for increasing research activities for US corporate income tax. The Orphan Drug credit under IRC 45C is not applicable to this analysis because XARELTO does not qualify by statute nor has Johnson & Johnson filed to receive orphan drug designation from the FDA for the selected drug.

[REDACTED]

[REDACTED]

Consistent with ICR guidance, no adjustment has been made for federal financial support in questions 2 through 5, as the research tax credit is not specific to the costs as defined by the ICR.



## F. Patents, Exclusivities, and Approvals

### Patents (Expired and Non-Expired) and Patent Applications

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. This table lists each patent that is related to the selected drug, as well as each application for a patent related to the selected drug that is pending with the USPTO.

Patent #	Date Filed	Patent Expiry Date	Drug Product Patent	Drug Substance Patent	Drug Method of Use Patent	Patent Application Pending	Patent Type	Listed in FDA Orange Book / Purple Book
7,585,860	2000-12-11	2020-12-11	N	Y	N	N	UTL	N
7,592,339	2000-12-11	2020-12-11	N	N	Y	N	UTL	N
7,157,456	2000-12-11	2024-08-28	Y	Y	Y	N	UTL	Y
9,415,053	2004-11-13	2024-11-13	Y	N	Y	N	UTL	Y
9,539,218	2006-01-19	2034-02-17	N	N	Y	N	UTL	Y
10,828,310	2019-01-31	2039-01-31	N	N	Y	N	UTL	Y
17/553,340	2021-12-16	9999-12-31	N	N	Y	Y	UTL	N

**Explanations:** This response, and all accompanying data in Section F, is confidential and proprietary and subject to projections under IRA §1193(c) and FOIA.

Question 12 relates to “Patents (Expired and Non-Expired) and Patent Applications.” The patents and patent applications listed in response to Question 12 have patent claims directed to the selected drug product, selected drug substance, methods of using the selected drug, and/or methods of manufacturing the selected drug.

Question 12 requests reporting of the “Date Filed.” In response, the date reported for all patents and patent applications is the effective filing date.

Question 12 requests reporting of the “Patent Expiry Date.” In response, the patent expiry date that is listed for the patents includes the 20-year patent term plus any available patent term adjustment (PTA) or patent term extension (PTE). The pediatric exclusivity (PED) that is attached to

U.S. Pat. Nos. 7,157,456, 9,415,053, 9,539,218, and 10,828,310 is not included in the “Patent Expiry Date” since it is a regulatory exclusivity. The additional term resulting from the granted 6 months of PED exclusivity is provided below for U.S. Pat. Nos. 7,157,456, 9,415,053, 9,539,218, and 10,828,310. The patent expiry date listed for U.S. Pat. Application Nos. [REDACTED] and 17/553,340 is “12/31/9999,” because these applications are pending and have not yet issued.

U.S. Pat. Nos. 7,585,860 and 7,592,339 have expired and are not currently in the Orange Book.

U.S. Pat. No. 7,157,456 expires August 28, 2024 (and 6 months PED exclusivity extends expiry to February 28, 2025). Patent Use Codes listed for this patent in the Orange Book are: (a) U-1301 (treatment of Deep Vein Thrombosis (DVT)), and (b) U-1302 (treatment of Pulmonary Embolism (PE)).

U.S. Pat. No. 9,415,053 expires November 13, 2024 (and 6 months PED exclusivity extends expiry to May 13, 2025). Patent Use Codes listed for this patent in the Orange Book in conjunction with the 2.5 mg tablet are: (a) U-2435 (reduction of risk of major cardiovascular events (CV death, MI, and stroke) in chronic coronary artery disease (CAD) or Peripheral Artery Disease (PAD)), (b) U-3205 (reduction of risk of major cardiovascular events (cardiovascular death, myocardial infarction, and stroke) in patients with CAD), and (c) U-3206 (reduction of risk of major thrombotic vascular events (myocardial infarction, ischemic stroke, acute limb ischemia, and major amputation of vascular etiology) in patients with PAD). Additional Use Codes listed for this patent in conjunction with the 10 mg tablet listing are U-1167, U-2142, U-2640, and U-3284. Use Codes listed for this patent in conjunction with the 15 mg tablet listing are U-1200, U-1301, U-1302, and U-3286. Use Codes listed for this patent in conjunction with the 20 mg tablet listing are U-1200, U-1301, U-1302, and U-3287. A description of these use codes (and the other use codes described herein can be found in the Orange Book; see also on the FDA’s website (e.g., [https://www.accessdata.fda.gov/scripts/cder/ob/results\\_patent.cfm](https://www.accessdata.fda.gov/scripts/cder/ob/results_patent.cfm)).

U.S. Pat. No. 9,539,218 expires February 17, 2034 (and 6 months PED exclusivity extends expiry to August 17, 2034). Patent Use Codes listed for this patent in the Orange Book in conjunction with the 10 mg tablet are:

(a) U-1957 (prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism in patients undergoing knee or hip replacement surgery, with once daily, rapid-release tablet administered for at least five consecutive days); (b) U-2143 (after completion of initial treatment lasting at least 6 months, to reduce the risk of recurrence of deep vein thrombosis and/or pulmonary embolism in certain patients with once daily, rapid-release tablet administered for at least five consecutive days), (c) U-2641 (prophylaxis of venous thromboembolism in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding with once daily, rapid-release tablet administered for at least five consecutive days), and U-3288 (prophylaxis of PE, DVT, and/or stroke in pediatric patients ( $\geq 50$  kg) aged 2 years and older with congenital heart disease after Fontan procedure with once daily, rapid-release tablet administered for at least five consecutive days). Patent Use Codes listed for this patent in the Orange Book in conjunction with the 15 mg tablet are: U-1953 and U-3289. Patent Use Codes listed for this patent in the Orange Book in conjunction with the 20 mg tablet are: U-1953, U-1954, U-1955, and U-3285.

The claims of U.S. Pat. No. 10,828,310 have been found invalid by the Patent Trial and Appeal Board. See Mylan Pharma. Inc. v. Bayer Pharma Aktiengesellschaft, IPR2022-00517, Patent No. 10,828,310, paper No. 70 (July 28, 2023). The deadline to file an appeal has not yet passed. If the patent owner appeals this decision and one or more claims are found not to be invalid, then U.S. Pat. No. 10,828,310 will expire January 31, 2039 (and 6 months PED exclusivity extends expiry to July 31, 2039). Patent Use Codes listed for this patent in the Orange Book are: (a) U-3207 (reduction of risk of cardiovascular death, myocardial infarction, and stroke in patients with CAD by administering clinically proven effective amounts that are 2.5 mg rivaroxaban twice daily and 75-100 mg aspirin daily), and (b) U-3208 (reduction of risk of myocardial infarction and ischemic stroke in patients with PAD by administering clinically proven effective amounts that are 2.5 mg rivaroxaban twice daily and 75-100 mg aspirin daily).

Alternatively, if the claims of U.S. Pat. No. 10,828,310 are found to be invalid on appeal, then there could be generic competition for the 2.5 mg dose of Xarelto® as early as March 1, 2025.

U.S. Pat. Application Nos. [REDACTED] and 17/553,340 are pending and relate to methods of using the selected drug. [REDACTED]

and Patent Application No. 17/553,340 is titled, "Methods of Thromboprophylaxis."

## F. Patents, Exclusivities, and Approvals

### Regulatory Exclusivity Periods

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. Manufacturers reported all regulatory exclusivity periods under the FD&C Act or the PHS Act that are listed in the Orange Book or the Purple Book and in effect or have expired for the selected drug.

Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
CEE	2016-07-01	22406	50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	This response, and all accompanying data in Section F, is confidential and proprietary and subject to projections under IRA §1193(c) and FOIA. New Chemical Entity (NCE) exclusivity The following statements about NDCs apply to all listed exclusivities in this submission. The Orange Book and FDA do not identify NDC-9s that are covered by regulatory exclusivities. The NDCs listed herein are not intended to address the scope of any exclusivity period. The submission does not include NDCs that are associated with other labelers beyond the NDA holder (secondary manufacturers or repackagers). We consider the Xarelto® NDCs (regardless of labeler) to be covered by the listed exclusivities to the same extent as our corresponding NDC for the relevant strength. Several exclusivities listed in this submission, including some that expired, were associated with both NDA N022406 and NDA N202439. The latter was administratively closed on 04/20/2022. Accordingly, we are listing all exclusivities under NDA N022406.
CIE	2014-11-04	22406	50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	New clinical investigation exclusivity for “I-643,” which pertains to “reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.”



## F. Patents, Exclusivities, and Approvals

### Regulatory Exclusivity Periods

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. Manufacturers reported all regulatory exclusivity periods under the FD&C Act or the PHS Act that are listed in the Orange Book or the Purple Book and in effect or have expired for the selected drug.

Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
CIE	2015-11-02	22406	50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	New clinical investigation exclusivity for “I-660,” which pertains to “treatment of deep vein thrombosis.”
CIE	2015-11-02	22406	50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	New clinical investigation exclusivity for “I-661,” which pertains to “treatment of pulmonary embolism.”
CIE	2015-11-02	22406	50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	New clinical investigation exclusivity for “I-662,” which pertains to “reduction in risk for deep vein thrombosis and the reduction in risk for pulmonary embolism.”
CIE	2020-10-27	22406	50458-0580-10	New clinical investigation exclusivity for “D-168,” which pertains to a “new dosing regimen of 10 mg once daily for the reduction in the risk of recurrence of deep vein thrombosis (DVT) and/or pulmonary embolism (PE) in patients at continued risk for DVT and/or PE after completion of initial treatment lasting at least 6 months.”
CIE	2023-03-10	22406	50458-0577 (2.5 mg) 50458-0578 (15 mg) 50458-0579 (20	New clinical investigation exclusivity for “M-284,” which pertains to “revisions to the labeling to include results from the Galileo trial.”

## F. Patents, Exclusivities, and Approvals

### Regulatory Exclusivity Periods

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. Manufacturers reported all regulatory exclusivity periods under the FD&C Act or the PHS Act that are listed in the Orange Book or the Purple Book and in effect or have expired for the selected drug.

Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
			mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	
PED	2023-09-10	22406	50458-0577 (2.5 mg) 50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	Pediatric Exclusivity extension of new clinical investigation exclusivity “M-284,” which pertains to “revisions to the labeling to include results from the Galileo trial.”
CIE	2022-10-11	22406	50458-0577 (2.5 mg) 50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	New clinical investigation exclusivity for “I-810,” which pertains to “prophylaxis of venous thromboembolism in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding.”
PED	2023-04-11	22406	50458-0577 (2.5 mg) 50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	Pediatric exclusivity extension of the new clinical investigation exclusivity “I-810,” which pertains to “prophylaxis of venous thromboembolism in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding.”
CIE	2021-10-11	22406	50458-0577-25	New clinical investigation exclusivity for “I-824,” which pertains to “rivaroxaban in combination with aspirin, is indicated to reduce the risk of major CV events (CV death, MI, and stroke) in patients with chronic coronary artery disease (CAD) or peripheral artery disease (PAD).”
CIE	2024-08-23	22406	50458-0577 (2.5 mg) 50458-0578 (15 mg) 50458-0579 (20	New clinical investigation exclusivity for “I-867,” which is “indicated to reduce the risk of major thrombotic vascular events



## F. Patents, Exclusivities, and Approvals

### Regulatory Exclusivity Periods

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. Manufacturers reported all regulatory exclusivity periods under the FD&C Act or the PHS Act that are listed in the Orange Book or the Purple Book and in effect or have expired for the selected drug.

Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
			mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	(myocardial infarction, ischemic stroke, acute limb ischemia, and major amputation of vascular etiology) in patients with PAD, including patients who have recently undergone a lower extremity revascularization procedure due to symptomatic PAD."
PED	2025-02-23	22406	50458-0577 (2.5 mg) 50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	Pediatric exclusivity extension of the new clinical investigation exclusivity for "I-867," which is "indicated to reduce the risk of major thrombotic vascular events (myocardial infarction, ischemic stroke, acute limb ischemia, and major amputation of vascular etiology) in patients with PAD, including patients who have recently undergone a lower extremity revascularization procedure due to symptomatic PAD."
CIE	2024-12-20	215859	50458-0575	New clinical investigation exclusivity for "NP," which is new product exclusivity.
PED	2025-06-20	215859	50458-0575	Pediatric Exclusivity extension of new product exclusivity.
PED	2025-02-28	22406	50458-0577 (2.5 mg) 50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 7,157,456. U.S. Pat. No. 7,157,456 expires August 28, 2024 (and related 6 months PED exclusivity expires on February 28, 2025).

## F. Patents, Exclusivities, and Approvals

### Regulatory Exclusivity Periods

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. Manufacturers reported all regulatory exclusivity periods under the FD&C Act or the PHS Act that are listed in the Orange Book or the Purple Book and in effect or have expired for the selected drug.

Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
PED	2025-05-13	22406	50458-0577 (2.5 mg) 50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 9,415,053. U.S. Pat. No. 9,415,053 expires November 13, 2024 (and related 6 months PED exclusivity expires on May 13, 2025).
PED	2034-08-17	22406	50458-0578 (15 mg) 50458-0579 (20 mg) 50458-0580 (10 mg) 50458-0584 (Xarelto® Starter kit)	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 9,539,218. U.S. Pat. No. 9,539,218 expires February 17, 2034 (and related 6 months PED exclusivity expires on August 17, 2034).
PED	2039-07-13	22406	50458-0577-25	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 10,828,310. The claims of U.S. Pat. No. 10,828,310 have been found invalid by the Patent Trial and Appeal Board. See Mylan Pharma. Inc. v. Bayer Pharma Aktiengesellschaft, IPR2022-00517, Patent No. 10,828,310, paper No. 70 (July 28, 2023). The deadline to file an appeal has not yet passed. If the patent owner appeals this decision and one or more claims are found on appeal to be valid, then U.S. Pat. No. 10,828,310 will expire January 31, 2039 (and related 6 months PED exclusivity will expire on July 31, 2039). Alternatively, if the claims of U.S. Pat. No. 10,828,310 are found to be invalid on appeal, then the exclusivity period would be removed from the Orange Book.



## F. Patents, Exclusivities, and Approvals

### Regulatory Exclusivity Periods

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. Manufacturers reported all regulatory exclusivity periods under the FD&C Act or the PHS Act that are listed in the Orange Book or the Purple Book and in effect or have expired for the selected drug.

Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
PED	2025-02-28	215859	50458-0575	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 7,157,456. U.S. Pat. No. 7,157,456 expires August 28, 2024 (and related 6 months PED exclusivity expires on February 28, 2025).

**Explanations:** None.

## F. Patents, Exclusivities, and Approvals

### All Active and Pending FDA Applications and Approvals

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. This list contains all active and pending FDA applications and approvals for the selected drug under section 505(c) of the FD&C Act and 351(a) of the PHS Act.

Application (NDA / BLA) Number	Application Type (NDA; BLA)	Class Code	Approval Date	Indication	Dosage Form and Strength	Sponsor	Application Status	Comments
22406	NDA	1	2011-07-01	The prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery	Tablet 10 mg	Janssen Pharmaceuticals, Inc.	APP	
202439	NDA	10	2011-11-04	To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation	Tablet 15 mg, 20mg	Janssen Pharmaceuticals, Inc	OTH	On 04/20/2022, this NDA was administratively closed; NDA has been re-classified from Type 10 to Type 9 NDA.
22406	NDA	6	2012-11-02	(a) Treatment of deep vein thrombosis (DVT) (b) Treatment of pulmonary embolism (PE) (c) Reduction in the risk of recurrence of DVT or PE	Tablet 10mg 15mg, 20mg	Janssen Pharmaceuticals, Inc	APP	An efficacy sNDA was approved in October 2017 for a new dosage regimen of 10 mg for "Reduction in the risk of recurrence of DVT or PE."

## F. Patents, Exclusivities, and Approvals

### All Active and Pending FDA Applications and Approvals

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. This list contains all active and pending FDA applications and approvals for the selected drug under section 505(c) of the FD&C Act and 351(a) of the PHS Act.

Application (NDA / BLA) Number	Application Type (NDA; BLA)	Class Code	Approval Date	Indication	Dosage Form and Strength	Sponsor	Application Status	Comments
202439	NDA	6	2018-10-11	To reduce the risk of major cardiovascular events in patients with coronary artery disease	Tablet 2.5 mg	Janssen Pharmaceuticals, Inc.	OTH	Note that NDA 202439 was administratively closed on 04/20/2022.
22406	NDA	6	2019-10-11	Prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients.	Tablet 10 mg	Janssen Pharmaceuticals, Inc.	APP	
202439	NDA	6	2021-08-23	To reduce the risk of major thrombotic vascular events in patients with peripheral artery disease (PAD), including patients after recent lower extremity revascularization due to symptomatic PAD	Tablet 2.5 mg	Janssen Pharmaceuticals, Inc.	OTH	Corresponds to NDA 022406/S-037. Note that NDA 202439 was administratively closed on 04/20/2022.



## F. Patents, Exclusivities, and Approvals

### All Active and Pending FDA Applications and Approvals

**Description:** Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. This list contains all active and pending FDA applications and approvals for the selected drug under section 505(c) of the FD&C Act and 351(a) of the PHS Act.

Application (NDA / BLA) Number	Application Type (NDA; BLA)	Class Code	Approval Date	Indication	Dosage Form and Strength	Sponsor	Application Status	Comments
215859	NDA	3	2021-12-20	(a) Treatment of VTE and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years (b) Thromboprophylaxis in pediatric patients 2 years and older with congenital heart disease after the Fontan procedure	Oral suspension 1 mg/mL once reconstituted	Janssen Pharmaceuticals, Inc	APP	

**Explanations:** None.

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0575-01	2018-Q1		ML	
50458-0575-01	2018-Q2		ML	
50458-0575-01	2018-Q3		ML	
50458-0575-01	2018-Q4		ML	
50458-0575-01	2019-Q1		ML	
50458-0575-01	2019-Q2		ML	
50458-0575-01	2019-Q3		ML	
50458-0575-01	2019-Q4		ML	
50458-0575-01	2020-Q1		ML	
50458-0575-01	2020-Q2		ML	
50458-0575-01	2020-Q3		ML	
50458-0575-01	2020-Q4		ML	
50458-0575-01	2021-Q1		ML	
50458-0575-01	2021-Q2		ML	
50458-0575-01	2021-Q3		ML	
50458-0575-01	2021-Q4		ML	
50458-0575-01	2022-Q1		ML	
50458-0575-01	2022-Q2		ML	
50458-0575-01	2022-Q3		ML	
50458-0575-01	2022-Q4		ML	
50458-0577-10	2018-Q1		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0577-10	2018-Q2		EA	
50458-0577-10	2018-Q3		EA	
50458-0577-10	2018-Q4		EA	
50458-0577-10	2019-Q1		EA	
50458-0577-10	2019-Q2		EA	
50458-0577-10	2019-Q3		EA	
50458-0577-10	2019-Q4		EA	
50458-0577-10	2020-Q1		EA	
50458-0577-10	2020-Q2		EA	
50458-0577-10	2020-Q3		EA	
50458-0577-10	2020-Q4		EA	
50458-0577-10	2021-Q1		EA	
50458-0577-10	2021-Q2		EA	
50458-0577-10	2021-Q3		EA	
50458-0577-10	2021-Q4		EA	
50458-0577-10	2022-Q1		EA	
50458-0577-10	2022-Q2		EA	
50458-0577-10	2022-Q3		EA	
50458-0577-10	2022-Q4		EA	
50458-0577-18	2018-Q1		EA	
50458-0577-18	2018-Q2		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0577-18	2018-Q3		EA	
50458-0577-18	2018-Q4		EA	
50458-0577-18	2019-Q1		EA	
50458-0577-18	2019-Q2		EA	
50458-0577-18	2019-Q3		EA	
50458-0577-18	2019-Q4		EA	
50458-0577-18	2020-Q1		EA	
50458-0577-18	2020-Q2		EA	
50458-0577-18	2020-Q3		EA	
50458-0577-18	2020-Q4		EA	
50458-0577-18	2021-Q1		EA	
50458-0577-18	2021-Q2		EA	
50458-0577-18	2021-Q3		EA	
50458-0577-18	2021-Q4		EA	
50458-0577-18	2022-Q1		EA	
50458-0577-18	2022-Q2		EA	
50458-0577-18	2022-Q3		EA	
50458-0577-18	2022-Q4		EA	
50458-0577-60	2018-Q1		EA	
50458-0577-60	2018-Q2		EA	
50458-0577-60	2018-Q3		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0577-60	2018-Q4		EA	
50458-0577-60	2019-Q1		EA	
50458-0577-60	2019-Q2		EA	
50458-0577-60	2019-Q3		EA	
50458-0577-60	2019-Q4		EA	
50458-0577-60	2020-Q1		EA	
50458-0577-60	2020-Q2		EA	
50458-0577-60	2020-Q3		EA	
50458-0577-60	2020-Q4		EA	
50458-0577-60	2021-Q1		EA	
50458-0577-60	2021-Q2		EA	
50458-0577-60	2021-Q3		EA	
50458-0577-60	2021-Q4		EA	
50458-0577-60	2022-Q1		EA	
50458-0577-60	2022-Q2		EA	
50458-0577-60	2022-Q3		EA	
50458-0577-60	2022-Q4		EA	
50458-0578-10	2018-Q1		EA	
50458-0578-10	2018-Q2		EA	
50458-0578-10	2018-Q3		EA	
50458-0578-10	2018-Q4		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0578-10	2019-Q1		EA	
50458-0578-10	2019-Q2		EA	
50458-0578-10	2019-Q3		EA	
50458-0578-10	2019-Q4		EA	
50458-0578-10	2020-Q1		EA	
50458-0578-10	2020-Q2		EA	
50458-0578-10	2020-Q3		EA	
50458-0578-10	2020-Q4		EA	
50458-0578-10	2021-Q1		EA	
50458-0578-10	2021-Q2		EA	
50458-0578-10	2021-Q3		EA	
50458-0578-10	2021-Q4		EA	
50458-0578-10	2022-Q1		EA	
50458-0578-10	2022-Q2		EA	
50458-0578-10	2022-Q3		EA	
50458-0578-10	2022-Q4		EA	
50458-0578-30	2018-Q1		EA	
50458-0578-30	2018-Q2		EA	
50458-0578-30	2018-Q3		EA	
50458-0578-30	2018-Q4		EA	
50458-0578-30	2019-Q1		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0578-30	2019-Q2		EA	
50458-0578-30	2019-Q3		EA	
50458-0578-30	2019-Q4		EA	
50458-0578-30	2020-Q1		EA	
50458-0578-30	2020-Q2		EA	
50458-0578-30	2020-Q3		EA	
50458-0578-30	2020-Q4		EA	
50458-0578-30	2021-Q1		EA	
50458-0578-30	2021-Q2		EA	
50458-0578-30	2021-Q3		EA	
50458-0578-30	2021-Q4		EA	
50458-0578-30	2022-Q1		EA	
50458-0578-30	2022-Q2		EA	
50458-0578-30	2022-Q3		EA	
50458-0578-30	2022-Q4		EA	
50458-0578-90	2018-Q1		EA	
50458-0578-90	2018-Q2		EA	
50458-0578-90	2018-Q3		EA	
50458-0578-90	2018-Q4		EA	
50458-0578-90	2019-Q1		EA	
50458-0578-90	2019-Q2		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0578-90	2019-Q3		EA	
50458-0578-90	2019-Q4		EA	
50458-0578-90	2020-Q1		EA	
50458-0578-90	2020-Q2		EA	
50458-0578-90	2020-Q3		EA	
50458-0578-90	2020-Q4		EA	
50458-0578-90	2021-Q1		EA	
50458-0578-90	2021-Q2		EA	
50458-0578-90	2021-Q3		EA	
50458-0578-90	2021-Q4		EA	
50458-0578-90	2022-Q1		EA	
50458-0578-90	2022-Q2		EA	
50458-0578-90	2022-Q3		EA	
50458-0578-90	2022-Q4		EA	
50458-0579-10	2018-Q1		EA	
50458-0579-10	2018-Q2		EA	
50458-0579-10	2018-Q3		EA	
50458-0579-10	2018-Q4		EA	
50458-0579-10	2019-Q1		EA	
50458-0579-10	2019-Q2		EA	
50458-0579-10	2019-Q3		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0579-10	2019-Q4		EA	
50458-0579-10	2020-Q1		EA	
50458-0579-10	2020-Q2		EA	
50458-0579-10	2020-Q3		EA	
50458-0579-10	2020-Q4		EA	
50458-0579-10	2021-Q1		EA	
50458-0579-10	2021-Q2		EA	
50458-0579-10	2021-Q3		EA	
50458-0579-10	2021-Q4		EA	
50458-0579-10	2022-Q1		EA	
50458-0579-10	2022-Q2		EA	
50458-0579-10	2022-Q3		EA	
50458-0579-10	2022-Q4		EA	
50458-0579-30	2018-Q1		EA	
50458-0579-30	2018-Q2		EA	
50458-0579-30	2018-Q3		EA	
50458-0579-30	2018-Q4		EA	
50458-0579-30	2019-Q1		EA	
50458-0579-30	2019-Q2		EA	
50458-0579-30	2019-Q3		EA	
50458-0579-30	2019-Q4		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0579-30	2020-Q1		EA	
50458-0579-30	2020-Q2		EA	
50458-0579-30	2020-Q3		EA	
50458-0579-30	2020-Q4		EA	
50458-0579-30	2021-Q1		EA	
50458-0579-30	2021-Q2		EA	
50458-0579-30	2021-Q3		EA	
50458-0579-30	2021-Q4		EA	
50458-0579-30	2022-Q1		EA	
50458-0579-30	2022-Q2		EA	
50458-0579-30	2022-Q3		EA	
50458-0579-30	2022-Q4		EA	
50458-0579-89	2018-Q1		EA	
50458-0579-89	2018-Q2		EA	
50458-0579-89	2018-Q3		EA	
50458-0579-89	2018-Q4		EA	
50458-0579-89	2019-Q1		EA	
50458-0579-89	2019-Q2		EA	
50458-0579-89	2019-Q3		EA	
50458-0579-89	2019-Q4		EA	
50458-0579-89	2020-Q1		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0579-89	2020-Q2		EA	
50458-0579-89	2020-Q3		EA	
50458-0579-89	2020-Q4		EA	
50458-0579-89	2021-Q1		EA	
50458-0579-89	2021-Q2		EA	
50458-0579-89	2021-Q3		EA	
50458-0579-89	2021-Q4		EA	
50458-0579-89	2022-Q1		EA	
50458-0579-89	2022-Q2		EA	
50458-0579-89	2022-Q3		EA	
50458-0579-89	2022-Q4		EA	
50458-0579-90	2018-Q1		EA	
50458-0579-90	2018-Q2		EA	
50458-0579-90	2018-Q3		EA	
50458-0579-90	2018-Q4		EA	
50458-0579-90	2019-Q1		EA	
50458-0579-90	2019-Q2		EA	
50458-0579-90	2019-Q3		EA	
50458-0579-90	2019-Q4		EA	
50458-0579-90	2020-Q1		EA	
50458-0579-90	2020-Q2		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0579-90	2020-Q3		EA	
50458-0579-90	2020-Q4		EA	
50458-0579-90	2021-Q1		EA	
50458-0579-90	2021-Q2		EA	
50458-0579-90	2021-Q3		EA	
50458-0579-90	2021-Q4		EA	
50458-0579-90	2022-Q1		EA	
50458-0579-90	2022-Q2		EA	
50458-0579-90	2022-Q3		EA	
50458-0579-90	2022-Q4		EA	
50458-0580-10	2018-Q1		EA	
50458-0580-10	2018-Q2		EA	
50458-0580-10	2018-Q3		EA	
50458-0580-10	2018-Q4		EA	
50458-0580-10	2019-Q1		EA	
50458-0580-10	2019-Q2		EA	
50458-0580-10	2019-Q3		EA	
50458-0580-10	2019-Q4		EA	
50458-0580-10	2020-Q1		EA	
50458-0580-10	2020-Q2		EA	
50458-0580-10	2020-Q3		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0580-10	2020-Q4		EA	
50458-0580-10	2021-Q1		EA	
50458-0580-10	2021-Q2		EA	
50458-0580-10	2021-Q3		EA	
50458-0580-10	2021-Q4		EA	
50458-0580-10	2022-Q1		EA	
50458-0580-10	2022-Q2		EA	
50458-0580-10	2022-Q3		EA	
50458-0580-10	2022-Q4		EA	
50458-0580-30	2018-Q1		EA	
50458-0580-30	2018-Q2		EA	
50458-0580-30	2018-Q3		EA	
50458-0580-30	2018-Q4		EA	
50458-0580-30	2019-Q1		EA	
50458-0580-30	2019-Q2		EA	
50458-0580-30	2019-Q3		EA	
50458-0580-30	2019-Q4		EA	
50458-0580-30	2020-Q1		EA	
50458-0580-30	2020-Q2		EA	
50458-0580-30	2020-Q3		EA	
50458-0580-30	2020-Q4		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0580-30	2021-Q1		EA	
50458-0580-30	2021-Q2		EA	
50458-0580-30	2021-Q3		EA	
50458-0580-30	2021-Q4		EA	
50458-0580-30	2022-Q1		EA	
50458-0580-30	2022-Q2		EA	
50458-0580-30	2022-Q3		EA	
50458-0580-30	2022-Q4		EA	
50458-0580-90	2018-Q1		EA	
50458-0580-90	2018-Q2		EA	
50458-0580-90	2018-Q3		EA	
50458-0580-90	2018-Q4		EA	
50458-0580-90	2019-Q1		EA	
50458-0580-90	2019-Q2		EA	
50458-0580-90	2019-Q3		EA	
50458-0580-90	2019-Q4		EA	
50458-0580-90	2020-Q1		EA	
50458-0580-90	2020-Q2		EA	
50458-0580-90	2020-Q3		EA	
50458-0580-90	2020-Q4		EA	
50458-0580-90	2021-Q1		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0580-90	2021-Q2		EA	
50458-0580-90	2021-Q3		EA	
50458-0580-90	2021-Q4		EA	
50458-0580-90	2022-Q1		EA	
50458-0580-90	2022-Q2		EA	
50458-0580-90	2022-Q3		EA	
50458-0580-90	2022-Q4		EA	
50458-0584-51	2018-Q1		EA	
50458-0584-51	2018-Q2		EA	
50458-0584-51	2018-Q3		EA	
50458-0584-51	2018-Q4		EA	
50458-0584-51	2019-Q1		EA	
50458-0584-51	2019-Q2		EA	
50458-0584-51	2019-Q3		EA	
50458-0584-51	2019-Q4		EA	
50458-0584-51	2020-Q1		EA	
50458-0584-51	2020-Q2		EA	
50458-0584-51	2020-Q3		EA	
50458-0584-51	2020-Q4		EA	
50458-0584-51	2021-Q1		EA	
50458-0584-51	2021-Q2		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0584-51	2021-Q3		EA	
50458-0584-51	2021-Q4		EA	
50458-0584-51	2022-Q1		EA	
50458-0584-51	2022-Q2		EA	
50458-0584-51	2022-Q3		EA	
50458-0584-51	2022-Q4		EA	
50458-0578-14	2018-Q1		EA	
50458-0578-14	2018-Q2		EA	
50458-0578-14	2018-Q3		EA	
50458-0578-14	2018-Q4		EA	
50458-0578-14	2019-Q1		EA	
50458-0578-14	2019-Q2		EA	
50458-0578-14	2019-Q3		EA	
50458-0578-14	2019-Q4		EA	
50458-0578-14	2020-Q1		EA	
50458-0578-14	2020-Q2		EA	
50458-0578-14	2020-Q3		EA	
50458-0578-14	2020-Q4		EA	
50458-0578-14	2021-Q1		EA	
50458-0578-14	2021-Q2		EA	
50458-0578-14	2021-Q3		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0578-14	2021-Q4		EA	
50458-0578-14	2022-Q1		EA	
50458-0578-14	2022-Q2		EA	
50458-0578-14	2022-Q3		EA	
50458-0578-14	2022-Q4		EA	
50458-0580-07	2018-Q1		EA	
50458-0580-07	2018-Q2		EA	
50458-0580-07	2018-Q3		EA	
50458-0580-07	2018-Q4		EA	
50458-0580-07	2019-Q1		EA	
50458-0580-07	2019-Q2		EA	
50458-0580-07	2019-Q3		EA	
50458-0580-07	2019-Q4		EA	
50458-0580-07	2020-Q1		EA	
50458-0580-07	2020-Q2		EA	
50458-0580-07	2020-Q3		EA	
50458-0580-07	2020-Q4		EA	
50458-0580-07	2021-Q1		EA	
50458-0580-07	2021-Q2		EA	
50458-0580-07	2021-Q3		EA	
50458-0580-07	2021-Q4		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0580-07	2022-Q1		EA	
50458-0580-07	2022-Q2		EA	
50458-0580-07	2022-Q3		EA	
50458-0580-07	2022-Q4		EA	
50458-0577-14	2018-Q1		EA	
50458-0577-14	2018-Q2		EA	
50458-0577-14	2018-Q3		EA	
50458-0577-14	2018-Q4		EA	
50458-0577-14	2019-Q1		EA	
50458-0577-14	2019-Q2		EA	
50458-0577-14	2019-Q3		EA	
50458-0577-14	2019-Q4		EA	
50458-0577-14	2020-Q1		EA	
50458-0577-14	2020-Q2		EA	
50458-0577-14	2020-Q3		EA	
50458-0577-14	2020-Q4		EA	
50458-0577-14	2021-Q1		EA	
50458-0577-14	2021-Q2		EA	
50458-0577-14	2021-Q3		EA	
50458-0577-14	2021-Q4		EA	
50458-0577-14	2022-Q1		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0577-14	2022-Q2		EA	
50458-0577-14	2022-Q3		EA	
50458-0577-14	2022-Q4		EA	
50458-0578-07	2018-Q1		EA	
50458-0578-07	2018-Q2		EA	
50458-0578-07	2018-Q3		EA	
50458-0578-07	2018-Q4		EA	
50458-0578-07	2019-Q1		EA	
50458-0578-07	2019-Q2		EA	
50458-0578-07	2019-Q3		EA	
50458-0578-07	2019-Q4		EA	
50458-0578-07	2020-Q1		EA	
50458-0578-07	2020-Q2		EA	
50458-0578-07	2020-Q3		EA	
50458-0578-07	2020-Q4		EA	
50458-0578-07	2021-Q1		EA	
50458-0578-07	2021-Q2		EA	
50458-0578-07	2021-Q3		EA	
50458-0578-07	2021-Q4		EA	
50458-0578-07	2022-Q1		EA	
50458-0578-07	2022-Q2		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0578-07	2022-Q3		EA	
50458-0578-07	2022-Q4		EA	
50458-0579-07	2018-Q1		EA	
50458-0579-07	2018-Q2		EA	
50458-0579-07	2018-Q3		EA	
50458-0579-07	2018-Q4		EA	
50458-0579-07	2019-Q1		EA	
50458-0579-07	2019-Q2		EA	
50458-0579-07	2019-Q3		EA	
50458-0579-07	2019-Q4		EA	
50458-0579-07	2020-Q1		EA	
50458-0579-07	2020-Q2		EA	
50458-0579-07	2020-Q3		EA	
50458-0579-07	2020-Q4		EA	
50458-0579-07	2021-Q1		EA	
50458-0579-07	2021-Q2		EA	
50458-0579-07	2021-Q3		EA	
50458-0579-07	2021-Q4		EA	
50458-0579-07	2022-Q1		EA	
50458-0579-07	2022-Q2		EA	
50458-0579-07	2022-Q3		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0579-07	2022-Q4		EA	
50458-0579-99	2018-Q1		EA	
50458-0579-99	2018-Q2		EA	
50458-0579-99	2018-Q3		EA	
50458-0579-99	2018-Q4		EA	
50458-0579-99	2019-Q1		EA	
50458-0579-99	2019-Q2		EA	
50458-0579-99	2019-Q3		EA	
50458-0579-99	2019-Q4		EA	
50458-0579-99	2020-Q1		EA	
50458-0579-99	2020-Q2		EA	
50458-0579-99	2020-Q3		EA	
50458-0579-99	2020-Q4		EA	
50458-0579-99	2021-Q1		EA	
50458-0579-99	2021-Q2		EA	
50458-0579-99	2021-Q3		EA	
50458-0579-99	2021-Q4		EA	
50458-0579-99	2022-Q1		EA	
50458-0579-99	2022-Q2		EA	
50458-0579-99	2022-Q3		EA	
50458-0579-99	2022-Q4		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0584-52	2018-Q1		EA	
50458-0584-52	2018-Q2		EA	
50458-0584-52	2018-Q3		EA	
50458-0584-52	2018-Q4		EA	
50458-0584-52	2019-Q1		EA	
50458-0584-52	2019-Q2		EA	
50458-0584-52	2019-Q3		EA	
50458-0584-52	2019-Q4		EA	
50458-0584-52	2020-Q1		EA	
50458-0584-52	2020-Q2		EA	
50458-0584-52	2020-Q3		EA	
50458-0584-52	2020-Q4		EA	
50458-0584-52	2021-Q1		EA	
50458-0584-52	2021-Q2		EA	
50458-0584-52	2021-Q3		EA	
50458-0584-52	2021-Q4		EA	
50458-0584-52	2022-Q1		EA	
50458-0584-52	2022-Q2		EA	
50458-0584-52	2022-Q3		EA	
50458-0584-52	2022-Q4		EA	
55154-1422-00	2018-Q1		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
55154-1422-00	2018-Q2		EA	
55154-1422-00	2018-Q3		EA	
55154-1422-00	2018-Q4		EA	
55154-1422-00	2019-Q1		EA	
55154-1422-00	2019-Q2		EA	
55154-1422-00	2019-Q3		EA	
55154-1422-00	2019-Q4		EA	
55154-1422-00	2020-Q1		EA	
55154-1422-00	2020-Q2		EA	
55154-1422-00	2020-Q3		EA	
55154-1422-00	2020-Q4		EA	
55154-1422-00	2021-Q1		EA	
55154-1422-00	2021-Q2		EA	
55154-1422-00	2021-Q3		EA	
55154-1422-00	2021-Q4		EA	
55154-1422-00	2022-Q1		EA	
55154-1422-00	2022-Q2		EA	
55154-1422-00	2022-Q3		EA	
55154-1422-00	2022-Q4		EA	
55154-1424-00	2018-Q1		EA	
55154-1424-00	2018-Q2		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
55154-1424-00	2018-Q3		EA	
55154-1424-00	2018-Q4		EA	
55154-1424-00	2019-Q1		EA	
55154-1424-00	2019-Q2		EA	
55154-1424-00	2019-Q3		EA	
55154-1424-00	2019-Q4		EA	
55154-1424-00	2020-Q1		EA	
55154-1424-00	2020-Q2		EA	
55154-1424-00	2020-Q3		EA	
55154-1424-00	2020-Q4		EA	
55154-1424-00	2021-Q1		EA	
55154-1424-00	2021-Q2		EA	
55154-1424-00	2021-Q3		EA	
55154-1424-00	2021-Q4		EA	
55154-1424-00	2022-Q1		EA	
55154-1424-00	2022-Q2		EA	
55154-1424-00	2022-Q3		EA	
55154-1424-00	2022-Q4		EA	
55154-1424-08	2018-Q1		EA	
55154-1424-08	2018-Q2		EA	
55154-1424-08	2018-Q3		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
55154-1424-08	2018-Q4		EA	
55154-1424-08	2019-Q1		EA	
55154-1424-08	2019-Q2		EA	
55154-1424-08	2019-Q3		EA	
55154-1424-08	2019-Q4		EA	
55154-1424-08	2020-Q1		EA	
55154-1424-08	2020-Q2		EA	
55154-1424-08	2020-Q3		EA	
55154-1424-08	2020-Q4		EA	
55154-1424-08	2021-Q1		EA	
55154-1424-08	2021-Q2		EA	
55154-1424-08	2021-Q3		EA	
55154-1424-08	2021-Q4		EA	
55154-1424-08	2022-Q1		EA	
55154-1424-08	2022-Q2		EA	
55154-1424-08	2022-Q3		EA	
55154-1424-08	2022-Q4		EA	
55154-1423-08	2018-Q1		EA	
55154-1423-08	2018-Q2		EA	
55154-1423-08	2018-Q3		EA	
55154-1423-08	2018-Q4		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
55154-1423-08	2019-Q1		EA	
55154-1423-08	2019-Q2		EA	
55154-1423-08	2019-Q3		EA	
55154-1423-08	2019-Q4		EA	
55154-1423-08	2020-Q1		EA	
55154-1423-08	2020-Q2		EA	
55154-1423-08	2020-Q3		EA	
55154-1423-08	2020-Q4		EA	
55154-1423-08	2021-Q1		EA	
55154-1423-08	2021-Q2		EA	
55154-1423-08	2021-Q3		EA	
55154-1423-08	2021-Q4		EA	
55154-1423-08	2022-Q1		EA	
55154-1423-08	2022-Q2		EA	
55154-1423-08	2022-Q3		EA	
55154-1423-08	2022-Q4		EA	
50458-0577-01	2018-Q1		EA	
50458-0577-01	2018-Q2		EA	
50458-0577-01	2018-Q3		EA	
50458-0577-01	2018-Q4		EA	
50458-0577-01	2019-Q1		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0577-01	2019-Q2		EA	
50458-0577-01	2019-Q3		EA	
50458-0577-01	2019-Q4		EA	
50458-0577-01	2020-Q1		EA	
50458-0577-01	2020-Q2		EA	
50458-0577-01	2020-Q3		EA	
50458-0577-01	2020-Q4		EA	
50458-0577-01	2021-Q1		EA	
50458-0577-01	2021-Q2		EA	
50458-0577-01	2021-Q3		EA	
50458-0577-01	2021-Q4		EA	
50458-0577-01	2022-Q1		EA	
50458-0577-01	2022-Q2		EA	
50458-0577-01	2022-Q3		EA	
50458-0577-01	2022-Q4		EA	
50458-0578-01	2018-Q1		EA	
50458-0578-01	2018-Q2		EA	
50458-0578-01	2018-Q3		EA	
50458-0578-01	2018-Q4		EA	
50458-0578-01	2019-Q1		EA	
50458-0578-01	2019-Q2		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0578-01	2019-Q3		EA	
50458-0578-01	2019-Q4		EA	
50458-0578-01	2020-Q1		EA	
50458-0578-01	2020-Q2		EA	
50458-0578-01	2020-Q3		EA	
50458-0578-01	2020-Q4		EA	
50458-0578-01	2021-Q1		EA	
50458-0578-01	2021-Q2		EA	
50458-0578-01	2021-Q3		EA	
50458-0578-01	2021-Q4		EA	
50458-0578-01	2022-Q1		EA	
50458-0578-01	2022-Q2		EA	
50458-0578-01	2022-Q3		EA	
50458-0578-01	2022-Q4		EA	
50458-0579-01	2018-Q1		EA	
50458-0579-01	2018-Q2		EA	
50458-0579-01	2018-Q3		EA	
50458-0579-01	2018-Q4		EA	
50458-0579-01	2019-Q1		EA	
50458-0579-01	2019-Q2		EA	
50458-0579-01	2019-Q3		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0579-01	2019-Q4		EA	
50458-0579-01	2020-Q1		EA	
50458-0579-01	2020-Q2		EA	
50458-0579-01	2020-Q3		EA	
50458-0579-01	2020-Q4		EA	
50458-0579-01	2021-Q1		EA	
50458-0579-01	2021-Q2		EA	
50458-0579-01	2021-Q3		EA	
50458-0579-01	2021-Q4		EA	
50458-0579-01	2022-Q1		EA	
50458-0579-01	2022-Q2		EA	
50458-0579-01	2022-Q3		EA	
50458-0579-01	2022-Q4		EA	
50458-0580-01	2018-Q1		EA	
50458-0580-01	2018-Q2		EA	
50458-0580-01	2018-Q3		EA	
50458-0580-01	2018-Q4		EA	
50458-0580-01	2019-Q1		EA	
50458-0580-01	2019-Q2		EA	
50458-0580-01	2019-Q3		EA	
50458-0580-01	2019-Q4		EA	



**G. Market Data and Revenue and Sales Volume Data****Wholesale Acquisition Cost Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Wholesale Acquisition Cost (WAC) unit price of the selected drug.

National Drug Code (NDC-11)	Quarter	WAC	Unit type (each, ML, GM)	Total Unit Volume
50458-0580-01	2020-Q1		EA	
50458-0580-01	2020-Q2		EA	
50458-0580-01	2020-Q3		EA	
50458-0580-01	2020-Q4		EA	
50458-0580-01	2021-Q1		EA	
50458-0580-01	2021-Q2		EA	
50458-0580-01	2021-Q3		EA	
50458-0580-01	2021-Q4		EA	
50458-0580-01	2022-Q1		EA	
50458-0580-01	2022-Q2		EA	
50458-0580-01	2022-Q3		EA	
50458-0580-01	2022-Q4		EA	

**Explanations:** Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

Thirty-six NDC-11s for “XARELTO” are included in the “Selected Drug List for Initial Price Applicability Year (IPAY) 2026”.

Consistent with CMS guidance, this submission reflects information on NDC-11s of the selected drug marketed by the Primary Manufacturer (Janssen Pharmaceuticals, Inc. or “JPI”) and any Secondary Manufacturer.

CMS has prepopulated Section A to include NDC-11s for XARELTO that include NDC-11s for XARELTO distributed by entities that do not meet the definition of “Secondary Manufacturer” because they are not listed in the XARELTO NDA and do not market XARELTO pursuant to an agreement with a Johnson & Johnson company. These NDC-11s are: One for Aphena Pharma Solutions -Tennessee, LLC (71610-0690-42), four for A-S Medication Solutions (50090-3625-00, 50090-3639-00, 50090-4468-00, 50090-4469-00), and one for Avera McKennan Hospital (69189-0578-01).



The NDC under Avera (69189-0578-01) was discontinued, and, after reasonable investigations, the following NDCs under A-S Medication Solutions do not appear to have ever been in use (i.e., 50090-3625-00, 50090-3639-00, 50090-4468-00, and 50090-4469-00).

Seven NDC-11s are sample NDCs under JPI labeler 50458: 50458-0577-14, 50458-0578-07, 50458-0578-14, 50458-0579-07, 50458-0579-99, 50458-0580-07, 50458-0584-52; Rows were added to – “enter “0” in the total unit volume field and left blank for other calculated fields.

Four NDC-11s are inner NDCs under JPI labeler 50458: 50458-0577-01, 50458-0578-01, 50458-0579-01, 50458-0580-01: Rows were added to – “enter “0” in the total unit volume field and left blank for other calculated fields.

Four NDC- 11s [55154-1422-00, 55154-1423-08, 55154-1424-08, and 55154-1424-00 discontinued] for Xarelto are repackaged by Cardinal Health LLC 107 (“Cardinal”) [REDACTED]

The WAC and units reported are per tablet or ML (labeled per NDC).

Units = gross trade product sales units only, which excludes product returns.

Quarters tie to our J&J financial calendar (e.g., Q1 2023 is the 12 week period January 2, 2023 through April 2, 2023). Most recent 5 years utilized for analysis (FY 2018 through FY 2022). Based on US data only.

**G. Market Data and Revenue and Sales Volume Data**

**Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	50458-0575	2018-Q1		ML	
Y	50458-0577	2018-Q1		EA	
Y	50458-0578	2018-Q1		EA	
Y	50458-0579	2018-Q1		EA	
Y	50458-0580	2018-Q1		EA	
Y	50458-0584	2018-Q1		EA	
Y	50458-0575	2018-Q2		ML	
Y	50458-0577	2018-Q2		EA	
Y	50458-0578	2018-Q2		EA	
Y	50458-0579	2018-Q2		EA	
Y	50458-0580	2018-Q2		EA	
Y	50458-0584	2018-Q2		EA	
Y	50458-0575	2018-Q3		ML	
Y	50458-0577	2018-Q3		EA	
Y	50458-0578	2018-Q3		EA	
Y	50458-0579	2018-Q3		EA	
Y	50458-0580	2018-Q3		EA	
Y	50458-0584	2018-Q3		EA	
Y	50458-0575	2018-Q4		ML	

**G. Market Data and Revenue and Sales Volume Data**

**Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	50458-0577	2018-Q4		EA	
Y	50458-0578	2018-Q4		EA	
Y	50458-0579	2018-Q4		EA	
Y	50458-0580	2018-Q4		EA	
Y	50458-0584	2018-Q4		EA	
Y	50458-0575	2019-Q1		ML	
Y	50458-0577	2019-Q1		EA	
Y	50458-0578	2019-Q1		EA	
Y	50458-0579	2019-Q1		EA	
Y	50458-0580	2019-Q1		EA	
Y	50458-0584	2019-Q1		EA	
Y	50458-0575	2019-Q2		ML	
Y	50458-0577	2019-Q2		EA	
Y	50458-0578	2019-Q2		EA	
Y	50458-0579	2019-Q2		EA	
Y	50458-0580	2019-Q2		EA	
Y	50458-0584	2019-Q2		EA	
Y	50458-0575	2019-Q3		ML	
Y	50458-0577	2019-Q3		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	50458-0578	2019-Q3		EA	
Y	50458-0579	2019-Q3		EA	
Y	50458-0580	2019-Q3		EA	
Y	50458-0584	2019-Q3		EA	
Y	50458-0575	2019-Q4		ML	
Y	50458-0577	2019-Q4		EA	
Y	50458-0578	2019-Q4		EA	
Y	50458-0579	2019-Q4		EA	
Y	50458-0580	2019-Q4		EA	
Y	50458-0584	2019-Q4		EA	
Y	50458-0575	2020-Q1		ML	
Y	50458-0577	2020-Q1		EA	
Y	50458-0578	2020-Q1		EA	
Y	50458-0579	2020-Q1		EA	
Y	50458-0580	2020-Q1		EA	
Y	50458-0584	2020-Q1		EA	
Y	50458-0575	2020-Q2		ML	
Y	50458-0577	2020-Q2		EA	
Y	50458-0578	2020-Q2		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	50458-0579	2020-Q2		EA	
Y	50458-0580	2020-Q2		EA	
Y	50458-0584	2020-Q2		EA	
Y	50458-0575	2020-Q3		ML	
Y	50458-0577	2020-Q3		EA	
Y	50458-0578	2020-Q3		EA	
Y	50458-0579	2020-Q3		EA	
Y	50458-0580	2020-Q3		EA	
Y	50458-0584	2020-Q3		EA	
Y	50458-0575	2020-Q4		ML	
Y	50458-0577	2020-Q4		EA	
Y	50458-0578	2020-Q4		EA	
Y	50458-0579	2020-Q4		EA	
Y	50458-0580	2020-Q4		EA	
Y	50458-0584	2020-Q4		EA	
Y	50458-0575	2021-Q1		ML	
Y	50458-0577	2021-Q1		EA	
Y	50458-0578	2021-Q1		EA	
Y	50458-0579	2021-Q1		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	50458-0580	2021-Q1		EA	
Y	50458-0584	2021-Q1		EA	
Y	50458-0575	2021-Q2		ML	
Y	50458-0577	2021-Q2		EA	
Y	50458-0578	2021-Q2		EA	
Y	50458-0579	2021-Q2		EA	
Y	50458-0580	2021-Q2		EA	
Y	50458-0584	2021-Q2		EA	
Y	50458-0575	2021-Q3		ML	
Y	50458-0577	2021-Q3		EA	
Y	50458-0578	2021-Q3		EA	
Y	50458-0579	2021-Q3		EA	
Y	50458-0580	2021-Q3		EA	
Y	50458-0584	2021-Q3		EA	
Y	50458-0575	2021-Q4		ML	
Y	50458-0577	2021-Q4		EA	
Y	50458-0578	2021-Q4		EA	
Y	50458-0579	2021-Q4		EA	
Y	50458-0580	2021-Q4		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	50458-0584	2021-Q4		EA	
Y	50458-0575	2022-Q1		ML	
Y	50458-0577	2022-Q1		EA	
Y	50458-0578	2022-Q1		EA	
Y	50458-0579	2022-Q1		EA	
Y	50458-0580	2022-Q1		EA	
Y	50458-0584	2022-Q1		EA	
Y	50458-0575	2022-Q2		ML	
Y	50458-0577	2022-Q2		EA	
Y	50458-0578	2022-Q2		EA	
Y	50458-0579	2022-Q2		EA	
Y	50458-0580	2022-Q2		EA	
Y	50458-0584	2022-Q2		EA	
Y	50458-0575	2022-Q3		ML	
Y	50458-0577	2022-Q3		EA	
Y	50458-0578	2022-Q3		EA	
Y	50458-0579	2022-Q3		EA	
Y	50458-0580	2022-Q3		EA	
Y	50458-0584	2022-Q3		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	50458-0575	2022-Q4		ML	
Y	50458-0577	2022-Q4		EA	
Y	50458-0578	2022-Q4		EA	
Y	50458-0579	2022-Q4		EA	
Y	50458-0580	2022-Q4		EA	
Y	50458-0584	2022-Q4		EA	
Y	55154-1422	2018-Q1		EA	
Y	55154-1422	2018-Q2		EA	
Y	55154-1422	2018-Q3		EA	
Y	55154-1422	2018-Q4		EA	
Y	55154-1422	2019-Q1		EA	
Y	55154-1422	2019-Q2		EA	
Y	55154-1422	2019-Q3		EA	
Y	55154-1422	2019-Q4		EA	
Y	55154-1422	2020-Q1		EA	
Y	55154-1422	2020-Q2		EA	
Y	55154-1422	2020-Q3		EA	
Y	55154-1422	2020-Q4		EA	
Y	55154-1422	2021-Q1		EA	



**G. Market Data and Revenue and Sales Volume Data**

**Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	55154-1422	2021-Q2		EA	
Y	55154-1422	2021-Q3		EA	
Y	55154-1422	2021-Q4		EA	
Y	55154-1422	2022-Q1		EA	
Y	55154-1422	2022-Q2		EA	
Y	55154-1422	2022-Q3		EA	
Y	55154-1423	2018-Q1		EA	
Y	55154-1423	2018-Q2		EA	
Y	55154-1423	2018-Q3		EA	
Y	55154-1423	2018-Q4		EA	
Y	55154-1423	2019-Q1		EA	
Y	55154-1423	2019-Q2		EA	
Y	55154-1423	2019-Q3		EA	
Y	55154-1423	2019-Q4		EA	
Y	55154-1423	2020-Q1		EA	
Y	55154-1423	2020-Q2		EA	
Y	55154-1423	2020-Q3		EA	
Y	55154-1423	2020-Q4		EA	
Y	55154-1423	2021-Q1		EA	

**G. Market Data and Revenue and Sales Volume Data**

**Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	55154-1423	2021-Q2		EA	
Y	55154-1423	2021-Q3		EA	
Y	55154-1423	2021-Q4		EA	
Y	55154-1423	2022-Q1		EA	
Y	55154-1423	2022-Q2		EA	
Y	55154-1423	2022-Q3		EA	
Y	55154-1423	2022-Q4		EA	
Y	55154-1424	2018-Q1		EA	
Y	55154-1424	2018-Q2		EA	
Y	55154-1424	2018-Q3		EA	
Y	55154-1424	2018-Q4		EA	
Y	55154-1424	2019-Q1		EA	
Y	55154-1424	2019-Q2		EA	
Y	55154-1424	2019-Q3		EA	
Y	55154-1424	2019-Q4		EA	
Y	55154-1424	2020-Q1		EA	
Y	55154-1424	2020-Q2		EA	
Y	55154-1424	2020-Q3		EA	
Y	55154-1424	2020-Q4		EA	

**G. Market Data and Revenue and Sales Volume Data****Medicaid Best Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Medicaid best price of the selected drug. The Medicaid best price information reflects what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – determination of best price.

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	55154-1424	2021-Q1		EA	
Y	55154-1424	2021-Q2		EA	
Y	55154-1424	2021-Q3		EA	
Y	55154-1424	2021-Q4		EA	
Y	55154-1424	2022-Q1		EA	
Y	55154-1424	2022-Q2		EA	
Y	55154-1424	2022-Q3		EA	
Y	55154-1424	2022-Q4		EA	
Y	55154-1422	2022-Q4		EA	

**Explanations:** Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

Fifteen NDC-9s for “XARELTO” are included in the “Selected Drug List for Initial Price Applicability Year (IPAY) 2026”. Not all fifteen NDC-9s are included in this submission.

Consistent with CMS guidance, this submission reflects information on NDC-9s of the selected drug marketed by the Primary Manufacturer and any Secondary Manufacturer.

\*Six NDC-9s are excluded: 71610-0690, 50090-3625, 50090-3639, 50090-4468, 50090-4469, and 69189-0578 (exclusions as referenced in the Section B Non-FAMP data collection section within “Explanation of Non-FAMP Calculation” field).

\*Nine NDC-9s are included in the submission for the most “recent five years” and include NDCs from both Janssen Pharmaceuticals, Inc. (“JPI”) 50458 labeler and Cardinal Health 107, LLC (“Cardinal”) 55154 labeler, respectively the “Primary Manufacturer” and the “Secondary

Manufacturer” as defined by the IRA ICR Final Guidance August 3, 2023. Total submission includes six JPI NDC-9s and three Cardinal NDC-9. Please note:

For the “Medicaid Best Price” the most recent five years is assumed to be 2018-2022, and the quarters within the five-year period are 1Q2018-4Q2022.

Where the NDC-9 did not have a Medicaid Best Price for a particular quarter within the most recent five years, rows were added to align with ICR instructions with unit type information “0” in the total unit volume field and Medicaid Best Price field “blank”.

- This applies to the XARELTO NDC 50458-0575 (first sale date of January 18, 2022) and XARELTO NDC 50458-0577 (first sale date of October 16, 2018).

- This also applies to the Cardinal secondary manufacturer NDCs 55154-1422, 55154-1423, 55154-1424 where there is no Best Price information available for these NDCs for the most recent five years.

The reported Best Price information reflects BP at NDC-9 level and reflects the lowest unit of measure by Medicaid unit type as submitted under the Medicaid Drug Rebate Program (MDRP) and reflect any restatements at the point in time of submission per the requirements under the ICR.

The submission has been modified in two ways to accommodate system limitations in HPMS. First, the IRA ICR requires "The Medicaid best price information must reflect what was submitted to Medicaid under the MDRP". Medicaid Best Price is submitted under the MDRP out to six decimal places, however, the IRA ICR format permits reporting only to two decimal places. Second, the Medicaid AMP unit type “Tabs” used by JPI in AMP submissions is not available in the unit type drop-down selection in HPMS. HPMS does not allow the user to move forward in the system unless information is submitted in the format available. In order to advance the primary manufacturer’s submission in HPMS, the primary manufacturer Best Price is at the lowest unit of measure rounded to the closest two decimals and “Each (EA)” for unit type where “Tabs” is the unit type under the MDRP.

The reported quarterly AMP unit volume is the sum of monthly AMP units within the quarter as reported under the MDRP government price reporting regulation and Medicaid Drug Program (MDP) system user guidance. AMP unit volume reflects the lowest unit of measure by Medicaid unit type to match ICR requirements. AMP units are not required as part of Best Price reporting under the MDRP.



## G. Market Data and Revenue and Sales Volume Data

### Federal Supply Schedule Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0575-01	2022-02-01 - 2022-04-14	\$227.59	ML	
Y	50458-0575-01	2022-04-15 - 2022-12-31	\$389.42	ML	
Y	50458-0577-10	2022-01-01 - 2022-12-31	\$597.89	EA	
Y	50458-0577-18	2022-01-01 - 2022-12-31	\$1,076.21	EA	
Y	50458-0577-60	2022-01-01 - 2022-12-31	\$358.73	EA	
Y	50458-0578-10	2022-01-01 - 2022-12-31	\$1,195.78	EA	
Y	50458-0578-30	2022-01-01 - 2022-12-31	\$358.73	EA	
Y	50458-0578-90	2022-01-01 - 2022-12-31	\$1,076.21	EA	
Y	50458-0579-10	2022-01-01 - 2022-12-31	\$1,195.78	EA	
Y	50458-0579-30	2022-01-01 - 2022-12-31	\$358.73	EA	

## G. Market Data and Revenue and Sales Volume Data

### Federal Supply Schedule Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0579-89	2022-01-01 - 2022-12-31	\$15,306.05	EA	
Y	50458-0579-90	2022-01-01 - 2022-12-31	\$1,076.21	EA	
Y	50458-0580-10	2022-01-01 - 2022-12-31	\$1,195.78	EA	
Y	50458-0580-30	2022-01-01 - 2022-12-31	\$358.73	EA	
Y	50458-0580-90	2022-01-01 - 2022-12-31	\$1,076.21	EA	
Y	50458-0584-51	2022-01-01 - 2022-12-31	\$609.86	EA	
Y	50458-0577-10	2021-01-01 - 2021-12-31	\$570.50	EA	
Y	50458-0577-18	2021-01-01 - 2021-12-31	\$1,026.91	EA	
Y	50458-0577-60	2021-01-01 - 2021-12-31	\$342.30	EA	

## G. Market Data and Revenue and Sales Volume Data

### Federal Supply Schedule Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0578-10	2021-01-01 - 2021-12-31	\$1,141.02	EA	
Y	50458-0578-30	2021-01-01 - 2021-12-31	\$342.30	EA	
Y	50458-0578-90	2021-01-01 - 2021-12-31	\$1,026.91	EA	
Y	50458-0579-10	2021-01-01 - 2021-12-31	\$1,141.02	EA	
Y	50458-0579-30	2021-01-01 - 2021-12-31	\$342.30	EA	
Y	50458-0579-89	2021-01-01 - 2021-12-31	\$14,605.01	EA	
Y	50458-0579-90	2021-01-01 - 2021-12-31	\$1,026.91	EA	
Y	50458-0580-10	2021-01-01 - 2021-12-31	\$1,141.02	EA	
Y	50458-0580-30	2021-01-01 - 2021-12-31	\$342.30	EA	



## G. Market Data and Revenue and Sales Volume Data

### Federal Supply Schedule Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0580-90	2021-01-01 - 2021-12-31	\$1,026.91	EA	
Y	50458-0584-51	2021-01-01 - 2021-12-31	\$581.93	EA	
Y	50458-0577-10	2020-01-01 - 2020-12-31	\$562.79	EA	
Y	50458-0577-18	2020-01-01 - 2020-12-31	\$1,013.04	EA	
Y	50458-0577-60	2020-01-01 - 2020-12-31	\$337.68	EA	
Y	50458-0578-10	2020-01-01 - 2020-12-31	\$1,125.60	EA	
Y	50458-0578-30	2020-01-01 - 2020-12-31	\$337.68	EA	
Y	50458-0578-90	2020-01-01 - 2020-12-31	\$1,013.04	EA	
Y	50458-0579-10	2020-01-01 - 2020-12-31	\$1,125.60	EA	
Y	50458-0579-30	2020-01-01 - 2020-12-31	\$337.68	EA	



## G. Market Data and Revenue and Sales Volume Data

### Federal Supply Schedule Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0579-89	2020-01-01 - 2020-12-31	\$14,407.62	EA	
Y	50458-0579-90	2020-01-01 - 2020-12-31	\$1,013.04	EA	
Y	50458-0580-10	2020-01-01 - 2020-12-31	\$1,125.60	EA	
Y	50458-0580-30	2020-01-01 - 2020-12-31	\$337.68	EA	
Y	50458-0580-90	2020-01-01 - 2020-12-31	\$1,013.04	EA	
Y	50458-0584-51	2020-01-01 - 2020-12-31	\$574.06	EA	
Y	50458-0577-10	2018-12-19 - 2019-02-12	\$287.80	EA	
Y	50458-0577-10	2019-02-13 - 2019-05-16	\$526.47	EA	
Y	50458-0577-10	2019-05-17 - 2019-08-31	\$562.79	EA	

## G. Market Data and Revenue and Sales Volume Data

### Federal Supply Schedule Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0577-10	2019-09-01 - 2019-12-31	\$562.79	EA	
Y	50458-0577-18	2018-12-19 - 2019-02-12	\$518.04	EA	
Y	50458-0577-18	2019-02-13 - 2019-05-16	\$947.65	EA	
Y	50458-0577-18	2019-05-17 - 2019-08-31	\$1,013.04	EA	
Y	50458-0577-18	2019-09-01 - 2019-12-31	\$1,013.04	EA	
Y	50458-0577-60	2018-12-19 - 2019-02-12	\$172.68	EA	
Y	50458-0577-60	2019-02-13 - 2019-05-16	\$315.88	EA	
Y	50458-0577-60	2019-05-17 - 2019-08-31	\$337.68	EA	
Y	50458-0577-60	2019-09-01 - 2019-12-31	\$337.68	EA	
Y	50458-0578-10	2019-01-01 - 2019-08-31	\$1,052.94	EA	

## G. Market Data and Revenue and Sales Volume Data

### Federal Supply Schedule Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0578-10	2019-09-01 - 2019-12-31	\$1,125.60	EA	
Y	50458-0578-30	2019-01-01 - 2019-08-31	\$315.88	EA	
Y	50458-0578-30	2019-09-01 - 2019-12-31	\$337.68	EA	
Y	50458-0578-90	2019-01-01 - 2019-08-31	\$947.65	EA	
Y	50458-0578-90	2019-09-01 - 2019-12-31	\$1,013.04	EA	
Y	50458-0579-10	2019-01-01 - 2019-08-31	\$1,052.94	EA	
Y	50458-0579-10	2019-09-01 - 2019-12-31	\$1,125.60	EA	
Y	50458-0579-30	2019-01-01 - 2019-08-31	\$315.88	EA	
Y	50458-0579-30	2019-09-01 - 2019-12-31	\$337.68	EA	
Y	50458-0579-89	2019-02-20 - 2019-03-06	\$8,000.00	EA	



**G. Market Data and Revenue and Sales Volume Data**

**Federal Supply Schedule Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

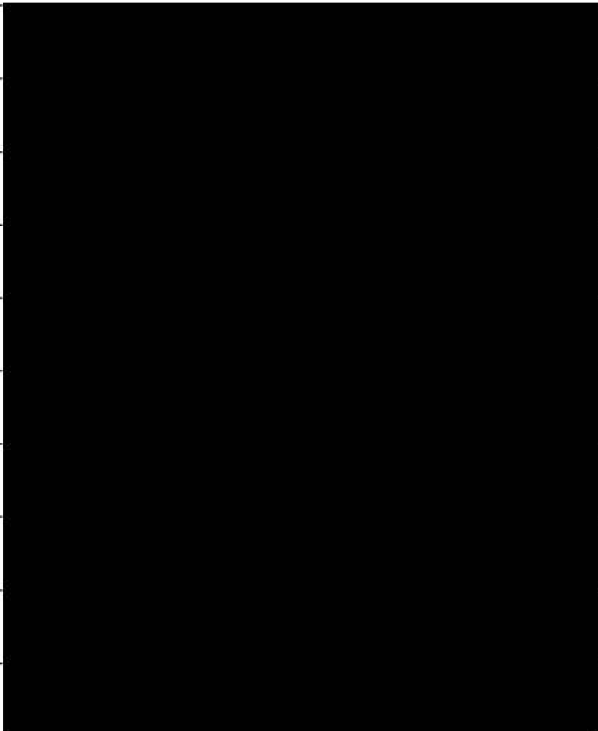
Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0579-89	2019-03-07 - 2019-05-31	\$6,153.26	EA	
Y	50458-0579-89	2019-06-01 - 2019-08-31	\$6,153.26	EA	
Y	50458-0579-89	2019-09-01 - 2019-12-31	\$14,407.62	EA	
Y	50458-0579-90	2019-01-01 - 2019-08-31	\$947.65	EA	
Y	50458-0579-90	2019-09-01 - 2019-12-31	\$1,013.04	EA	
Y	50458-0580-10	2019-01-01 - 2019-08-31	\$1,052.94	EA	
Y	50458-0580-10	2019-09-01 - 2019-12-31	\$1,125.60	EA	
Y	50458-0580-30	2019-01-01 - 2019-08-31	\$315.88	EA	
Y	50458-0580-30	2019-09-01 - 2019-12-31	\$337.68	EA	



## G. Market Data and Revenue and Sales Volume Data

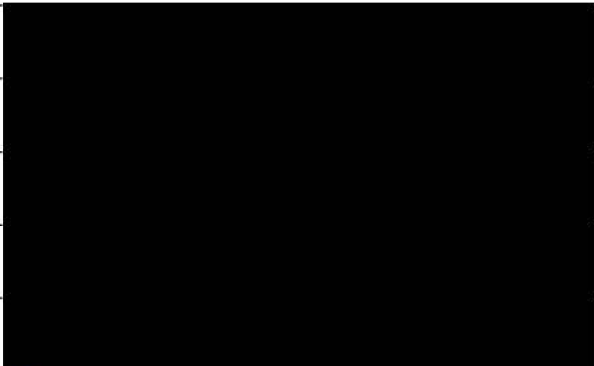
### Federal Supply Schedule Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0580-90	2019-01-01 - 2019-08-31	\$947.65	EA	
Y	50458-0580-90	2019-09-01 - 2019-12-31	\$1,013.04	EA	
Y	50458-0584-51	2019-01-01 - 2019-08-31	\$537.01	EA	
Y	50458-0584-51	2019-09-01 - 2019-12-31	\$574.06	EA	
Y	50458-0578-10	2018-01-01 - 2018-12-31	\$758.65	EA	
Y	50458-0578-30	2018-01-01 - 2018-12-31	\$227.60	EA	
Y	50458-0578-90	2018-01-01 - 2018-12-31	\$682.78	EA	
Y	50458-0579-10	2018-01-01 - 2018-12-31	\$758.65	EA	
Y	50458-0579-30	2018-01-01 - 2018-12-31	\$227.60	EA	
Y	50458-0579-90	2018-01-01 - 2018-12-31	\$682.78	EA	

**G. Market Data and Revenue and Sales Volume Data****Federal Supply Schedule Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. Manufacturers reported any federal supply schedule (FSS) price for the selected drug made available during the most recent five years. The FSS price information reflects what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Federal Supply Schedule Price	National Drug Code (NDC-11)	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0580-10	2018-01-01 - 2018-12-31	\$758.65	EA	
Y	50458-0580-30	2018-01-01 - 2018-12-31	\$227.60	EA	
Y	50458-0580-90	2018-02-15 - 2018-09-14	\$515.67	EA	
Y	50458-0580-90	2018-09-15 - 2018-12-31	\$947.65	EA	
Y	50458-0584-51	2018-01-01 - 2018-12-31	\$418.27	EA	

**Explanations:** Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

Thirty-six NDC-11s for “XARELTO” are included in the “Selected Drug List for Initial Price Applicability Year (IPAY) 2026”. Not all thirty-six NDC-11s are included in this submission.

\*Twenty-one NDC-11s are excluded from submission because Federal Supply Schedule (FSS) prices for these NDCs are not included in FSS contracts with Janssen Pharmaceuticals, Inc. (“JPI”) and not listed on the VA National Acquisition Center (VA NAC) website:

Six NDC-11s are from third parties: 71610-0690-42, 50090-3625-00, 50090-3639-00, 50090-4468-00, 50090-4469-00, 69189-0578-01 as referenced in the Section B Non-FAMP data collection section within “Explanation of Non-FAMP Calculation” field.

Seven NDC-11s are sample NDCs under JPI labeler 50458: 50458-0577-14, 50458-0578-07, 50458-0578-14, 50458-0579-07, 50458-0579-99, 50458-0580-07, 50458-0584-52.

Four NDC-11s are inner NDCs under JPI labeler 50458 NDCs: 50458-0577-01, 50458-0578-01, 50458-0579-01, 50458-0580-01.

Four NDC-11s are repacking NDCs under Cardinal ("Secondary Manufacturer") labeler 55154 NDCs: 55154-1422-00, 55154-1423-08, 55154-1424-00, 55154-1424-08. As instructed by Cardinal these products are only made available to the customers that contracted to have them repackaged into the applicable configuration. They are not otherwise available for purchase.

\*Fifteen NDC-11s are included in FSS price submission under the JPI labeler 50458.

The "Federal Supply Schedule Price" reflects those that can be found online in the Pharmaceutical pricing data for all VA NAC Programs by NDC-11 to match ICR requirements. In order to reconcile to the VA NAC, the pricing submitted includes IFF. Note, the ICR requests a data point "Federal Supply Schedule Service Price" which we are unfamiliar with and are not reporting. In its place we are reporting the "Federal Supply Schedule Price".

FSS Total Unit Volume: The reported FSS total unit volume captures unit quantity at the package level used to calculate the FSS price in accordance with the Veteran's Health Care Act (VHCA) public law. ICR required reporting total unit volume sold to "direct federal purchasers".

[REDACTED]

[REDACTED] For purposes of this submission, the 2018-2022 invoice data was pulled at a point in time in May 2023 to prepare for the IRA ICR submissions. It is our assumption that for this request, CMS intends to correlate the reported FSS price to the units sold during the time period that price was in effect.

**G. Market Data and Revenue and Sales Volume Data**

**Big Four Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Big Four price of the selected drug. The Big Four price information reflects the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Big Four Price	National Drug Code (NDC-11)	Price Start Date to End Date	Big Four Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0575-01	2022-02-01 - 2022-04-14	\$227.59	ML	
Y	50458-0575-01	2022-04-15 - 2022-08-14	\$384.82	ML	
Y	50458-0575-01	2022-08-15 - 2022-12-31	\$378.21	ML	
Y	50458-0577-10	2022-01-01 - 2022-12-31	\$569.87	EA	
Y	50458-0577-18	2022-01-01 - 2022-12-31	\$1,076.21	EA	
Y	50458-0577-60	2022-01-01 - 2022-12-31	\$358.73	EA	
Y	50458-0578-10	2022-01-01 - 2022-12-31	\$733.88	EA	
Y	50458-0578-30	2022-01-01 - 2022-12-31	\$358.73	EA	
Y	50458-0578-90	2022-01-01 - 2022-12-31	\$1,070.53	EA	
Y	50458-0579-10	2022-01-01 - 2022-12-31	\$776.08	EA	
Y	50458-0579-30	2022-01-01 - 2022-12-31	\$358.73	EA	



**G. Market Data and Revenue and Sales Volume Data**

**Big Four Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Big Four price of the selected drug. The Big Four price information reflects the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Big Four Price	National Drug Code (NDC-11)	Price Start Date to End Date	Big Four Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0579-89	2022-01-01 - 2022-12-31	\$11,656.09	EA	
Y	50458-0579-90	2022-01-01 - 2022-12-31	\$1,068.10	EA	
Y	50458-0580-10	2022-01-01 - 2022-12-31	\$757.76	EA	
Y	50458-0580-30	2022-01-01 - 2022-12-31	\$358.69	EA	
Y	50458-0580-90	2022-01-01 - 2022-12-31	\$1,068.23	EA	
Y	50458-0584-51	2022-01-01 - 2022-12-31	\$577.12	EA	
Y	50458-0577-10	2021-01-01 - 2021-12-31	\$546.50	EA	
Y	50458-0577-18	2021-01-01 - 2021-12-31	\$998.88	EA	
Y	50458-0577-60	2021-01-01 - 2021-12-31	\$330.41	EA	
Y	50458-0578-10	2021-01-01 - 2021-12-31	\$739.79	EA	
Y	50458-0578-30	2021-01-01 - 2021-12-31	\$328.89	EA	

### G. Market Data and Revenue and Sales Volume Data

#### Big Four Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Big Four price of the selected drug. The Big Four price information reflects the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Big Four Price	National Drug Code (NDC-11)	Price Start Date to End Date	Big Four Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0578-90	2021-01-01 - 2021-12-31	\$977.38	EA	
Y	50458-0579-10	2021-01-01 - 2021-12-31	\$792.27	EA	
Y	50458-0579-30	2021-01-01 - 2021-12-31	\$329.61	EA	
Y	50458-0579-89	2021-01-01 - 2021-12-31	\$10,936.58	EA	
Y	50458-0579-90	2021-01-01 - 2021-12-31	\$982.50	EA	
Y	50458-0580-10	2021-01-01 - 2021-12-31	\$749.24	EA	
Y	50458-0580-30	2021-01-01 - 2021-12-31	\$327.99	EA	
Y	50458-0580-90	2021-01-01 - 2021-12-31	\$976.44	EA	
Y	50458-0584-51	2021-01-01 - 2021-12-31	\$526.74	EA	
Y	50458-0577-10	2020-01-01 - 2020-12-31	\$535.76	EA	
Y	50458-0577-18	2020-01-01 - 2020-12-31	\$1,000.02	EA	

### G. Market Data and Revenue and Sales Volume Data

#### Big Four Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Big Four price of the selected drug. The Big Four price information reflects the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Big Four Price	National Drug Code (NDC-11)	Price Start Date to End Date	Big Four Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0577-60	2020-01-01 - 2020-12-31	\$330.27	EA	
Y	50458-0578-10	2020-01-01 - 2020-12-31	\$721.19	EA	
Y	50458-0578-30	2020-01-01 - 2020-12-31	\$305.71	EA	
Y	50458-0578-90	2020-01-01 - 2020-12-31	\$906.57	EA	
Y	50458-0579-10	2020-01-01 - 2020-12-31	\$742.03	EA	
Y	50458-0579-30	2020-01-01 - 2020-12-31	\$306.03	EA	
Y	50458-0579-89	2020-01-01 - 2020-12-31	\$10,967.28	EA	
Y	50458-0579-90	2020-01-01 - 2020-12-31	\$917.28	EA	
Y	50458-0580-10	2020-01-01 - 2020-12-31	\$749.61	EA	
Y	50458-0580-30	2020-01-01 - 2020-12-31	\$303.86	EA	
Y	50458-0580-90	2020-01-01 - 2020-12-31	\$906.22	EA	



### G. Market Data and Revenue and Sales Volume Data

#### Big Four Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Big Four price of the selected drug. The Big Four price information reflects the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Big Four Price	National Drug Code (NDC-11)	Price Start Date to End Date	Big Four Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0584-51	2020-01-01 - 2020-12-31	\$513.66	EA	
Y	50458-0577-10	2018-12-19 - 2019-02-12	\$287.80	EA	
Y	50458-0577-10	2019-02-13 - 2019-05-16	\$501.97	EA	
Y	50458-0577-10	2019-05-17 - 2019-08-31	\$521.49	EA	
Y	50458-0577-10	2019-09-01 - 2019-12-31	\$521.49	EA	
Y	50458-0577-18	2018-12-19 - 2019-02-12	\$518.04	EA	
Y	50458-0577-18	2019-02-13 - 2019-05-16	\$914.94	EA	
Y	50458-0577-18	2019-05-17 - 2019-08-31	\$965.74	EA	
Y	50458-0577-18	2019-09-01 - 2019-12-31	\$965.74	EA	
Y	50458-0577-60	2018-12-19 - 2019-02-12	\$172.68	EA	
Y	50458-0577-60	2019-02-13 - 2019-05-16	\$304.11	EA	



**G. Market Data and Revenue and Sales Volume Data**

**Big Four Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Big Four price of the selected drug. The Big Four price information reflects the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Big Four Price	National Drug Code (NDC-11)	Price Start Date to End Date	Big Four Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0577-60	2019-05-17 - 2019-08-31	\$320.36	EA	
Y	50458-0577-60	2019-09-01 - 2019-12-31	\$320.36	EA	
Y	50458-0578-10	2019-01-01 - 2019-08-31	\$725.84	EA	
Y	50458-0578-10	2019-09-01 - 2019-12-31	\$725.84	EA	
Y	50458-0578-30	2019-01-01 - 2019-08-31	\$284.13	EA	
Y	50458-0578-30	2019-09-01 - 2019-12-31	\$284.13	EA	
Y	50458-0578-90	2019-01-01 - 2019-08-31	\$844.58	EA	
Y	50458-0578-90	2019-09-01 - 2019-12-31	\$844.58	EA	
Y	50458-0579-10	2019-01-01 - 2019-08-31	\$800.00	EA	
Y	50458-0579-10	2019-09-01 - 2019-12-31	\$800.00	EA	
Y	50458-0579-30	2019-01-01 - 2019-08-31	\$285.08	EA	

## G. Market Data and Revenue and Sales Volume Data

### Big Four Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Big Four price of the selected drug. The Big Four price information reflects the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Big Four Price	National Drug Code (NDC-11)	Price Start Date to End Date	Big Four Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0579-30	2019-09-01 - 2019-12-31	\$285.08	EA	
Y	50458-0579-89	2019-02-20 - 2019-03-06	\$8,000.00	EA	
Y	50458-0579-89	2019-03-07 - 2019-05-31	\$6,153.26	EA	
Y	50458-0579-89	2019-06-01 - 2019-08-31	\$6,153.26	EA	
Y	50458-0579-89	2019-09-01 - 2019-12-31	\$11,008.90	EA	
Y	50458-0579-90	2019-01-01 - 2019-08-31	\$850.29	EA	
Y	50458-0579-90	2019-09-01 - 2019-12-31	\$850.29	EA	
Y	50458-0580-10	2019-01-01 - 2019-08-31	\$700.96	EA	
Y	50458-0580-10	2019-09-01 - 2019-12-31	\$700.96	EA	
Y	50458-0580-30	2019-01-01 - 2019-08-31	\$281.53	EA	
Y	50458-0580-30	2019-09-01 - 2019-12-31	\$281.53	EA	

### G. Market Data and Revenue and Sales Volume Data

#### Big Four Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Big Four price of the selected drug. The Big Four price information reflects the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Big Four Price	National Drug Code (NDC-11)	Price Start Date to End Date	Big Four Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0580-90	2019-01-01 - 2019-08-31	\$914.08	EA	
Y	50458-0580-90	2019-09-01 - 2019-12-31	\$914.08	EA	
Y	50458-0584-51	2019-01-01 - 2019-08-31	\$471.19	EA	
Y	50458-0584-51	2019-09-01 - 2019-12-31	\$471.19	EA	
Y	50458-0578-10	2018-01-01 - 2018-12-31	\$698.18	EA	
Y	50458-0578-30	2018-01-01 - 2018-12-31	\$227.60	EA	
Y	50458-0578-90	2018-01-01 - 2018-12-31	\$682.78	EA	
Y	50458-0579-10	2018-01-01 - 2018-12-31	\$736.73	EA	
Y	50458-0579-30	2018-01-01 - 2018-12-31	\$227.60	EA	
Y	50458-0579-90	2018-01-01 - 2018-12-31	\$682.78	EA	
Y	50458-0580-10	2018-01-01 - 2018-12-31	\$686.98	EA	



## G. Market Data and Revenue and Sales Volume Data

### Big Four Price

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides responses about the Big Four price of the selected drug. The Big Four price information reflects the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.

Big Four Price	National Drug Code (NDC-11)	Price Start Date to End Date	Big Four Price	Unit Type (EA, ML, GM)	Total Unit Volume
Y	50458-0580-30	2018-01-01 - 2018-12-31	\$227.60	EA	
Y	50458-0580-90	2018-02-15 - 2018-09-14	\$515.67	EA	
Y	50458-0580-90	2018-09-15 - 2018-12-31	\$909.34	EA	
Y	50458-0584-51	2018-01-01 - 2018-12-31	\$418.27	EA	

**Explanations:** Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

Thirty-six NDC-11s for “XARELTO” are included in the “Selected Drug List for Initial Price Applicability Year (IPAY) 2026”. Not all thirty-six NDC-11s are included in this submission.

\*Twenty-one NDC-11s are excluded from submission because Big Four prices for these NDCs are not included in FSS contracts with Janssen Pharmaceuticals, Inc. (“JPI”) and not listed on the VA National Acquisition Center (VA NAC) website.

Six NDC-11s are from third parties: 71610-0690-42, 50090-3625-00, 50090-3639-00, 50090-4468-00, 50090-4469-00, 69189-0578-01 as referenced in the Section B Non-FAMP data collection section within “Explanation of Non-FAMP Calculation” field.

Seven NDC-11s are sample NDCs under JPI labeler 50458: 50458-0577-14, 50458-0578-07, 50458-0578-14, 50458-0579-07, 50458-0579-99, 50458-0580-07, 50458-0584-52.

Four NDC-11s are inner NDCs under JPI labeler 50458 NDCs: 50458-0577-01, 50458-0578-01, 50458-0579-01, 50458-0580-01.



Four NDC-11s are repacking NDCs under Cardinal (“Secondary Manufacturer”) labeler 55154 NDCs: 55154-1422-00; 55154-1423-08; 55154-1424-00, 55154-1424-08. [REDACTED]

\*Fifteen NDC-11s are included in Big Four information submission under the JPI labeler 50458.

“Big Four Price” for NDC-11 (50458-0579-89), a start date difference was identified between the contract modification received by JPI (September, 1, 2019) and the information reported on the VA NAC website (September 10, 2019). Data in this submission is based on the documentation received by JPI confirming the start date of September, 1, 2019.

“Big Four Price” reflects those that can be found online in the Pharmaceutical pricing data for all VA NAC Programs by NDC-11 to match ICR requirements. In order to reconcile to the VA NAC, the pricing submitted includes IFF.

Provisional prices for newly launched products were found on the VA NAC website only under the FSS pricing but the submitted data also included the provisional prices available for the Big Four Price not listed on the VA NAC.

“Big Four Total Unit Volume” is the total number of units for each NDC-11 sold to Big Four federal customers and could include units sold with prices that reflect temporary price reduction and/or uniform formulary blanket purchase agreement price.

Big Four Total Unit Volume: The reported total unit volume captures unit quantity at the package level used to calculate the Big Four price in accordance with the Veteran’s Health Care Act (VHCA) public law.

[REDACTED] For purposes of this submission, the 2018-2022 invoice data was pulled at a point in time in May 2023 to prepare for the IRA ICR submissions. It is our assumption that for this request, CMS intends to correlate the reported Big Four price to the units sold during the time period that price was in effect.

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0575-01	2018-Q1				ML	
50458-0575-01	2018-Q2				ML	
50458-0575-01	2018-Q3				ML	
50458-0575-01	2018-Q4				ML	
50458-0575-01	2019-Q1				ML	
50458-0575-01	2019-Q2				ML	
50458-0575-01	2019-Q3				ML	
50458-0575-01	2019-Q4				ML	
50458-0575-01	2020-Q1				ML	
50458-0575-01	2020-Q2				ML	
50458-0575-01	2020-Q3				ML	
50458-0575-01	2020-Q4				ML	
50458-0575-01	2021-Q1				ML	
50458-0575-01	2021-Q2				ML	
50458-0575-01	2021-Q3				ML	
50458-0575-01	2021-Q4				ML	
50458-0575-01	2022-Q1				ML	
50458-0575-01	2022-Q2				ML	
50458-0575-01	2022-Q3				ML	
50458-0575-01	2022-Q4				ML	
50458-0577-10	2018-Q1				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0577-10	2018-Q2				EA	
50458-0577-10	2018-Q3				EA	
50458-0577-10	2018-Q4				EA	
50458-0577-10	2019-Q1				EA	
50458-0577-10	2019-Q2				EA	
50458-0577-10	2019-Q3				EA	
50458-0577-10	2019-Q4				EA	
50458-0577-10	2020-Q1				EA	
50458-0577-10	2020-Q2				EA	
50458-0577-10	2020-Q3				EA	
50458-0577-10	2020-Q4				EA	
50458-0577-10	2021-Q1				EA	
50458-0577-10	2021-Q2				EA	
50458-0577-10	2021-Q3				EA	
50458-0577-10	2021-Q4				EA	
50458-0577-10	2022-Q1				EA	
50458-0577-10	2022-Q2				EA	
50458-0577-10	2022-Q3				EA	
50458-0577-10	2022-Q4				EA	
50458-0577-18	2018-Q1				EA	
50458-0577-18	2018-Q2				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0577-18	2018-Q3				EA	
50458-0577-18	2018-Q4				EA	
50458-0577-18	2019-Q1				EA	
50458-0577-18	2019-Q2				EA	
50458-0577-18	2019-Q3				EA	
50458-0577-18	2019-Q4				EA	
50458-0577-18	2020-Q1				EA	
50458-0577-18	2020-Q2				EA	
50458-0577-18	2020-Q3				EA	
50458-0577-18	2020-Q4				EA	
50458-0577-18	2021-Q1				EA	
50458-0577-18	2021-Q2				EA	
50458-0577-18	2021-Q3				EA	
50458-0577-18	2021-Q4				EA	
50458-0577-18	2022-Q1				EA	
50458-0577-18	2022-Q2				EA	
50458-0577-18	2022-Q3				EA	
50458-0577-18	2022-Q4				EA	
50458-0577-60	2018-Q1				EA	
50458-0577-60	2018-Q2				EA	
50458-0577-60	2018-Q3				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0577-60	2018-Q4				EA	
50458-0577-60	2019-Q1				EA	
50458-0577-60	2019-Q2				EA	
50458-0577-60	2019-Q3				EA	
50458-0577-60	2019-Q4				EA	
50458-0577-60	2020-Q1				EA	
50458-0577-60	2020-Q2				EA	
50458-0577-60	2020-Q3				EA	
50458-0577-60	2020-Q4				EA	
50458-0577-60	2021-Q1				EA	
50458-0577-60	2021-Q2				EA	
50458-0577-60	2021-Q3				EA	
50458-0577-60	2021-Q4				EA	
50458-0577-60	2022-Q1				EA	
50458-0577-60	2022-Q2				EA	
50458-0577-60	2022-Q3				EA	
50458-0577-60	2022-Q4				EA	
50458-0578-10	2018-Q1				EA	
50458-0578-10	2018-Q2				EA	
50458-0578-10	2018-Q3				EA	
50458-0578-10	2018-Q4				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0578-10	2019-Q1				EA	
50458-0578-10	2019-Q2				EA	
50458-0578-10	2019-Q3				EA	
50458-0578-10	2019-Q4				EA	
50458-0578-10	2020-Q1				EA	
50458-0578-10	2020-Q2				EA	
50458-0578-10	2020-Q3				EA	
50458-0578-10	2020-Q4				EA	
50458-0578-10	2021-Q1				EA	
50458-0578-10	2021-Q2				EA	
50458-0578-10	2021-Q3				EA	
50458-0578-10	2021-Q4				EA	
50458-0578-10	2022-Q1				EA	
50458-0578-10	2022-Q2				EA	
50458-0578-10	2022-Q3				EA	
50458-0578-10	2022-Q4				EA	
50458-0578-30	2018-Q1				EA	
50458-0578-30	2018-Q2				EA	
50458-0578-30	2018-Q3				EA	
50458-0578-30	2018-Q4				EA	
50458-0578-30	2019-Q1				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0578-30	2019-Q2				EA	
50458-0578-30	2019-Q3				EA	
50458-0578-30	2019-Q4				EA	
50458-0578-30	2020-Q1				EA	
50458-0578-30	2020-Q2				EA	
50458-0578-30	2020-Q3				EA	
50458-0578-30	2020-Q4				EA	
50458-0578-30	2021-Q1				EA	
50458-0578-30	2021-Q2				EA	
50458-0578-30	2021-Q3				EA	
50458-0578-30	2021-Q4				EA	
50458-0578-30	2022-Q1				EA	
50458-0578-30	2022-Q2				EA	
50458-0578-30	2022-Q3				EA	
50458-0578-30	2022-Q4				EA	
50458-0578-90	2018-Q1				EA	
50458-0578-90	2018-Q2				EA	
50458-0578-90	2018-Q3				EA	
50458-0578-90	2018-Q4				EA	
50458-0578-90	2019-Q1				EA	
50458-0578-90	2019-Q2				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0578-90	2019-Q3				EA	
50458-0578-90	2019-Q4				EA	
50458-0578-90	2020-Q1				EA	
50458-0578-90	2020-Q2				EA	
50458-0578-90	2020-Q3				EA	
50458-0578-90	2020-Q4				EA	
50458-0578-90	2021-Q1				EA	
50458-0578-90	2021-Q2				EA	
50458-0578-90	2021-Q3				EA	
50458-0578-90	2021-Q4				EA	
50458-0578-90	2022-Q1				EA	
50458-0578-90	2022-Q2				EA	
50458-0578-90	2022-Q3				EA	
50458-0578-90	2022-Q4				EA	
50458-0579-10	2018-Q1				EA	
50458-0579-10	2018-Q2				EA	
50458-0579-10	2018-Q3				EA	
50458-0579-10	2018-Q4				EA	
50458-0579-10	2019-Q1				EA	
50458-0579-10	2019-Q2				EA	
50458-0579-10	2019-Q3				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0579-10	2019-Q4				EA	
50458-0579-10	2020-Q1				EA	
50458-0579-10	2020-Q2				EA	
50458-0579-10	2020-Q3				EA	
50458-0579-10	2020-Q4				EA	
50458-0579-10	2021-Q1				EA	
50458-0579-10	2021-Q2				EA	
50458-0579-10	2021-Q3				EA	
50458-0579-10	2021-Q4				EA	
50458-0579-10	2022-Q1				EA	
50458-0579-10	2022-Q2				EA	
50458-0579-10	2022-Q3				EA	
50458-0579-10	2022-Q4				EA	
50458-0579-30	2018-Q1				EA	
50458-0579-30	2018-Q2				EA	
50458-0579-30	2018-Q3				EA	
50458-0579-30	2018-Q4				EA	
50458-0579-30	2019-Q1				EA	
50458-0579-30	2019-Q2				EA	
50458-0579-30	2019-Q3				EA	
50458-0579-30	2019-Q4				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0579-30	2020-Q1				EA	
50458-0579-30	2020-Q2				EA	
50458-0579-30	2020-Q3				EA	
50458-0579-30	2020-Q4				EA	
50458-0579-30	2021-Q1				EA	
50458-0579-30	2021-Q2				EA	
50458-0579-30	2021-Q3				EA	
50458-0579-30	2021-Q4				EA	
50458-0579-30	2022-Q1				EA	
50458-0579-30	2022-Q2				EA	
50458-0579-30	2022-Q3				EA	
50458-0579-30	2022-Q4				EA	
50458-0579-89	2018-Q1				EA	
50458-0579-89	2018-Q2				EA	
50458-0579-89	2018-Q3				EA	
50458-0579-89	2018-Q4				EA	
50458-0579-89	2019-Q1				EA	
50458-0579-89	2019-Q2				EA	
50458-0579-89	2019-Q3				EA	
50458-0579-89	2019-Q4				EA	
50458-0579-89	2020-Q1				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0579-89	2020-Q2				EA	
50458-0579-89	2020-Q3				EA	
50458-0579-89	2020-Q4				EA	
50458-0579-89	2021-Q1				EA	
50458-0579-89	2021-Q2				EA	
50458-0579-89	2021-Q3				EA	
50458-0579-89	2021-Q4				EA	
50458-0579-89	2022-Q1				EA	
50458-0579-89	2022-Q2				EA	
50458-0579-89	2022-Q3				EA	
50458-0579-89	2022-Q4				EA	
50458-0579-90	2018-Q1				EA	
50458-0579-90	2018-Q2				EA	
50458-0579-90	2018-Q3				EA	
50458-0579-90	2018-Q4				EA	
50458-0579-90	2019-Q1				EA	
50458-0579-90	2019-Q2				EA	
50458-0579-90	2019-Q3				EA	
50458-0579-90	2019-Q4				EA	
50458-0579-90	2020-Q1				EA	
50458-0579-90	2020-Q2				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0579-90	2020-Q3				EA	
50458-0579-90	2020-Q4				EA	
50458-0579-90	2021-Q1				EA	
50458-0579-90	2021-Q2				EA	
50458-0579-90	2021-Q3				EA	
50458-0579-90	2021-Q4				EA	
50458-0579-90	2022-Q1				EA	
50458-0579-90	2022-Q2				EA	
50458-0579-90	2022-Q3				EA	
50458-0579-90	2022-Q4				EA	
50458-0580-10	2018-Q1				EA	
50458-0580-10	2018-Q2				EA	
50458-0580-10	2018-Q3				EA	
50458-0580-10	2018-Q4				EA	
50458-0580-10	2019-Q1				EA	
50458-0580-10	2019-Q2				EA	
50458-0580-10	2019-Q3				EA	
50458-0580-10	2019-Q4				EA	
50458-0580-10	2020-Q1				EA	
50458-0580-10	2020-Q2				EA	
50458-0580-10	2020-Q3				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0580-10	2020-Q4				EA	
50458-0580-10	2021-Q1				EA	
50458-0580-10	2021-Q2				EA	
50458-0580-10	2021-Q3				EA	
50458-0580-10	2021-Q4				EA	
50458-0580-10	2022-Q1				EA	
50458-0580-10	2022-Q2				EA	
50458-0580-10	2022-Q3				EA	
50458-0580-10	2022-Q4				EA	
50458-0580-30	2018-Q1				EA	
50458-0580-30	2018-Q2				EA	
50458-0580-30	2018-Q3				EA	
50458-0580-30	2018-Q4				EA	
50458-0580-30	2019-Q1				EA	
50458-0580-30	2019-Q2				EA	
50458-0580-30	2019-Q3				EA	
50458-0580-30	2019-Q4				EA	
50458-0580-30	2020-Q1				EA	
50458-0580-30	2020-Q2				EA	
50458-0580-30	2020-Q3				EA	
50458-0580-30	2020-Q4				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0580-30	2021-Q1				EA	
50458-0580-30	2021-Q2				EA	
50458-0580-30	2021-Q3				EA	
50458-0580-30	2021-Q4				EA	
50458-0580-30	2022-Q1				EA	
50458-0580-30	2022-Q2				EA	
50458-0580-30	2022-Q3				EA	
50458-0580-30	2022-Q4				EA	
50458-0580-90	2018-Q1				EA	
50458-0580-90	2018-Q2				EA	
50458-0580-90	2018-Q3				EA	
50458-0580-90	2018-Q4				EA	
50458-0580-90	2019-Q1				EA	
50458-0580-90	2019-Q2				EA	
50458-0580-90	2019-Q3				EA	
50458-0580-90	2019-Q4				EA	
50458-0580-90	2020-Q1				EA	
50458-0580-90	2020-Q2				EA	
50458-0580-90	2020-Q3				EA	
50458-0580-90	2020-Q4				EA	
50458-0580-90	2021-Q1				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0580-90	2021-Q2				EA	
50458-0580-90	2021-Q3				EA	
50458-0580-90	2021-Q4				EA	
50458-0580-90	2022-Q1				EA	
50458-0580-90	2022-Q2				EA	
50458-0580-90	2022-Q3				EA	
50458-0580-90	2022-Q4				EA	
50458-0584-51	2018-Q1				EA	
50458-0584-51	2018-Q2				EA	
50458-0584-51	2018-Q3				EA	
50458-0584-51	2018-Q4				EA	
50458-0584-51	2019-Q1				EA	
50458-0584-51	2019-Q2				EA	
50458-0584-51	2019-Q3				EA	
50458-0584-51	2019-Q4				EA	
50458-0584-51	2020-Q1				EA	
50458-0584-51	2020-Q2				EA	
50458-0584-51	2020-Q3				EA	
50458-0584-51	2020-Q4				EA	
50458-0584-51	2021-Q1				EA	
50458-0584-51	2021-Q2				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0584-51	2021-Q3				EA	
50458-0584-51	2021-Q4				EA	
50458-0584-51	2022-Q1				EA	
50458-0584-51	2022-Q2				EA	
50458-0584-51	2022-Q3				EA	
50458-0584-51	2022-Q4				EA	
50458-0578-14	2018-Q1				EA	
50458-0578-14	2018-Q2				EA	
50458-0578-14	2018-Q3				EA	
50458-0578-14	2018-Q4				EA	
50458-0578-14	2019-Q1				EA	
50458-0578-14	2019-Q2				EA	
50458-0578-14	2019-Q3				EA	
50458-0578-14	2019-Q4				EA	
50458-0578-14	2020-Q1				EA	
50458-0578-14	2020-Q2				EA	
50458-0578-14	2020-Q3				EA	
50458-0578-14	2020-Q4				EA	
50458-0578-14	2021-Q1				EA	
50458-0578-14	2021-Q2				EA	
50458-0578-14	2021-Q3				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0578-14	2021-Q4				EA	
50458-0578-14	2022-Q1				EA	
50458-0578-14	2022-Q2				EA	
50458-0578-14	2022-Q3				EA	
50458-0578-14	2022-Q4				EA	
50458-0580-07	2018-Q1				EA	
50458-0580-07	2018-Q2				EA	
50458-0580-07	2018-Q3				EA	
50458-0580-07	2018-Q4				EA	
50458-0580-07	2019-Q1				EA	
50458-0580-07	2019-Q2				EA	
50458-0580-07	2019-Q3				EA	
50458-0580-07	2019-Q4				EA	
50458-0580-07	2020-Q1				EA	
50458-0580-07	2020-Q2				EA	
50458-0580-07	2020-Q3				EA	
50458-0580-07	2020-Q4				EA	
50458-0580-07	2021-Q1				EA	
50458-0580-07	2021-Q2				EA	
50458-0580-07	2021-Q3				EA	
50458-0580-07	2021-Q4				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0580-07	2022-Q1				EA	
50458-0580-07	2022-Q2				EA	
50458-0580-07	2022-Q3				EA	
50458-0580-07	2022-Q4				EA	
50458-0577-14	2018-Q1				EA	
50458-0577-14	2018-Q2				EA	
50458-0577-14	2018-Q3				EA	
50458-0577-14	2018-Q4				EA	
50458-0577-14	2019-Q1				EA	
50458-0577-14	2019-Q2				EA	
50458-0577-14	2019-Q3				EA	
50458-0577-14	2019-Q4				EA	
50458-0577-14	2020-Q1				EA	
50458-0577-14	2020-Q2				EA	
50458-0577-14	2020-Q3				EA	
50458-0577-14	2020-Q4				EA	
50458-0577-14	2021-Q1				EA	
50458-0577-14	2021-Q2				EA	
50458-0577-14	2021-Q3				EA	
50458-0577-14	2021-Q4				EA	
50458-0577-14	2022-Q1				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0577-14	2022-Q2				EA	
50458-0577-14	2022-Q3				EA	
50458-0577-14	2022-Q4				EA	
50458-0578-07	2018-Q1				EA	
50458-0578-07	2018-Q2				EA	
50458-0578-07	2018-Q3				EA	
50458-0578-07	2018-Q4				EA	
50458-0578-07	2019-Q1				EA	
50458-0578-07	2019-Q2				EA	
50458-0578-07	2019-Q3				EA	
50458-0578-07	2019-Q4				EA	
50458-0578-07	2020-Q1				EA	
50458-0578-07	2020-Q2				EA	
50458-0578-07	2020-Q3				EA	
50458-0578-07	2020-Q4				EA	
50458-0578-07	2021-Q1				EA	
50458-0578-07	2021-Q2				EA	
50458-0578-07	2021-Q3				EA	
50458-0578-07	2021-Q4				EA	
50458-0578-07	2022-Q1				EA	
50458-0578-07	2022-Q2				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0578-07	2022-Q3				EA	
50458-0578-07	2022-Q4				EA	
50458-0579-07	2018-Q1				EA	
50458-0579-07	2018-Q2				EA	
50458-0579-07	2018-Q3				EA	
50458-0579-07	2018-Q4				EA	
50458-0579-07	2019-Q1				EA	
50458-0579-07	2019-Q2				EA	
50458-0579-07	2019-Q3				EA	
50458-0579-07	2019-Q4				EA	
50458-0579-07	2020-Q1				EA	
50458-0579-07	2020-Q2				EA	
50458-0579-07	2020-Q3				EA	
50458-0579-07	2020-Q4				EA	
50458-0579-07	2021-Q1				EA	
50458-0579-07	2021-Q2				EA	
50458-0579-07	2021-Q3				EA	
50458-0579-07	2021-Q4				EA	
50458-0579-07	2022-Q1				EA	
50458-0579-07	2022-Q2				EA	
50458-0579-07	2022-Q3				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0579-07	2022-Q4				EA	
50458-0579-99	2018-Q1				EA	
50458-0579-99	2018-Q2				EA	
50458-0579-99	2018-Q3				EA	
50458-0579-99	2018-Q4				EA	
50458-0579-99	2019-Q1				EA	
50458-0579-99	2019-Q2				EA	
50458-0579-99	2019-Q3				EA	
50458-0579-99	2019-Q4				EA	
50458-0579-99	2020-Q1				EA	
50458-0579-99	2020-Q2				EA	
50458-0579-99	2020-Q3				EA	
50458-0579-99	2020-Q4				EA	
50458-0579-99	2021-Q1				EA	
50458-0579-99	2021-Q2				EA	
50458-0579-99	2021-Q3				EA	
50458-0579-99	2021-Q4				EA	
50458-0579-99	2022-Q1				EA	
50458-0579-99	2022-Q2				EA	
50458-0579-99	2022-Q3				EA	
50458-0579-99	2022-Q4				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0584-52	2018-Q1				EA	
50458-0584-52	2018-Q2				EA	
50458-0584-52	2018-Q3				EA	
50458-0584-52	2018-Q4				EA	
50458-0584-52	2019-Q1				EA	
50458-0584-52	2019-Q2				EA	
50458-0584-52	2019-Q3				EA	
50458-0584-52	2019-Q4				EA	
50458-0584-52	2020-Q1				EA	
50458-0584-52	2020-Q2				EA	
50458-0584-52	2020-Q3				EA	
50458-0584-52	2020-Q4				EA	
50458-0584-52	2021-Q1				EA	
50458-0584-52	2021-Q2				EA	
50458-0584-52	2021-Q3				EA	
50458-0584-52	2021-Q4				EA	
50458-0584-52	2022-Q1				EA	
50458-0584-52	2022-Q2				EA	
50458-0584-52	2022-Q3				EA	
50458-0584-52	2022-Q4				EA	
55154-1422-00	2018-Q1				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
55154-1422-00	2018-Q2				EA	
55154-1422-00	2018-Q3				EA	
55154-1422-00	2018-Q4				EA	
55154-1422-00	2019-Q1				EA	
55154-1422-00	2019-Q2				EA	
55154-1422-00	2019-Q3				EA	
55154-1422-00	2019-Q4				EA	
55154-1422-00	2020-Q1				EA	
55154-1422-00	2020-Q2				EA	
55154-1422-00	2020-Q3				EA	
55154-1422-00	2020-Q4				EA	
55154-1422-00	2021-Q1				EA	
55154-1422-00	2021-Q2				EA	
55154-1422-00	2021-Q3				EA	
55154-1422-00	2021-Q4				EA	
55154-1422-00	2022-Q1				EA	
55154-1422-00	2022-Q2				EA	
55154-1422-00	2022-Q3				EA	
55154-1422-00	2022-Q4				EA	
55154-1424-00	2018-Q1				EA	
55154-1424-00	2018-Q2				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
55154-1424-00	2018-Q3				EA	
55154-1424-00	2018-Q4				EA	
55154-1424-00	2019-Q1				EA	
55154-1424-00	2019-Q2				EA	
55154-1424-00	2019-Q3				EA	
55154-1424-00	2019-Q4				EA	
55154-1424-00	2020-Q1				EA	
55154-1424-00	2020-Q2				EA	
55154-1424-00	2020-Q3				EA	
55154-1424-00	2020-Q4				EA	
55154-1424-00	2021-Q1				EA	
55154-1424-00	2021-Q2				EA	
55154-1424-00	2021-Q3				EA	
55154-1424-00	2021-Q4				EA	
55154-1424-00	2022-Q1				EA	
55154-1424-00	2022-Q2				EA	
55154-1424-00	2022-Q3				EA	
55154-1424-00	2022-Q4				EA	
55154-1424-08	2018-Q1				EA	
55154-1424-08	2018-Q2				EA	
55154-1424-08	2018-Q3				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
55154-1424-08	2018-Q4				EA	
55154-1424-08	2019-Q1				EA	
55154-1424-08	2019-Q2				EA	
55154-1424-08	2019-Q3				EA	
55154-1424-08	2019-Q4				EA	
55154-1424-08	2020-Q1				EA	
55154-1424-08	2020-Q2				EA	
55154-1424-08	2020-Q3				EA	
55154-1424-08	2020-Q4				EA	
55154-1424-08	2021-Q1				EA	
55154-1424-08	2021-Q2				EA	
55154-1424-08	2021-Q3				EA	
55154-1424-08	2021-Q4				EA	
55154-1424-08	2022-Q1				EA	
55154-1424-08	2022-Q2				EA	
55154-1424-08	2022-Q3				EA	
55154-1424-08	2022-Q4				EA	
55154-1423-08	2018-Q1				EA	
55154-1423-08	2018-Q2				EA	
55154-1423-08	2018-Q3				EA	
55154-1423-08	2018-Q4				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
55154-1423-08	2019-Q1				EA	
55154-1423-08	2019-Q2				EA	
55154-1423-08	2019-Q3				EA	
55154-1423-08	2019-Q4				EA	
55154-1423-08	2020-Q1				EA	
55154-1423-08	2020-Q2				EA	
55154-1423-08	2020-Q3				EA	
55154-1423-08	2020-Q4				EA	
55154-1423-08	2021-Q1				EA	
55154-1423-08	2021-Q2				EA	
55154-1423-08	2021-Q3				EA	
55154-1423-08	2021-Q4				EA	
55154-1423-08	2022-Q1				EA	
55154-1423-08	2022-Q2				EA	
55154-1423-08	2022-Q3				EA	
55154-1423-08	2022-Q4				EA	
50458-0577-01	2018-Q1				EA	
50458-0577-01	2018-Q2				EA	
50458-0577-01	2018-Q3				EA	
50458-0577-01	2018-Q4				EA	
50458-0577-01	2019-Q1				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0577-01	2019-Q2				EA	
50458-0577-01	2019-Q3				EA	
50458-0577-01	2019-Q4				EA	
50458-0577-01	2020-Q1				EA	
50458-0577-01	2020-Q2				EA	
50458-0577-01	2020-Q3				EA	
50458-0577-01	2020-Q4				EA	
50458-0577-01	2021-Q1				EA	
50458-0577-01	2021-Q2				EA	
50458-0577-01	2021-Q3				EA	
50458-0577-01	2021-Q4				EA	
50458-0577-01	2022-Q1				EA	
50458-0577-01	2022-Q2				EA	
50458-0577-01	2022-Q3				EA	
50458-0577-01	2022-Q4				EA	
50458-0578-01	2018-Q1				EA	
50458-0578-01	2018-Q2				EA	
50458-0578-01	2018-Q3				EA	
50458-0578-01	2018-Q4				EA	
50458-0578-01	2019-Q1				EA	
50458-0578-01	2019-Q2				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0578-01	2019-Q3				EA	
50458-0578-01	2019-Q4				EA	
50458-0578-01	2020-Q1				EA	
50458-0578-01	2020-Q2				EA	
50458-0578-01	2020-Q3				EA	
50458-0578-01	2020-Q4				EA	
50458-0578-01	2021-Q1				EA	
50458-0578-01	2021-Q2				EA	
50458-0578-01	2021-Q3				EA	
50458-0578-01	2021-Q4				EA	
50458-0578-01	2022-Q1				EA	
50458-0578-01	2022-Q2				EA	
50458-0578-01	2022-Q3				EA	
50458-0578-01	2022-Q4				EA	
50458-0579-01	2018-Q1				EA	
50458-0579-01	2018-Q2				EA	
50458-0579-01	2018-Q3				EA	
50458-0579-01	2018-Q4				EA	
50458-0579-01	2019-Q1				EA	
50458-0579-01	2019-Q2				EA	
50458-0579-01	2019-Q3				EA	



**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0579-01	2019-Q4				EA	
50458-0579-01	2020-Q1				EA	
50458-0579-01	2020-Q2				EA	
50458-0579-01	2020-Q3				EA	
50458-0579-01	2020-Q4				EA	
50458-0579-01	2021-Q1				EA	
50458-0579-01	2021-Q2				EA	
50458-0579-01	2021-Q3				EA	
50458-0579-01	2021-Q4				EA	
50458-0579-01	2022-Q1				EA	
50458-0579-01	2022-Q2				EA	
50458-0579-01	2022-Q3				EA	
50458-0579-01	2022-Q4				EA	
50458-0580-01	2018-Q1				EA	
50458-0580-01	2018-Q2				EA	
50458-0580-01	2018-Q3				EA	
50458-0580-01	2018-Q4				EA	
50458-0580-01	2019-Q1				EA	
50458-0580-01	2019-Q2				EA	
50458-0580-01	2019-Q3				EA	
50458-0580-01	2019-Q4				EA	

**G. Market Data and Revenue and Sales Volume Data**

**U.S. Commercial Average Net Unit Price**

**Description:** The purpose of this section is to collect the market data, revenue and sales volume data described in section 1194(e)(1)(E) of the Act. The following table provides the U.S. commercial average net unit price, including group and individual commercial plans on- and off- exchange of the selected drug.

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
50458-0580-01	2020-Q1				EA	
50458-0580-01	2020-Q2				EA	
50458-0580-01	2020-Q3				EA	
50458-0580-01	2020-Q4				EA	
50458-0580-01	2021-Q1				EA	
50458-0580-01	2021-Q2				EA	
50458-0580-01	2021-Q3				EA	
50458-0580-01	2021-Q4				EA	
50458-0580-01	2022-Q1				EA	
50458-0580-01	2022-Q2				EA	
50458-0580-01	2022-Q3				EA	
50458-0580-01	2022-Q4				EA	

**Explanations:** Confidential & Proprietary, Subject to Protections Under IRA §1193(c) and FOIA

Thirty-six NDC-11s for “XARELTO” are included in the “Selected Drug List for Initial Price Applicability Year (IPAY) 2026”.

Consistent with CMS guidance, this submission reflects information on NDC-11s of the selected drug marketed by the Primary Manufacturer (Janssen Pharmaceuticals, Inc. or “JPI”) and any Secondary Manufacturer.

CMS has prepopulated Section A to include NDC-11s for XARELTO that include NDC-11s for XARELTO distributed by entities that do not meet the definition of “Secondary Manufacturer” because they are not listed in the XARELTO NDA and do not market XARELTO pursuant to an agreement with a Johnson & Johnson company. These NDC-11s are: One for Aphenia Pharma Solutions -Tennessee, LLC (71610-0690-42), four for A-S Medication Solutions (50090-3625-00, 50090-3639-00, 50090-4468-00, 50090-4469-00), and one for Avera McKennan Hospital (69189-0578-01).

The NDC under Avera (69189-0578-01) was discontinued, and, after reasonable investigations, the following NDCs under A-S Medication Solutions do not appear to have ever been in use (i.e., 50090-3625-00, 50090-3639-00, 50090-4468-00, and 50090-4469-00).

Seven NDC-11s are sample NDCs under JPI labeler 50458: 50458-0577-14, 50458-0578-07, 50458-0578-14, 50458-0579-07, 50458-0579-99, 50458-0580-07, 50458-0584-52; Rows were added to – “enter “0” in the total unit volume field and left blank for other calculated fields.

Four NDC-11s are inner NDCs under JPI labeler 50458: 50458-0577-01, 50458-0578-01, 50458-0579-01, 50458-0580-01: Rows were added to – “enter “0” in the total unit volume field and left blank for other calculated fields.

Four NDC- 11s [55154-1422-00, 55154-1423-08, 55154-1424-08, and 55154-1424-00 discontinued] for Xarelto are repackaged by Cardinal Health LLC 107 (“Cardinal”) [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Based on US data only.



Manufacturer E2 Submissions – Johnson & Johnson Health Care Systems



Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Respondent Name	Laura D'Meza
	Organization Name (if applicable)	Johnson & Johnson Health Care Systems
	Respondent Email	ldmeza@its.jnj.com
	Who is completing this form?	
Question 27: Prescribing Information	Prescribing Information	<p>Section I (Question 27 through 30 and 32) is confidential &amp; proprietary, use subject to IRA 1193(c); FOIA exemptions apply</p> <p>NOTE: Please review the executive summary prior to this section.</p> <p>XARELTO® (rivaroxaban), a Factor Xa inhibitor direct oral anticoagulant (DOAC), is a clinical advancement in the treatment and prevention of thrombotic events compared to warfarin. [1] Over one-third of Medicare beneficiaries are impacted by conditions that put them at risk for formation of blood clots that can lead to thrombotic events such as heart attack, stroke, and pulmonary embolism. [2] In 2019, ~327,000 deaths of Americans 65+ were attributed to atrial fibrillation (including nonvalvular atrial fibrillation [NVAf]), venous thromboembolism (VTE), coronary artery disease (CAD), or peripheral artery disease (PAD). [3] Total Medicare spending for beneficiaries with these conditions was over \$350 billion in 2019. [2] XARELTO® has 11 FDA approved indications with proven efficacy in preventing, treating, and reducing the risk of costly thrombotic events in NVAf, VTE, CAD, and PAD. XARELTO® is available as an oral tablet and an oral suspension formulation that is unique amongst DOACs for pediatric patients.</p> <p>Therapeutic Alternative: Based on CMS guidance that therapeutic alternatives are first identified within the same drug class before considering other drug classes, XARELTO®'s therapeutic alternative is ELIQUIS® (apixaban) (Factor Xa inhibitors). [4] There are two other approved and marketed DOACs: dabigatran etexilate (direct thrombin inhibitor) and edoxaban (Factor Xa inhibitor). [REDACTED]</p> <p>[2]</p> <p>An important differentiator between XARELTO® and ELIQUIS® is the dosing regimen, with XARELTO® predominantly once-daily for most indications, while ELIQUIS® is twice-daily for all indications.</p>

Question	Sub-Question	Response
		<p>Major treatment guidelines endorse DOACs including XARELTO® for indications #1-#6 (see Table 3 in Question 28). [5-11]</p> <p>XARELTO® Indication #1: to reduce the risk of stroke and systemic embolism (a blood clot in the bloodstream that can cause a blockage) in NVAf</p> <p>* XARELTO® Use in Course of Care: The recommended dose of XARELTO® is 15 mg once daily with an evening meal in patients with creatinine clearance (CrCl) <math>\leq 50</math> mL/min or 20 mg once daily with the evening meal in patients with CrCl <math>&gt; 50</math> mL/min. Clearance of creatinine is a measure of how well the kidneys are functioning.</p> <p>* ELIQUIS® Use in Course of Care: The recommended dose of ELIQUIS® is 5 mg orally twice daily or 2.5 mg twice daily in patients with at least two of the following characteristics: age greater than or equal to 80 years, body weight less than or equal to 60 kg, or serum creatinine greater than or equal to 1.5 mg/dL.</p> <p>XARELTO® Indication #2: for the treatment of deep vein thrombosis (DVT)</p> <p>* XARELTO® Use in Course of Care: The recommended dose of XARELTO® in patients with CrCl <math>\geq 15</math> mL/min is 15 mg orally twice daily with food, then after 21 days, transition to XARELTO® 20 mg orally once daily with food at the same time each day. Avoid use in patients with CrCl <math>&lt; 15</math> mL/min.</p> <p>* ELIQUIS® Use in Course of Care: The recommended dose of ELIQUIS® is 10 mg taken orally twice daily for the first seven days of therapy. After seven days, the recommended dose is 5 mg taken orally twice daily.</p> <p>XARELTO® Indication #3: for the treatment of pulmonary embolism (PE)</p> <p>* XARELTO® Use in Course of Care: The recommended dose of XARELTO® in patients with CrCl <math>\geq 15</math> mL/min is 15 mg orally twice daily with food, then after 21 days, transition to XARELTO® 20 mg orally once daily with food at the same time each day. Avoid use in patients with CrCl <math>&lt; 15</math> mL/min.</p> <p>* ELIQUIS® Use in Course of Care: The recommended dose of ELIQUIS® is 10 mg taken orally twice daily for the first seven days of therapy. After seven days, the recommended dose is 5 mg taken orally twice daily.</p> <p>XARELTO® Indication #4: for the reduction in the risk of recurrence of DVT and/or PE in adult patients at continued risk for recurrent DVT and/or PE after completion of initial treatment lasting at least six months</p> <p>* XARELTO® Use in Course of Care: The recommended dose of XARELTO® in patients with CrCl <math>\geq 15</math> mL/min is 10 mg once daily, after at least six months of standard anticoagulant treatment, with or without food. Avoid use in patients with CrCl <math>&lt; 15</math> mL/min.</p> <p>* ELIQUIS® Use in Course of Care: ELIQUIS® is indicated to reduce the risk of recurrent DVT and PE following initial therapy. The recommended dose of ELIQUIS® is 2.5 mg taken orally twice daily after at least six months of treatment for DVT or PE.</p>



Question	Sub-Question	Response
		<p>XARELTO® Indication #5: for the prophylaxis of DVT, which may lead to PE in adult patients undergoing knee replacement surgery.</p> <p>* XARELTO® Use in Course of Care: The recommended dose of XARELTO® in patients with CrCl <math>\geq</math>15 mL/min is 10 mg once daily for 12 days, 6 to 10 hours after surgery once hemostasis has been established, with or without food. Avoid use in patients with CrCl &lt;15 mL/min.</p> <p>* ELIQUIS® Use in Course of Care: The recommended dose of ELIQUIS® is 2.5 mg taken orally twice daily. The initial dose should be taken 12 to 24 hours after surgery. The recommended duration of treatment is 12 days.</p> <p>XARELTO® Indication #6: for the prophylaxis of DVT, which may lead to PE in adult patients undergoing hip replacement surgery</p> <p>* XARELTO® Use in Course of Care: The recommended dose of XARELTO® in patients with CrCl <math>\geq</math>15 mL/min is 10 mg once daily for 35 days, 6 to 10 hours after surgery once hemostasis has been established. Avoid use in patients with CrCl &lt;15 mL/min.</p> <p>* ELIQUIS® Use in Course of Care: The recommended dose of ELIQUIS® is 2.5 mg taken orally twice daily. The initial dose should be taken 12 to 24 hours after surgery. The recommended duration of treatment is 35 days.</p> <p>Janssen has made additional investments in the cardiovascular therapeutic area which has resulted in FDA approval of 5 additional indications (#7-#11) for XARELTO®. XARELTO® is the only Factor Xa inhibitor that is FDA approved and marketed in these 5 indications, further augmenting the value XARELTO® provides to patients, including Medicare beneficiaries. While there are other treatments for these conditions, XARELTO® offers a therapeutic advancement to these treatments. Moreover, we do not believe these other treatments are appropriate therapeutic alternatives to XARELTO® for establishing a price as they are not within the same therapeutic class, chemical class, or mechanism of action.</p> <p>XARELTO® Indication #7: (in combination with aspirin) to reduce the risk of serious heart problems, heart attack and stroke in adults with coronary artery disease (a condition where the blood supply to the heart is reduced or blocked). XARELTO® is the only DOAC indicated for use in combination with aspirin for patients with CAD. Dual pathway inhibition, which includes the anticoagulant (XARELTO®) with the antiplatelet (aspirin), inhibits both thrombin and platelets and represents an important advance in the management of patients with chronic CAD. [12, 13] Clinical guidelines (AHA/ACC/ACCP/ASPC/NLA/PCNA guidelines) were recently updated to include a recommendation for XARELTO®. [14]</p> <p>* XARELTO® Use in Course of Care: The recommended dose of XARELTO® is 2.5 mg orally twice daily with or without food, in combination with aspirin (75-100 mg) once daily.</p> <p>* Other Treatments Used in Course of Care: Aspirin or clopidogrel dosed 75 mg once daily orally without a loading</p>



Question	Sub-Question	Response
		<p>dose.</p> <p>XARELTO® Indication #8: (in combination with aspirin) to reduce the risk of a sudden decrease in blood flow to the legs, major amputation, serious heart problems or stroke in adults with peripheral artery disease (a condition where the blood flow to the legs is reduced) and includes adults who have recently had a procedure to improve blood flow to the legs.</p> <p>XARELTO® is the only DOAC indicated for use in combination with aspirin for patients with PAD, including patients after recent lower extremity revascularization due to symptomatic PAD. This dual pathway inhibition, which includes the anticoagulant (XARELTO®) with the antiplatelet (aspirin), inhibits both thrombin and platelets and represents an important advance in the management of patients with PAD. [12, 13] National guidelines are currently evolving in PAD where therapeutic alternatives are limited.</p> <p>* XARELTO® Use in Course of Care: The recommended dose of XARELTO® is dosed 2.5 mg orally twice daily with or without food, in combination with aspirin (75-100 mg) once daily. When starting therapy after a successful lower extremity revascularization procedure, initiate once hemostasis has been established.</p> <p>* Other Treatments Used in Course of Care: Clopidogrel is dosed 75 mg once daily orally without a loading dose.</p> <p>XARELTO® Indication #9: for the prophylaxis of VTE and VTE-related death during hospitalization and post hospital discharge in adult patients admitted for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE, and not at high risk for bleeding</p> <p>* XARELTO® Use in Course of Care: The recommended dose of XARELTO® in patients with CrCl <math>\geq</math>15 mL/min is 10 mg once daily, with or without food, in the hospital and after hospital discharge for a total recommended duration of 31 to 39 days.</p> <p>* Other Treatments Used in Course of Care: Low molecular weight heparin, unfractionated heparin, or fondaparinux all of which are subcutaneous injections. [15]</p> <p>XARELTO® Indication #10: for the treatment of venous thromboembolism (VTE) and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years after at least five days of initial parenteral anticoagulant treatment</p> <p>* XARELTO® Use in Course of Care: Please refer to the XARELTO® Full Prescribing Information (PI), Medication Guide, and Instructions for Use for complete information regarding dosage and administration in pediatric patients.</p> <p>* Other Treatments Used in Course of Care: Low molecular weight heparin (subcutaneous injection), unfractionated heparin (intravenous infusion), or warfarin. [16, 17]</p> <p>XARELTO® Indication #11: for thromboprophylaxis (prevention of clots) in pediatric patients aged two years and older with congenital heart disease who have undergone the Fontan procedure</p>





Question	Sub-Question	Response
		<p>Some children are born with a heart condition that prevents normal amounts of oxygen from circulating through the body. The Fontan procedure reroutes the blood flow from the lower body to the lungs to help increase the levels of oxygen in the blood. Because the Fontan procedure is an open-heart surgery, the risk of blood clots increases after the procedure. Approximately 1,000 Fontan procedures are performed each year in the US. [18, 19]</p> <p>* XARELTO® Use in Course of Care: Please refer to the XARELTO® Full Prescribing Information, Medication Guide, and Instructions for Use for complete information regarding dosage and administration in pediatric patients.</p> <p>* Other Treatments Used in Course of Care: Low molecular weight heparin (subcutaneous injection), unfractionated heparin (intravenous infusion), warfarin, or aspirin. [17, 20]</p> <p>XARELTO® has 6 indications in common with ELIQUIS®. XARELTO® offers once daily dosing for the majority of the treatment duration, simplifying use for Medicare beneficiaries. In contrast, ELIQUIS® is dosed twice daily.</p> <p>XARELTO® has 5 additional FDA approved indications and provides an important treatment and prevention option for at-risk populations including: CAD, PAD, acutely ill medical patients, and pediatric patients. ELIQUIS® is not FDA approved in these populations.</p> <p>References</p> <ol style="list-style-type: none"> <li>1. Nasiri A, AlQahtani A, Rayes NH, AlQahtani R, Alkharras R, Alghethber H. Direct oral anticoagulant: Review article. Journal of Family Medicine and Primary Care. 2022;11(8):4180-3. doi: 10.4103/jfmpc.jfmpc_2253_21. PubMed PMID: 01697686-202208000-00013.</li> <li>2. Janssen Scientific Affairs, LLC. Data on File.</li> <li>3. National Vital Statistics System, Mortality 1999-2020 on CDC WONDER Online Database, released in 2021. Data are from the Multiple Cause of Death Files, 1999-2020, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program.: Centers for Disease Control and Prevention, National Center for Health Statistics; [cited 2023 September 11]. Available from: <a href="https://wonder.cdc.gov/ucd-icd10.html">https://wonder.cdc.gov/ucd-icd10.html</a>.</li> <li>4. Seshamani M. Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026. In: Services DoHH, editor. 2023.</li> <li>5. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration With the Society of Thoracic Surgeons. Circulation. 2019;140(2):e125-e51. doi: doi:10.1161/CIR.0000000000000665.</li> <li>6. Lip GYH, Banerjee A, Boriani G, Chiang Ce, Fargo R, Freedman B, et al. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. Chest. 2018;154(5):1121-201. doi:</li> </ol>



Question	Sub-Question	Response
		<p><a href="https://doi.org/10.1016/j.chest.2018.07.040">https://doi.org/10.1016/j.chest.2018.07.040</a>.</p> <p>7. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021;42(5):373-498. doi: 10.1093/eurheartj/ehaa612.</p> <p>8. Ortel TL, Neumann I, Ageno W, Beyth R, Clark NP, Cuker A, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Advances. 2020;4(19):4693-738. doi: 10.1182/bloodadvances.2020001830.</p> <p>9. Stevens SM, Woller SC, Kreuziger LB, Bounameaux H, Doerschug K, Geersing G-J, et al. Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. Chest. 2021;160(6):e545-e608. doi: <a href="https://doi.org/10.1016/j.chest.2021.07.055">https://doi.org/10.1016/j.chest.2021.07.055</a>.</p> <p>10. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41(4):543-603. doi: 10.1093/eurheartj/ehz405. PubMed PMID: 31504429.</p> <p>11. Mazzolai L, Ageno W, Alatri A, Bauersachs R, Becattini C, Brodmann M, et al. Second consensus document on diagnosis and management of acute deep vein thrombosis: updated document elaborated by the ESC Working Group on aorta and peripheral vascular diseases and the ESC Working Group on pulmonary circulation and right ventricular function. Eur J Prev Cardiol. 2022;29(8):1248-63. doi: 10.1093/eurjpc/zwab088. PubMed PMID: 34254133.</p> <p>12. Ramacciotti E, Weitz JI. Rivaroxaban plus aspirin for cardiovascular protection: Rationale for the vascular dose and dual pathway inhibition. Thrombosis Research. 2019;184:44-9. doi: <a href="https://doi.org/10.1016/j.thromres.2019.09.033">https://doi.org/10.1016/j.thromres.2019.09.033</a>.</p> <p>13. Rivera-Caravaca JM, Camelo-Castillo A, Ramírez-Macías I, Gil-Pérez P, López-García C, Esteve-Pastor MA, et al. Antithrombotic Therapy in Patients with Peripheral Artery Disease: A Focused Review on Oral Anticoagulation. Int J Mol Sci. 2021;22(13). Epub 20210701. doi: 10.3390/ijms22137113. PubMed PMID: 34281167; PubMed Central PMCID: PMC8267774.</p> <p>14. Virani SS, Newby LK, Arnold SV, Bittner V, Brewer LC, Demeter SH, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. Circulation. 2023;148(9):e9-e119. doi: doi:10.1161/CIR.0000000000001168.</p> <p>15. Schünemann HJ, Cushman M, Burnett AE, Kahn SR, Beyer-Westendorf J, Spencer FA, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. Blood Adv. 2018;2(22):3198-225. doi: 10.1182/bloodadvances.2018022954. PubMed PMID: 30482763; PubMed Central PMCID: PMC6258910.</p>



Question	Sub-Question	Response
		<p>16. Monagle P, Cuello CA, Augustine C, Bonduel M, Brandão LR, Capman T, et al. American Society of Hematology 2018 Guidelines for management of venous thromboembolism: treatment of pediatric venous thromboembolism. Blood Adv. 2018;2(22):3292-316. doi: 10.1182/bloodadvances.2018024786. PubMed PMID: 30482766; PubMed Central PMCID: PMC6258911.</p> <p>17. Monagle P, Chan AKC, Goldenberg NA, Ichord RN, Journeycake JM, Nowak-Göttl U, Vesely SK. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e737S-e801S. doi: 10.1378/chest.11-2308. PubMed PMID: 22315277; PubMed Central PMCID: PMC3278066.</p> <p>18. Fontan Procedure: Cleveland Clinic; 2022 [cited 2023 July 27]. Available from: <a href="https://my.clevelandclinic.org/health/treatments/24545-fontan-procedure#:~:text=Each%20year%2C%20healthcare%20providers%20in,have%20had%20a%20Fontan%20procedure.">https://my.clevelandclinic.org/health/treatments/24545-fontan-procedure#:~:text=Each%20year%2C%20healthcare%20providers%20in,have%20had%20a%20Fontan%20procedure.</a></p> <p>19. Akintoye E, Miranda WR, Veldtman GR, Connolly HM, Egbe AC. National trends in Fontan operation and in-hospital outcomes in the USA. Heart. 2019;105(9):708-14. doi: 10.1136/heartjnl-2018-313680.</p> <p>20. Giglia TM, Massicotte MP, Tweddell JS, Barst RJ, Bauman M, Erickson CC, et al. Prevention and treatment of thrombosis in pediatric and congenital heart disease: a scientific statement from the American Heart Association. Circulation. 2013;128(24):2622-703. Epub 20131113. doi: 10.1161/01.cir.0000436140.77832.7a. PubMed PMID: 24226806.</p>
	Evidence Submitted include a cost-effectiveness measure?	N
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	<p>Section I (Question 27 through 30 and 32) is confidential &amp; proprietary, use subject to IRA 1193(c); FOIA exemptions apply</p> <p>NOTE: Please review the executive summary prior to this section.</p> <p>XARELTO® (rivaroxaban) is a Factor Xa inhibitor direct oral anticoagulant (DOAC), with the broadest set of FDA approved indications to prevent, treat, and reduce the risk of thrombotic events (see Table 1).</p> <p>As described in Question 27, ELIQUIS® is the therapeutic alternative for XARELTO® (see Table 2). [REDACTED] [1] DOACs are a substantial therapeutic advance over older agents like warfarin and injectable low molecular weight heparin (LMWH). [2-4] [REDACTED]</p>



Question	Sub-Question	Response
		<p>[1]</p> <p>Major treatment guidelines consistently recommend DOACs, including XARELTO®, over warfarin for the management of patients with nonvalvular atrial fibrillation (NVAF) and for venous thromboembolism (VTE) treatment (see Table 3). [5-14]</p> <p>DOACs, including XARELTO®, have clear therapeutic and patient-oriented advantages over warfarin with fewer food/drug interactions and standardized dosing to eliminate the requirement for frequent (daily to approximately monthly) blood tests to determine and maintain a safe and effective dose (adds costs [~\$1,900 annually] and inconvenience to beneficiaries). [1, 2] LMWHs require subcutaneous injections which may cause bruising and has been reported to result in higher rates of non-administration based on patient/family member refusal which may hinder everyday adherence to therapy. [3, 4]</p> <p>The most common use of DOACs within Medicare beneficiaries is to treat, prevent, and reduce the risk of thrombotic events among NVAF and VTE patients.</p> <p>XARELTO® provides clinical and economic benefits among NVAF and VTE populations. In a systematic literature review of 29 real-world studies focused on elderly NVAF and VTE patients (&gt;=65 years of age) comparing XARELTO® and warfarin, data showed:</p> <ul style="list-style-type: none"> <li>* More than two-thirds of real-world studies found statistically significant reductions in stroke and systemic embolism (a blood clot in the bloodstream that can cause a blockage), ischemic stroke, and intracranial hemorrhage risk with XARELTO®.</li> <li>* Significant reduction in stroke and systemic embolism costs with XARELTO® in the studies that reported data on cost.</li> <li>* Approximately 58% of studies showed similar major bleeding risk to warfarin (see Figure 1).[15]</li> </ul> <p>The therapeutic alternative to XARELTO® is ELIQUIS®, each delivering similar value for Medicare beneficiaries in the 6 common indications.</p> <p>A real world, observational study of &gt;77,000 NVAF patients taking XARELTO® or ELIQUIS® illuminated that these products are used in different patient populations. XARELTO® patients have:</p> <ul style="list-style-type: none"> <li>* Fewer comorbidities: Lower Quan-Charlson comorbidity index (mean 2.50 vs 3.02), XARELTO® vs ELIQUIS®: higher number indicates greater mortality risk and more severe comorbid conditions</li> <li>* Lower risk of stroke: CHA2DS2-VASc score (mean 2.43 vs 2.75) XARELTO® vs. ELIQUIS®: higher number indicates higher risk of stroke. CHA2DS2-VASc is a risk stratification measure used by physicians that includes sex, age,</li> </ul>





Question	Sub-Question	Response
		<p>congestive heart failure, hypertension, stroke/TIA, vascular disease, and diabetes.</p> <p>* Lower risk of bleeding: Lower HAS-BLED score (mean 1.48 vs 1.59) XARELTO® vs. ELIQUIS®: higher score indicates higher bleeding risk. HAS-BLED is a risk stratification measure based on hypertension, renal disease, liver disease, stroke history, prior major bleeding or predisposition to bleeding, unstable international normalized ratio (INR), age &gt;65 years, medication usage predisposing to bleeding, and alcohol use. [16]</p> <p>XARELTO®'s unique benefits in comparison to ELIQUIS® include better adherence and additional value in underserved patient populations with CAD and PAD where there is no other FDA approved and marketed DOAC</p> <p>NVAF patients are often complex with multiple comorbidities typically associated with polypharmacy that may increase overall pill burden and dosing errors. [17-20] XARELTO® is taken once daily for NVAF and VTE (after an initial three week twice-daily dosing) treatment, while ELIQUIS® is taken twice daily for both indications. Physicians and patients often make medication decisions based on their dosing frequency. Several real-world studies have shown that adherence to treatment with once-daily DOACs (XARELTO® and edoxaban) is higher than with twice-daily DOACs (dabigatran and ELIQUIS®). [21, 22] Multiple real-world studies have reported that adherence to XARELTO® in patients with NVAF or VTE is higher than with ELIQUIS®. [23-27]</p> <p>No randomized clinical trials have been conducted that directly compare XARELTO® and ELIQUIS® in NVAF or VTE populations. Comparative data is limited to observational, retrospective studies assessing effectiveness and safety.</p> <p>The most common adverse event for all blood thinners including DOACs is bleeding. The contraindications listed on the FDA approved labels for XARELTO® and ELIQUIS® are identical.</p> <div data-bbox="632 1109 1997 1255" style="background-color: black; height: 90px; width: 100%;"></div> <p>While real world evidence can shed light on utilization patterns and outcomes, there are several important limitations to these anticoagulant observational studies that need to be considered:</p> <p>* Underdosing or overdosing may impact effectiveness and safety outcomes due to the narrow therapeutic window for these drugs. [28]</p> <p>* In these observational studies, &gt;75% have short duration of follow-up of less than one year, which limits the ability to compare the benefit-risk profiles of XARELTO® and ELIQUIS® (see Table 4). For anticoagulants, bleeding adverse events (risk) typically manifest earlier while thrombotic events occur over a longer period of time during a patient's</p>



Question	Sub-Question	Response
		<p>treatment: therefore, these short-duration studies may overestimate the risk and underestimate the benefit.</p> <p>* Observational studies can capture the exposure of drugs to large numbers of patients in diverse settings. Still, they leverage a relatively small proportion of real-world patients, that may not represent the general population treated with XARELTO® and ELIQUIS®. For example, among five large, retrospective, observational analyses comparing XARELTO® and ELIQUIS® in Medicare-age NVAf populations, only 9% to 31% of the total possible patient populations remained in the final analyses based on matching criteria [29-33].</p> <p>In an observational study conducted ex-US over 6 years, investigators found that XARELTO® was associated with lower all-cause mortality (Figure 2) and ischemic stroke rates compared to ELIQUIS® while gastrointestinal bleed rates were higher for XARELTO®. [34]</p> <p>FDA Sentinel assessments of DOACs in 2020 and 2022 resulted in no updates to the risk of bleeding in the warnings and precautions, or adverse reactions sections of either XARELTO®'s or ELIQUIS®'s prescribing information.</p> <p>The FDA Sentinel analyzed the standard dose of DOACs among NVAf patients ≥65 years of age. No significant differences were observed between XARELTO® and ELIQUIS® for incidence of thromboembolic stroke and intracranial hemorrhage, while there was a statistically significant increase with XARELTO® for major extracranial bleeding and gastrointestinal bleeding of 2.5 per 100PY and 2.3 per 100PY relative to ELIQUIS®, respectively (see Table 5). [35, 36]</p> <p>Due to continued investment from Janssen, XARELTO® has 5 unique indications that impact both Medicare beneficiaries and underserved populations where no other Factor Xa inhibitor alternative is FDA approved and marketed, further augmenting the value XARELTO® provides to Medicare beneficiaries.</p> <p>XARELTO®'s 5 unique indications are in the following conditions:</p> <p>Coronary Artery Disease (CAD) and Peripheral Artery Disease (PAD)</p> <p>XARELTO®'s treatment for CAD and PAD is in combination with aspirin (antiplatelet). This dual pathway inhibition is unique and inhibits both thrombin and platelets, which represents an important advance in the management of patients with chronic CAD or PAD. [37, 38]</p> <p>1. Coronary Artery Disease (CAD)</p> <p>In the COMPASS trial comparing XARELTO® + aspirin therapy vs. aspirin alone, XARELTO® + aspirin significantly reduced the primary major adverse cardiovascular events (MACE) composite (cardiovascular death, stroke, and heart</p>

Question	Sub-Question	Response
		<p>attack) compared with aspirin alone [39] and had a higher Net Clinical Benefit defined as fewer adverse events of the composite of MACE, fatal bleeding or symptomatic bleeding into a critical organ (see Table 6). [40]</p> <p>The following clinical guidelines recommend XARELTO® + aspirin:</p> <ul style="list-style-type: none"> <li>* The American Diabetes Association (ADA) guidelines for cardiovascular disease and risk management recommend that combination therapy with aspirin plus low dose XARELTO® be considered for patients with stable CAD and/or peripheral artery disease (PAD) and low bleeding risk to prevent MACE and major adverse limb events (MALE). [41]</li> <li>* The European Society of Cardiology-European Association for the Study of Diabetes (ESC-EASD) guidelines on diabetes, pre-diabetes, and cardiovascular disease recommends that low-dose XARELTO® + aspirin may be beneficial for management of CAD in high risk patients. [42]</li> <li>* The recently published AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients with Chronic Coronary Disease (CCD), which includes CAD, recommend the addition of XARELTO® to aspirin for long-term reduction of risk for MACE in patients with CCD without an indication for therapeutic DOAC or dual antiplatelet therapy and who are at high risk of recurrent ischemic events but low-to-moderate bleeding risk. In patients with CCD and no indication for oral anticoagulant therapy, low-dose aspirin is recommended to reduce MACE. [43]</li> </ul> <p>2. Peripheral Artery Disease (PAD)</p> <ul style="list-style-type: none"> <li>* In the VOYAGER trial comparing XARELTO® + aspirin therapy vs. aspirin monotherapy (see Table 7): <ul style="list-style-type: none"> <li>- Almost 85% of adults who took XARELTO® + aspirin did not have a heart attack, stroke, sudden decrease in blood flow in the legs, or amputation after revascularization procedure.</li> <li>- The rate of the first event like a stroke, heart attack, poor blood flow in the legs, and amputation was 15.5% for people taking XARELTO® + aspirin vs 17.8% for aspirin alone— a statistically significant result.</li> <li>- The occurrence of major bleeding at three years, defined according to the Thrombolysis in myocardial infarction (TIMI) classification, occurred in more patients treated with XARELTO® + aspirin vs. aspirin alone, but the difference was not statistically significant. There were no differences between groups for the occurrence of fatal bleeding and the composite of intracranial hemorrhage and fatal bleeding. [44]</li> </ul> </li> <li>* The COMPASS trial PAD subgroup analysis of rates of major thrombotic vascular events (heart attack, stroke, cardiovascular death, acute limb ischemia, or major amputation of vascular etiology) were 3.4% per year in XARELTO® + aspirin vs. 4.8% per year in aspirin monotherapy treated patients (refer to XARELTO® prescribing information for more detail). The net clinical benefit, defined as fewer adverse events of the composite of MACE, fatal bleeding or symptomatic bleeding into a critical organ was higher with XARELTO® + aspirin vs. aspirin alone (see Table 6). [45] The following clinical guidelines recommend XARELTO® + aspirin for PAD: <ul style="list-style-type: none"> <li>- The ADA guidelines for cardiovascular disease and risk management recommend that combination therapy with XARELTO® + aspirin be considered for patients with stable CAD and/or PAD and low bleeding risk to prevent MACE and MALE. [41]</li> <li>- The ESC-EASD guidelines on diabetes, pre-diabetes, and cardiovascular disease recommend that XARELTO® +</li> </ul> </li> </ul>



Question	Sub-Question	Response
		<p>aspirin be considered in patients with diabetes and symptomatic lower-extremity artery disease/PAD without high bleeding risk. [42]</p> <p>- The AHA/ACC guidelines for PAD are undergoing updates and are anticipated to be published in early 2024.</p> <p>3. Acutely Ill Medical Patients</p> <p>* In the MAGELLAN trial comparing XARELTO® with enoxaparin/placebo, XARELTO® demonstrated similar rates of VTE at day 10 – per protocol population and lower rates at day 35 – modified intent-to-treat population (see Table 8). [46, 47]</p> <p>* Approximately 99% of patients taking XARELTO® did not experience a major bleeding event; ~97% of patients taking XARELTO® did not experience a clinically relevant nonmajor bleeding event, however these events were higher with XARELTO® than enoxaparin/placebo. [46]</p> <p>* Current guidelines for acute medically ill patients do not include XARELTO®.</p> <p>4. Pediatric DVT/PE</p> <p>* The EINSTEIN-Jr trial was the largest pediatric DOAC trial conducted for the treatment of VTE. Recurrent VTE rates were 1.2% for XARELTO® vs. 3% for standard anticoagulation, however the trial was not powered to find a difference between the two treatment groups (see Table 3 in Question 29). [48]</p> <p>* Similar rates of major and clinically relevant nonmajor bleeding were observed with XARELTO® vs. standard anticoagulation (3% XARELTO® vs. 1.8% standard anticoagulation). [48]</p> <p>* XARELTO® is the only DOAC with an approved liquid formulation in this population.</p> <p>* Current guidelines for pediatric patients with DVT/PE do not include XARELTO®.</p> <p>5. Pediatric Post-Fontan Procedure</p> <p>* In the UNIVERSE trial comparing XARELTO® with aspirin, XARELTO® was evaluated for the prevention of thrombotic events in pediatric patients post-Fontan procedure, which is a procedure used to treat children with single ventricle heart defect. Comparable rates of thrombotic events (1.6% XARELTO® vs. 8.8% aspirin), major bleeding events (1.6% XARELTO® vs. 0% aspirin), and clinically nonmajor bleeding events (6.3% XARELTO® vs. 8.8% aspirin) were observed. The UNIVERSE clinical trial was not powered for statistical significance (see to Table 4 in Question 29). [49]</p> <p>* XARELTO® is the only DOAC with an approved liquid formulation in this population.</p> <p>* Current guidelines for pediatric patients post-Fontan procedure do not include XARELTO®.</p> <p>* See Question 27 for a description of Fontan procedure.</p> <p>DOACs, including XARELTO®, represent a therapeutic advancement over warfarin. The therapeutic alternative to XARELTO® is ELIQUIS®.</p>





Question	Sub-Question	Response
		Relative to ELIQUIS®, the 5 unique indications provide additional value to Medicare beneficiaries and underserved populations and should be considered in XARELTO®'s value assessment.
	Hyperlink to Citation - Additional Materials for Question 28	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	
	Evidence Submitted include a cost-effectiveness measure?	N
	What type of Evidence is shown?	
Question 29: Comparative Effectiveness on Specific Populations	Response to Question 29	<p>Section I (Question 27 through 30 and 32) is confidential &amp; proprietary, use subject to IRA 1193(c); FOIA exemptions apply</p> <p>NOTE: Please review the executive summary prior to this section.</p> <p>XARELTO® is the first-in-class Factor Xa inhibitor with the broadest set of FDA approved indications (11 indications). The breadth of indications brings clear value to many patients over 65, with data showing consistent value in specific populations, including in Black patients with nonvalvular atrial fibrillation (NVAf) and venous thromboembolism (VTE), pediatric patients, and beneficiaries with coronary artery disease (CAD) and peripheral artery disease (PAD) who have multiple comorbidities. [1-15] These underserved populations face disproportionate clinical burdens; providing health care professionals with data in these specific populations to support treatment decisions is critical to advance health equity. [16-20]</p>



Question	Sub-Question	Response
		<p>There is limited real world data and no head-to-head clinical trials in these specific populations comparing XARELTO® to ELIQUIS® (therapeutic alternative).</p> <p>Black Medicare beneficiaries with NVAF are at higher risk of stroke: The risks of death and stroke in atrial fibrillation patients 65 years of age or older is higher in Black patients compared to White patients. [16] Medicare fee-for-service (FFS) beneficiaries aged 65+ years had a higher prevalence rate of stroke (3.9%) compared to those beneficiaries under 65 years (2.7%). Black patients had the highest prevalence rate (6%) of stroke compared to the other racial/ethnic groups (3-4%). [21] No head-to-head randomized clinical trials directly compare the safety and efficacy of XARELTO® and ELIQUIS® for any indications or specific populations.</p> <p>* A sub-group analysis of XARELTO®’s registrational trial, ROCKET AF, suggested XARELTO®’s efficacy and safety compared to warfarin was consistent among Black patients for the outcomes of stroke or systemic embolism (a blood clot in the bloodstream that can cause a blockage) and major or clinically relevant nonmajor bleeding. [6]</p> <p>* An electronic health record (EHR) based, real-world observational analysis among Black patients with NVAF found that XARELTO® use was associated with a 23% lower risk of stroke or systemic embolism and a 16% reduction in major bleeding risk compared to warfarin (see Table 1). [7]</p> <p>Black beneficiaries with VTE are at higher risk of deep vein thrombosis (DVT) and pulmonary embolism (PE): Black patients have 30% to 60% higher rates of VTE than White patients. [17] Black patients hospitalized with PE are younger with more severe disease compared to White patients. [22] Hospitalization rates for DVT among Black patients have increased from 316 per 100,000 person-years in 1999 to 382 per 100,000 person-years in 2010, a relative increase of 20.8%, while hospitalizations among White patients and other races have declined by 42.2% and 28.1% respectively. [23]</p> <p>* Analyses of XARELTO®’s registrational trials, EINSTEIN DVT and EINSTEIN PE, suggested XARELTO®’s efficacy and safety compared to warfarin was consistent among Black patients for the outcomes of recurrent VTE and major or clinically relevant nonmajor bleeding. [3, 4]</p> <p>* An EHR-based, real-world observational analysis found that in Black patients experiencing an acute VTE, no significant differences in the incidence of the composite endpoint of recurrent VTE or major bleeding, recurrent VTE, or major bleeding were observed between patients receiving XARELTO® or warfarin at six months (see Table 2). [5]</p> <p>Pediatric patients who have VTE or are post-Fontan procedure require anticoagulation: XARELTO® offers an oral suspension formulation for pediatric patients with these conditions to help with dosing and administration. XARELTO® is the only DOAC that is FDA approved to treat VTE and reduce the risk of VTE recurrence in children from birth to 18 years of age, and for anticoagulation post-Fontan procedure. XARELTO®, unlike alternative options, does not require routine monitoring or frequent needle sticks.</p>

Question	Sub-Question	Response
		<p>* In the EINSTEIN Jr clinical trial for pediatric patients with VTE, XARELTO® was associated with recurrent VTE rate of 1.2% vs. 3% for heparin / warfarin (trial was not powered for statistical significance) (see Table 3). [2] XARELTO® and dabigatran etexilate are the only approved DOACs for this indication (see Table 1 in Question 28).</p> <p>* In the UNIVERSE clinical trial for pediatric patients post-Fontan procedure, XARELTO® was associated with a 1.6% thrombotic event rate vs. 8.8% for aspirin (trial was not powered for statistical significance) (see Table 4). [1] XARELTO® is the only FDA approved or studied drug in this indication (see Table 1 in Question 28).</p> <p>Patients with CAD/PAD have multiple comorbidities including diabetes, obesity, and chronic kidney disease (CKD): XARELTO® is the only approved DOAC for the treatment of CAD and PAD. Approximately 25% of Medicare beneficiaries have CAD and/or PAD, and these conditions are strong predictors of future cardiovascular event risk. [24, 25] One in seven Medicare beneficiaries with chronic CAD and/or PAD experienced major adverse cardiovascular events (MACE) or major adverse limb events (MALE) within two years. [26]</p> <p>COMPASS trial in CAD/PAD: The combination of XARELTO® + aspirin reduced the primary major adverse MACE composite (cardiovascular death, stroke, and heart attack) by 24% compared with aspirin alone. Discontinuing XARELTO® + aspirin and switching to non-study aspirin was associated with a loss of MACE benefit and excess of stroke, particularly during the six months post switching, highlighting the need to maintain CAD/PAD patients on XARELTO® + aspirin combination. [8, 14] For the net clinical benefit (NCB) outcome including the composite of cardiovascular death, stroke, heart attack, fatal bleeding, or symptomatic bleeding into a critical organ, fewer NCB events occurred in the XARELTO® + aspirin group relative to aspirin monotherapy group [27, 28]. Results were consistent across specific populations with greater risk of thrombotic events/amputations including obese patients, diabetics, and those with mild-to-moderate CKD (see Table 5). [8, 10-12]</p> <p>VOYAGER trial in PAD: The combination of XARELTO® + aspirin reduced the relative risk of the primary endpoint of composite acute limb ischemia, major amputation for vascular causes, heart attack, stroke, or death from cardiovascular disease by 15% compared to aspirin alone. There were no significant differences between groups for the occurrence of major bleeding (see Table 6). [13]</p> <p>Many CAD/PAD patients have comorbidities such as obesity, diabetes, and moderate CKD which are difficult to treat. [29-35] In addition, beneficiaries that are 75 and older with CAD/PAD have an increased risk for cardiovascular events. [29-36] In addition, beneficiaries that are 75 and older with CAD/PAD have an increased risk for cardiovascular events. [36]</p> <p>* Obese patients have a significantly increased risk of cardiovascular events and incur increased costs to Medicare. [29] An estimated 21% of Medicare FFS beneficiaries had a diagnosis of obesity in 2019. [30]</p> <p>* Diabetics are at an increased risk for MACE and MALE. An estimated 27.5% of Medicare FFS beneficiaries had a</p>



Question	Sub-Question	Response
		<p>diagnosis of diabetes in 2019. [31-33]</p> <p>* Patients with moderate CKD often require different dosing of anticoagulants due to the impact on kidney function. XARELTO® does not require different dosing in CAD/PAD populations. [11, 37]</p> <p>Results from studies of XARELTO® + aspirin in patients with CAD/PAD show consistent outcomes amongst the elderly and hard-to-treat populations, offering additional value to Medicare beneficiaries. [8-15]</p> <p>XARELTO® delivers value in specific populations as well as addresses health equity needs in undeserved groups such as Black patients. XARELTO® is FDA approved for the treatment of CAD/PAD, treatment and prevention of recurrent VTE (pediatrics), and prevention of VTE post-Fontan procedure (pediatrics), unlike its therapeutic alternative ELIQUIS®. XARELTO® has shown comparable outcomes to the overall trial populations in CAD/PAD patients with multiple comorbidities such as obesity, diabetes, and moderate CKD. XARELTO® has demonstrated value for underserved and overlooked patient populations through FDA approved indications, clinical trials, and real-world evidence.</p>
	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	N
	What type of Evidence is shown?	





Question	Sub-Question	Response
Question 30: Addressing Unmet Medical Needs	Response to Question 30	<p>Section I (Question 27 through 30 and 32) is confidential &amp; proprietary, use subject to IRA 1193(c); FOIA exemptions apply</p> <p>NOTE: Please review the executive summary prior to this section.</p> <p>Direct oral anticoagulants (DOACs), including XARELTO® and its therapeutic alternative ELIQUIS®, continue to address unmet medical needs for Medicare beneficiaries with nonvalvular atrial fibrillation (NVAf) and venous thromboembolism (VTE) by providing greater effectiveness over warfarin as reported in RWE studies. [1, 2] Only XARELTO® has FDA approved indications to address additional unmet medical needs by offering a novel mechanism (Factor Xa inhibitor) to treat the growing population of Medicare beneficiaries, many of which are Black patients, with coronary artery disease (CAD) and peripheral artery disease (PAD).</p> <p>Current treatment options have underlying limitations, such as warfarin requiring routine monitoring and ELIQUIS® having twice daily dosing for NVAf. XARELTO® offers simplified once daily dosing without routine monitoring for Medicare beneficiaries with NVAf to prevent or reduce the risk of stroke and systemic embolism (a blood clot in the bloodstream that can cause a blockage).</p> <p>Atrial fibrillation (AF), the most common heart arrhythmia, increases the risk of ischemic stroke (blood clot blocking blood flow to brain) five-fold which accounts for 1 in 21 deaths in the US. [3, 4] An estimated 3-6 million people in the US have AF, and the population of AF patients older than 65 expected to nearly double from 12% to 22% (2010 to 2040) due to an aging population. [5, 6] More than 454,000 hospitalizations with AF as the primary diagnosis happen each year in the US. Nonvalvular atrial fibrillation (NVAf) is a subset AF, which is the most common heart arrhythmia. [4] The average cost for stroke in the US is ~\$60,000 per patient. [7]</p> <p>Prior to XARELTO®, beneficiaries with NVAf were treated with warfarin for ongoing anticoagulation. Treatment with warfarin requires routine monitoring as well as lifestyle changes which may impact a beneficiary's adherence, outcomes, and quality of life. [8] XARELTO®, unlike its therapeutic alternative ELIQUIS®, provides a more convenient treatment option with once daily dosing.</p> <p>XARELTO® addresses unmet medical needs in Medicare beneficiaries with VTE including deep vein thrombosis (DVT) and pulmonary embolism (PE) by offering a simplified treatment regimen versus warfarin and injectable LMWH.</p> <p>VTE is a thrombotic disease that occurs when a blood clot forms in a vein and includes DVT and PE. DVT occurs when a blood clot forms in one or more of the deep veins in the body, usually in the legs. A serious complication of DVT happens if part of the clot breaks off and travels to the lungs, which can cause a blockage called PE. [9] VTE affects</p>



Question	Sub-Question	Response
		<p>~600,000 Medicare beneficiaries each year. [3, 10] VTE is a major morbidity cause, leading to an estimated 548,000 hospitalizations annually in the US alone, with hospitalization rates being higher among older patients. [11] Treatment for VTE can be as much as \$15,000 to \$20,000 per person and often results in readmission to the hospital. As many as 100,000 Americans die of blood clots each year. [9]</p> <p>In EINSTEIN DVT and PE trials, almost 98% of adults being treated for a DVT with XARELTO® did not experience another DVT/PE and almost 98% of adults being treated for a PE with XARELTO® did not experience another DVT/PE. Bleeding rates were comparable to enoxaparin/vitamin K antagonist across these trials. [12]</p> <p>XARELTO® reduces the risk of recurrent DVT/PE with extended treatment after greater than 6 months initial treatment vs. aspirin and is the only DOAC to demonstrate a major bleeding rate as low as aspirin in patients at continued risk for DVT/PE. [13]</p> <p>XARELTO® is the only DOAC with an oral suspension for pediatric patients in need of anticoagulation for the treatment and prevention of recurrent VTE and for the prevention of VTE post-Fontan procedure. XARELTO®, unlike alternative treatments such as injectable LMWH or warfarin, does not require routine monitoring or frequent needle sticks.</p> <p>XARELTO® offers a novel treatment mechanism for CAD/PAD which impacts one-quarter of Medicare beneficiaries. [14, 15] XARELTO® is the only DOAC FDA approved for these indications.</p> <p>PAD is the leading cause of the ~400 nontraumatic amputations each day in the US. Black patients are four times more likely to have an amputation due to PAD than White patients. [16] The Amputations Reduction and Compassion Act, recently introduced into Congress, aims to bring greater awareness for the need to screen patients for PAD to reduce amputations. [17]</p> <p>A real-world study reported that one in seven patients with chronic CAD/PAD experienced major adverse cardiovascular events (MACE) or major adverse limb events (MALE) within two years. These events were associated with healthcare costs that were three times higher than those without MACE or MALE, with average difference in healthcare costs being \$48,000 to \$58,000 higher in patients that had a stroke or heart attack, respectively. [18] Approximately 200,000 people each year experience recurrent heart attack and 185,000 people experience recurrent stroke. [3] Overall, the risk of major adverse outcomes remains despite the availability of other treatment options. [19, 20]</p> <p>Studies show 25% to 90% of amputations within PAD populations are associated with diabetes. This risk is thought to</p>



Question	Sub-Question	Response
		<p>be attributable to the combination of peripheral neuropathy and infection stemming from diabetes and the presence of impaired arterial flow due to PAD. [21]</p> <p>XARELTO® + aspirin therapy reduced MACE events in patients with CAD/PAD and major thrombotic vascular events in patients with PAD compared to aspirin alone. [22, 23] Treatment for CAD/PAD is evolving because there are still unmet medical needs. AHA/ACC/ACCP/ASPC/NLA/PCNA guidelines for CAD were updated in July 2023 to include XARELTO® as a treatment option and guidelines for PAD are anticipated to be updated in early 2024. [24]</p> <p>Both XARELTO® and its therapeutic alternative, ELIQUIS®, address important unmet medical needs in NVAf and VTE. XARELTO® provides additional value over its therapeutic alternative, ELIQUIS®, by offering a unique formulation for pediatrics and a novel mechanism of treatment for Medicare beneficiaries with CAD and/or PAD.</p>
	Hyperlink to Citation - Additional Materials for Question 30	<p>[REDACTED]</p>
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	<p>[REDACTED]</p>
	Evidence Submitted include a cost-effectiveness measure?	<p>N</p>
	What type of Evidence is shown?	





Question	Sub-Question	Response
Question 31: Patient and Caregiver Experience	Response to Question 31	
Question 32: Executive Summary	Response to Question 32	<p>Key Takeaways:</p> <ul style="list-style-type: none"> <li>*Over one-third of Medicare beneficiaries are impacted by conditions that put them at risk for formation of blood clots that can lead to thrombotic events such as heart attack, stroke, and pulmonary embolism (PE) which may lead to death.</li> <li>*XARELTO®, which is in a class of blood thinners known as Factor Xa inhibitor direct oral anticoagulants (DOACs), is a therapeutic advancement over warfarin. XARELTO® has clear advantages over warfarin including fewer food/drug interactions, standardized dosing, and elimination of ongoing invasive and costly blood tests to monitor response to therapy.</li> <li>*XARELTO® is preferred over warfarin in major treatment guidelines for nonvalvular atrial fibrillation (NVAf) and venous thromboembolism (VTE).</li> <li>*XARELTO® has 11 FDA approved indications, 5 of which are unique and impact underserved populations where no other Factor Xa inhibitor DOACs are approved or marketed. XARELTO® has treated &gt;10 million U.S. patients across all indications.</li> <li>*ELIQUIS®, also a DOAC, is the therapeutic alternative to XARELTO®.</li> </ul> <p>[REDACTED]</p> <p>Disease Burden: Blood clots form in veins and arteries, and if they become dislodged, they can travel to the brain or lungs and cause thrombotic events such as stroke or PE. Thrombotic events (stroke, heart attack, deep vein thrombosis [DVT], and PE) are major complications of cardiovascular disease. These events are leading causes of death and disability among Medicare beneficiaries and are significant drivers of Medicare costs. In 2019, ~327,000 deaths of Americans 65+ were attributed to atrial fibrillation (including NVAf), VTE, coronary artery disease (CAD), or peripheral artery disease (PAD). In that same year, over one-third of Medicare beneficiaries were impacted by conditions that put them at risk of thrombotic events. Total Medicare spending on beneficiaries with these conditions in 2019 was over \$350 billion.</p> <p>*The specific type of thrombotic events include:</p> <ul style="list-style-type: none"> <li>-Stroke due to NVAf, a heart arrhythmia condition that can lead to the formation of blood clots that can travel to the</li> </ul>





Question	Sub-Question	Response
		<p>brain.</p> <p>-VTE which includes DVT, blood clots in the deep veins of the body (e.g., legs), and PE, which is a blood clot in the pulmonary artery (i.e., lungs).</p> <p>-CAD and PAD cause narrowing of arteries in the heart and usually legs. Narrowed arteries reduce blood flow and can result in the formation of blood clots leading to tissue damage (e.g., stroke, heart attack, amputation).</p> <p>Treatment Options: DOACs, including XARELTO®, are a therapeutic advancement over warfarin. Major treatment guidelines endorse DOACs (including XARELTO®) over warfarin for stroke and systemic embolism (a blood clot in the bloodstream that can cause a blockage) prevention in NVAf, VTE treatment, and reduction of VTE recurrence. (See Table 3 in Question 28)</p> <p>XARELTO's® Value to Beneficiaries: XARELTO® has 11 FDA approved indications, including 5 unique indications compared to ELIQUIS®, with proven efficacy in preventing, treating, and reducing the risk of costly thrombotic events in NVAf, VTE, CAD, and PAD.</p> <p>*XARELTO® plays a critical role in treating and reducing the risk of thrombotic events for Medicare beneficiaries with CAD/PAD.</p> <p>*Heart disease is the number one cause of death of which CAD is the most common type. CAD affects approximately 25% of Medicare beneficiaries and is a strong predictor of future cardiovascular events such as heart attacks and stroke. Recent statistics show that every year 200,000 people experience recurrent heart attacks and 185,000 people experience recurrent strokes.</p> <p>*PAD is the leading cause of the ~400 nontraumatic amputations each day in the US. Studies show 25% to 90% of amputations within studied populations are associated with diabetes. Black Americans are twice as likely to have PAD.</p> <p>*XARELTO® has clear advantages over warfarin:</p> <ul style="list-style-type: none"> <li>-Fewer food/drug interactions</li> <li>-Standardized dosing (no titration)</li> <li>-Elimination of ongoing requirement for frequent, invasive, and costly blood tests to find and maintain a safe and effective dose.</li> <li>-XARELTO® is associated with cost savings compared to warfarin (22% hospitalization cost saving in DVT and 33% in PE).</li> </ul> <p>Conclusion: XARELTO® represents a therapeutic advance over warfarin in NVAf and VTE. XARELTO's® 5 unique indications provide additional value to patients, including Medicare beneficiaries, and should be considered in XARELTO's® value assessment.</p>



Question	Sub-Question	Response
		<div data-bbox="634 289 1990 365" style="background-color: black; height: 47px; width: 100%;"></div> <p>APPENDIX</p> <p>DOAC Clinical Overview:</p> <p>*DOACs have been extensively studied. During clinical development, 34,947 adults were treated with XARELTO® vs. 24,685 with ELIQUIS®.</p> <p>*All anticoagulants carry the risk of bleeding and similar warnings and precautions. The contraindications listed on the FDA approved labels for XARELTO® and ELIQUIS® are identical. Use of DOACs requires a benefit risk assessment as bleeding events may be observed in a shorter timeframe whereas assessment of treatment and prevention of thrombotic events may require a longer timeframe.</p> <p>*There are no head-to-head randomized clinical trials that directly compare the safety and efficacy of XARELTO® to ELIQUIS® for any indication. Comparative data is limited to observational, retrospective studies where the majority have a follow up period of &lt;1 year, which is not long enough to assess the benefit risk profile.</p> <p>*In an observational study conducted ex-US over 6 years, investigators found that XARELTO® was associated with lower all-cause mortality and ischemic stroke rates compared to ELIQUIS® while gastrointestinal bleed rates were higher for XARELTO®.</p> <p>*FDA Sentinel has conducted analyses of the effectiveness and safety for Factor Xa inhibitors, which have not resulted in any changes to the risk of bleeding in the safety section of either XARELTO®'s or ELIQUIS®'s prescribing information to date.</p>

**Table 1: XARELTO® has the most FDA approved indications of all direct oral anticoagulants**

Indication		XARELTO (rivaroxaban)	ELIQUIS (apixaban)	PRADAXA (dabigatran)	SAVAYSA (edoxaban)	BEVYXXA (betrixaban)
NVAF		✓	✓	✓	✓†	
PE treatment		✓	✓	✓	✓	
DVT treatment		✓	✓	✓	✓	
DVT/PE extended treatment		✓	✓			
Hip replacement DVT/PE prophylaxis		✓	✓	✓		
Knee replacement DVT/PE prophylaxis		✓	✓			
Acute medically ill		✓				✓‡
CAD		✓				
PAD		✓				
Pediatric DVT/PE		✓		✓		
Pediatric post-Fontan procedure		✓				

CAD, coronary artery disease; DVT, deep vein thrombosis; NA, not available; NVAF, nonvalvular atrial fibrillation; PAD, peripheral artery disease; PE, pulmonary embolism.

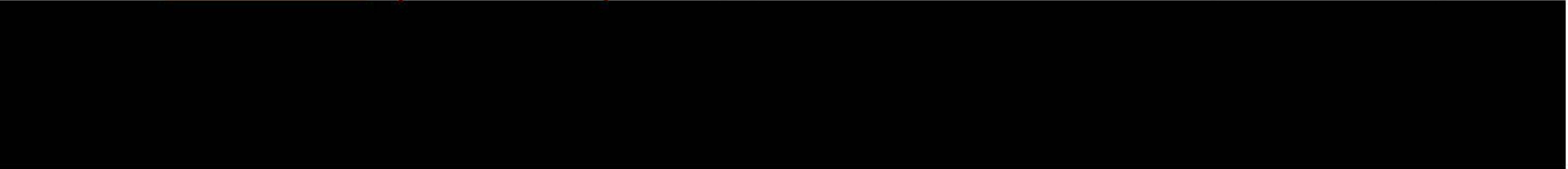
†Limitation of use in NVAF patients with creatinine clearance >95 mL/min because of increased risk of ischemic stroke compared to warfarin at the highest dose studied (60 mg).

\*Ceased commercialization in 2019.

||PRADAXA Capsules are indicated for the treatment of VTE in pediatric patients aged 8 to <18 years who have been treated with a parenteral anticoagulation ≥5 days and to reduce the risk of recurrence of VTE in pediatric patients aged 8 to <18 years who have been previously treated. PRADAXA Oral Pellets are indicated for the treatment of VTE in pediatric patients aged 3 months to <12 years of age who have been treated with a parenteral anticoagulant for at least 5 days and to reduce the risk of recurrence of VTE in pediatric patients aged 3 months to <12 years of age who have been previously treated.

Table 2: Comparison of attributes of alternative therapies

	Direct Oral Anticoagulants				VKA	LMWH
Product	XARELTO® (rivaroxaban)	★ ELIQUIS® (apixaban)	PRADAXA® (dabigatran)	SAVAYSA® (edoxaban)	Warfarin	Enoxaparin
AB-rated Generic Available	No	No	Yes	No	Yes	Yes
Therapeutic Class	Direct Oral Anticoagulant	✓	✓	✓	✗	✗
Chemical Class	Oxazolidinone	✗	✗	✗	✗	✗
MOA	Factor Xa Inhibitor	✓	✗	✓	✗	✗



Therapeutic Alternative

\*Enoxaparin dosing for treatment for an 80 kg adult, dosed 1 mg/ kg twice daily  
VKA: Vitamin K Antagonist  
LMWH: Low Molecular Weight Heparin



**Table 3: Clinical Guideline Recommendations for Atrial Fibrillation and Venous Thromboembolism Recommend DOACs over Warfarin**

Organization	Guideline Title	Summary of DOAC Recommendation
<b>Atrial Fibrillation Guidelines</b>		
AHA/ACC/HRS	2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation (January 2019)	<ul style="list-style-type: none"> <li>Rivaroxaban is recommended as one anticoagulant option for patients with atrial fibrillation and an elevated CHA<sub>2</sub>DS<sub>2</sub>-VASc score of <math>\geq 2</math> in men or <math>\geq 3</math> in women (COR 1, LOE B).</li> <li>Rivaroxaban, dabigatran, apixaban, and edoxaban are recommended over warfarin in NOAC-eligible patients with atrial fibrillation (except with moderate-to-severe mitral stenosis or mechanical heart valve) (COR 1, LOE A).</li> <li>In patients with atrial fibrillation, anticoagulant therapy should be individualized on the basis of shared decision-making after discussion of the absolute risks and relative risks of stroke and bleeding, as well as the patient's values and preferences (COR 1, LOE C).</li> </ul>
AHA/ASA	2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association (Kleindorfer 2021)	<ul style="list-style-type: none"> <li>Oral anticoagulation (eg, apixaban, dabigatran, edoxaban, rivaroxaban, or warfarin) is recommended to reduce the risk of recurrent stroke in patients with NVAF and stroke or transient ischemic attack (TIA) (COR 1, LOE A).</li> <li>In patients with stroke or TIA and AF who do not have moderate to severe mitral stenosis or a mechanical heart valve, apixaban, dabigatran, edoxaban, or rivaroxaban is recommended in preference to warfarin to reduce the risk of recurrent stroke (COR 1, LOE BENEFIT-RISK).</li> </ul>
CCS	The 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive Guidelines for the Management of Atrial Fibrillation (Andrade 2020)	<ul style="list-style-type: none"> <li>We recommend most patients should receive a DOAC (apixaban, dabigatran, edoxaban, or rivaroxaban) in preference to warfarin when OAC therapy is indicated for patients with NVAF (Strong Recommendation, High-Quality Evidence).</li> <li>We recommend that OAC be prescribed for most frail elderly patients with AF (Strong Recommendation, Moderate-Quality Evidence).</li> </ul>
CHEST	2018 Antithrombotic Therapy for Atrial Fibrillation CHEST Guideline and Expert Panel Report (Lip 2018)	<ul style="list-style-type: none"> <li>In patients with AF who are eligible for OAC, we recommend NOACs over VKA (Strength of recommendation: Strong; Quality of evidence: Moderate)</li> </ul>
ESC	2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation Developed in Collaboration with the European Association for Cardio-Thoracic Surgery (EACTS) (Hindricks 2020)	<ul style="list-style-type: none"> <li>For stroke prevention in AF patients who are eligible for OAC, NOACs are recommended in preference to VKAs, excluding patients with mechanical heart valves or moderate-to-severe mitral stenosis (COR 1, LOE A).</li> <li>The elderly and frail with atrial fibrillation: older people are less likely to receive OAC despite sufficient evidence supporting the use of OAC in this population. Frailty, comorbidities, and increased risk of falls do not outweigh the benefits of OAC given the small absolute risk of bleeding in anticoagulated elderly patients.</li> <li>Evidence from randomized controlled trials, meta-analyses and large registries support the use of OAC in this age group. Antiplatelets are neither more effective nor safer than warfarin and may even be harmful, whereas NOACs appear to have a better overall risk-</li> </ul>



		benefit profile compared with warfarin. Prescribing a reduced dose of OAC is less effective in preventing AF adverse outcomes.
ESO	2019 Antithrombotic Treatment for Secondary Prevention of Stroke and Other Thromboembolic Events in Patients with Stroke or Transient Ischemic Attack and Nonvalvular Atrial Fibrillation: A European Stroke Organisation Guideline (Klijn 2019)	<ul style="list-style-type: none"> <li>• In patients with nonvalvular AF and previous ischemic stroke or TIA, we recommend non-vitamin K antagonist oral anticoagulants over vitamin K antagonists for secondary prevention of all events (Strength of recommendation: Strong; Quality of evidence: High)</li> <li>• In elderly patients with nonvalvular AF and a history of ischemic stroke or TIA, we suggest NOACs over VKAs (Strength of recommendation: Weak; Quality of evidence: Low)</li> </ul>
NICE	2021 National Institute for Health and Care Excellence Atrial Fibrillation: Diagnosis and Management (NICE 2021)	<ul style="list-style-type: none"> <li>• Offer anticoagulation with a direct-acting oral anticoagulant to people with atrial fibrillation and a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 or above, considering the risk of bleeding. Apixaban, dabigatran, edoxaban and rivaroxaban are all recommended as options, when used in line with the criteria specified in the relevant NICE technology appraisal guidance.</li> <li>• Based on the evidence and their experience, the committee decided not to recommend one direct-acting oral anticoagulant over the others, but instead to emphasize that treatment should be tailored to the person's clinical needs and preferences. Each anticoagulant has different risks and benefits that should be considered and fully discussed with the person as part of informed shared decision making.</li> </ul>
<b>Venous Thromboembolism Guidelines</b>		
ASH	American Society of Hematology 2020 Guidelines for Management of Venous Thromboembolism: Treatment of Deep Vein Thrombosis and Pulmonary Embolism (Ortel 2020)	<ul style="list-style-type: none"> <li>• For patients with DVT and/or PE, the ASH guideline panel suggests using DOACs over VKAs (conditional recommendation based on moderate certainty in the evidence of effects)</li> <li>• For patients with DVT and/or PE, the ASH guideline panel does not suggest 1 DOAC over another (conditional recommendation based on very low certainty in the evidence of comparative effects).</li> <li>• For patients who will be treated with a DOAC, the ASH guideline panel does not suggest 1 medication over another given the very low certainty in the evidence on comparative effects. However, for patients who will be taking a DOAC, there are differences that should be taken into consideration.</li> <li>• For patients with DVT and/or PE who have completed primary treatment and will continue with a DOAC for secondary prevention, the ASH guideline panel suggests using standard dose DOAC or lower-dose DOAC (conditional recommendation based on moderate certainty in the evidence of effects).</li> </ul>
CHEST	2021 Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report (Stevens 2021)	<ul style="list-style-type: none"> <li>• In patients with VTE (DVT of the leg or PE) we recommend apixaban, dabigatran, edoxaban, or rivaroxaban over VKA as treatment-phase (first 3 months) anticoagulant therapy (strong recommendation, moderate-certainty evidence)</li> </ul>

		In patients offered extended-phase anticoagulation, we suggest the use of reduced-dose apixaban or rivaroxaban over full-dose apixaban or rivaroxaban (weak recommendation, very low certainty evidence).
ESC	2022 Second Consensus Document on Diagnosis and Management of Acute Deep Vein Thrombosis: Updated Document Elaborated by the ESC Working Group on Aorta and Peripheral Vascular Diseases and the ESC Working Group on Pulmonary Circulation and Right Ventricular Function (Mazzolai 2022)	<ul style="list-style-type: none"> <li>Initial and long-term DVT management in non-cancer patients: NOACs should be preferred as first-line anticoagulant therapy in absence of contraindications.</li> </ul> <p>Extended management (&gt;first 3 months) of DVT (without PE): In absence of contraindications, NOACs should be preferred as first-line extended anticoagulant therapy in non-cancer patients, except in patients with antiphospholipid syndrome.</p>
ESC	2019 ESC Guidelines for the Diagnosis and Management of Acute Pulmonary Embolism Developed in Collaboration with the European Respiratory Society (ERS): The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) (Konstantinides 2020)	<ul style="list-style-type: none"> <li>Recommendations for acute-phase treatment of intermediate- or low-risk pulmonary embolism: When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a VKA (COR 1, LOE A).</li> </ul> <p>NOAC dose in extended anticoagulation: If extended oral anticoagulation is decided after PE in a patient without cancer, a reduced dose of the NOACs apixaban (2.5 mg b.i.d.) or rivaroxaban (10 mg o.d.) should be considered after 6 months of therapeutic anticoagulation (COR 2a, LOE A).</p>
NICE	2020 National Institute for Health and Care Excellence Venous Thromboembolic Diseases: Diagnosis, Management and Thrombophilia Testing (NICE 2020)	<ul style="list-style-type: none"> <li>Anticoagulation treatment for confirmed DVT or PE: Offer either apixaban or rivaroxaban to people with confirmed proximal DVT or PE (but see recommendations 1.3.11 to 1.3.20 for people with any of the clinical features listed in recommendation 1.3.7). <ul style="list-style-type: none"> <li>... the committee were not confident that apixaban should be the only option for a DOAC and recommended a choice of apixaban or rivaroxaban.</li> <li>The committee recognized that apixaban or rivaroxaban might not be suitable for everyone, so they included options for treatment with LMWH followed by dabigatran or edoxaban, or LMWH with a VKA.</li> </ul> </li> </ul> <p>Long-term anticoagulation for secondary prevention: Take into account the person's preferences and their clinical situation when selecting an anticoagulant for long-term treatment</p>
<ul style="list-style-type: none"> <li>January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task</li> </ul>		

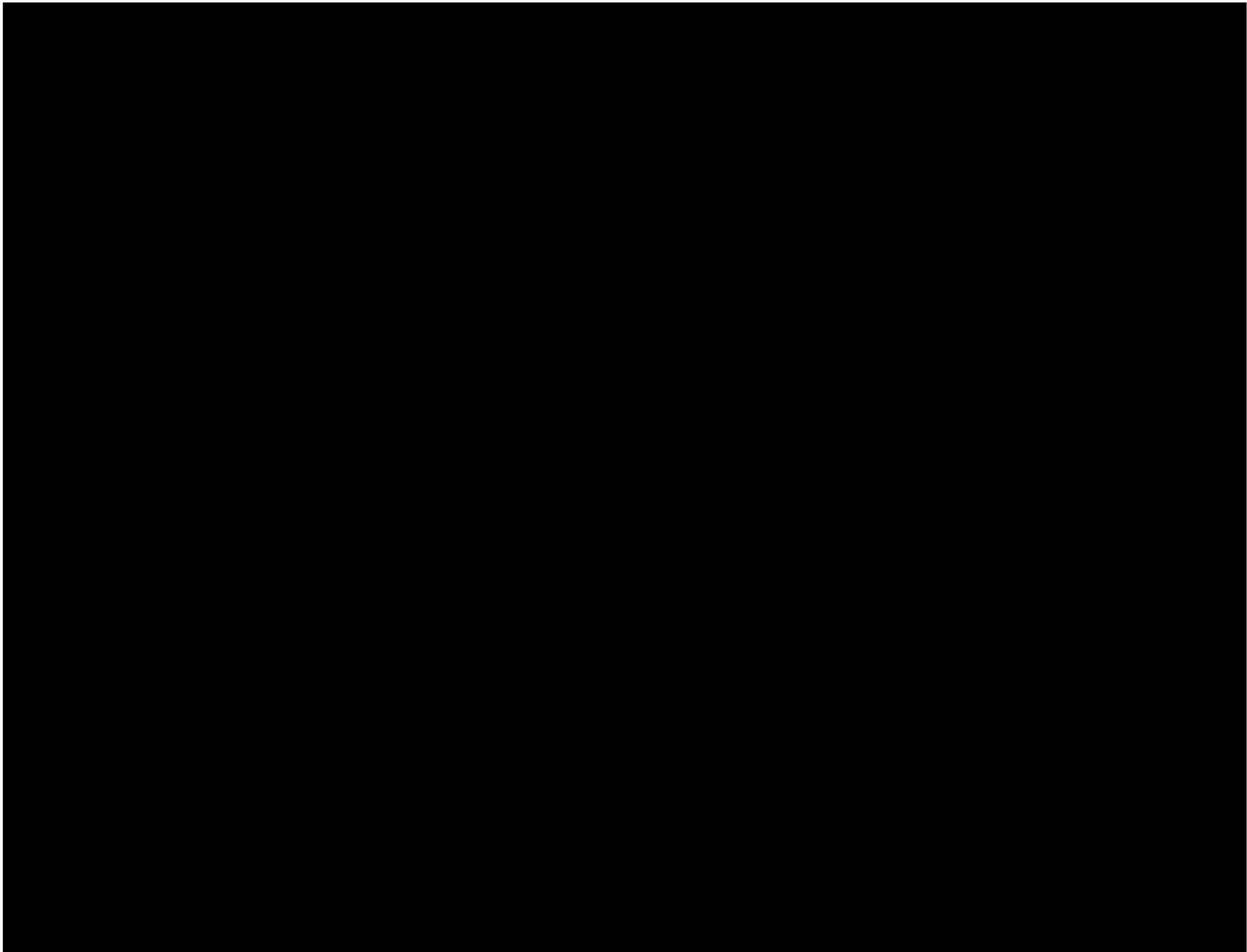
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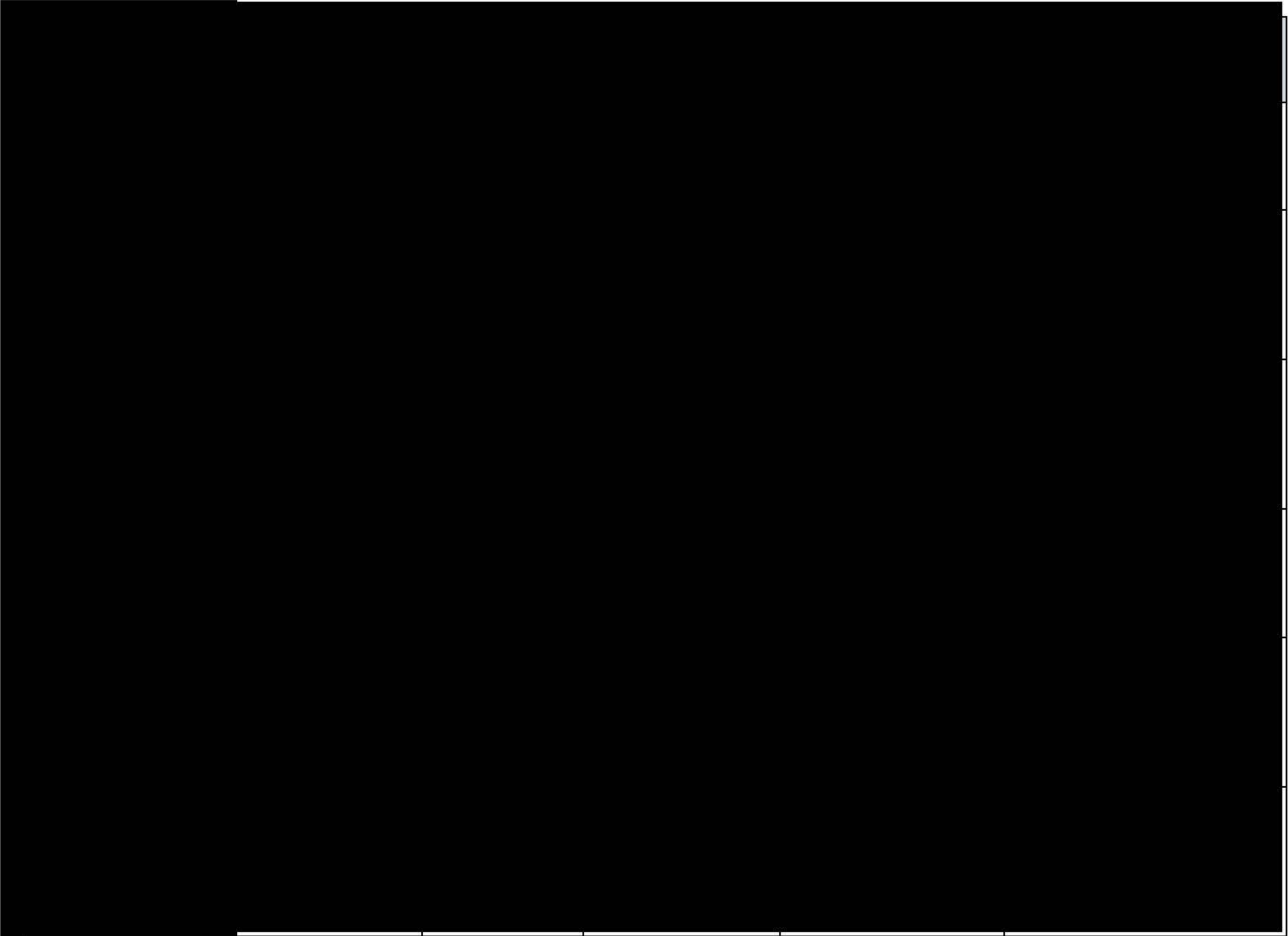
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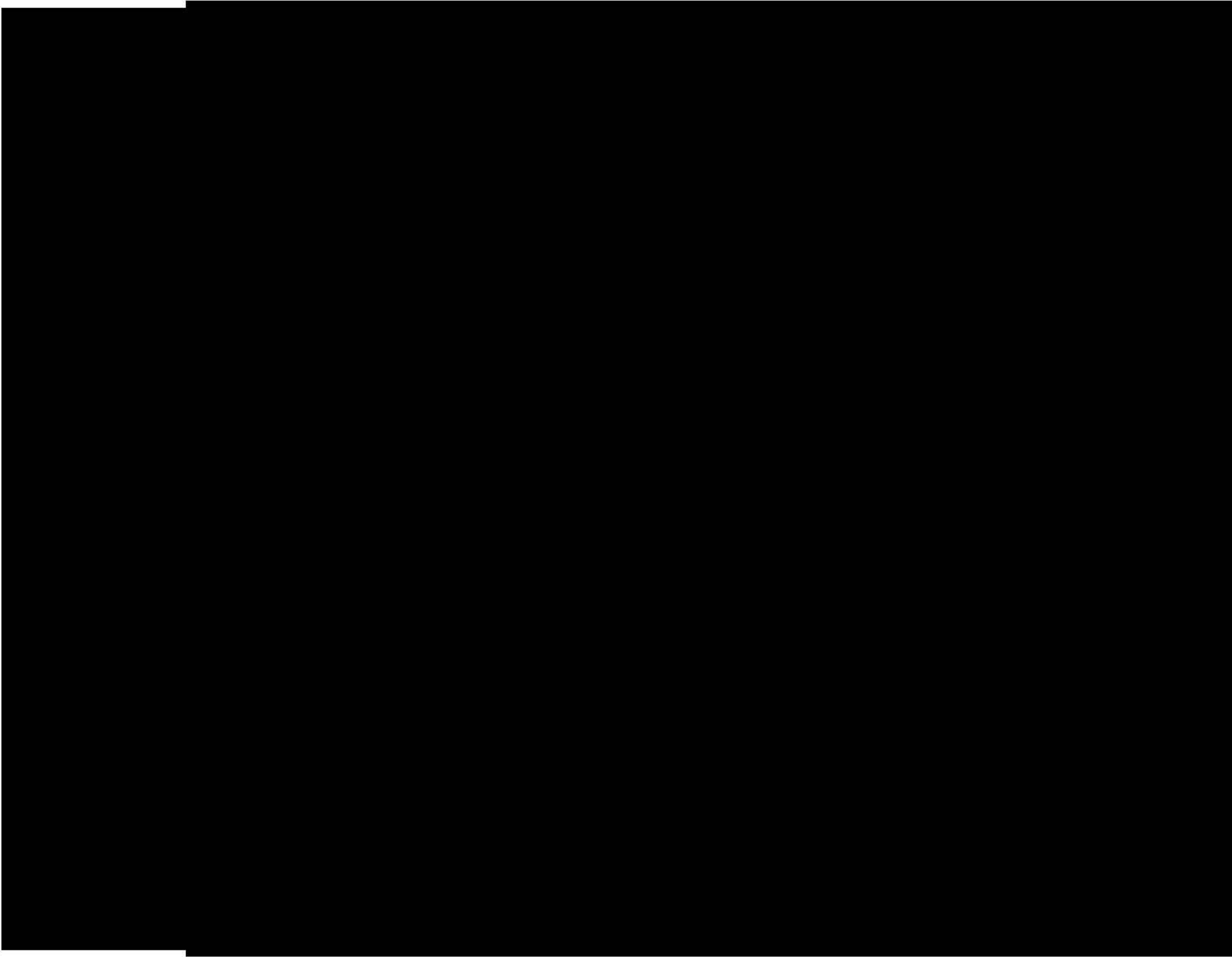


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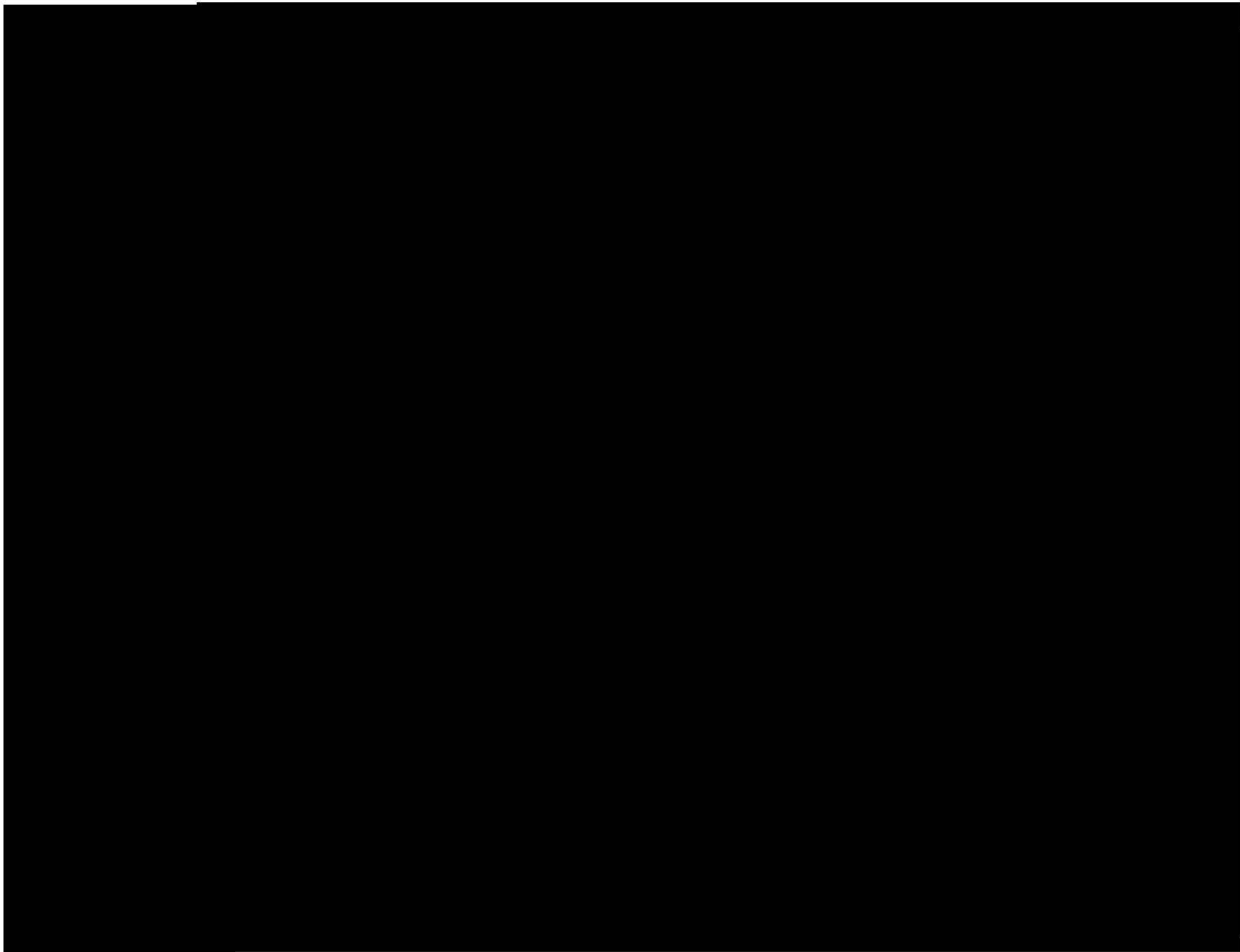


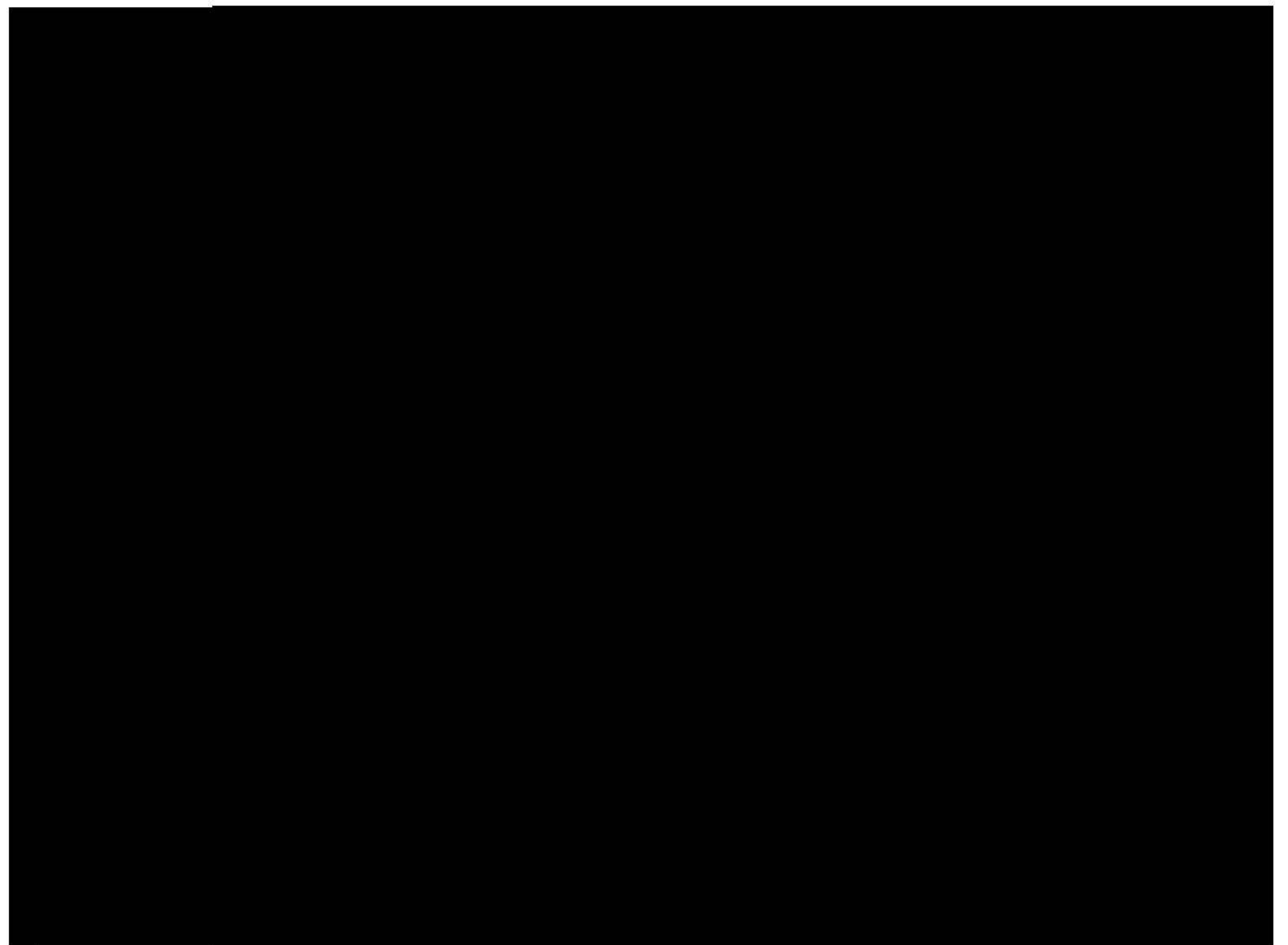




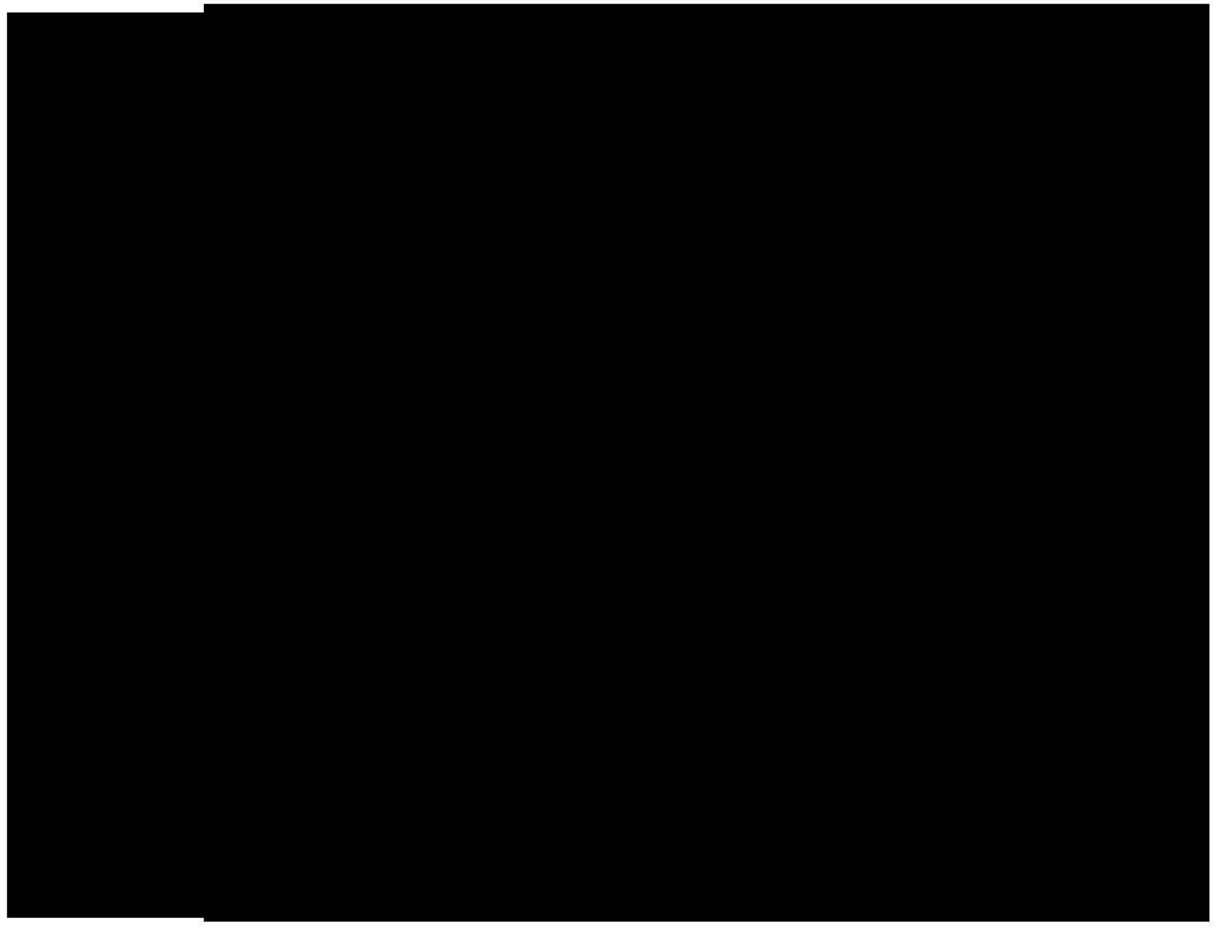




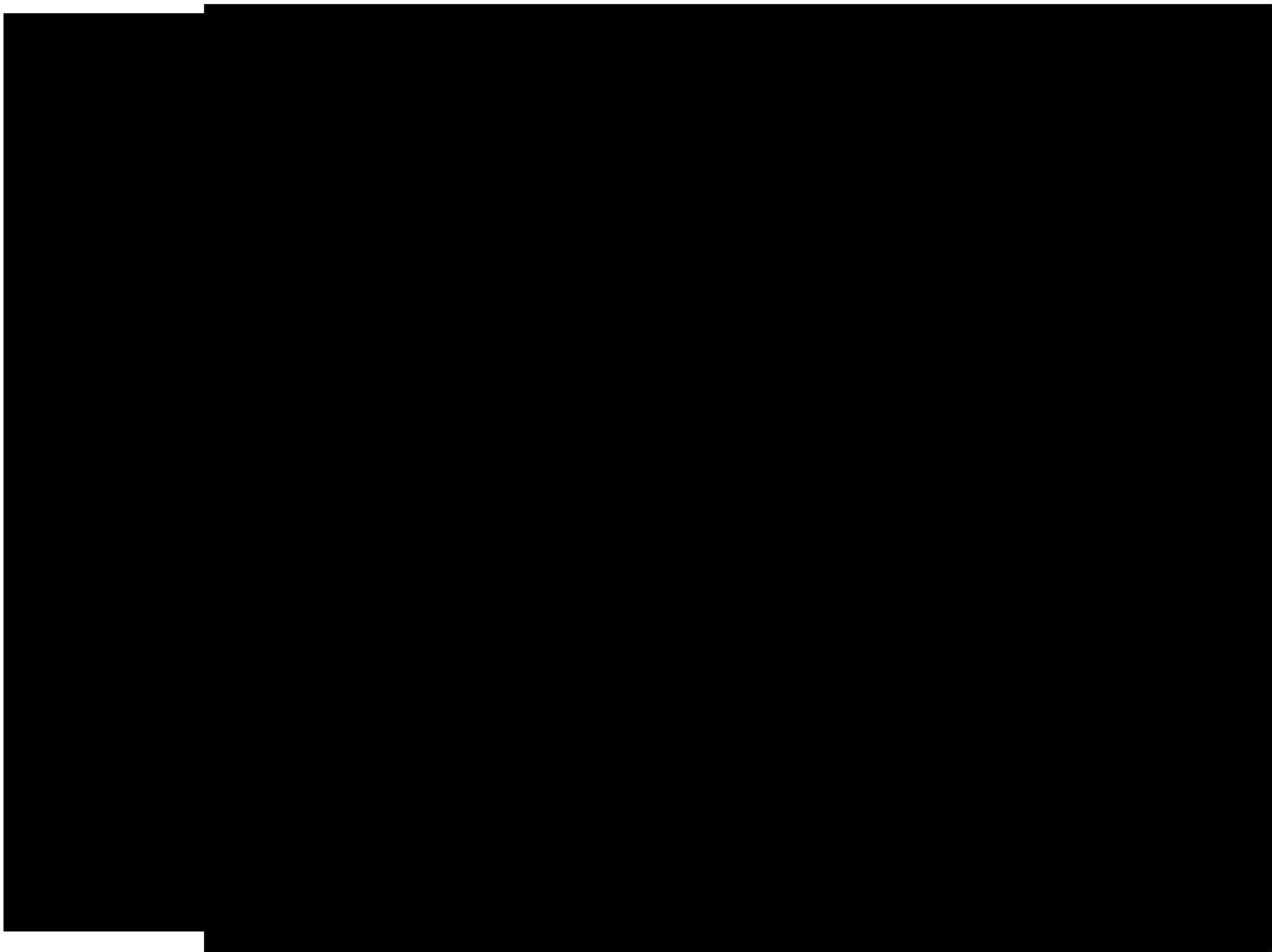


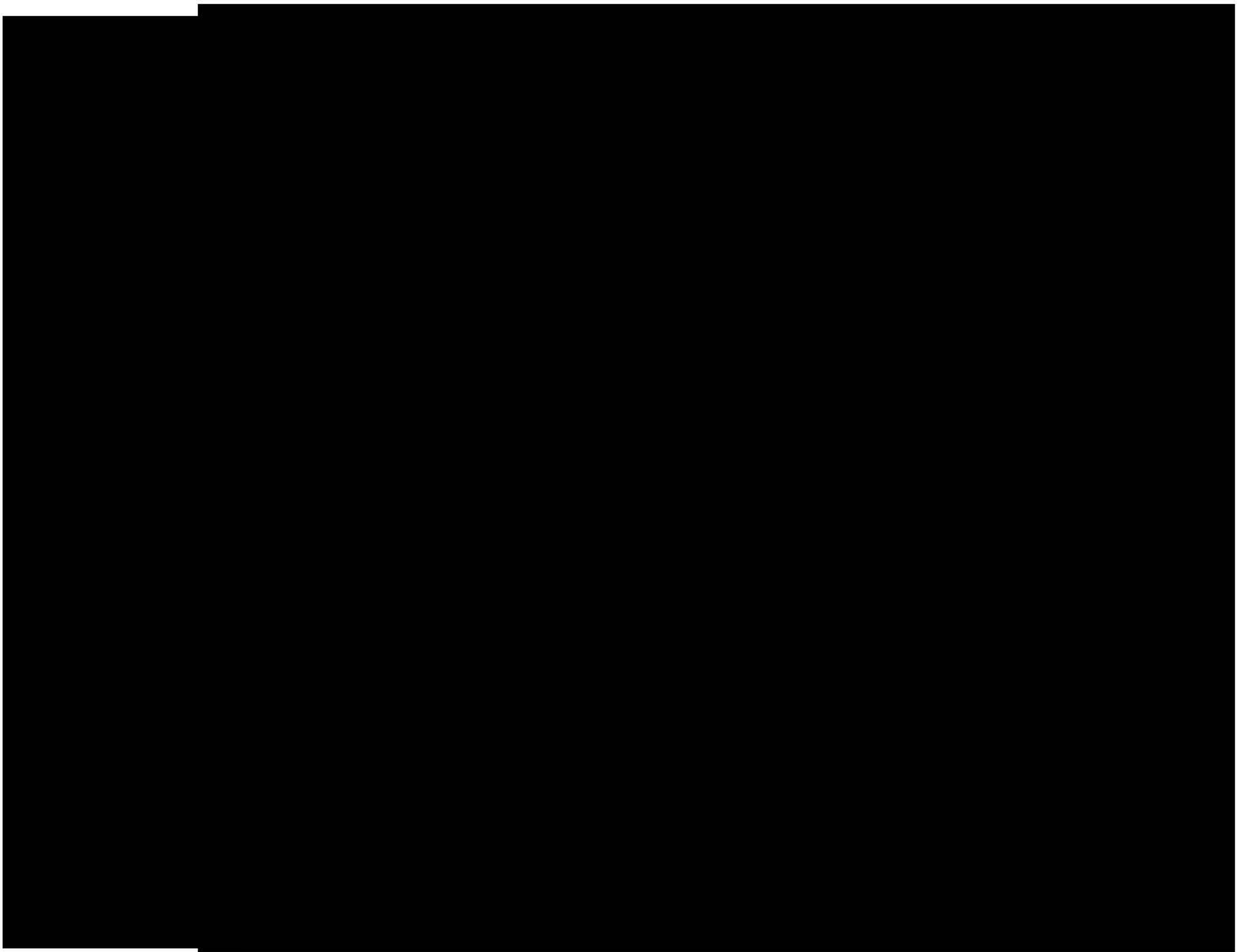




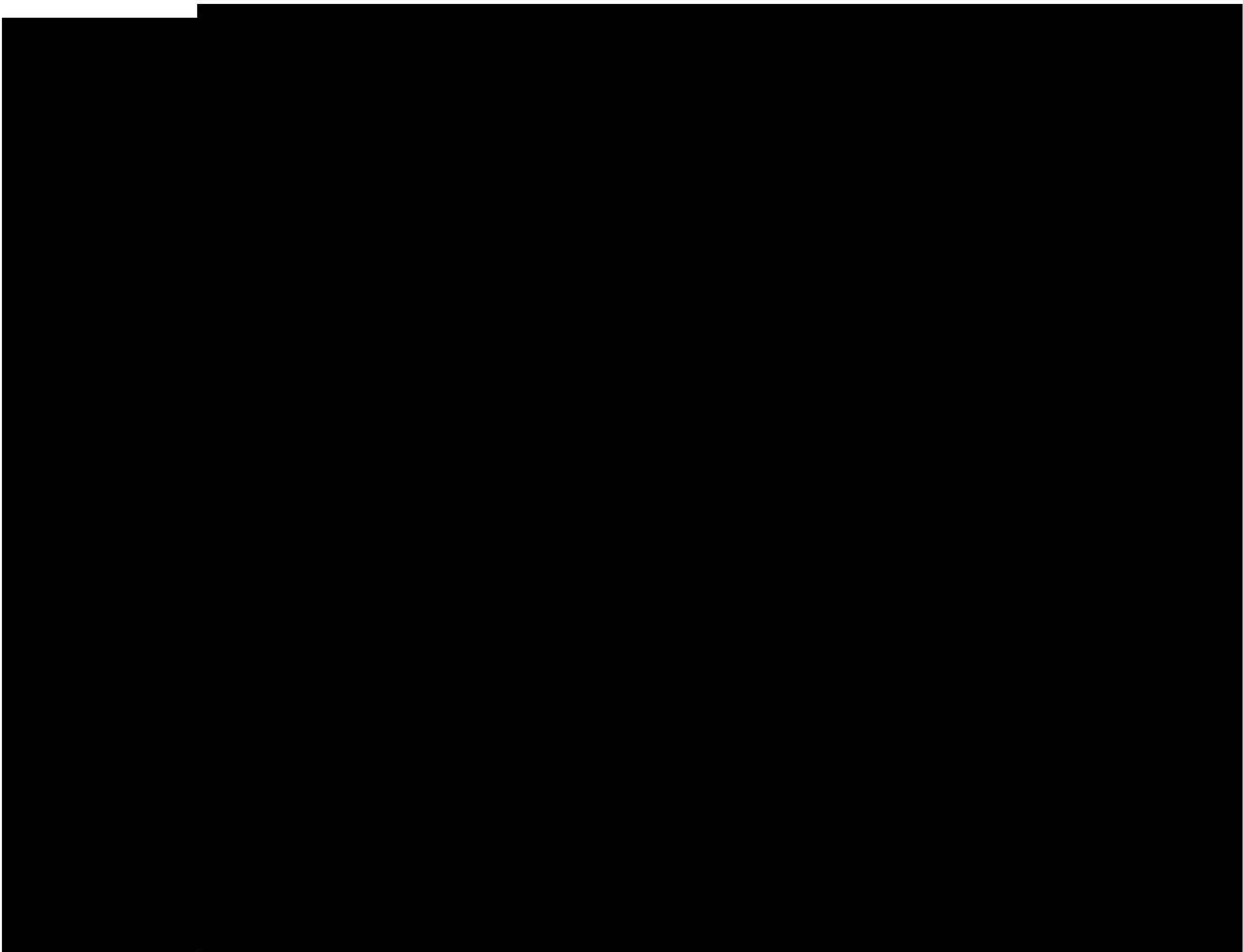


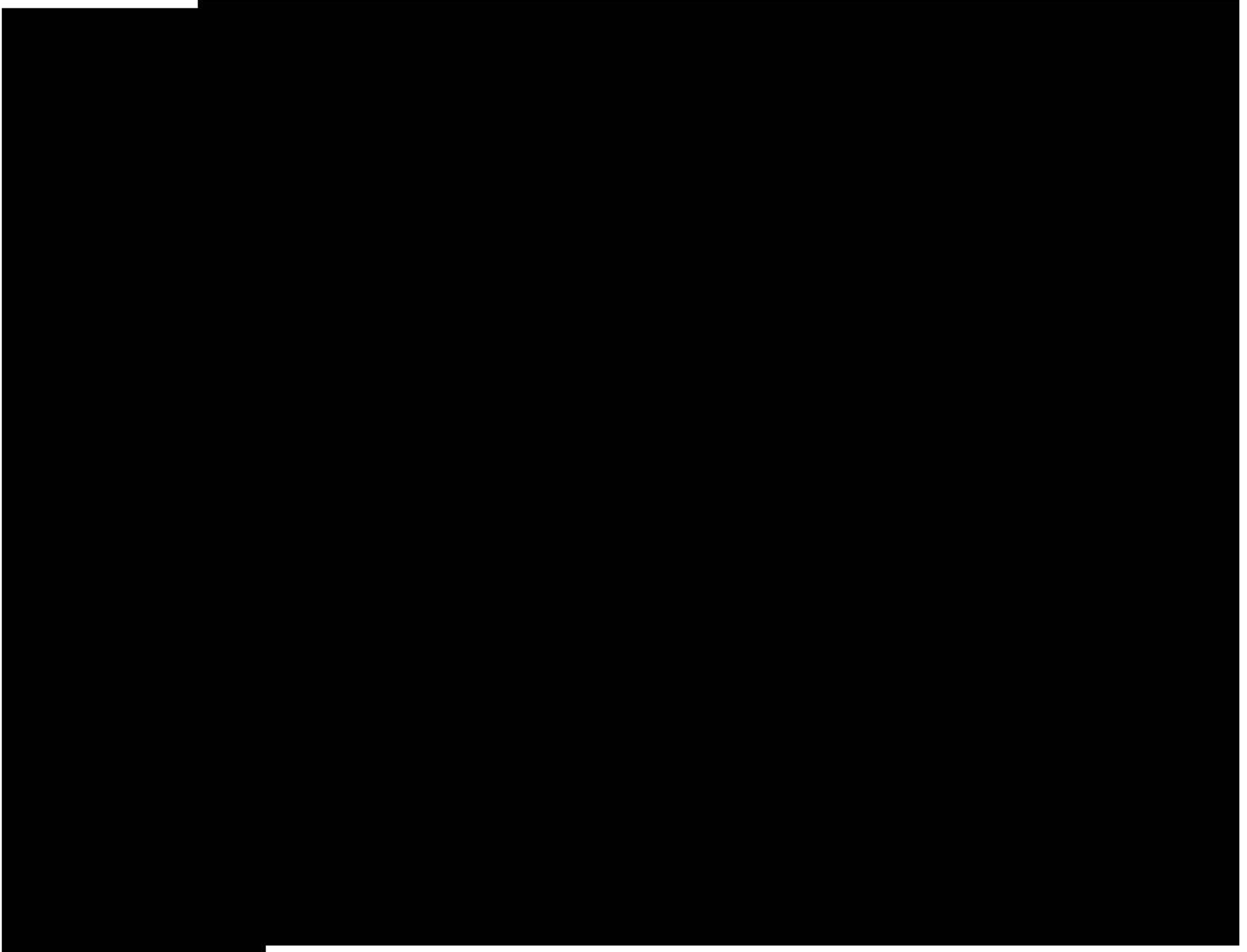
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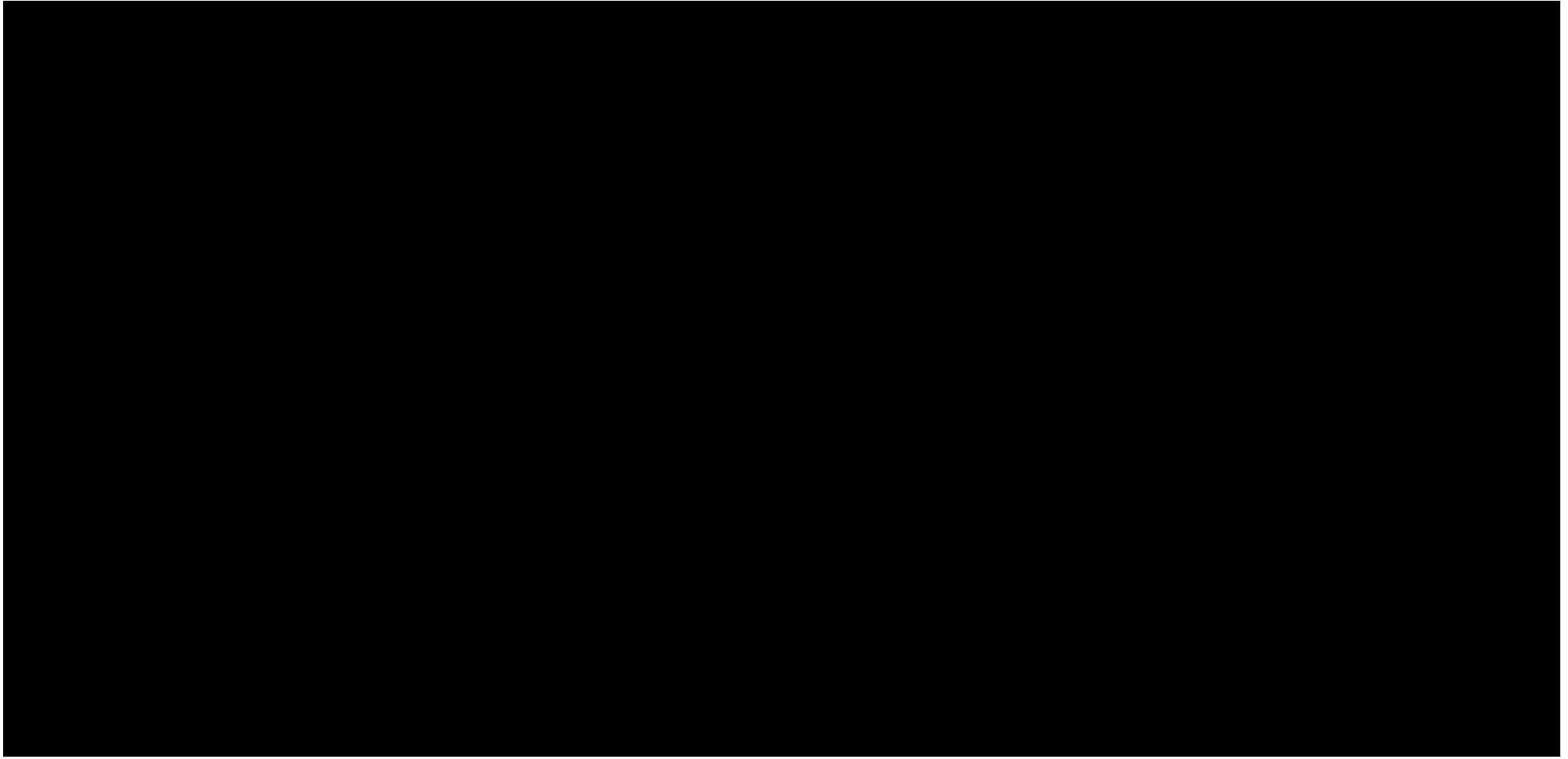












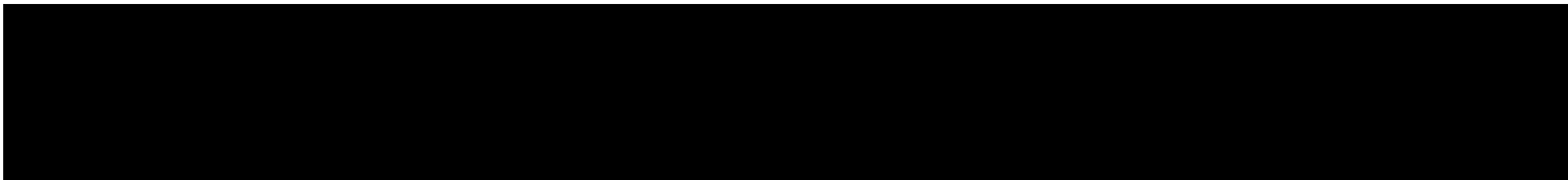
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**Table 5 FDA Sentinel Summary of Findings**

	<b>XARELTO® N=75,889</b> Incidence Rate per 100PY	<b>Apixaban N=75,889</b> Incidence Rate per 100PY	<b>Incidence Rate Difference, per 100PY</b>	<b>Hazard Ratio (95% CI)</b>
<b>2020 FDA Sentinel Report<sup>1</sup></b>				
<b>Thromboembolic stroke</b>	0.837	0.911	-0.074	1.00 (0.82, 1.22)
<b>Intracranial hemorrhage</b>	0.568	0.451	0.118	1.28 (0.99, 1.67)
<b>Major extracranial bleeding</b>	4.871	2.311	2.56	2.29 (2.06, 2.55)
<b>Gastrointestinal hemorrhage</b>	4.389	2.067	2.323	2.32 (2.07, 2.59)
	<b>XARELTO® N= 111,814</b> Incidence Rate per 100PY	<b>Apixaban N=77,234</b> Incidence Rate per 100PY	<b>Incidence Rate Difference, per 100PY</b>	<b>Hazard Ratio (95% CI)</b>
<b>2022 FDA Sentinel Report<sup>2</sup></b>				
<b>Thromboembolic stroke</b>	0.809	0.895	-0.086	0.99 (0.82, 1.19)
<b>Intracranial hemorrhage</b>	0.533	0.436	0.097	1.23 (0.96, 1.58)
<b>Major extracranial bleeding</b>	4.744	2.221	2.523	2.33 (2.11, 2.58)
<b>Gastrointestinal hemorrhage</b>	4.253	1.981	2.272	2.35 (2.11, 2.61)
<p>Note: Incidence rates in the FDA sentinel reports were reported as per 1000 person-years (PY), which was converted to per 100PY in this summary table.</p> <ol style="list-style-type: none"> <li>Center for Drug Evaluation &amp; Research (CDER). Stroke, intracranial hemorrhage, and bleeding following dabigatran, rivaroxaban, and apixaban use in patients aged 65 or older: A propensity score matched analysis. September 14, 2020. <a href="https://www.sentinelinitiative.org/studies/drugs/individual-drug-analyses/stroke-intracranial-hemorrhage-and-bleeding-following">https://www.sentinelinitiative.org/studies/drugs/individual-drug-analyses/stroke-intracranial-hemorrhage-and-bleeding-following</a>. Accessed May 1, 2023.</li> <li>Center for Drug Evaluation and Research (CDER). Intracranial hemorrhage following direct oral anticoagulant use: An inverse probability of treatment weighting analysis. April 25, 2022. <a href="https://www.sentinelinitiative.org/studies/drugs/individual-drug-analyses/thromboembolic-stroke-major-extracranial-bleeding-0">https://www.sentinelinitiative.org/studies/drugs/individual-drug-analyses/thromboembolic-stroke-major-extracranial-bleeding-0</a>. Accessed May 1, 2023.</li> </ol>				

**Table 6: COMPASS CAD/PAD Trial - Primary Efficacy, Safety and Net Clinical Benefit Outcomes**



Outcome	XARELTO plus Aspirin (N=9152)	Aspirin Alone (N=9126)	XARELTO plus Aspirin vs Aspirin Alone	
	n (%)		HR (95% CI)	P Value
Primary Efficacy and Safety Outcomes in Overall COMPASS CAD/PAD Patients <sup>1</sup>				
MI, stroke, or CV death*	379 (4.1)	496 (5.4)	0.76 (0.66-0.86)	<0.001
Major bleeding	288 (3.1)	170 (1.9)	1.70 (1.40-2.05)	<0.001
Outcome	XARELTO plus Aspirin (N=8313)	Aspirin Alone (N=8261)	XARELTO plus Aspirin vs Aspirin Alone	
	n (%)		HR (95% CI)	P Value
Primary Efficacy, Safety, and Net Clinical Benefit Outcomes in the COMPASS Trial: Patients with CAD <sup>2</sup>				
MI, stroke, or CV death	347 (4)	460 (6)	0.74 (0.65-0.86)	<0.0001
Major bleeding	263 (3)	158 (2)	1.66 (1.37-2.03)	<0.0001
Net clinical benefit (CV death, stroke, MI, fatal bleeding, or symptomatic bleeding into critical organ) <sup>†</sup>	392 (5)	494 (6)	0.78 (0.69-0.90)	0.0003
Outcome	XARELTO plus Aspirin (N=2492)	Aspirin Alone (N=2504)	XARELTO plus Aspirin vs Aspirin Alone	
	n (%)		HR (95% CI)	P Value
Primary Efficacy, Safety, and Net Clinical Benefit Outcomes in the COMPASS Trial: Patients with PAD <sup>3</sup>				
CV death, stroke, MI	126 (5)	174 (7)	0.72 (0.57-0.90)	0.0047
Major bleeding	77 (3)	48 (2)	1.61 (1.12-2.31)	0.0089
Net clinical benefit (CV death, MI, stroke, and critical organ or fatal bleeding) <sup>‡</sup>	140 (6)	185 (7)	0.75 (0.60-0.94)	0.011
Abbreviations: CI, confidence interval; CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction.				
*P value for the primary efficacy outcome is confirmatory.				
†Provisions to address multiple testing for subgroups, such as coronary artery disease, were not specified and, therefore, any HRs, corresponding CIs, and P values reported for subgroup analyses cannot be interpreted as statistically significant (Eikelboom JW et al. Rivaroxaban with or without aspirin in stable cardiovascular disease [Supplementary Appendix]. N Engl J Med. 2017;377(14):S1-S37.)				
‡Prespecified net clinical benefit outcome.				
1. Eikelboom JW, Connolly SJ, Bosch J, Dagenais GR, Hart RG, Shestakovska O, et al. Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease: from the COMPASS trial. N Engl J Med. 2017;377(14):1319-30. Epub 20170827. doi: 10.1056/NEJMoa1709118.				

2. Connolly SJ, Eikelboom JW, Bosch J, Dagenais G, Dyal L, Lanas F, et al. Rivaroxaban with or without aspirin in patients with stable coronary artery disease: an international, randomised, double-blind, placebo-controlled trial. *Lancet*. 2018;391(10117):205-18. Epub 20171110. doi: 10.1016/s0140-6736(17)32458-3.
3. Anand SS, Caron F, Eikelboom JW, Bosch J, Dyal L, Aboyans V, et al. Major Adverse Limb Events and Mortality in Patients With Peripheral Artery Disease: The COMPASS Trial. *J Am Coll Cardiol*. 2018;71(20):2306-15. Epub 20180311. doi: 10.1016/j.jacc.2018.03.008.

Table 7: VOYAGER PAD Trial - Efficacy and Safety Outcomes

Outcome	XARELTO (N=3286)		Placebo (N=3278)		HR (95% CI)	P Value
	Patients with Event no. (%)	K-M Estimate at 3 years (%)	Patients with Event no. (%)	K-M Estimate at 3 years (%)		
<b>Primary efficacy outcome*</b>						
Composite of ALI, major amputation for vascular causes, MI, ischemic stroke, or death from CV causes	508 (15.5)	17.3	584 (17.8)	19.9	0.85 (0.76–0.96)	0.009
Outcome	XARELTO (N=3256)		Placebo (N=3248)		HR (95% CI)	P Value
	Patients with Event no. (%)	K-M Estimate at 3 years (%)	Patients with Event no. (%)	K-M Estimate at 3 years (%)		
<b>Principal safety outcome†</b>						
TIMI major bleeding	62 (1.90)	2.65	44 (1.35)	1.87	1.43 (0.97–2.10)	0.07

Abbreviations: ALI, acute limb ischemia; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; K-M, Kaplan-Meier; MI, myocardial infarction. TIMI, Thrombolysis in Myocardial Infarction.

\*Efficacy outcome analyzed on an intention-to-treat basis.

†Safety analysis included all patients who underwent randomization and had received at least one dose of trial medication (on-treatment).

Bonaca MP, Bauersachs RM, Anand SS, Debus ES, Nehler MR, Patel MR, et al. Rivaroxaban in Peripheral Artery Disease after Revascularization. New England Journal of Medicine. 2020;382(21):1994-2004. doi: 10.1056/NEJMoa2000052.



**Table 8: MAGELLAN Subpopulation Trial – Efficacy and Safety Outcomes**

The MAGELLAN subpopulation excluded patients with: history of bronchiectasis, pulmonary cavitation, or pulmonary hemorrhage, active cancer (i.e. undergoing acute, in-hospital treatment), active gastroduodenal ulcer in the three months prior to treatment, history of bleeding in the three months prior to treatment, or dual antiplatelet therapy.

Modified ITT - Day 35 Efficacy Outcomes	XARELTO N=2419	Enoxaparin/Placebo N=2506	RR (95% CI)
	n (%)		
Primary efficacy outcome (composite of asymptomatic proximal DVT, symptomatic proximal or distal DVT, symptomatic nonfatal PE, and VTE-related death)	94 (3.9%)	143 (5.7%)	0.680 (0.527-0.877)
Symptomatic lower-extremity DVT	9 (0.4%)	10 (0.4%)	-
Symptomatic nonfatal PE	7 (0.3%)	10 (0.4%)	-
Asymptomatic proximal DVT	73 (3.0%)	110 (4.4%)	-
VTE-related death	15 (0.6%)	26 (1.0%)	-
Per-Protocol - Day 10 Efficacy Outcomes	XARELTO N=2385	Enoxaparin N=2433	RR (95% CI)
	n (%)		
Primary efficacy outcome (composite of asymptomatic proximal DVT, symptomatic proximal or distal DVT, symptomatic nonfatal PE, and VTE-related death)	58 (2.4%)	72 (3.0%)	0.820 (0.583-1.154)
Symptomatic lower-extremity DVT	6 (0.3%)	4 (0.2%)	-
Symptomatic nonfatal PE	5 (0.2%)	2 (<0.1%)	-
Asymptomatic proximal DVT	52 (2.2%)	62 (2.5%)	-
VTE-related death	2 (<0.1%)	6 (0.2%)	-
Safety Population*	XARELTO N=3218	Enoxaparin/Placebo N=3229	RR (95% CI)
	n (%)		
Day 1 to 35*			
Clinically relevant bleeding	114 (3.5%)	49 (1.5%)	2.345 (1.685-3.264)
Major bleeding	22 (0.7%)	15 (0.5%)	1.480 (0.771-2.842)
CRNM bleeding	93 (2.9%)	34 (1.1%)	-
Fatal bleeding	3 (<0.1%)	1 (<0.1%)	-
Day 1 to 10*			
Clinically relevant bleeding	80 (2.5%)	35 (1.1%)	2.306 (1.556-3.418)
Major bleeding	13 (0.4%)	11 (0.3%)	1.191 (0.535-2.651)
CRNM bleeding	67 (2.1%)	24 (0.7%)	-
Fatal bleeding	1 (<0.1%)	1 (<0.1%)	-



Abbreviations: CI, confidence interval; CRNM, clinically relevant nonmajor; DVT, deep vein thrombosis; ITT, intent-to-treat; PE, pulmonary embolism; RR, risk reduction; VTE, venous thromboembolism.

\*On treatment +2 days

Spyropoulos AC, Lipardi C, Xu J, Lu W, Suh E, Yuan Z, et al. Improved Benefit Risk Profile of Rivaroxaban in a Subpopulation of the MAGELLAN Study. Clin Appl Thromb Hemost. 2019;25:1076029619886022. doi: 10.1177/1076029619886022. .

**Table 1. Summary of XARELTO® findings among Black NVAf Patients in a Real-World Observational EHR Study– Effectiveness and Safety Outcomes – Intention to Treat**

	<b>XARELTO® N=4102 Incidence (%/year)</b>	<b>Warfarin N=4102 Incidence (%/year)</b>	<b>Hazard Ratio (95% CI)</b>
Stroke or Systemic Embolism	1.99	2.48	0.77 (0.60-0.99)
Major Bleeding	4.22	4.98	0.84 (0.70-0.99)

Abbreviations: CI, confidence interval; HR, hazard ratio; NVAf, nonvalvular atrial fibrillation

A retrospective cohort analysis of adult African American patients with a diagnosis of NVAf who were anticoagulant-naïve during the 12-months prior to initiation of rivaroxaban or warfarin. Based on 1:1 propensity score matched analysis (4102 rivaroxaban and 4102 warfarin patients) using Optum® De-Identified Electronic Health Record (EHR) data from January 2012-September 2018. Patients were followed for up to 2-years or until a thrombotic or bleeding event, end of EHR activity or end of data availability (an intent-to-treat approach). Cohort risk was compared using doubly robust Cox regression models and reported as hazard ratios (HRs) with 95% confidence intervals (CIs).

Coleman CI, Thompson S, Ashton V, Palladino M, Bunz TJ. Rivaroxaban Versus Warfarin in African American Patients with Nonvalvular Atrial Fibrillation. *Journal of the National Medical Association*. 2020;112(4):395-401. doi: <https://doi.org/10.1016/j.jnma.2020.04.014>.

**Table 2. Summary of XARELTO® findings among Black VTE Patients in a Real-World Observational EHR Study - Effectiveness and Safety Outcomes – Intention to Treat**

	<b>XARELTO® N=2097 n (%)</b>	<b>Warfarin N=2842 n (%)</b>	<b>Hazard Ratio (95% CI)</b>
<b>3-month Follow-up</b>			
Composite of recurrent VTE or major bleeding	96 (4.58)	130 (4.57)	1.08 (0.82-1.42)
Recurrent VTE	74 (3.53)	96 (3.38)	1.07 (0.78-1.46)
Major Bleeding	27 (1.29)	40 (1.41)	1.19 (0.72-1.97)
<b>6-month Follow-up</b>			
Composite of recurrent VTE or major bleeding	105 (5.01)	166 (5.84)	0.96 (0.75-1.24)
Recurrent VTE	81 (3.86)	115 (4.05)	1.01 (0.76-1.36)
Major Bleeding	30 (1.43)	59 (2.08)	0.93 (0.59-1.47)
<b>12-month Follow-up</b>			
Composite of recurrent VTE or major bleeding	122 (5.82)	208 (7.32)	0.93 (0.74-1.16)
Recurrent VTE	89 (4.24)	140 (4.93)	0.95 (0.72-1.20)
Major Bleeding	39 (1.86)	80 (2.81)	0.92 (0.62-1.36)
<p>Abbreviations: CI, confidence interval; EHR, electronic healthcare record; HR, hazard ratio; VTE, venous thromboembolism</p> <p>Retrospective cohort analysis using Optum® De-Identified Electronic Health Record data from November 1, 2012 through September 30, 2018. African Americans admitted to the hospital, emergency department or observation unit for acute deep vein thrombosis or pulmonary embolism, who received rivaroxaban or warfarin as their first oral anticoagulant within 7-days of the acute event and had ≥1 provider visit in the 12-months prior were included in the study. Differences in baseline characteristics between cohorts were adjusted using inverse probability-of-treatment weighting (IPTW). Cohort risk was compared using Cox regression and reported as hazard ratios (HRs) with 95% confidence intervals (CIs).</p> <p>Costa OS, Thompson S, Ashton V, Palladino M, Bunz TJ, Coleman CI. Rivaroxaban versus warfarin for treatment and prevention of recurrence of venous thromboembolism in African American patients: a retrospective cohort analysis. Thrombosis Journal. 2020;18(1):6. doi: 10.1186/s12959-020-00219-w.</p>			



**Table 3 EINSTEIN Jr. Trial Findings**

Efficacy Outcome – Full Analysis Set	XARELTO* N=335	Comparator Group† N=165	XARELTO vs. Comparator Group Risk Difference (95% CI)	XARELTO vs. Comparator Group Hazard Ratio (95% CI)
	n (%)			
Primary efficacy outcome: Symptomatic recurrent VTE	4 (1.2)	5 (3.0)	-1.8% (-6.0%, 0.6%)	0.40 (0.11, 1.41)
Secondary efficacy outcome: Symptomatic recurrent VTE or asymptomatic deterioration on repeat imaging	5 (1.5)	6 (3.6)	-2.1% (-6.5%, 0.6%)	---
Safety Outcome – Safety Analysis Set – Main Treatment Period‡	XARELTO* N=329	Comparator Group† N=162	---	---
	n (%)		---	---
Major bleeding§	0	2 (1.2)	---	---
Clinically relevant non-major bleeding¶	10 (3.0)	1 (0.6)	---	---
Trivial bleeding	113 (34.3)	44 (27.2)	---	---
Any bleeding	119 (36.2)	45 (27.8)	---	---

Abbreviations: CI, confidence interval; VTE, venous thromboembolism

\*Treatment schedule: body weight-adjusted doses of XARELTO (exposures to match that of 20 mg daily dose in adults); randomized 2:1 (XARELTO: Comparator).

†Unfractionated heparin (UFH), low molecular weight heparin (LMWH), fondaparinux or VKA.

‡These events occurred after randomization until 3 months of treatment (1 month for patients <2 years with central venous catheter-related VTE (CVC-VTE). Patients may have more than one event.

§Defined as clinically overt bleeding associated with a decrease in hemoglobin of  $\geq 2$  g/dL, a transfusion of  $\geq 2$  units of packed red blood cells or whole blood, bleeding at a critical site, or with a fatal outcome.

¶¶Defined as clinically overt bleeding, which did not meet the criteria for major bleeding, but was associated with medical intervention, unscheduled contact with a physician, temporary cessation of treatment, discomfort for the patient, or impairment of activities of daily life.

Trial was not powered for statistical significance

Male C, Lensing AWA, Palumbo JS, Kumar R, Nurmeev I, Hege K, et al. Rivaroxaban compared with standard anticoagulants for the treatment of acute venous thromboembolism in children: a randomised, controlled, phase 3 trial. The Lancet Haematology. 2020;7(1):e18-e27. doi: [https://doi.org/10.1016/S2352-3026\(19\)30219-4](https://doi.org/10.1016/S2352-3026(19)30219-4).



**Table 4 UNIVERSE Trial Findings**

Efficacy Outcome – Full Analysis Set	Part A (single arm; not randomized)	Part B (Randomized 2 XARELTO:1 aspirin)		XARELTO vs. Aspirin Group Risk Difference (95% CI)
	XARELTO N=12	XARELTO* N=64	Aspirin* N=34	
	n (%)	n (%)		
Primary efficacy outcome: any thrombotic event	1 (8.3)	1 (1.6)	3 (8.8)	-7.3% (-21.7%, 1.1%)
Ischemic stroke	0	0	1 (2.9)	-2.9% (-16.2%, 2.9%)
Pulmonary embolism	0	1 (1.6)	0	1.6% (-9.9%, 8.4%)
Venous thrombosis	1 (8.3)	0	2 (5.9)	-5.9% (-20.6%, -0.1%)
Safety Outcomes – Safety Analysis Set – On Treatment Plus 2 days	XARELTO N=12	XARELTO* N=64	Aspirin* N=34	---
	n (%)	n (%)		---
Major Bleeding†	0	1 (1.6)	0	---
Clinically relevant non-major bleeding‡	1 (8.3)	4 (6.3)	3 (8.8)	---
Trivial bleeding	3 (25)	21 (32.8)	12 (35.3)	---
Any bleeding	4 (33.3)	23 (35.9)	14 (41.2)	---
Abbreviations: CI, confidence interval				
*Treatment schedule: body weight-adjusted doses of XARELTO (exposures to match that of 20 mg daily dose in adults); randomized 2:1 (XARELTO: Comparator).				
†Defined as clinically overt bleeding associated with a decrease in hemoglobin of ≥2 g/dL, a transfusion of the equivalent of ≥2 units of packed red blood cells or whole blood, bleeding at a critical site, or with a fatal outcome.				
‡Defined as clinically overt bleeding, which did not meet the criteria for major bleeding, but was associated with medical intervention, unscheduled contact with a physician, temporary cessation of treatment, discomfort for the patient, or impairment of activities of daily life.				
Trial was not powered for statistical significance				

McCrindle BW, Michelson AD, Bergen AHV, Horowitz ES, Sandoval JP, Justino H, et al. Thromboprophylaxis for Children Post-Fontan Procedure: Insights From the UNIVERSE Study. *Journal of the American Heart Association*. 2021;10(22):e021765. doi:10.1161/JAHA.120.021765.

Table 5 COMPASS CAD/PAD Trial Findings

Outcome	XARELTO plus Aspirin	Aspirin Alone	XARELTO plus Aspirin vs Aspirin Alone	
	n/N (%)		HR (95% CI)	P Value
Primary Efficacy Outcome (MI, stroke, CV death*) in COMPASS CAD/PAD Patients Overall and in Key Subgroups				
COMPASS Overall Population <sup>1</sup>	379/9152 (4.1)	496/9126 (5.4)	0.76 (0.66-0.86)	<0.001
COMPASS Diabetes <sup>2</sup>	179/3448 (5.2)	239/3474 (6.9)	0.74 (0.61-0.90)	---
COMPASS Moderate Renal Dysfunction (eGFR<60ml/min) <sup>3</sup>	132/2054 (6.4)	177/2114 (8.4)	0.75 (0.60-0.94)	---
COMPASS Obese (BMI≥30kg/m2) <sup>4</sup>	120/2872 (4.2)	181/2963 (6.1)	0.71 (0.57-0.86)	---
Primary Safety Outcome (major bleeding) in COMPASS CAD/PAD Patients Overall and in Key Subgroups				
COMPASS Overall Population <sup>1</sup>	288/9152 (3.1)	170/9126 (1.9)	1.70 (1.40-2.05)	<0.001
COMPASS Diabetes <sup>2</sup>	110/3448 (3.2)	65/3474 (1.9)	1.70 (1.25-2.31)	---
COMPASS Moderate Renal Dysfunction (eGFR<60ml/min) <sup>3</sup>	81/2054 (3.9)	57/2114 (2.7)	1.47 (1.05-2.07)	---
COMPASS Obese (BMI≥30kg/m2) <sup>4</sup>	91/2872 (3.2)	63/2963 (2.1)	1.59 (1.21-2.06)	---
Outcome	XARELTO plus Aspirin (N=8313)	Aspirin Alone (N=8261)	XARELTO plus Aspirin vs Aspirin Alone	
	n (%)		HR (95% CI)	P Value
Primary Efficacy, Safety, and Net Clinical Benefit Outcomes in the COMPASS Trial: Patients with CAD <sup>5</sup>				
MI, stroke, or CV death	347 (4)	460 (6)	0.74 (0.65-0.86)	<0.0001
Major bleeding	263 (3)	158 (2)	1.66 (1.37-2.03)	<0.0001
Net clinical benefit (CV death, stroke, MI, fatal bleeding, or symptomatic bleeding into critical organ) <sup>†</sup>	392 (5)	494 (6)	0.78 (0.69-0.90)	0.0003
Outcome	XARELTO plus Aspirin (N=2492)	Aspirin Alone (N=2504)	XARELTO plus Aspirin vs Aspirin Alone	
	n (%)		HR (95% CI)	P Value
Primary Efficacy, Safety, and Net Clinical Benefit Outcomes in the COMPASS Trial: Patients with PAD <sup>6</sup>				

CV death, stroke, MI	126 (5)	174 (7)	0.72 (0.57-0.90)	0.0047
Major bleeding	77 (3)	48 (2)	1.61 (1.12-2.31)	0.0089
Net clinical benefit (CV death, MI, stroke, and critical organ or fatal bleeding) <sup>‡</sup>	140 (6)	185 (7)	0.75 (0.60-0.94)	0.011

Abbreviations: CI, confidence interval; CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction.

\*P value for the primary efficacy outcome is confirmatory.

†Provisions to address multiple testing for subgroups, such as coronary artery disease, were not specified and, therefore, any HRs, corresponding CIs, and P values reported for subgroup analyses cannot be interpreted as statistically significant (Eikelboom JW et al. Rivaroxaban with or without aspirin in stable cardiovascular disease [Supplementary Appendix]. N Engl J Med. 2017;377(14):S1-S37.)

‡Prespecified net clinical benefit outcome.

1. Eikelboom JW, Connolly SJ, Bosch J, Dagenais GR, Hart RG, Shestakovska O, et al. Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease: from the COMPASS trial. N Engl J Med.
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### Table 6 VOYAGER-PAD Trial Findings

Outcome	XARELTO (N=3286)		Placebo (N=3278)		HR (95% CI)	P Value
	Patients with Event no. (%)	K-M Estimate at 3 years (%)	Patients with Event no. (%)	K-M Estimate at 3 years (%)		
Primary efficacy outcome*						
Composite of ALI, major amputation for vascular causes, MI, ischemic stroke, or death from CV causes	508 (15.5)	17.3	584 (17.8)	19.9	0.85 (0.76–0.96)	0.009
Outcome	XARELTO (N=3256)		Placebo (N=3248)		HR (95% CI)	P Value
	Patients with Event no. (%)	K-M Estimate at 3 years (%)	Patients with Event no. (%)	K-M Estimate at 3 years (%)		
Principal safety outcome†						
TIMI major bleeding	62 (1.90)	2.65	44 (1.35)	1.87	1.43 (0.97–2.10)	0.07

Abbreviations: ALI, acute limb ischemia; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; K-M, Kaplan-Meier; MI, myocardial infarction. TIMI, Thrombolysis in Myocardial Infarction.

\*Efficacy outcome analyzed on an intention-to-treat basis.

†Safety analysis included all patients who underwent randomization and had received at least one dose of trial medication (on-treatment).

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### Question 30

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**Public E2 Submission**

IPAY: 2026



Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	AARP
	Respondent Email	
	Who is completing this form?	PAT
Question 27: Prescribing Information	Prescribing Information	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
	Response to Question 29	

## Public E2 Submission

IPAY: 2026



Question	Sub-Question	Response
Question 29: Comparative Effectiveness on Specific Populations	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	
	Hyperlink to Citation - Additional Materials for Question 30	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	



## Public E2 Submission

IPAY: 2026



Question	Sub-Question	Response
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Question 31: Patient and Caregiver Experience	Response to Question 31	<p><b>Response</b></p> <p>AARP, which advocates for the more than 100 million Americans age 50 and over, is pleased to submit the following comments in response to the Centers for Medicare and Medicaid Services' (CMS) Medicare Drug Price Negotiation Program Patient-Focused Listening Sessions. AARP commends CMS for soliciting feedback from the public and appreciates its efforts to ensure that patients, caregivers, and health care providers have a voice in the negotiation process. ..Data shows that brand-name drug prices have increased dramatically faster than inflation for decades. List prices for the 25 brand-name drugs with the highest total Medicare Part D spending in 2021 have increased by an average of 226 - or more than tripled - since they first entered the market. Data also shows that all but one of the top 25 drugs' lifetime price increases greatly exceeded the corresponding annual rate of general inflation (Consumer Price Index All Urban Consumers for All Items; CPI-U) over the period that each product has been on the market (i.e., product launch date until May 2023). For example, the price of Enbrel (Etanercept), used to treat rheumatoid arthritis and psoriatic arthritis, has increased by 701% since coming to market in 1998, and the price of Januvia (Sitagliptin), used to treat diabetes, has increased by 275% since entering the market in 2006. Further, the median price of a new brand-name prescription drug is now approximately \$200,000 per year, so even relatively small percentage price increases can translate into thousands of dollars and put life-saving medications out of reach of the patients who need them...High prescription drug prices can negatively affect older adults' health and financial security. [REDACTED], a Medicare enrollee from [REDACTED], is living with a health condition and takes Xarelto to treat the condition. Earlier this year, [REDACTED] had to pay over \$400 for a 90-day supply of his prescription. "That price varies over the year. It was over \$600 when I was in the donut hole." [REDACTED] also witnesses older Americans leaving pharmacy counters without their prescriptions because they cannot afford them. "Older people trying to live on very limited fixed incomes, that just don't have the funds, and they're not taking their medications as they should. That leads to lower life expectancy and quality of life and just about every bad thing." ..AARP fiercely believes that the needs of Medicare beneficiaries should remain paramount as the agency implements the Negotiation Program. In 2022, about 1 in 5 adults ages 65 and up either skipped, delayed, took less medication than was prescribed, or took someone else's medication last year because of concerns about cost. It is not fair or right to ask patients and taxpayers to continue paying for high prescription drug prices that are the result of broken markets. ..Successful implementation of the new federal law will help reduce prescription drug prices and costs and ensure that millions of older Americans are better able to access the prescription drugs they need at a price they can afford. The Medicare drug price negotiation process will also finally allow CMS to push back on indiscriminately escalating drug prices and ensure that taxpayer funds are paying for value – all while saving billions for Medicare and its beneficiaries. The CBO estimates that the Negotiation Program will save Medicare and the American taxpayers nearly \$98.5 billion over 10 years, reduce the budget deficit by \$25 billion in 2031, and save Medicare Part D enrollees \$7 billion in 2031 due to lower out-of-pocket costs and premiums. ..This is about real people whose lives are on the line. For decades, older Americans have paid the highest prices in the world for prescription drugs - often three times higher than people in other countries. Now is the time to change that. Effective implementation of this Program will represent a major victory for older Americans and</p>
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# Public E2 Submission

IPAY: 2026



Question	Sub-Question
Question 32: Executive Summary	Response to Question 32

**Response**  
their families across the country who are struggling to afford their prescriptions. It will also help encourage and appropriately reward the development of truly innovative products. AARP stands ready to assist in any way with these and other efforts to bring down drug prices and help older Americans afford the medications and treatments they need. If you have any questions, please do not hesitate to contact me or Gidget Benitez at [gbenitez@aarp.org](mailto:gbenitez@aarp.org)...Sincerely, ..Nancy LeaMond.Executive Vice President and Chief Advocacy & Engagement Officer







October 2, 2023

Meena Seshamani, M.D., Ph.D.  
Director, Center for Medicare  
Centers for Medicare & Medicaid Services  
U.S. Department of Health and Human Services

Dear Dr. Seshamani:

AARP, which advocates for the more than 100 million Americans age 50 and over, is pleased to submit the following comments in response to the Centers for Medicare and Medicaid Services' (CMS) Medicare Drug Price Negotiation Program Patient-Focused Listening Sessions. AARP commends CMS for soliciting feedback from the public and appreciates its efforts to ensure that patients, caregivers, and health care providers have a voice in the negotiation process.

Data shows that brand-name drug prices have increased dramatically faster than inflation for decades. List prices for the 25 brand-name drugs with the highest total Medicare Part D spending in 2021 have increased by an average of 226%—or more than tripled—since they first entered the market.<sup>1</sup> Data also shows that all but one of the top 25 drugs' lifetime price increases greatly exceeded the corresponding annual rate of general inflation (Consumer Price Index All Urban Consumers for All Items; CPI-U) over the period that each product has been on the market (i.e., product launch date until May 2023).<sup>2</sup> For example, the price of Enbrel (Etanercept), used to treat rheumatoid arthritis and psoriatic arthritis, has increased by 701% since coming to market in 1998, and the price of Januvia (Sitagliptin), used to treat diabetes, has increased by 275% since entering the market in 2006.<sup>3</sup> Further, the median price of a new brand-name prescription drug is now approximately \$200,000 per year,<sup>4</sup> so even relatively small percentage price increases can translate into thousands of dollars and put life-saving medications out of reach of the patients who need them.

High prescription drug prices can negatively affect older adults' health and financial security. [REDACTED], a Medicare enrollee from [REDACTED], is living with a health condition and takes Xarelto to treat the condition. Earlier this year, [REDACTED] had to pay over \$400 for a 90-day supply of his prescription. "That price varies over the year. It was over \$600 when I was in the donut hole." [REDACTED] also witnesses older Americans leaving pharmacy counters without their prescriptions because they cannot afford them. "Older people trying to live on very limited fixed incomes, that

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<sup>1</sup> Leigh Purvis, "Prices for Top Medicare Part D Drugs Have More Than Tripled Since Entering the Market." Washington, DC: AARP Public Policy Institute, August 10, 2023. <https://doi.org/10.26419/ppi.00202.001>.

<sup>2</sup> *Id.*

<sup>3</sup> *Id.*

<sup>4</sup> Benjamin N. Rome, Alexander C. Egilman, and Aaron S. Kesselheim, "Trends in Prescription Drug Launch Prices, 2008–2021," *Journal of the American Medical Association* 327, no. 21 (2022): 2145–47, <https://jamanetwork.com/journals/jama/fullarticle/2792986>; Deena Beasley, "U.S. New Drug Price Exceeds \$200,000 Median in 2022," *Reuters*, January 5, 2023, <https://www.reuters.com/business/healthcare-pharmaceuticals/us-new-drug-price-exceeds-200000-median-2022-2023-01-05/>.

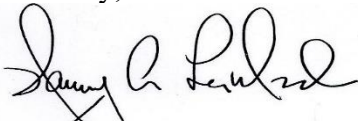
just don't have the funds, and they're not taking their medications as they should. That leads to lower life expectancy and quality of life and just about every bad thing."

AARP fiercely believes that the needs of Medicare beneficiaries should remain paramount as the agency implements the Negotiation Program. In 2022, about 1 in 5 adults ages 65 and up either skipped, delayed, took less medication than was prescribed, or took someone else's medication last year because of concerns about cost.<sup>5</sup> It is not fair or right to ask patients and taxpayers to continue paying for high prescription drug prices that are the result of broken markets.

Successful implementation of the new federal law will help reduce prescription drug prices and costs and ensure that millions of older Americans are better able to access the prescription drugs they need at a price they can afford. The Medicare drug price negotiation process will also finally allow CMS to push back on indiscriminately escalating drug prices and ensure that taxpayer funds are paying for value – all while saving billions for Medicare and its beneficiaries. The CBO estimates that the Negotiation Program will save Medicare and the American taxpayers nearly \$98.5 billion over 10 years,<sup>6</sup> reduce the budget deficit by \$25 billion in 2031,<sup>7</sup> and save Medicare Part D enrollees \$7 billion in 2031 due to lower out-of-pocket costs and premiums.<sup>8</sup>

This is about real people whose lives are on the line. For decades, older Americans have paid the highest prices in the world for prescription drugs - often three times higher than people in other countries. Now is the time to change that. Effective implementation of this Program will represent a major victory for older Americans and their families across the country who are struggling to afford their prescriptions. It will also help encourage and appropriately reward the development of truly innovative products. AARP stands ready to assist in any way with these and other efforts to bring down drug prices and help older Americans afford the medications and treatments they need. If you have any questions, please do not hesitate to contact me or Gidget Benitez at [gbenitez@aarp.org](mailto:gbenitez@aarp.org).

Sincerely,



Nancy A. LeaMond  
Executive Vice President and  
Chief Advocacy & Engagement Officer

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<sup>5</sup> Stacie B. Dusetzina et al., "Cost-Related Medication Nonadherence and Desire for Medication Cost Information Among Adults Aged 65 Years and Older in the US in 2022," *JAMA Network Open* 6, no. 5 (2023): e2314211, <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2805012>.

<sup>6</sup> Congressional Budget Office, "Estimated Budgetary Effects of Public Law 117-169, to Provide for Reconciliation Pursuant to Title II of S. Con. Res. 14," [https://www.cbo.gov/system/files/2022-09/PL117-169\\_9-7-22.pdf](https://www.cbo.gov/system/files/2022-09/PL117-169_9-7-22.pdf). Accessed September 27, 2023.

<sup>7</sup> Congressional Budget Office, "How CBO Estimated the Budgetary Impact of Key Prescription Drug Provisions in the 2022 Reconciliation Act," <https://www.cbo.gov/system/files/2023-02/58850-IRA-Drug-Provs.pdf>. Accessed September 27, 2023.

<sup>8</sup> *Id.*

**Public E2 Submission**

IPAY: 2026



Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	Aimed Alliance
	Respondent Email	
	Who is completing this form?	PAO
Question 27: Prescribing Information	Prescribing Information	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
	Response to Question 29	



## Public E2 Submission

IPAY: 2026



Question	Sub-Question	Response
Question 29: Comparative Effectiveness on Specific Populations	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	
	Hyperlink to Citation - Additional Materials for Question 30	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	

# Public E2 Submission

IPAY: 2026



Question	Sub-Question	Response
Question 31: Patient and Caregiver Experience	Response to Question 31	
Question 32: Executive Summary	Response to Question 32	





September 28, 2023

Chiquita Brooks-LaSure  
Administrator  
U.S. Centers for Medicare & Medicaid Services  
7500 Security Boulevard  
Baltimore, MD 21244

Re: IRA Patient Listening Sessions

Dear Administrator Brooks-LaSure:

Aimed Alliance is a not-for-profit health policy organization that seeks to protect and enhance the rights of health care consumers and providers. We are writing to express our concerns with the Inflation Reduction Act's (IRA) Medicare Drug Price Negotiation Program Patient-Focused Listening Sessions.

While we support efforts aimed at making prescription drugs more affordable for Medicare Part D beneficiaries, Aimed Alliance strongly urges the Centers for Medicare & Medicaid Services (CMS) to ensure the patient voice and perspective is valued in a genuine, long-term, and sustainable manner.

## **I. Background**

In August 2022, Congress passed the IRA, which provided CMS the authority to directly negotiate the prices of certain prescription drugs with drug manufacturers.<sup>1</sup> The negotiations are limited to single source drugs, without generic or biosimilar alternatives, that have been on the market for at least 7 years, or 11 years for biologics.<sup>2</sup> On August 29, 2023, CMS published a list of 10 prescription drugs that are subject to the Medicare negotiation process. These drugs cover treatments for cardiovascular diseases, diabetes, chronic kidney disease, psoriasis, rheumatoid arthritis, psoriatic arthritis, Crohn's disease, and ulcerative colitis.<sup>3</sup> CMS stated these drugs were identified as the ten most expensive covered Part D drugs.

In determining the negotiated price CMS will impose, CMS stated it will consider various factors, including comparative effectiveness and impact on specific populations, such as individuals with disabilities, the elderly, terminally ill patients, children, and others; and the extent to which the drug and its alternatives address an unmet medical need.<sup>4</sup> Aimed Alliance urges CMS to ensure patient and provider lived experiences are adequately valued when considering these factors and throughout this process.

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<sup>1</sup> CMS, *Fact Sheet: Key Information on the Process for the First Round of Negotiations for the Medicare Drug Price Negotiation Program*, <https://www.cms.gov/files/document/fact-sheet-negotiation-process-flow.pdf>

<sup>2</sup> *Id.*; CMS, *Medicare Drug Price Negotiation Program: Selected Drugs for Initial Price Applicability Year 2026*, <https://www.cms.gov/files/document/fact-sheet-medicare-selected-drug-negotiation-list-ipay-2026.pdf>

<sup>3</sup> *Id.*

<sup>4</sup> <https://www.cms.gov/files/document/fact-sheet-medicare-selected-drug-negotiation-list-ipay-2026.pdf>



## II. Appropriately Value Patient and Provider Lived Experiences

Aimed Alliance applauds CMS for incorporating patient and provider lived experiences in the drug negotiation process. However, we urge CMS to expand the current process to ensure a wider network of patients and providers can participate, and to guarantee patient and provider voices are genuinely valued.

Internationally, several countries employ mechanisms that allow governments to negotiate drug prices with manufacturers. For example, France and Sweden base drug pricing on factors such as therapeutic value, the price of comparable treatments, and the contributions of the drug's sales to the national economy.<sup>5</sup> Sweden further incorporates ethical considerations, prioritizing those with the greatest health care needs and ensuring the process upholds and respects individual human dignity.<sup>6</sup> By valuing the needs of patients and providers, Sweden maintains an overall high health care satisfaction rate.<sup>7</sup> In contrast, the United Kingdom, which also implements a government negotiation program, has seen reports of patients being unable to access innovative treatments that may improve their condition and quality of life due to non-patient-centered valuations.<sup>8</sup> As a result of failing to appropriately value patient-perspectives on the benefits of treatments, patients in the United Kingdom also experience reduced uptake of new cancer treatments.<sup>9</sup>

Ultimately, while various systems have provided means to center patient-perspectives and lived experiences, not all systems genuinely value these insights in determining drug prices, ultimately impacting treatment accessibility. Aimed Alliance urges CMS to properly value the lived experiences of patients, providers, and caregivers, and recognize the benefits these treatments provide to consumer's health and quality of life.

## III. Expand the Number of Listening Sessions to Ensure Diverse Representation

Under the current framework, CMS offers only one listening session for each selected prescription drug, with each session lasting less than two hours and accommodating only 20 in-person speakers. Members of the public who are not selected to speak also have the option to submit written comments.<sup>10</sup> Aimed Alliance urges CMS to expand the number of listening

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<sup>5</sup> David J. Gross, Jonathan Ratner, James Perez & Sarah Glavin, *International Pharmaceutical Controls: France, Germany, Sweden, and the United Kingdom*, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4193451/#:~:text=New%20product%20prices%20emerge%20from,sales%20to%20the%20national%20economy>.

<sup>6</sup> Global Legal Rights, *Pricing & Reimbursement Laws and Regulations 2023*, <https://www.globallegalinsights.com/practice-areas/pricing-and-reimbursement-laws-and-regulations/sweden>

<sup>7</sup> Roosa Tikkanen, et al., *Sweden Scorecard*, <https://www.commonwealthfund.org/international-health-policy-center/countries/sweden>; Keteven Kandelaki, *Patient-centeredness as a quality domain in Swedish healthcare: results from the first national surveys in difference Swedish health care setting*, <https://bmjopen.bmj.com/content/6/1/e009056>.

<sup>8</sup> Houses of Parliament: Parliamentary Office of Science & Technology, *Drug Pricing*, [https://www.parliament.uk/globalassets/documents/post/postpn\\_364\\_Drug\\_Pricing.pdf](https://www.parliament.uk/globalassets/documents/post/postpn_364_Drug_Pricing.pdf)

<sup>9</sup> *Id.*

<sup>10</sup> CMS, *Medicare Drug Price Negotiations Program Patient-Focused Listening Sessions*, <https://www.cms.gov/inflation-reduction-act-and-medicare/medicare-drug-price-negotiation-program-patient-focused-listening-sessions>

sessions to ensure patients, organizations, and caregivers have the opportunity to speak on behalf of their communities.

The 20 speakers selected to participate in each session are requested to address patients' day-to-day experiences living with their condition and under their treatment; the benefits and side effects of the treatments; patient access, adherence, and affordability; and any additional information the speaker considers significant.<sup>11</sup> While Aimerd Alliance believes this information is crucial for appropriately determining the negotiated prices, we are concerned that relying on 20 randomly selected speakers will not provide CMS with a comprehensive perspective on these medications and their benefits to patients, providers, and caregivers. We are also concerned that this random selection process could unintentionally exclude speakers who shed light on health equity, minority health, and other access issues.<sup>12</sup> Therefore, we urge CMS to expand the number of listening sessions to ensure CMS appropriately considers the broad implications and health equity considerations of these treatments; and how these price negotiations could impact access for diverse communities.

Lastly, we strongly encourage CMS to value and give due consideration to both written and spoken comments provided by patient advocacy organizations. Individuals with chronic illnesses such as multiple sclerosis and inflammatory bowel disease (IBD) frequently experience social stigma, rejection, and workplace discrimination resulting from their condition.<sup>13</sup> For instance, one study found that out of 105 patients with IBD, 84 percent reported experiencing stigma associated with their condition.<sup>14</sup> Consequently, it is critical to recognize that some individuals with chronic conditions may not feel comfortable discussing their health, treatments, and challenges openly. As a result, they often rely on advocacy organizations to share their stories, perspectives, and experiences.

#### **IV. Conclusion**

In conclusion, we sincerely appreciate the opportunity to provide feedback on the IRA process and CMS's efforts to ensure the voices of patients, providers, and caregivers are at the forefront of this process. Please contact us at [policy@aimedalliance.org](mailto:policy@aimedalliance.org) if you have any additional questions.

Sincerely,  
Ashira Vantrees  
Counsel

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<sup>11</sup> *Id.*

<sup>12</sup> Khiara Bridges, *Implicit Bias and Racial Disparities in Health Care*, [https://www.americanbar.org/groups/crsj/publications/human\\_rights\\_magazine\\_home/the-state-of-healthcare-in-the-united-states/racial-disparities-in-health-care/](https://www.americanbar.org/groups/crsj/publications/human_rights_magazine_home/the-state-of-healthcare-in-the-united-states/racial-disparities-in-health-care/)

<sup>13</sup> Valerie A Earnshaw, Diane M. Quinn & Crystall L. Park, *Anticipated stigma and quality of life among people living with chronic illnesses*, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3644808/>

<sup>14</sup> Marco Vinenzco Lenti, et al., *Stigmatization and resilience in inflammatory bowel disease patients at one-year follow up*, <https://www.frontiersin.org/articles/10.3389/fgstr.2022.1063325/full>

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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	Chronic Care Policy Alliance
	Respondent Email	
Question 27: Prescribing Information	Who is completing this form?	PAO The Chronic Care Policy Alliance (CCPA) is a network of advocates focused on issues affecting patients living with chronic conditions. While we will let other disease-specific organizations offer their detailed perspectives on this drug, CCPA wishes to convey its views on how CMS should use the information gathered from the public. ..As CMS weighs information on how this product is prescribed and factors that information into the negotiation process, CMS should ensure that the negotiated price continues to support the patients using the product and their current usage. Patients using the product off-label or in different doses than the label should continue to have the same access after the negotiation process. Additionally, ensuring that the negotiation does not spur greater restrictions to access or utilization management, is also important to patients.
	Prescribing Information	
	Evidence Submitted include a cost-effectiveness measure?	N
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	The Chronic Care Policy Alliance (CCPA) is a network of advocates focused on issues affecting patients living with chronic conditions. While we will let other disease-specific organizations offer their detailed perspectives on this drug, CCPA wishes to convey its views on how CMS should use the information gathered from the public...As CMS weighs information on the therapeutic impact and comparative effectiveness of this product, it is paramount that CMS recognize that individual patients may experience substantial benefit from a product that may not be apparent in aggregated data. Because of this, as CMS considers how this area factors into the overall price negotiation, CMS should ensure a negotiated price reflects the value the product provides to each unique patient. CCPA believes it is important that the incentives to continue developing treatments for chronic diseases be preserved, and it is important to reward the value treatments bring to patients.



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Question	Sub-Question	Response
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	
	Evidence Submitted include a cost-effectiveness measure?	N
	What type of Evidence is shown?	
	Response to Question 29	<p>The Chronic Care Policy Alliance (CCPA) is a network of advocates focused on issues affecting patients living with chronic conditions. While we will let other disease-specific organizations offer their detailed perspectives on this drug, CCPA wishes to convey its views on how CMS should use the information gathered from the public...Patients with chronic diseases all have their own unique experiences – in considering comparative effectiveness, CMS should weigh equally the experiences of individuals the same as measurements of experiences of specific populations – in a way that elevates all voices, instead of letting larger voices outweigh single patients. CCPA also encourages CMS to take into account populations that may be uniquely adversely affected by negotiation, such as specific patient populations that may face new utilization or formulary restrictions. In this way, CMS can ensure that it pursues a patient-centered approach.</p>
Question 29: Comparative Effectiveness on Specific Populations	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	N



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Question	Sub-Question	Response
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	The Chronic Care Policy Alliance (CCPA) is a network of advocates focused on issues affecting patients living with chronic conditions. While we will let other disease-specific organizations offer their detailed perspectives on this drug, CCPA wishes to convey its views on how CMS should use the information gathered from the public...CMS should ensure that its negotiation process on this product does not disadvantage any patient with an unmet medical need. Specifically, CMS should guard against the results of negotiations undercutting research into the product that may meet other unmet medical needs or may negatively impact the development of other products focused on unmet medical needs.
	Hyperlink to Citation - Additional Materials for Question 30	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	N
	What type of Evidence is shown?	
Question 31: Patient and Caregiver Experience	Response to Question 31	
Question 32: Executive Summary	Response to Question 32	



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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	
	Respondent Email	
	Who is completing this form?	HCW
Question 27: Prescribing Information	Prescribing Information	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
	Response to Question 29	

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Question	Sub-Question	Response
Question 29: Comparative Effectiveness on Specific Populations	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	
	Hyperlink to Citation - Additional Materials for Question 30	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	



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Question	Sub-Question	Response
Question 31: Patient and Caregiver Experience	Response to Question 31	
Question 32: Executive Summary	Response to Question 32	<p>Thank you for the opportunity to provide comments on rivaroxaban for the Medicare Drug Price Negotiation Program for initial price applicability year 2026. ..I am a cardiologist based in Memphis, TN and serve patients in both Tennessee and Mississippi. I am a fellow of the National Lipid Association, the American Society for Preventive Cardiology, the American College of Cardiology and serve on a number of boards supporting cardiovascular patients and providers. . .The state of Mississippi, where most of my patients call home, has the worst rates of cardiovascular disease and cardiovascular death in the country. My colleagues and I oftentimes feel that we are on the front lines battling the #1 killer not only in our state, but in the country as well. Having therapies available to treat my patients is of the utmost importance, and rivaroxaban has provided and continues to provide immense value for my patients. ..Rivaroxaban is a Factor Xa inhibitor, novel oral anticoagulant (NOAC), used to treat and manage deep vein thrombosis (DVT). It is also used postoperatively to prevent blood clots and stroke in patients with atrial fibrillation and is used in secondary prevention of acute coronary syndrome and peripheral artery disease. Compared with warfarin, NOACs are associated with a statistically significant risk reduction in thromboembolic stroke (20-29% reduction) intracranial hemorrhage (35-62% reduction) and mortality (19-34% reduction).<sup>1</sup> Fewer people in America have strokes, pulmonary embolism and deep vein thrombosis as a result. ..I am grateful that the legislation that promulgated the Medicare Drug Price Negotiation Program capped out-of-pocket maximums for drugs and created a mechanism that America's seniors can pay down their deductible over the course of a plan year. However, I must impress upon you that any cost savings that are negotiated through this program must be passed to the patient. Individuals that I treat who are on agents like Entresto often have comorbidities and are taking many medications to treat their cardiovascular disease and/or metabolic conditions. If cost savings from this program are not passed to the patient, then patient-centered care is transparently not the goal of the program. Furthermore, if access to these medications is limited as a result of this program, the results could be disastrous for patient health and outcomes. Please ensure that access remains open. ..Thank you. ...1. Graham DJ, Baro E, Zhang R, Liao J, Wernecke M, Reichman ME, Hu M, Illoh O, Wei Y, Goulding MR, Chillarige Y, Southworth MR, MaCurdy TE, Kelman JA. Comparative Stroke, Bleeding, and Mortality Risks in Older Medicare Patients Treated with Oral Anticoagulants for Nonvalvular Atrial Fibrillation. Am J Med. 2019 May;132(5):596-604.e11. doi: 10.1016/j.amjmed.2018.12.023. Epub 2019 Jan 9. PMID: 30639551.</p>



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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	Advancecardiohealth.org
	Respondent Email	
	Who is completing this form?	PAT
Question 27: Prescribing Information	Prescribing Information	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
	Response to Question 29	

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Question	Sub-Question	Response
Question 29: Comparative Effectiveness on Specific Populations	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	
	Hyperlink to Citation - Additional Materials for Question 30	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	





Question	Sub-Question	Response
Question 31: Patient and Caregiver Experience	Response to Question 31	<p>Thank you for allowing me the opportunity to comment on the Medicare Drug Price Negotiation Program...I have taken Xarelto since 2013 to prevent blood clots after being diagnosed with atrial fibrillation. I can directly credit Xarelto for improving my quality of life and keeping me active in a variety of groups, such as Voices of AFIB Patients, the Partnership to Advance Cardiovascular Health, StopAfib.org, and PCORI Alumnus...I was excited when I heard about the Medicare Drug Price Negotiation Program, because of the program's aim to make specific medicines more affordable for our nation's seniors. I am a Medicare beneficiary myself, and though lower costs sound nice, I am extremely concerned that the negotiations will result in me being nonmedically switched from Xarelto to another drug. ..I have only tried one other medicine since my diagnosis. I took Eliquis for one week in preparation for my second ablation. I did not experience any difference in effectiveness, but it was notably more inconvenient for me, as Eliquis must be taken twice a day as opposed to just once a day like Xarelto. This might sound like a simple issue of convenience but is not that simple. Missing a dose puts patients at risk of developing blood clots, which can lead to stroke. Particularly among Medicare patients, having convenient and effective options is crucial to maximizing health. ..Furthermore, Xarelto is more cost effective for me compared to Eliquis. I do not want to be moved to a less effective and/or more expensive option, and I am very concerned that will happen under the current guidelines. CMS must ensure patients are at the center of the conversation and incorporate each patient's feedback into the negotiation process. CMS must ensure utilization management techniques, like step therapy, non-medical switching, and prior authorization, are not used to withhold medicines from patients. Medicine choices should be solely a decision between the Doctor and the Patient.</p>
Question 32: Executive Summary	Response to Question 32	



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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	
	Respondent Email	
	Who is completing this form?	HCW
Question 27: Prescribing Information	Prescribing Information	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
	Response to Question 29	

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Question	Sub-Question	Response
Question 29: Comparative Effectiveness on Specific Populations	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	
	Hyperlink to Citation - Additional Materials for Question 30	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	



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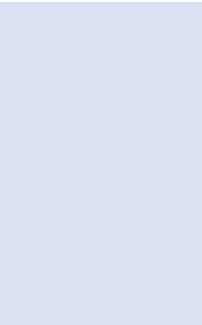
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Question	Sub-Question	Response
Question 31: Patient and Caregiver Experience	Response to Question 31	<p>Thank you for affording the opportunity for clinicians and patients to comment on the Centers for Medicare and Medicaid Services (CMS) Drug Price Negotiation Program for implementation in year 2026...My name is [REDACTED], PharmD, PhC, CACP, and I serve as [REDACTED].</p> <p>[REDACTED] Over my career, I have published extensively on anticoagulation, thrombosis and bleeding management. [REDACTED]</p> <p>[REDACTED] ..The AC Forum includes more than 13,000 physicians, nurses, and pharmacists representing over 3,000 anticoagulation services (clinics). Our members directly support over 1 million patients annually. Founded 30 years ago, the Anticoagulation Forum is the largest organization of anticoagulation management specialists working to improve the quality of care for patients taking antithrombotic medications by educating healthcare professionals and advocating for clinical best practices. ..As you know, the number of Medicare beneficiaries using direct oral anticoagulants (DOACs) has risen considerably in the last 15 years. The reasons for this increase are numerous: Atrial fibrillation (AF) is the most common cardiac arrhythmia in the United States, and patients with AF are five times more likely to experience an ischemic stroke. Venous thromboembolism is the third most common life-threatening cardiovascular disease in the United States. DOACs like rivaroxaban prevent blood clots and prevent stroke in people with nonvalvular atrial fibrillation and are the mainstay treatment for deep vein thrombosis and pulmonary embolism. For example, one major trial demonstrated a significant reduction in the rate of stroke and systemic embolism with rivaroxaban, while also significantly reducing life-threatening intracranial hemorrhage and fatal bleeding as compared to warfarin. DOACs are safe, effective and have far fewer side effects than warfarin for most patients. They also offer fewer drug-drug interactions and provide value for both patients and the healthcare system. For example, in contrast to warfarin, they do not require frequent clinic appointments and/or routine monitoring, both of which have associated financial and social costs that must be considered. ..I believe that provisions in the Inflation Reduction Act (IRA) are well-intentioned and will help Medicare beneficiaries. Making drugs affordable for patients is essential, and I know that patients will benefit from the out-of-pocket maximum provision and the deductible smoothing mechanism. In order for price negotiation to have the most benefit for patients, however, savings achieved through IRA negotiations must be realized by patients rather than within prescription benefit managers (PBMs). Most importantly, equal access to all therapeutic options should be available for shared decision-making between patients and prescribers and decisions should not be driven by outside influences (i.e., insurance companies, non-medical switching, etc.) It</p>
Question 32: Executive Summary	Response to Question 32	



Question	Sub-Question
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	<p><b>Response</b></p> <p>is of the utmost importance that CMS can ensure that, through this process, patients can retain access to the therapy decided upon between the patient and their prescriber. ..Lastly, it is important to emphasize that increased access to medications will inevitably be tied to increased prescribing. At present, more than 5 million people in the US are prescribed an anticoagulant, a number that is anticipated to at least double by 2050 due to secular trends in the population. Concerningly, anticoagulants are the leading cause of emergency department visits and hospital readmissions due to anticoagulant-associated bleeding or thrombotic events. Hence, it is imperative that increased access and prescribing be closely coupled with improved anticoagulant care delivery models such as anticoagulation stewardship which has been shown to improve patient safety and outcomes.</p>
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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	StopAfib.org
	Respondent Email	
	Who is completing this form?	PAT
Question 27: Prescribing Information	Prescribing Information	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
	Response to Question 29	



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Question	Sub-Question	Response
Question 29: Comparative Effectiveness on Specific Populations	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	
	Hyperlink to Citation - Additional Materials for Question 30	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	

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Question	Sub-Question	Response
Question 31: Patient and Caregiver Experience	Response to Question 31	<p>Thank you for the opportunity to share my experience as an afib patient on oral anticoagulants and that of other afib patients on rivaroxaban. ..Warfarin was our only option before the DOACs (rivaroxaban, apixaban, edoxaban, and dabigatran). But, I was never stable on it. My International Normalized Ratio (INR) would swing wildly between too low (risk of a clot/stroke) and too high (risk of a bleed); I often required multiple blood draws per week to adjust my dose, which took many hours away from work and family. ..In 2005, research showed that one-fourth of those on warfarin were unstable for genetic reasons. I finally understood why I had been through such challenges when it seemed to work fine for others. In talking with afib patients, I found that these challenges with being stable on warfarin appeared to be much more common in women than men. ..Additionally, with warfarin, you must avoid or consistently consume foods containing Vitamin K (i.e., green vegetables). You spend countless hours managing your diet. Warfarin has numerous drug interactions, too. And side effects such as hair loss (falling out in chunks) were common with warfarin...The DOACs were lifesavers – few food and drug interactions and no testing – so we regained our lives and freedom. ..However, pharmacy benefits managers (PBMs) brought back our nightmares. In 2022, one of the largest PBMs dropped three DOACs from their formulary. Hence, patients either paid 100%, applied for Prior Authorizations, or changed meds, returning them to warfarin nightmares. ..As a result of these price negotiations, Prior Authorizations are likely to become even more pervasive and pernicious as payers seek to recapture margins eroded by subsidizing a more significant portion of drug costs. ..My experience with Prior Authorizations is an example of how this hurts patients. As a heart disease patient, I have been on a statin drug for two decades. I tried the generic when my statin went off-patent, and the brand was removed from the formulary. Within two days, my right (dominant) hand was paralyzed; within days of stopping it, I regained the use of my hand. My doctor then requested a Prior Authorization for me to continue on the brand I had been stable on for years. That was approved for several years but has been denied in the past two years. Since then, I have wasted 40-60 hours per year on Prior Authorizations. Most patients cannot spend that time dealing with this (and the stress of doing so is aging me). Last year, my Prior Authorization was denied multiple times, and we went all the way to an Administrative Law Judge Hearing, where the judge found in my favor. Even after that, the insurer has rejected it numerous times this year. ..I am now out of this lifesaving medication. I must wait until next year to try again for Prior Authorization (or take the generic that paralyzed my hand). These games are killing people. I do not want to be one of them, but I cannot afford to pay 100% of the cost of the brand statin I had been stable on for two decades. ..We patients are asking CMS to engage with us throughout this negotiation process and protect us from abusive payers and PBMs. ..While Part D plans must cover drugs selected for negotiation, we fear they will find a way (Tier 4 or non-medical switching) to either make patients pay most of the cost or reduce our access to them and our other medications. They are already working on such strategies; many patients have just received notice that 2024 Part D premiums are doubling. ..These negotiations will pressure PBMs to non-medically switch us (playing doctor once again), which is deadly for us. With many afib patients being on beta blockers that cause confusion, being non-medically switched among different anticoagulant dosing regimens can result in overdosing or underdosing, thus leading to deadly bleeds</p>

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Question

Sub-Question

Response

and strokes. ..Please protect us from these catastrophic consequences caused by payers/PBMs decreasing our access to lifesaving meds...Thank you.

Question 32:  
Executive  
Summary

Response to Question 32





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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	Institute for Clinical and Economic Review
	Respondent Email Who is completing this form?	NAR
Question 27: Prescribing Information	Prescribing Information	<p>1.1. Introduction..As a result of the Inflation Reduction Act (IRA), the Centers for Medicare &amp; Medicaid Services (CMS) will soon begin negotiating prices for certain high-expenditure drugs. This submission examines the direct-acting oral anticoagulants (DOACs) apixaban (Eliquis®, Bristol Myers Squibb / Pfizer) and rivaroxaban (Xarelto®, Janssen Pharmaceuticals, Inc.), two of the 10 drugs that CMS has selected for negotiation in the first round. The information in the submission is tailored to reflect legislative specifications in the IRA and subsequent CMS guidance. It is not comprehensive but does include sections on multiple elements related to drug value, providing different options for translating evidence into initial offer prices and for assessing counteroffers from drug makers. We focused on the use of these two drugs for non-valvular atrial fibrillation (NVAf) since that represents the vast majority of use for drugs in this class. As clinical and cost comparators, we selected warfarin, an older generic medication that was the standard therapy for atrial fibrillation prior to the DOACs, and dabigatran, which is the first DOAC available as a generic medication as of 2022...These DOACs have several FDA indications. However, data suggest that the vast majority of DOAC use is for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation (NVAf) [IPD Analytics, 2021]. CMS will be able to use its own data to confirm the relative percentage of use of apixaban and rivaroxaban for different indications. ..Specialty society guidelines (e.g., the American College of Chest Physicians [CHEST] guidelines) suggest that the use of these medications for NVAf be guided by the risk for stroke using one of two risk prediction tools: the CHADS<sub>2</sub> score (one point for each of congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and one points for stroke) or an updated version: the CHA<sub>2</sub>DS<sub>2</sub>-VASc score which adds three additional risk factors (vascular disease [coronary artery disease, peripheral artery disease, aortic atherosclerosis], age 65-74 years, and female sex). The benefits of stroke prevention with these medications are balanced by the risk for bleeding, which is most commonly estimated using the HAS-BLED score (one point for each risk factor: hypertension, abnormal renal and liver function, stroke, bleeding, labile INR [international normalized ratio], elderly, drugs or alcohol). For all three risk prediction tools, higher scores correspond to higher risk for the predicted outcome...1.2. Prescribing Information..The prescribing information for the four drugs is summarized below.</p>

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		<ul style="list-style-type: none"><li>• Apixaban (Eliquis®, Bristol Myers Squibb / Pfizer)</li><li>• Mechanism of Action: Factor Xa inhibitor</li><li>• Dose: 2.5 or 5 mg by mouth twice daily. For NVAf, 5 mg orally twice daily. In patients with at least two of the following characteristics: age greater than or equal to 80 years, body weight less than or equal to 60 kg, or serum creatinine greater than or equal to 1.5 mg/dL, the recommended dose is 2.5 mg orally twice daily.</li><li>• Indication:</li><li>• Reduce the risk of stroke and systemic embolism in patients with NVAf</li><li>• Prophylaxis of deep vein thrombosis (DVT) in patients who have undergone knee or hip replacement</li><li>• Treatment of DVT and pulmonary embolism (PE) and to reduce the risk of recurrent DVT and PE</li></ul> <ul style="list-style-type: none"><li>• Rivaroxaban (Xarelto®, Janssen Pharmaceuticals Inc.)</li><li>• Mechanism of Action: Factor Xa inhibitor.o Dose: 15 or 20 mg by mouth once daily with food</li><li>• Indications:</li><li>• To reduce risk of stroke and systemic embolism in nonvalvular atrial fibrillation</li><li>• For treatment of DVT</li><li>• For treatment of PE</li><li>• For reduction in the risk of recurrence of DVT or PE</li><li>• For the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery</li><li>• For prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients</li><li>• To reduce the risk of major cardiovascular events in patients with CAD</li><li>• To reduce the risk of major thrombotic vascular events in patients with PAD, including patients after recent lower extremity revascularization due to symptomatic PAD</li><li>• For treatment of VTE and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years</li><li>• For thromboprophylaxis in pediatric patients two years and older with congenital heart disease after the Fontan procedure</li></ul> <ul style="list-style-type: none"><li>• Warfarin</li><li>• Mechanism of Action: Vitamin K antagonist</li><li>• Dose: By mouth once daily with individualized dosing regimen based on INR results</li><li>• Indications:</li><li>• Prophylaxis and treatment of venous thrombosis and its extension, pulmonary embolism</li></ul>



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		<ul style="list-style-type: none"> <li>• Prophylaxis and treatment of thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement</li> <li>• Reduction in the risk of death, recurrent myocardial infarction, and thromboembolic events such as stroke or systemic embolization after myocardial infarction</li> <li>• Dabigatran</li> <li>• Mechanism of Action: Direct thrombin inhibitor</li> <li>• Dose: 75 or 150 mg by mouth once daily. For NVAf: 150 mg orally, twice daily for patients with CrCl &gt;30 mL/min or 75mg orally, twice daily for patients with CrCl 15-30 mL/min.</li> <li>• Generics first approved on March 11, 2020 (Alkem Labs LTD) and May 6, 2020 (Hetero Labs LTD), and launched in 2022</li> <li>• Indications:</li> <li>• To reduce the risk of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation</li> <li>• For the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in adult patients who have been treated with a parenteral anticoagulant for 5-10 days</li> <li>• To reduce the risk of recurrence of DVT and PE in adult patients who have been previously treated</li> <li>• For the prophylaxis of DVT and PE in adult patients who have undergone hip replacement surgery</li> <li>• For the treatment of venous thromboembolic events (VTE) in pediatric patients 8 to less than 18 years of age who have been treated with a parenteral anticoagulant for at least 5 days</li> <li>• To reduce the risk of recurrence of VTE in pediatric patients 8 to less than 18 years of age who have been previously treated</li> </ul>
	<p>Evidence Submitted include a cost-effectiveness measure?</p> <p>What type of Evidence is shown?</p>	N
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	<p>3.1. Interventions and Therapeutic Alternatives..To estimate the comparative therapeutic impact of apixaban and rivaroxaban in NVAf, we compared each drug to both warfarin and dabigatran...3.2. Comparative Clinical Effectiveness..3.2.1. Methods Overview..We focused on patient-important outcomes and adverse events, including stroke/systemic embolism (SE), myocardial infarction (MI), bleeding rates, and all-cause mortality. Outcome definitions are reported in Supplement Table A1.(1) For comparisons with warfarin, we focused on head-to-head randomized controlled trials (RCTs) with the interventions of interest. For comparisons with dabigatran, we conducted Bayesian network meta-analyses (NMAs) of RCTs. We also reviewed evidence from high-quality observational studies on long-term outcomes and harms. The full scope and procedures for the</p>

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		<p>systematic literature review are detailed in the Supplement.(1)..Evidence Base..We examined direct evidence comparing apixaban and rivaroxaban with warfarin from the ARISTOTLE and ROCKET AF trials, respectively. We used the RE-LY trial of dabigatran versus warfarin to conduct indirect analyses comparing the DOACs. These trials are described in the Supplement and in Table 3.1...3.2.2. Results..Clinical Benefits..Apixaban..Direct Evidence: Apixaban versus Warfarin..In the ARISTOTLE trial, patients receiving apixaban had a lower rate of stroke/SE (1.27% per year) compared to those in the warfarin group (1.6%) (HR: 0.79; 95% CI: 0.66 to 0.95; p=0.02). Risk of MI with apixaban was not statistically significantly different from that with warfarin (HR: 0.88; 95% CI: 0.66 to 1.17; p=0.37). The rate of all-cause mortality was lower in the apixaban group compared to the warfarin group (HR: 0.89; 95% CI: 0.80 to 0.998; p=0.047).(2) ..Indirect Evidence: Apixaban versus Dabigatran ..Tables 3.2 and 3.3 provide point estimates of the relative effect of apixaban and rivaroxaban versus dabigatran and warfarin for the NMA outcomes. Risk of stroke/SE with apixaban was not statistically significantly different from that with dabigatran (HR: 1.2; 95% CrI: 0.9 to 1.59). In contrast, apixaban was more efficacious than dabigatran in reducing MI (HR: 0.64; 95% CrI: 0.41 to 0.98). There was no difference in all-cause mortality (HR: 1.01; 95% CrI: 0.85 to 1.2)...Rivaroxaban..Direct Evidence: Rivaroxaban versus Warfarin..In the ROCKET AF trial, patients receiving rivaroxaban had a lower rate of stroke/SE (1.7% per year) compared to those in the warfarin group (2.2%) (HR: 0.79; 95% CI: 0.66 to 0.96; p=0.02). The risk of MI and all-cause mortality were not statistically significantly lower, but the point estimates favored rivaroxaban (MI HR: 0.81; 95% CI: 0.63 to 1.06; p=0.12; mortality HR: 0.85; 95% CI: 0.70 to 1.02; p=0.07). ..Indirect Evidence: Rivaroxaban versus Dabigatran ..The risk of stroke/SE with rivaroxaban was not statistically significantly different from that with dabigatran (HR: 1.2; 95% CrI: 0.89 to 1.6); however, the risk of MI was lower (HR: 0.59; 95% CrI: 0.38 to 0.9). There was no statistically significant difference in all-cause mortality (HR: 0.97; 95% CrI: 0.77 to 1.21)...All other outcomes are reported in Supplement D.(1) ..Harms..Apixaban ..In the ARISTOTLE trial, the rate of major bleeding was lower in the apixaban group compared to the warfarin group (2.13% vs. 3.09% per year, HR: 0.69; 95% CI: 0.60 to 0.80; p&lt;0.001), as was intracranial bleeding (HR: 0.42; 95% CI: 0.30 to 0.58), though absolute rates were small.(2) Estimates from the NMA reported that the risk of major bleeding was lower with apixaban compared to dabigatran (HR: 0.74; 95% CrI: 0.61 to 0.91), but there was no difference for intracranial bleeding (HR: 1.05; 95% CrI: 0.63 to 1.77). See Table 3.5 and Supplement Table D2.5...Patients in the apixaban arm of ARISTOTLE were less likely to discontinue the study drug (Table 3.4), but the absolute difference was small. Results of the NMA showed that apixaban had lower total discontinuation and discontinuation due to AEs compared to dabigatran (Supplement Tables D2.9 and D2.10)...Rivaroxaban ..In the ROCKET AF trial, the rate of major bleeding was similar in the rivaroxaban and warfarin groups. Patients receiving rivaroxaban had a lower rate of intracranial bleeding (HR: 0.67; 95% CI: 0.47 to 0.93), though absolute rates were small.(3) The NMA results for rivaroxaban versus dabigatran showed no statistically significant difference in major bleeding (HR: 1.12; 95% CrI: 0.92 to 1.37) or intracranial bleeding (HR: 1.67; 95% CrI: 0.99 to 2.82)...Patients in the rivaroxaban arm of ROCKET AF were more likely to discontinue the study drug and discontinue due to AEs compared with warfarin, though the absolute differences were small. The NMA results for rivaroxaban versus</p>



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	<p><b>Response</b></p> <p>dabigatran showed lower rates for total discontinuation and discontinuation due to AEs for rivaroxaban...See Supplement D for additional NMA results for harms and discontinuation.(1)..Observational Data..Two large high-quality observational studies were identified that examined long-term safety and effectiveness of apixaban and rivaroxaban.(4-6) These studies used propensity scoring to account for confounding, and are described in detail in Supplement D...Findings in Lau et al. (N=527,226) comparing both drugs to dabigatran in a multinational sample (US, UK, France, and Germany) were generally similar to those in our NMAs with the following exceptions (4):</p> <ul style="list-style-type: none"> <li>• Lower relative major gastrointestinal bleeding risk with apixaban (HR: 0.81; 95% CI: 0.70 to 0.94)</li> <li>• Higher relative point estimates for all-cause mortality with apixaban (HR: 1.22; 95% CI: 0.94 to 1.60) and with rivaroxaban (HR: 1.16; 95% CI: 0.89-1.59), although these were non-significant with relatively wide confidence intervals.</li> <li>• Higher relative major gastrointestinal bleeding risk with rivaroxaban (HR: 1.15; 95% CI: 1.04 to 1.28)</li> </ul> <p>Findings in Chan et al. (N=106,044) comparing both drugs to warfarin in a Taiwanese sample found both apixaban and rivaroxaban were associated with a significantly higher risk of interstitial lung disease (ILD) compared to warfarin, though the absolute risk was low (0.29 per 100 person years with DOACs, 0.17 per 100 person years with warfarin).(5) Observational studies cannot prove causality, but ILD cannot be ruled out as a potential rare complication of DOACs. ..Findings from Graham et al. (N=134,414) comparing dabigatran and warfarin (comparators of interest) in a sample of Medicare patients are reported in the supplement.(1, 6)..Uncertainty and Controversies..Indirect analyses were necessary to compare apixaban and rivaroxaban to dabigatran. This increases the uncertainty in the findings. Our NMA results are similar to those observed in the large observational study identified that compares the DOACs, increasing our confidence in the results.(4)..Patients enrolled in the RCTs had some baseline differences compared to a Medicare population. Those in the RCTs had had higher rates of heart failure, prior stroke, and MI, and patients in ARISTOTLE and RE-LY were slightly younger than a Medicare population as these trials included patients under age 65.(7)..Uncertainties regarding findings for key patient subgroups are discussed in Section 4...3.2.3. Summary and Comment - Comparative Clinical Effectiveness..Summary evidence ratings are shown in Table 3.6. For apixaban, we rated the evidence on comparative clinical effectiveness as demonstrating a high certainty of a small net benefit compared with warfarin (B rating). In the pivotal randomized trial there were statistically significant benefits for apixaban in preventing strokes/systemic embolism and major bleeding, but the absolute differences were small. There was also a small, but non-significant trend towards lower total mortality. There were no important differences in adverse events or discontinuation rates. In addition, apixaban has the advantage of not requiring regular laboratory monitoring and dose adjustments that are required for safe and effective use of warfarin...We judged the evidence on apixaban versus dabigatran to demonstrate moderate certainty of a comparable or small net benefit (C+ rating). There were no randomized trials directly comparing the two therapies, and in our network meta-analyses, there was no significant difference in the prevention of</p>
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strokes/systemic embolism. There was a small, but statistically significant reduction in major bleeding, a finding also noted in a large, observational real-world study. There were no important differences in adverse events or discontinuation rates...For rivaroxaban versus warfarin, the evidence was rated as demonstrating high certainty of a small net benefit (B rating). The pivotal randomized trial showed small, but significant benefits in the prevention of strokes/systemic embolism and major bleeding. There was also a small, but non-significant trend towards lower total mortality. There were no important differences in adverse events or discontinuation rates, and rivaroxaban has the advantage of not requiring regular laboratory monitoring and dose adjustments that are required for safe and effective use of warfarin...For rivaroxaban versus dabigatran, however, we judge the evidence provides high certainty of only a comparable net benefit (C rating). In our network meta-analyses, there were no significant differences in the prevention of strokes/systemic embolism, bleeding rates, or total mortality. Furthermore, our decision-analytic model found the differences between the two DOACs in life-years and evLYs were near zero. In addition, in a large observational real-world study the bleeding rates for rivaroxaban and dabigatran were similar.(2)..3.3. Comparative Effectiveness and Cost

..3.3.1. Methods Overview..We developed a de novo decision-analytic model to assess the lifetime health outcomes and costs of apixaban and rivaroxaban relative to warfarin and dabigatran. If desired, ICER can provide an executable model file to CMS. Health outcomes included cardiovascular events (i.e., number of strokes, MIs, and major bleeds), life years, and equal value life years (evLYs). Importantly, evLYs are a measure of health that captures the impact of treatment on both length of life and quality of life while weighing the value of extended life of all individuals in exactly the same way. In doing so, the evLY eliminates any risk of valuing extended life lower for conditions in which people are elderly, disabled, or terminally ill. Additional details on the evLY are presented in Section 2.2. ..All patients in the model had NVAF and could be in a health state of “well,” chronic post-stroke (ischemic and hemorrhagic), chronic post-MI, or death. Acute events including stroke, MI, and major bleeds (intracranial hemorrhage [ICH], gastrointestinal [GI], and other) were captured as transient events within all living health states. Patients experiencing a stroke or MI who survived the event transitioned to a chronic health state with quality-of-life decrements and incurred costs reflective of individuals experiencing a prior stroke or MI. Patients in the post-stroke state were at risk of subsequent strokes and other events (except MI) and remained in the post-stroke state until they died. Patients in the post-MI state were at risk of subsequent MIs and other events and remained in that state unless they died or experienced a stroke. All patients could transition to death from all causes (including background and NVAF-specific mortality) from any of the alive health states. In addition, patients could die from acute events (stroke, MI, major bleeds). Health outcomes and costs were discounted at 3% per year...Key model inputs included clinical event probabilities, quality of life values, and health care costs. Where available, Medicare-specific costs based on the Agency for Healthcare Research and Quality’s (AHRQ) Healthcare Cost and Utilization Project (HCUP) were used. Productivity changes and other non-intervention indirect costs were included in a modified societal perspective analysis. Treatment effectiveness was estimated using findings from the clinical review, informed by a network meta-analysis. ..The model included non-intervention health care sector costs,

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including chronic NVAf-related condition costs, acute cardiovascular event-related costs, and chronic condition costs for post-stroke and post-MI-related care. Generic versions of dabigatran were first launched in the US in 2022.(8) Because of the recency of launch, no stable data on the effective Medicare price for dabigatran are available publicly. The model results therefore are framed as price premiums and, as such, can be informative regardless of the prices CMS determines are paid by Medicare for warfarin and dabigatran. For the same reason, and because the direction of the treatment efficacy varies by cardiovascular event, the presented model results do not include a cost-consequence analysis (e.g., cost per stroke averted). ..Detailed methods and results are presented in the Supplement.(1)..3.3.2. Results..Projected Discounted Lifetime Health Outcomes and Non-Intervention Healthcare Sector Costs for Apixaban and Rivaroxaban versus Warfarin and Dabigatran..Total lifetime discounted health outcomes and non-intervention health care sector costs (inclusive of acute event and chronic condition costs) for each intervention and comparator are shown in Table 3.7. ..Apixaban versus Warfarin..Compared to warfarin, apixaban resulted in fewer strokes, MIs, and major bleeds. Overall, apixaban resulted in more life years and evLYs gained and lower non-intervention health care sector costs...Apixaban versus Dabigatran..Compared to dabigatran, apixaban resulted in fewer MIs and major bleeds, and a greater number of strokes. Overall, apixaban resulted in more life years and evLYs gained and lower non-intervention health care sector costs over the lifetime of the model. ..Rivaroxaban versus Warfarin..Compared to warfarin, rivaroxaban resulted in fewer strokes and MIs, and a greater number of major bleeds. Overall, rivaroxaban resulted in more life years and evLYs gained, and lower non-intervention health care sector costs over the lifetime of the model...Rivaroxaban versus Dabigatran..Compared to dabigatran, rivaroxaban resulted in fewer MIs and a higher number of strokes and major bleeds. Overall, rivaroxaban resulted in the same life years and evLYs gained, with marginally lower non-intervention health care sector costs over the lifetime of the model. ..Price Premium Threshold Analyses..We framed our price threshold calculations as the price premiums for apixaban and for rivaroxaban over whatever the annualized price paid for warfarin and dabigatran may be (Table 3.9). Considering a range of cost-effectiveness thresholds is recommended, and the most commonly suggested thresholds in the US are \$100,000 and \$150,000 per QALY.(9, 10) We used these same thresholds when substituting the evLYG for the QALY, which would have the effect of increasing the premium prices at each threshold. We have included a wider range of thresholds to provide CMS with additional pricing points for consideration. ..Since CMS may want to consider comparative results for apixaban and rivaroxaban versus both warfarin and dabigatran, we present threshold price results versus both these potential comparators. The results are incremental to the price of the comparator agent, and as such, the results remain relevant regardless of whatever price CMS might pay for warfarin or dabigatran. ..Annual price premiums are shown in Table 3.9. Thirty-day price premiums above warfarin and dabigatran pricing can be calculated by dividing the annualized price by 12.175. For apixaban, calculated annual price premiums relative to the cost to CMS of warfarin are \$1,260 at a threshold of \$50,000/evLYG; \$2,290 at \$100,000/evLYG; \$3,320 at \$150,000/evLYG; and \$4,350 at \$200,000/evLYG. Annual price premiums for apixaban relative to dabigatran are: \$240 at \$50,000/evLYG; \$340 at \$100,000/evLYG; \$430 at

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\$150,000/evLYG; and \$530 at \$200,000/evLYG...For rivaroxaban, annual price premiums relative to the cost to CMS of warfarin are \$1,110 at a threshold of \$50,000/evLYG; \$2,050 at \$100,000/evLYG; \$2,980 at \$150,000/evLYG; and \$3,920 at \$200,000/evLYG. Compared to dabigatran, however, rivaroxaban was not associated with health gains, and therefore decision analytic modeling confirmed that the evidence does not support a price premium for rivaroxaban above CMS pricing for dabigatran...Uncertainty and Controversies..No measure of health gain, including individual cardiovascular events or summary measures such as the evLYG, captures all information important in value considerations. Additional considerations such as unmet need are relevant to consider in discussions on value and pricing negotiations...We recognize that quality of life associated with acute cardiovascular events and their longer-term sequelae vary across individual patients. Our modeling approach aggregates these impacts to find an average projected lifetime benefit to inform threshold pricing estimates. Given that CMS is seeking a single price for consideration as an initial offer, it is reasonable for an aggregated population-based approach to be used. ..No publicly available net price for apixaban and rivaroxaban from the Medicare population was available for our analysis; therefore, we are unable to compare our results to current Medicare prices for these agents. ..Sensitivity Analyses..Deterministic and probabilistic sensitivity analyses were conducted. In the Supplement, we present independent tornado diagrams for incremental non-intervention health care sector costs and incremental evLYGs for each intervention versus warfarin and dabigatran. Based on probabilistic analyses, model findings were robust to uncertainties in parameter estimates...Scenario Analyses..We conducted a scenario analysis from a modified societal perspective which included warfarin monitoring time and associated costs, and costs related to patient and caregiver productivity loss due to illness. The societal perspective analysis is considered “modified” because it does not include broader societal impacts such as effects on education, tax payments or benefits, or environmental impact. The modified societal perspective analysis supported annual value-based price premiums that were approximately \$120 higher for apixaban when compared to dabigatran across the evaluated thresholds; annual value-based price premiums were \$150 higher for rivaroxaban when compared to dabigatran. ..Detailed results from all scenario analyses can be found in the Supplement.(1)..Model Validation..Details related to model validation can be found in the Supplement.(1)..3.3.3. Summary and Comment - Comparative Effectiveness and Cost..We projected lifetime health outcomes and costs for a population of Medicare patients with NVAf receiving apixaban, rivaroxaban, dabigatran, or warfarin. There was an observed health benefit achieved for apixaban and rivaroxaban compared to warfarin, and marginal health gains for apixaban but not for rivaroxaban when compared to dabigatran. The marginal health benefits observed across DOACs is partially explained by the occurrence of competing events. For example, based on the network meta-analysis, dabigatran has a numerically favorable stroke risk profile, and a less favorable MI risk profile compared to apixaban and rivaroxaban. When considering the impact of these events on differences in life years and evLYs (which considers health related quality of life impacts and survival), very similar overall health benefits are observed between DOACs. In addition to the health differences observed, threshold pricing estimates include consideration for the cost-offsets observed between intervention and



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	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	comparator. ..In summary, both apixaban and rivaroxaban have demonstrated clinical benefits over warfarin that support a range of premium pricing options. Modeling of all health and cost effects showed incremental benefits for apixaban (greater evLYs and lower costs) compared to dabigatran, suggesting that a price premium, albeit marginal, would be reasonable. For rivaroxaban, the modeled health outcomes suggest overall comparable clinical effectiveness versus dabigatran, and as such, reference pricing to dabigatran could be considered a reasonable policy application of the cost-effectiveness findings.
	Evidence Submitted include a cost-effectiveness measure?	N
Question 29: Comparative Effectiveness on Specific Populations	What type of Evidence is shown?	N
	Response to Question 29	<p>4.1. Comparative Clinical Effectiveness – Subgroup Analyses and Heterogeneity..To evaluate subgroups of interest and heterogeneity, we evaluated subgroup analyses conducted in the three main trials reported in the response to question 28 and one observational study from Lau et al.(1) Subgroup analyses for the RE-LY trial, comparing dabigatran and warfarin, are reported in the Supplement.(2) We also identified two trials that specifically enrolled patients with NVAf and end-stage renal disease (ESRD).(3, 4) Ultimately, there are no persuasive findings in the clinical evidence of major differences in the balance of risks and benefits for patients with ESRD, the elderly, or those with terminal illness (e.g., cancer). There is currently no reported evidence that examined differences in risk and benefits for children or those with disabilities. The studies are described in detail below...4.1.1. End-Stage Renal Disease..Comparative Clinical Effectiveness - Trials in Patients with ESRD..Evidence informing our review of the interventions of interest in those with ESRD were derived from two Phase IV clinical trials: RENAL AF and Valkyrie.(3, 4) Both ESRD trials were small and underpowered to detect comparative efficacy of the intervention of interest versus the comparator. Overall, there are no persuasive findings in the clinical evidence to suggest major differences in the balance of risks and benefits for patients with ESRD. The studies are described in detail below. ..RENAL AF was a Phase IV open-label, blinded-outcome RCT that evaluated the efficacy of oral apixaban 5 mg twice daily (2.5 mg twice daily if weight ≤ 60 kg or age ≥ 80 years) versus warfarin (INR 2-3) in those with AF and ESRD in the US.(3) RENAL AF was designed to test for noninferiority on the primary outcome (major or clinically relevant nonmajor bleeding) and superiority for primary and secondary outcomes, including stroke/SE and death. There were challenges with participant recruitment and this study was ultimately terminated early, which meant that the study was underpowered to</p>

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detect a statistical effect. Patients were followed for a median of 330 (apixaban) or 340 (warfarin) days. See Supplement D2 for further description of the planned analysis and termination. Full inclusion and exclusion criteria for both ESRD trials are described in Supplement Table D3.1., and baseline characteristics are outlined in Table 4.1. and Supplement Table D3.30. Like ARISTOTLE, a greater proportion of patients were younger (37% were <65 years of age). Patients were more racially diverse (45% identified as Black) and were more likely to have heart failure, hypertension, and diabetes as compared to the three RCTs and the other ESRD trial. ..Rates of stroke, SE, and bleeding-related mortality were similar among those in the apixaban or warfarin group at one year.(3) In contrast, rates of major or non-major clinically relevant bleeding were high overall and numerically higher in the apixaban group (32%) versus warfarin group (26%) as was all-cause mortality (26% vs. 18% in apixaban versus warfarin, respectively). See Supplement Tables D3.31 and D3.32. However, due to the small sample size (N=154), the authors were not able to draw any conclusions from the clinical data. ..Valkyrie was a Phase IV open-label RCT that evaluated the efficacy of oral rivaroxaban 10 mg once daily versus warfarin (INR 2-3) in those with NVAf on chronic hemodialysis.(4) There was an additional group who received rivaroxaban and menquinone-7 (MK-7). As this intervention was not one of our interventions of interest, we did not include the results of this group in our analysis. The study was designed to examine whether the replacement of warfarin by rivaroxaban can slow progression of vascular calcification. Thus, the primary outcome was the absolute and relative change in coronary artery calcification score. Secondary outcomes included a composite of non-fatal stroke and cardiovascular events, death, and bleeding at a median of 1.8 years. Compared to the RCTs, patients were older with a median age of 80, were more likely to have had a prior stroke or MI, and had a higher CHA2DS2-VAS score; although the mean was comparable to the ROCKET AF trial. ..The primary clinical endpoint for the Valkyrie study was a composite of fatal cardiovascular disease and nonfatal stroke, cardiac events, and other vascular events at a median of 1.8 years. The rate of the composite outcome was significantly lower in the rivaroxaban compared to the warfarin group (HR: 0.34; 95% CI: 0.19 to 0.61; p=0.0003).(5) The rate of all-cause death and any bleeding events was numerically lower in the rivaroxaban group compared to the warfarin group. Stroke did not differ between the groups. See Supplement Table D3.31. Major bleeding outcomes were only available for the two rivaroxaban groups combined (rivaroxaban alone and rivaroxaban plus vitamin K2). Like RENAL AF, the study was not powered to detect clinical benefit and thus results of these two ESRD trials should be interpreted with caution...As noted above, both ESRD trials were small and underpowered to detect comparative efficacy of the intervention of interest versus the comparator. There are no persuasive findings in the clinical literature suggesting major differences in the overall balance of risks and benefits for patients with ESRD...Within-Trial Subgroups for ESRD..Within-trial subgroup analyses examined the effect of renal function or chronic kidney disease, as a proxy for ESRD, on treatment benefit. There were no consistent subgroup effects for renal function. This was especially true when using a continuous assessment of renal function, which may be considered a more sensitive variable than a categorical assessment...There was no effect modification by renal function reported across subgroup analyses of stroke/SE, MI, or all-cause mortality of the ARISTOTLE trial.(6-9) See Supplement

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Tables D3.5-6, and D3.11-12. There was a suggestion of a greater reduction in major bleeding in patients with moderate or severe renal impairment (creatinine clearance [CrCl]  $\leq 50$  mL/min) in those who received apixaban versus warfarin (p value for interaction = 0.03).(6) In a subsequent analyses of those with advanced chronic kidney disease (CrCl 25 to 30 mL/min), there were fewer major bleeding events in those in the apixaban group, compared to warfarin, but no difference in intracranial bleeding.(7) However, a secondary data analysis that used worsening renal function as a continuous independent variable reported no effect modification by renal function on any of the outcomes.(8) Renal function as a continuous variable could be considered a more sensitive measure to examine treatment modification and overcomes the issue of interpreting different categories of renal function that have been used across analyses...Differences in results when using categories versus continuous variables were also found in subgroup analyses of the ROCKET AF trial. In several analyses that categorized patients into renal function groups (e.g., 30-49,  $> 50$ ; or  $< 50$ , 50-80,  $> 80$  CrCl mL/min), there was no interaction between renal function and treatment group for major or non-major bleeding, major bleeding alone, stroke/SE, and ischemic or hemorrhagic stroke.(10-12) However, when median CrCl was used as a variable, Piccini et al. (2014) reported that those in the warfarin group who had a major bleed had lower CrCl at baseline as compared to patients in the rivaroxaban group.(13) This effect modification was not replicated by Fordyce et al. (2016).(14) Fordyce et al. identified patients who experienced a worsening of renal function during the study ( $> 20\%$  decrease in CrCl from screening to any point in the trial) and reported no treatment modification by worsening renal function for any bleeding, MI, or death. However, those who had worsening renal function and were given rivaroxaban had a larger reduction in stroke/SE compared to those given warfarin (HR: 0.50; 95% CI: 0.27 to 0.93;  $p=0.05$ ). See Supplement Tables D3.15, D.17, and D3.21-D3.25. The subgroup analyses from this trial were inconsistent. There are also issues with interpretation when including independent variables that change over the course of a study (e.g., worsening renal function) as it is unclear how the intervention or other uncontrolled factors in the trial may influence this relationship. ..The observational study from Lau et al. (2022) examined the primary endpoint (stroke/SE) and safety endpoints (bleeding and all-cause mortality) in patients with chronic kidney disease (CKD) for the comparisons of interest (apixaban versus dabigatran; dabigatran versus rivaroxaban).(1) See Supplement Table D3.39. Consistent with the overall sample of the Lau et al. study, the authors reported similar rates of stroke/SE, intracranial hemorrhage, and all-cause mortality in those with CKD. For GI bleeding, the findings were consistent with the overall sample for the apixaban versus dabigatran comparison. However, when comparing dabigatran versus rivaroxaban, the rates of GI bleeding were similar in those with CKD, suggesting less benefit from dabigatran in reducing GI bleeding in those with CKD. The authors note that apixaban may be more favorable in reducing the risk of GI bleeding in those with CKD...4.1.2. Individuals with Disabilities..No reported evidence examined the efficacy and safety of the interventions of interest in individuals with disabilities with NVAf. ..4.1.3. The Elderly..Within-trial subgroup analyses examined the effect of age on treatment benefit. There were no clear subgroup effects by age, except a potential signal for lower risk of extracranial bleeding, particularly GI bleeding, in older adults prescribed DOACs as compared to warfarin. ..There was no effect modification by age



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reported across multiple analyses of primary and secondary outcomes from the ARISTOTLE trial.(6, 15) See Supplement Tables D3.5, D3.6, and D3.13. ..In the main trial publication, there was no effect modification by age for stroke/SE nor major bleed in the ROCKET AF trial, which was confirmed in a secondary analysis.(10, 12) Additional secondary data analyses reported that there was no treatment modification for major bleeding, fatal bleeding, and intracranial hemorrhage alone.(12, 16) However, when examining major and non-major clinically relevant bleeding, there was a significant effect modification by age ( $p=0.009$ ). (12) There was a higher risk of bleeding in those 75 years and older in the rivaroxaban group versus warfarin (HR: 1.13; 95% CI: 1.02 to 1.25) but, in those less than 75 years, there was no significant difference in the bleeding risk between the groups (HR: 0.93; 95% CI: 0.84 to 1.04). See Supplement Tables D3.15-20 and D3.24. Given these results, it is likely that the subgroup effect, if real, may be driven by non-major clinically relevant bleeding and, as noted in the study, extracranial bleeding. Gastrointestinal bleeding was more common in those over 75 years in the rivaroxaban group as compared to the warfarin group. ..The observational study conducted by Lau et al. (2022) examined the effect of age in the comparisons of interest.(1) Similar to the subgroup analyses for CKD, the results for stroke/SE, intracranial hemorrhage, and all-cause mortality in those 80 years or older were consistent with the overall sample. See Supplement Table D3.40. Again, the rates of GI bleeding were similar in those 80 years or older when comparing dabigatran versus rivaroxaban, inconsistent with the overall sample. The authors noted that apixaban may be more favorable in reducing the risk of GI bleeding for older adults...4.1.4. Individuals Who Are Terminally Ill..A within-trial subgroup analysis of the ARISTOTLE trial examined the efficacy and safety of apixaban versus warfarin in those with AF and active cancer ( $N=157$ ), history of (remote) cancer ( $N=1,079$ ), or no cancer ( $N=16,947$ ). (17) Those with active or remote cancer were older (74 vs. 70) and had a slightly higher CHA2DS2-VASc score compared to those with no cancer. Those with active cancer had a higher rate of all-cause mortality compared to those with no or remote cancer. See Supplement Tables D3.7 to D3.9. When examining the effect on the primary efficacy and safety outcomes for apixaban versus warfarin according to cancer status, the results were consistent in patients with and without cancer. Apixaban versus warfarin was associated with fewer thrombotic events in patients with active cancer (HR: 0.30; 95% CI: 0.11 to 0.83) compared to those with no cancer (HR: 0.86; 95% CI: 0.78 to 0.95). There was also a trend towards greater reduction in mortality with apixaban versus warfarin in those without cancer. With further investigation, the authors noted that this effect was mostly driven by high rates of non-cardiovascular death in those with remote cancer who received apixaban versus those treated with warfarin. ..4.1.5. Children..No reported evidence examined the efficacy and safety of the interventions of interest in children with NVAf...Subgroups for the RE-LY trial are reported in Section D5 of the Supplement.(2) ..4.2 Subgroup Uncertainties and Controversies..There are uncertainties around the comparative effectiveness of the drugs in patients with ESRD. Both trials in this patient population were underpowered: one because it was a pilot study and the other stopped enrolling patients due to challenges in recruitment. However, an individual patient-level NMA that combined the results of four trials including the three in our NMA found that the DOACs were safer and more effective than warfarin in patients with NVAf at 5 levels of renal function down to



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		<p>a creatine clearance of 25-29.9 ml/min.(18) Dabigatran is renally cleared with dose reduction indicated for patients with a creatine clearance of 15-30 ml/min.(19).Older patients are a major subgroup of interest as they comprise most patients covered by Medicare. As noted above, there was no evidence of effect modification by age in any of the randomized trials included in our analyses. In addition, an individual patient-level NMA that combined the results of four trials including the three in our NMA found that the DOACs were safer and more effective than warfarin in patients without effect modification by age (&lt;65, 65-75, and &gt;75 years) for the outcomes of stroke / systemic embolism, major bleeding, and total mortality.(20)..4.3 Comparative Cost Effectiveness – Subgroup Analyses..There was no clinical evidence to support subgroup analyses within the cost-effectiveness model.</p> <ol style="list-style-type: none"><li>1. Lau WCY, Torre CO, Man KKC, Stewart HM, Seager S, Van Zandt M, et al. Comparative Effectiveness and Safety Between Apixaban, Dabigatran, Edoxaban, and Rivaroxaban Among Patients With Atrial Fibrillation : A Multinational Population-Based Cohort Study. Ann Intern Med. 2022;175(11):1515-24. Epub 2022/11/01. doi: 10.7326/m22-0511. PubMed PMID: 36315950.</li><li>2. Tice JA, Richardson M, Wright A, Seidner M, Rind DM, Pearson SD. Special Assessment to Inform CMS Drug Price Negotiation: Eliquis and Xarelto - Supplemental Materials: Institute for Clinical and Economic Review; 2023 [cited 2023 October 2]. Available from: <a href="https://icer.org/wp-content/uploads/2023/09/ICER_NVAF_Medicare_Supplement_100223.pdf">https://icer.org/wp-content/uploads/2023/09/ICER_NVAF_Medicare_Supplement_100223.pdf</a>.</li><li>3. Pokorney SD, Chertow GM, Al-Khalidi HR, Gallup D, Dignacco P, Mussina K, et al. Apixaban for Patients With Atrial Fibrillation on Hemodialysis: A Multicenter Randomized Controlled Trial. Circulation. 2022;146(23):1735-45. doi: 10.1161/CIRCULATIONAHA.121.054990.</li><li>4. De Vriese AS, Caluwé R, Pyfferoen L, De Bacquer D, De Boeck K, Delanote J, et al. Multicenter Randomized Controlled Trial of Vitamin K Antagonist Replacement by Rivaroxaban with or without Vitamin K2 in Hemodialysis Patients with Atrial Fibrillation: the Valkyrie Study. Journal of the American Society of Nephrology. 2020;31(1).</li><li>5. De Vriese AS, Caluwé R, Van Der Meersch H, De Boeck K, De Bacquer D. Safety and Efficacy of Vitamin K Antagonists versus Rivaroxaban in Hemodialysis Patients with Atrial Fibrillation: A Multicenter Randomized Controlled Trial. Journal of the American Society of Nephrology. 2021;32(6).</li><li>6. Granger CB, Alexander JH, McMurray JJV, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus Warfarin in Patients with Atrial Fibrillation. New England Journal of Medicine. 2011;365(11):981-92. doi: 10.1056/NEJMoa1107039.</li><li>7. Stanifer JW, Pokorney SD, Chertow GM, Hohnloser SH, Wojdyla DM, Garonzik S, et al. Apixaban Versus Warfarin in Patients With Atrial Fibrillation and Advanced Chronic Kidney Disease. Circulation. 2020;141(17):1384-92. doi: doi:10.1161/CIRCULATIONAHA.119.044059.</li><li>8. Hijazi Z, Hohnloser SH, Andersson U, Alexander JH, Hanna M, Keltai M, et al. Efficacy and Safety of Apixaban Compared With Warfarin in Patients With Atrial Fibrillation in Relation to Renal Function Over Time:</li></ol>

Hyperlink to Citation -  
Additional Materials for  
Question 29

Question	Sub-Question	Response
		<p>Insights From the ARISTOTLE Randomized Clinical Trial. JAMA Cardiology. 2016;1(4):451-60. doi: 10.1001/jamacardio.2016.1170.</p> <p>9. Hohnloser SH, Hijazi Z, Thomas L, Alexander JH, Amerena J, Hanna M, et al. Efficacy of apixaban when compared with warfarin in relation to renal function in patients with atrial fibrillation: insights from the ARISTOTLE trial. European Heart Journal. 2012;33(22):2821-30. doi: 10.1093/eurheartj/ehs274.</p> <p>10. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. New England Journal of Medicine. 2011;365(10):883-91. doi: 10.1056/NEJMoa1009638.</p> <p>11. Fox KAA, Piccini JP, Wojdyla D, Becker RC, Halperin JL, Nessel CC, et al. Prevention of stroke and systemic embolism with rivaroxaban compared with warfarin in patients with non-valvular atrial fibrillation and moderate renal impairment. European Heart Journal. 2011;32(19):2387-94. doi: 10.1093/eurheartj/ehr342.</p> <p>12. Halperin JL, Hankey GJ, Wojdyla DM, Piccini JP, Lokhnygina Y, Patel MR, et al. Efficacy and Safety of Rivaroxaban Compared With Warfarin Among Elderly Patients With Nonvalvular Atrial Fibrillation in the Rivaroxaban Once Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF). Circulation. 2014;130(2):138-46. doi: 10.1161/CIRCULATIONAHA.113.005008.</p> <p>13. Piccini JP, Garg J, Patel MR, Lokhnygina Y, Goodman SG, Becker RC, et al. Management of major bleeding events in patients treated with rivaroxaban vs. warfarin: results from the ROCKET AF trial. European Heart Journal. 2014;35(28):1873-80. doi: 10.1093/eurheartj/ehu083.</p> <p>14. Fordyce CB, Hellkamp AS, Lokhnygina Y, Lindner SM, Piccini JP, Becker RC, et al. On-Treatment Outcomes in Patients With Worsening Renal Function With Rivaroxaban Compared With Warfarin. Circulation. 2016;134(1):37-47. doi: 10.1161/CIRCULATIONAHA.116.021890.</p> <p>15. Halvorsen S, Atar D, Yang H, De Caterina R, Erol C, Garcia D, et al. Efficacy and safety of apixaban compared with warfarin according to age for stroke prevention in atrial fibrillation: observations from the ARISTOTLE trial. European Heart Journal. 2014;35(28):1864-72. doi: 10.1093/eurheartj/ehu046.</p> <p>16. Goodman SG, Wojdyla DM, Piccini JP, White HD, Paolini JF, Nessel CC, et al. Factors Associated With Major Bleeding Events: Insights From the ROCKET AF Trial (Rivaroxaban Once-daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation). Journal of the American College of Cardiology. 2014;63(9):891-900. doi: <a href="https://doi.org/10.1016/j.jacc.2013.11.013">https://doi.org/10.1016/j.jacc.2013.11.013</a>.</p> <p>17. Melloni C, Dunning A, Granger CB, Thomas L, Khouri MG, Garcia DA, et al. Efficacy and Safety of Apixaban Versus Warfarin in Patients with Atrial Fibrillation and a History of Cancer: Insights from the ARISTOTLE Trial. The American Journal of Medicine. 2017;130(12):1440-8.e1. doi: 10.1016/j.amjmed.2017.06.026.</p> <p>18. Harrington J CA, Hua K, Wallentin L, Patel MR, Hohnloser SH, Giugliano RP, Fox KA, Hijazi Z, Lopes RD, Pokorney SD. . Direct Oral Anticoagulants Versus Warfarin Across the Spectrum of Kidney Function: Patient-Level Network Meta-Analyses From COMBINE AF. Circulation. 2023;147(23):1748-57.</p>

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		<p>19. U.S. Food and Drug Administration. PRADAXA® (dabigatran etexilate) Package Insert. 2021.</p> <p>20. Carnicelli AP HH, Connolly SJ, Eikelboom J, Giugliano RP, Morrow DA, Patel MR, Wallentin L, Alexander JH, Cecilia Bahit M, Benz AP. Direct oral anticoagulants versus warfarin in patients with atrial fibrillation: patient-level network meta-analyses of randomized clinical trials with interaction testing by age and sex. Circulation. 2022;145(4):242-55.</p>
	<p>Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29</p> <p>Evidence Submitted include a cost-effectiveness measure?</p> <p>What type of Evidence is shown?</p>	<p>N</p>
Question 30: Addressing Unmet Medical Needs	Response to Question 30	<p>2.1. Qualitative Discussion..Revised guidance from CMS defines unmet need as “treating a disease or condition in cases where no other treatment options exist or existing treatments do not adequately address the disease or condition.”(1) DOACs improve outcomes in NVAf compared with warfarin as they generally provide better protection against stroke and systemic embolism for a similar bleeding risk or equivalent protection with a lower bleeding risk. For most patients, warfarin presents more burdens than DOACs, including the requirement for close laboratory monitoring, particularly at initiation. For many patients ongoing monitoring is required every few weeks. Warfarin also requires that patients adhere to a diet with a consistent intake of vitamin K, and initiation or discontinuation of many other medications will require a new phase of close laboratory monitoring and adjustment of warfarin dosing...Even with the DOACs, however, all patients face a residual risk of strokes and systemic emboli, and all have risks of bleeding events ranging from minor to catastrophic...2.1.1. Patient and Caregiver Perspectives..Patients told us that they did not like having to go to the laboratory at least once a month to monitor their INR when on warfarin. They also expressed frustration at limiting their intake of leafy green vegetables. Taking a pill once or twice a day without laboratory or dietary monitoring is much easier. However, for all four drugs, patients complained about bleeding, including unsightly bruises arising without trauma and prolonged bleeding after minor cuts. Some patients live in fear of more significant bleeding, leading them to limit activities (e.g., soccer, skiing, biking) that they had previously enjoyed but which now were felt to pose too great a risk. One patient told us about repeated emergency room visits at which he would urinate blood and blood clots due to complications arising from his prior radiation</p>

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therapy for prostate cancer. Finally, we heard about the fear of having a stroke with its risk of long-term disability and loss of independence. Patients are aware that none of the available drugs are 100% effective at preventing strokes...2.2 Quantitative Discussion..Decision-analytic models, often used to support estimates of value-based drug pricing, can also produce quantitative findings on unmet need. Calculations of proportional and absolute health “shortfall” are two different ways to estimate the reduction in lifetime health due to a condition compared with health in the age- and sex-matched general US population. Using the decision-analytic model described in Section 3.3, we calculated proportional and absolute shortfalls in health using the equal value of life years (evLY) measure.(2)..CMS revised guidance states: ..CMS requires respondents submitting information to indicate whether their submission contains information from studies that use measures that treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. CMS also requests that respondents submitting information under 1194(e)(2) provide a short description of any cost-effectiveness measures included in the research they are submitting, and how they believe the data avoids treating extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. ..We attest that all measures of health used throughout this submission, and specifically the evLY, do not treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. The evLY treats the value of extended life of all individuals in exactly the same way, with each year of life gained from treatment valued identically. As such, the evLY is a nondiscriminatory alternative to the quality-adjusted life year (QALY). The evLY has served for many years as a bedrock of ICER's drug price benchmarks that are used by the Veterans Administration, Medicaid programs, and private insurers. In our public comments on the CMS draft guidance, we provided further rationale for why the evLY is consistent with the IRA and will be helpful to CMS in its deliberations.(3)..To quantify unmet need for patients with NVAf, we present evLY shortfall calculations for two treatments: apixaban and dabigatran. We chose to calculate health shortfalls despite apixaban treatment because it is the market leader in utilization and produced the best lifetime health outcomes in analytic modeling (see Section 3.3). We also chose to calculate health shortfalls for patients treated with dabigatran since those shortfalls represent the “unmet need” for patients not treated with one of the two drugs being negotiated. ..To calculate the absolute evLY shortfall for each condition, we subtracted the lifetime undiscounted evLYs with apixaban treatment from the evLYs expected for the general population (calculated using age- and sex-adjusted estimates for mortality and a constant utility of 0.851 for quality of life). To calculate the proportional evLY shortfall, we divided the absolute evLY shortfall by the evLY life expectancy for the general population with the same age and sex distribution at baseline...The undiscounted absolute shortfall for Medicare patients with NVAf treated with apixaban was 2.29 evLYs versus the general age- and sex-adjusted US population. The undiscounted proportional shortfall was  $2.29/9.65 = 24\%$ . The undiscounted absolute shortfall for Medicare patients with NVAf treated with dabigatran was 2.31 evLYs versus the general



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age- and sex-adjusted US population. The undiscounted proportional shortfall was  $2.31/9.65 = 24\%$ . For context, as shown in Table 2.1, the absolute evLY shortfall for Medicare patients with NVAF treated with apixaban is comparable to that observed with osteoporosis but substantially less than with chronic depression or Alzheimer's disease. The proportional shortfall was comparable to that for patients living with ulcerative colitis, but substantially less than for patients with lupus nephritis or relapsing forms of multiple sclerosis.

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2. Granger CB, Alexander JH, McMurray JJV, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus Warfarin in Patients with Atrial Fibrillation. *New England Journal of Medicine*. 2011;365(11):981-92. doi: 10.1056/NEJMoa1107039.
3. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. *New England Journal of Medicine*. 2011;365(10):883-91. doi: 10.1056/NEJMoa1009638.
4. Lau WCY, Torre CO, Man KKC, Stewart HM, Seager S, Van Zandt M, et al. Comparative Effectiveness and Safety Between Apixaban, Dabigatran, Edoxaban, and Rivaroxaban Among Patients With Atrial Fibrillation : A Multinational Population-Based Cohort Study. *Ann Intern Med*. 2022;175(11):1515-24. Epub 2022/11/01. doi: 10.7326/m22-0511. PubMed PMID: 36315950.
5. Chan Y-H, Chao T-F, Chen S-W, Lee H-F, Chen W-M, Li P-R, et al. Development of Interstitial Lung Disease Among Patients With Atrial Fibrillation Receiving Oral Anticoagulants in Taiwan. *JAMA Network Open*. 2022;5(11):e2243307-e. doi: 10.1001/jamanetworkopen.2022.43307.
6. Graham DJ, Reichman ME, Wernecke M, Zhang R, Southworth MR, Levenson M, et al. Cardiovascular, Bleeding, and Mortality Risks in Elderly Medicare Patients Treated With Dabigatran or Warfarin for Nonvalvular Atrial Fibrillation. *Circulation*. 2015;131(2):157-64. doi: 10.1161/CIRCULATIONAHA.114.012061.
7. Graham DJ, Baro E, Zhang R, Liao J, Wernecke M, Reichman ME, et al. Comparative Stroke, Bleeding, and Mortality Risks in Older Medicare Patients Treated with Oral Anticoagulants for Nonvalvular Atrial Fibrillation. *Am J Med*. 2019;132(5):596-604.e11. Epub 2019/01/15. doi: 10.1016/j.amjmed.2018.12.023. PubMed PMID: 30639551.
8. IPD Analytics. Cardiovascular: Direct-acting Oral Anticoagulants (DOAC/NOAC). 2023 Contract No.: August 2023.
9. Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, et al. Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and Medicine. *Jama*. 2016;316(10):1093-103. Epub 2016/09/14. doi: 10.1001/jama.2016.12195. PubMed PMID: 27623463.

Hyperlink to Citation -  
Additional Materials for  
Question 30

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Question	Sub-Question	Response
		10. Neumann PJ, Cohen JT, Weinstein MC. Updating Cost-Effectiveness – The Curious Resilience of the \$50,000-per-QALY Threshold. The New England journal of medicine. 2014;371(9):796-7. doi: 10.1056/NEJMp1405158.
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	Y
	What type of Evidence is shown?	N
Question 31: Patient and Caregiver Experience	Response to Question 31	
Question 32: Executive Summary	Response to Question 32	As a result of the Inflation Reduction Act (IRA), the Centers for Medicare & Medicaid Services (CMS) will soon begin negotiating prices for certain high-expenditure drugs. This submission examines the direct-acting oral anticoagulants (DOACs) apixaban (Eliquis®, Bristol Myers Squibb / Pfizer) and rivaroxaban (Xarelto®, Janssen Pharmaceuticals, Inc.), two of the 10 drugs that CMS has selected for negotiation in the first round. The information in the submission is tailored to reflect legislative specifications in the IRA and subsequent CMS guidance. It is not comprehensive but does include sections on multiple elements related to drug value, providing different options for translating evidence into initial offer prices and for assessing counteroffers from drug makers. We focused on the use of these two drugs for non-valvular atrial fibrillation (NVAf) since that represents the vast majority of use for drugs in this class. As clinical and cost comparators, we selected warfarin, an older generic medication that was the standard therapy for atrial fibrillation prior to the DOACs, and dabigatran, which is the first DOAC available as a generic medication, launched in 2022...We sought patient input and were told of the impact of patients' ongoing fear of having a stroke and the potential for long term disability and loss of independence. We also heard about their lived experience with bleeding, including the time it takes to stop bleeding after cuts and common unsightly bruises without trauma. Some patients worry continually about more significant bleeding, leading them to limit their activities. As a quantitative measure of unmet need, we found the absolute equal value life years (evLY) shortfall for Medicare patients

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### Response

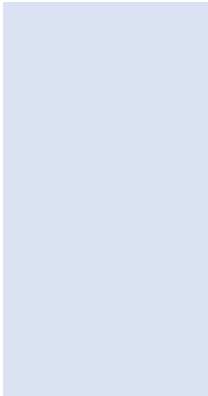
with NVAF was comparable to that observed with living with osteoporosis but substantially less than with chronic depression or Alzheimer's disease. The proportional evLY shortfall was comparable to that observed with ulcerative colitis, but substantially less than that with lupus nephritis or relapsing forms of multiple sclerosis. ..To estimate the comparative therapeutic impact of apixaban and rivaroxaban in NVAF, we compared each drug to warfarin and to dabigatran. Both apixaban and rivaroxaban had direct randomized controlled trial evidence versus warfarin, but we needed to conduct a network meta-analysis to assess comparisons with dabigatran. This evidence, consistent with results from observational studies, demonstrates that DOACs improve outcomes for patients with NVAF compared to treatment with warfarin. The DOACs generally provide better protection against stroke and systemic embolism for a similar bleeding risk or equivalent protection with a lower bleeding risk. Across the trials, there was no evidence of effect modification by age in any of the outcomes we examined...For apixaban, we have rated the evidence on comparative clinical effectiveness as demonstrating a high certainty of a small net benefit compared with warfarin (B rating). In the pivotal randomized trial there were statistically significant benefits for apixaban in preventing strokes/systemic embolism and major bleeding, but the absolute differences were small. There was also a small, but non-significant trend towards lower total mortality. There were no important differences in adverse events or discontinuation rates. In addition, apixaban has the advantage of not requiring regular laboratory monitoring and dose adjustments that are required for safe and effective use of warfarin...We judged the evidence on apixaban versus dabigatran to demonstrate moderate certainty of a comparable or small net benefit (C+ rating). There were no randomized trials directly comparing the two therapies, and in our network meta-analyses, there was no significant difference in the prevention of strokes/systemic embolism. There was a small, but statistically significant reduction in major bleeding, a finding also noted in a large, observational real-world study. There were no important differences in adverse events or discontinuation rates...For rivaroxaban versus warfarin, the evidence was rated as demonstrating high certainty of a small net benefit (B rating). The pivotal randomized trial showed small, but significant benefits in the prevention of strokes/systemic embolism and major bleeding. There was also a small, but non-significant trend towards lower total mortality. There were no important differences in adverse events or discontinuation rates, and rivaroxaban has the advantage of not requiring regular laboratory monitoring and dose adjustments that are required for safe and effective use of warfarin...For rivaroxaban versus dabigatran, however, we judge the evidence provides high certainty of only a comparable net benefit (C rating). In our network meta-analyses, there were no significant differences in the prevention of strokes/systemic embolism, bleeding rates, or total mortality. Furthermore, our decision-analytic model found the differences between the two DOACs in life-years and evLYs were near zero. In addition, in a large, observational real-world study the bleeding rates for rivaroxaban and dabigatran were similar. ..We used decision-analytic modeling to assess the lifetime projected effectiveness and cost of apixaban and rivaroxaban compared to warfarin and dabigatran. Based on their comparative clinical effectiveness, we report price premiums at various cost-effectiveness thresholds for apixaban and rivaroxaban relative to the prices that CMS pays for comparator agents (warfarin and dabigatran)

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to inform drug price negotiations alongside other considerations. We do not stipulate a specific cost-effectiveness threshold as most appropriate but note for CMS that academic health economics research supports consideration of pricing between \$100,000-\$150,000 per evLYG. .For apixaban, calculated annual price premiums relative to the cost to CMS of warfarin are \$1,260 at a threshold of \$50,000/evLYG; \$2,290 at \$100,000/evLYG; \$3,320 at \$150,000/evLYG; and \$4,350 at \$200,000/evLYG. Annual price premiums for apixaban relative to dabigatran are: \$240 at \$50,000/evLYG; \$340 at \$100,000/evLYG; \$430 at \$150,000/evLYG; and \$530 at \$200,000/evLYG...For rivaroxaban, annual price premiums relative to the cost to CMS of warfarin are \$1,110 at a threshold of \$50,000/evLYG; \$2,050 at \$100,000/evLYG; \$2,980 at \$150,000/evLYG; and \$3,920 at \$200,000/evLYG. Compared to dabigatran, however, rivaroxaban was not associated with health gains, and therefore decision analytic modeling confirmed that the evidence does not support a price premium for rivaroxaban above CMS pricing for dabigatran.





**Table 2.1. Absolute and Proportional evLY Shortfall for Medicare Patients with NVAf Treated with Apixaban Compared to Other Conditions.**

	Absolute evLY Shortfall	Proportional evLY Shortfall
Lupus nephritis	22.1	56%
Relapsing remitting multiple sclerosis	18.86	52%
Moderate to severe atopic dermatitis	9.92	28%
Chronic depression	9.65	32%
Ulcerative colitis	6.57	19%
Osteoporosis	2.61	19%
Nonvalvular atrial fibrillation	2.29	24%

evLY: equal-value life year

**Table 3.1. Overview of Main Trials**

	Arms	Arm size	Study Duration	Baseline Characteristics					
				Age, mean (SD)	% Male	% White	CHADS <sub>2</sub> , mean (SD)	CHA <sub>2</sub> DS <sub>2</sub> -VASc, mean (SD)	HAS-BLED, mean (SD)
ARISTOTLE	Apixaban§	9120	1.8 years*	69.1 (9.61)	64.5	82.6	2.1 (1.1)	3.7 (1.5)	1.8 (1.05)
	Warfarin‡	9081		69.0 (9.74)	65	82.5	2.1 (1.1)	3.7 (1.5)	1.8 (1.06)
ROCKET AF	Rivaroxaban¤	7131	1.6 years*	73 (65-78)†	60.3	82.3	3.5 (0.94)	4.8 (1.3)	2.8 (0.9)
	Warfarin‡	7133		73 (65-78)†	60.3	82.9	3.5 (0.95)	4.8 (1.3)	
RE-LY	Dabigatran**	6076	2 years*	71.5 (8.8)	63.2	70.2	2.2 (1.2)	NR	NR
	Warfarin‡	6022		71.6 (8.6)	63.3	69.8	2.1 (1.1)	NR	NR

AF: atrial fibrillation, CHADS<sub>2</sub>: congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), CHA<sub>2</sub>DS<sub>2</sub>-VASc: congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female), HAS-BLED: Hypertension, Abnormal liver/renal function, Stroke history, Bleeding history or predisposition, Labile INR, Elderly, Drug/alcohol usage, NR: not reported, SD: standard deviation, %: percent

\*median

†median(IQR)

‡INR 2-3 dose

§Apixaban 5mg or 2.5 twice daily

¤Rivaroxaban 20 mg or 15 mg once daily

\*\*Dabigatran 150 mg twice daily

**Table 3.2. Network Meta-Analysis Results for Stroke/Systemic Embolism.**

Apixaban (5 mg or 2.5 mg BID)			
1 (0.76, 1.31)	Rivaroxaban (20 mg or 15 mg QD)		
1.2 (0.9, 1.59)	1.2 (0.89, 1.6)	Dabigatran (150 mg BID)	
<b>0.79</b> <b>(0.66, 0.95)</b>	<b>0.79</b> <b>(0.65, 0.96)</b>	<b>0.66</b> <b>(0.53, 0.82)</b>	Warfarin (INR: 2-3)

BID: twice a day, QD: once a day.

Legend: Each box represents the estimated hazard ratio and 95% credible interval for the direct and indirect comparisons between two drugs: the drug at the top of the column compared to the drug at the right of the row. Estimates in bold signify that the 95% credible interval does not contain 1.0.

**Table 3.3. Network Meta-Analysis Results for Myocardial Infarction.**

Apixaban (5 mg or 2.5 mg BID)			
1.09 (0.73, 1.61)	Rivaroxaban (20 mg or 15 mg QD)		
<b>0.64</b> <b>(0.41, 0.98)</b>	<b>0.59</b> <b>(0.38, 0.9)</b>	Dabigatran (150 mg BID)	
0.88 (0.66, 1.17)	0.81 (0.62, 1.06)	1.38 (1, 1.91)	Warfarin (INR: 2-3)

BID: twice a day, QD: once a day.

Legend: Each box represents the estimated hazard ratio and 95% credible interval for the direct and indirect comparisons between two drugs: the drug at the top of the column compared to the drug at the right of the row. Estimates in bold signify that the 95% credible interval does not contain 1.0.



**Table 3.4. Discontinuations of DOACs versus Warfarin**

	All discontinuations	Discontinuation due to AEs
<b>ARISTOTLE</b>	Apixaban: 21.4%* Warfarin: 23.4%	Apixaban: 7.6% Warfarin: 8.4%
<b>ROCKET AF</b>	Rivaroxaban: 23.7%* Warfarin: 22.2%	Rivaroxaban: 8.3% Warfarin: 7%
<b>RE-LY</b>	Dabigatran: 17%* Warfarin: 12%	Dabigatran: 6.2% Warfarin: 3.3%

AEs: adverse events, AF: atrial fibrillation

\* Difference between the groups met statistical significance,  $p < 0.05$ .

**Table 3.5. Network Meta-Analysis Results for Major Bleeding.**

Apixaban (5 mg or 2.5 mg BID)			
<b>0.66</b> <b>(0.54, 0.81)</b>	Rivaroxaban (20 mg or 15 mg QD)		
<b>0.74</b> <b>(0.61, 0.91)</b>	<b>1.12</b> (0.92, 1.37)	Dabigatran (150 mg BID)	
<b>0.69</b> <b>(0.6, 0.8)</b>	1.04 (0.9, 1.2)	0.93 (0.81, 1.07)	Warfarin (INR: 2-3)

BID: twice a day, QD: once a day.

Legend: Each box represents the estimated hazard ratio and 95% credible interval for the direct and indirect comparisons between two drugs: the drug at the top of the column compared to the drug at the right of the row. Estimates in bold signify that the 95% credible interval does not contain 1.0.

Figure 3.1. ICER Evidence Rating Matrix

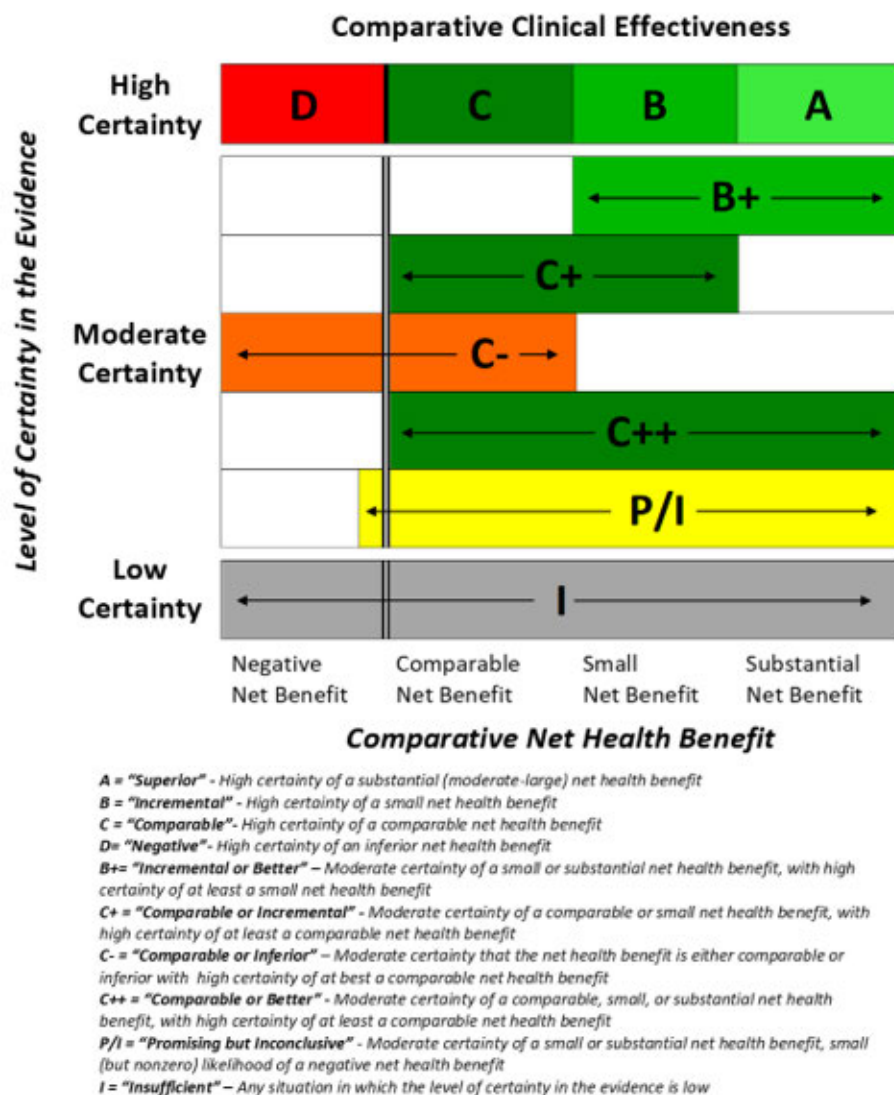


Table 3.6 Evidence Ratings

Treatment	Comparator	Evidence Rating
Apixaban	Warfarin	B
Apixaban	Dabigatran	C+
Rivaroxaban	Warfarin	B
Rivaroxaban	Dabigatran	C

**Table 3.7. Lifetime Health Outcomes and Annualized Average Non-Intervention Health Care Sector Costs by Treatment Strategy**

Treatment	Strokes*	MIs	Major Bleeds**	Life Years (Discounted)	evLYs (Discounted)	Annualized non-intervention health care sector costs† (Discounted)
Apixaban	0.184	0.148	0.170	7.82	6.15	\$40,600
Rivaroxaban	0.184	0.136	0.269	7.80	6.14	\$40,700
Dabigatran	0.155	0.237	0.253	7.80	6.14	\$40,800
Warfarin	0.236	0.167	0.227	7.74	5.99	\$41,200

evLYs: equal-value life years, LY: Life year, MI: myocardial infarction

\*Includes ischemic and hemorrhagic strokes

\*\*Includes major gastrointestinal bleeds, intracranial hemorrhages, and non- gastrointestinal extracranial hemorrhages.

†Inclusive of acute event and chronic condition costs estimated over the lifetime of the model and displayed as an annualized average for each treatment strategy (excludes intervention costs).

**Table 3.8. Incremental Lifetime Results for Apixaban and Rivaroxaban versus Warfarin and Dabigatran**

Treatment	Incremental Lifetime Outcomes					
	Strokes*	MIs	Major Bleeds**	Life Years (Discounted)	evLYs (Discounted)	Non-intervention health care sector costs† (Discounted)
Apixaban vs. Warfarin	-0.052	-0.019	-0.057	0.08	0.16	-\$1,800
Apixaban vs. Dabigatran	0.028	-0.089	-0.083	0.01	0.02	-\$1,100
Rivaroxaban vs. Warfarin	-0.052	-0.032	0.042	0.06	0.14	-\$1,300
Rivaroxaban vs. Dabigatran	0.028	-0.101	0.016	-0.005	-0.001	-\$600

evLYs: equal-value life years, LY: Life year, MI: myocardial infarction

**Note:** Negative LYs and evLYs represent life years lost with rivaroxaban vs. comparators; negative incremental strokes, Mis, and major bleeds represent events averted with rivaroxaban vs. comparators; negative costs represent cost savings for rivaroxaban vs. comparators.

\*Includes ischemic and hemorrhagic strokes

\*\*Includes major gastrointestinal bleeds, intracranial hemorrhages, and non- gastrointestinal extracranial hemorrhages.

†Inclusive of acute event and chronic condition costs (excludes intervention costs).

**Table 3.9. Maximum Annualized Price Premium for Apixaban and Rivaroxaban Above Warfarin and Dabigatran Pricing to Achieve a Range of Cost-Effectiveness Price Premium Thresholds**

	\$50,000/evLY	\$100,000/evLY	\$150,000/evLY	\$200,000/evLY
Apixaban vs. Warfarin	\$1,260	\$2,290	\$3,320	\$4,350
Apixaban vs. Dabigatran	\$240	\$340	\$430	\$530
Rivaroxaban vs. Warfarin	\$1,110	\$2,050	\$2,980	\$3,920
Rivaroxaban vs. Dabigatran	No price premium*	No price premium*	No price premium*	No price premium*

evLYs: equal-value life years

Note: Annualized price premiums are rounded to the nearest \$10.

\*Rivaroxaban resulted in fewer evLYs gained relative to dabigatran.



**Table 4.1. Overview of ESRD Studies**

	Arms	Arm size	Study Duration	Baseline Characteristics					
				Age, mean (SD)	% Male	% White	CHADS <sub>2</sub> , mean (SD)	CHA <sub>2</sub> DS <sub>2</sub> -VASc, mean (SD)	HAS-BLED, mean (SD)
<b>Valkyrie</b>	Rivaroxaban $\alpha$	46	1.88 years*	79.9 (74.4-83.9) $\ddagger$	76.1	NR	NR	4.7 (1.4)	4.7 (1.4)
	Warfarin $\ddagger$	44		80.3 (71.5-84.3) $\ddagger$	56.8	NR	NR	4.8 (1.5)	4.8 (1.5)
<b>RENAL-AF</b>	Apixaban $\#$	82	0.93 years* $\dagger$	69.0 (61.0, 76.0) $\ddagger$	58.5	52.4	NR	NR	NR
	Warfarin $\S$	72		68.0 (60.5, 72.5) $\ddagger$	69.4	50	NR	NR	NR

AF: atrial fibrillation, CHADS<sub>2</sub>: congestive heart failure, hypertension, age  $\geq 75$  (doubled), diabetes, stroke (doubled), CHA<sub>2</sub>DS<sub>2</sub>-VASc: congestive heart failure, hypertension, age  $\geq 75$  (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female), HAS-BLED: Hypertension, Abnormal liver/renal function, Stroke history, Bleeding history or predisposition, Labile INR, Elderly, Drug/alcohol usage, NR: not reported, SD: standard deviation, %: percent

\*median

$\dagger$ Treatment was planned for up to 15 months but the study was terminated early due to a lower recruitment rate.

$\ddagger$ median(IQR)

$\S$ INR 2-3 dose

$\#$ Apixaban 5mg or 2.5 twice daily

$\alpha$ Rivaroxaban 10 mg once daily

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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	Partnership to Advance Cardiovascular Health
	Respondent Email	
	Who is completing this form?	PAO
Question 27: Prescribing Information	Prescribing Information	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
	Response to Question 29	

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Question	Sub-Question	Response
Question 29: Comparative Effectiveness on Specific Populations	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	
	Hyperlink to Citation - Additional Materials for Question 30	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	

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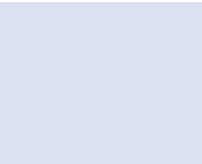


Question	Sub-Question	Response
Question 31: Patient and Caregiver Experience	Response to Question 31	<p>The Partnership to Advance Cardiovascular Health (PACH) is a nonprofit advocacy coalition of stakeholder groups that represent cardiovascular patients, patient advocates, health care providers, and medical researchers. On behalf of its members, PACH advocates for patient access to FDA-approved therapies and promotes innovation in cardiovascular healthcare for the millions of Americans at high risk for heart disease. ..Cardiovascular medicine has benefited from many years of breakthrough research, which has led to highly effective treatments that have enabled seniors to live longer, healthier lives. However, heart disease continues to be the #1 killer in America, accounting for 1 in every 5 deaths in 2021. .Cardiovascular disease disproportionately impacts vulnerable communities, including minorities, aging populations, rural communities, and those with lower socioeconomic status. For example, black men have a 70% higher risk of heart failure (HF), and black women have a 50% higher risk than their white counterparts. Yet racial and ethnic minorities receive less than 40% of total annual advanced HF therapies – and women receive less than a quarter. Similarly, atrial fibrillation (AF) is the most common cardiac arrhythmia in the United States, and patients with AF are five times more likely to experience an ischemic stroke. Medicare claims studies have shown that Black and Hispanic patients over 65 with AF had a higher unadjusted risk of death and stroke. ..Rivaroxaban is used to treat and manage venous thromboembolism (VTE) as a postoperative blood thinner for patients in non-valvular atrial fibrillation (AF). It is also used in secondary prevention of peripheral artery disease and coronary syndrome. Compared to warfarin, rivaroxaban reduces the risk of stroke and mortality significantly for patients with nonvalvular atrial fibrillation.<sup>1</sup> Its value is demonstrated by the tens of millions of patients that it has helped to prevent clotting events and strokes. ..As an organization that represents cardiovascular patients and prescribers, we believe it is notable that cardiovascular agents are disproportionately represented in price negotiations. Our goal is to ensure that the 42% of Medicare beneficiaries who have been diagnosed with a heart condition can still receive current and future medications they need to prevent heart attacks and strokes. While we steadfastly agree that lowering the cost of medications for our vulnerable seniors is a priority, we remain concerned that the Inflation Reduction Act Medicare Drug Price Negotiation Program could negatively impact innovation and access to life-saving medications. ..We recognize IRA has implications for future research and development as well as access to current medicines. We urge CMS to take steps now to ensure the drug negotiation program is patient-centric and equitable for the millions of Medicare beneficiaries diagnosed with cardiovascular disease today and in the long run. If PACH or our members can be a resource to CMS, please do not hesitate to contact us. Considering that the IRA will disproportionately impact cardiovascular patients, we would welcome meeting with CMS to discuss our concerns and offer insights from the community. . .1.                      Alberts, M. J., Chen, Y. W., Lin, J.,</p>
Question 32: Executive Summary	Response to Question 32	





Question	Sub-Question
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	<p><b>Response</b> Kogan, E., Twyman, K., &amp; Milentijevic, D. (2020). Risks of stroke and mortality in atrial fibrillation patients treated with Rivaroxaban and Warfarin. Stroke, 51(2), 549-555. <a href="https://doi.org/10.1161/strokeaha.119.025554">https://doi.org/10.1161/strokeaha.119.025554</a></p>
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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	RIVAROXABAN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	Pharmaceutical Care Management Association (PCMA)
	Respondent Email	
	Who is completing this form?	TRD
Question 27: Prescribing Information	Prescribing Information	
	Evidence Submitted include a cost-effectiveness measure?  What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	<p>The Pharmaceutical Care Management Association (PCMA) appreciates the opportunity to submit comments regarding the therapeutic alternatives for Rivaroxaban. Our members help administer the Part D prescription drug benefit on behalf of many Part D plan sponsors, and a central component of that function is the identification of therapeutic alternatives to develop comprehensive prescription drug formularies consistent with applicable statutory, regulatory, and clinical requirements, including ensuring formularies are not discriminatory...In general, while we understand that CMS cannot disclose the specifics of their negotiations with manufacturers of selected drugs, we believe the public is best served by CMS disclosing as much about this process as possible, and otherwise aligning its methodology for selecting therapeutic alternatives with how Part D plans select therapeutic alternatives. Our comments focus on emphasizing the differences between identifying therapeutic alternatives for purposes of the Medicare Drug Price Negotiation Program, and the role that the identification of therapeutic alternatives plays under the Medicare Part D program's formulary standards and enrollee communication requirements. PCMA has three main points...1. As a general principle, CMS should identify therapeutic alternatives under the Medicare Drug Price Negotiation Program consistent with the guardrails that apply to Part D plan sponsors when identifying therapeutic alternatives for the Part D program. ...2. CMS should clarify in an HPMS memo to Part D plans that CMS's identification of therapeutic alternatives for the Medicare Drug Price Negotiation Program will not impact the agency's existing approach towards evaluating Part D formulary design for compliance with Part D formulary requirements...3. CMS</p>

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should clarify in an HPMS memo that Part D plans retain discretion on how to communicate therapeutic alternatives to enrollees, and that CMS's identification of therapeutic alternatives for purposes of the Medicare Drug Price Negotiation Program will not affect these enrollee communications...We discuss these issues in more detail below...I. CMS should identify therapeutic alternatives under the Medicare Drug Price Negotiation Program consistent with the guardrails that apply to Part D plan sponsors when identifying therapeutic alternatives for their formulary submissions. ..Currently, Part D plan sponsors consider a variety of factors when identifying therapeutic alternatives for their formulary submissions, including but not limited to (i) clinical effectiveness, (ii) safety, (iii) price, (iv) availability, and (v) patient preferences. Importantly, these factors are considered within a regulatory framework that imposes certain overarching formulary requirements. ..First, Part D plans must ensure that their formulary designs are nondiscriminatory. CMS considers several criteria when assessing whether a formulary is nondiscriminatory. CMS may presumptively approve formulary designs which align with the United States Pharmacopoeia's (USP) Medicare Model Guidelines (MMGs) based on the view that the MMGs reflect a scientifically and-clinically-based taxonomy developed by an independent expert body without a vested financial interest in the Part D program. The MMGs are also important because they provide a guiding framework for Part D plans to use when determining therapeutic alternatives. The MMGs group drugs into categories and classes. These categories and classes generally encompass the universe of potential therapeutic alternatives for a given medical condition. This means that Part D plans can use the MMGs to identify the range of therapeutic alternatives to consider when developing their formularies...Second, Part D plans must provide an adequate formulary, which among other things, means including at least two Part D drugs within a particular category or class of Part D drugs. This minimum formulary standard helps ensure a wide range of treatment options for enrollees, even if they have complex or rare medical conditions. Additionally, this requirement promotes patient choice and competition among drug manufacturers because the ability for patients to access alternative treatments incentivizes drug manufacturers to lower prices and innovate. The requirement to include at least two drugs per category or class helps to ensure that patients with a given medical condition have at least two formulary treatment options available to them, even if there are few therapeutic alternatives. This requirement is important because it prevents Part D plans from excluding entire categories or classes of drugs from their formularies...Third, Part D plans must consider cost sharing in the development of formularies. For example, CMS could raise concerns about formularies that place drugs on high cost-sharing tiers without placing therapeutic alternatives in preferable positions. CMS has also expressed concerns about "adverse tiering" where a plan sponsor assigns most or all drugs in the same therapeutic class needed to treat a specific chronic, high-cost medical condition to a high cost-sharing tier. In short, Part D plans must consider the enrollee's share of costs for a particular drug when considering therapeutic alternatives...PCMA encourages CMS to identify therapeutic alternatives for the Medicare Drug Price Negotiation Program in the same way that Part D plans do for their formularies. This would ensure consistency in process across two closely related programs and avoid introducing multiple, confusing standards for the same underlying definitional term. At the very least, aligning



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	<p>the selection of therapeutic alternatives under the Medicare Drug Price Negotiation Program with Part D formulary submissions would give Part D plans some assurance that CMS's assessment of their formulary submissions will not be affected by CMS's own process of selecting therapeutic alternatives...II. CMS's identification of therapeutic alternatives for the Medicare Drug Price Negotiation Program should not compromise the agency's evaluation of the adequacy of Part D plan formulary design, ensuring that Medicare beneficiaries continue to have access to a broad range of affordable prescription drugs...PCMA acknowledges that CMS's identification of therapeutic alternatives under the Medicare Drug Price Negotiation Program is required by law and essential for successful drug pricing negotiations. As stated above, we urge CMS to attempt to align its selection of therapeutic alternatives with how Part D plans select therapeutic alternatives...That being said, it is important to recognize that the exercise of selecting therapeutic alternatives for the Medicare Drug Price Negotiation Program and the Part D program, while overlapping in some areas, are ultimately distinct. Selecting therapeutic alternatives for the Medicare Drug Price Negotiation Program requires unique considerations that are not fully applicable to how Part D plans identify and leverage therapeutic alternatives for formulary development. Accordingly, we do not expect CMS to perfectly align itself with Part D plan sponsor methodologies for selecting therapeutic alternatives..First, therapeutic alternatives are a statutory feature of the Medicare Drug Price Negotiation Program. CMS selects therapeutic alternatives when negotiating pricing for selected drugs because the statute requires the agency to do so. Even if the statute did not require CMS to identify therapeutic alternatives, CMS would likely need to do so because it supports the agency in carrying out its statutory mandate to negotiate a "maximum fair price" (MFP) with manufacturers. Importantly, the MFP applies in a vacuum without regards to affordability and relative competitiveness with other drugs that a beneficiary may access...By contrast, while Part D plans are required to select therapeutic alternatives for formulary submissions, Part D plans select therapeutic alternatives based on a delicate balance between clinical comparability, cost-effectiveness, and beneficiary access. Unlike CMS, which is required to focus on a single drug in isolation when assessing therapeutic alternatives, Part D plans, PBMs, and their pharmacy and therapeutics (P&amp;T) committees are tasked with developing comprehensive formularies that holistically meet the complex needs of their enrollees. Part D plans must, already, cover selected drugs on their formularies under the statute, and CMS's interpretation worryingly suggests that such coverage may also involve a preferred status designation. Additional indirect restrictions on formulary design stemming from CMS's evaluation criteria under the Medicare Drug Price Negotiation Program could significantly hamper Part D plans' ability to offer competitive plan designs. In light of the comprehensive considerations that Part D plans must consider in developing formularies, CMS must ensure plans retain flexibility to adequately weigh all of these factors when developing formularies, including identifying therapeutic alternatives...Second, CMS's selection of therapeutic alternatives is a one-time event, done solely to determine the MFP for a selected drug. Once the MFP is determined, the drug's therapeutic alternatives play no further role in how Medicare beneficiaries access the selected drug...In contrast, a Part D plan sponsor's selection of therapeutic alternatives is used in multiple ways, including formulary design, coverage</p>
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### Response

determination, tiering exceptions, and Part D appeals. This means that Part D plans must carefully consider all potential scenarios in which their selection of therapeutic alternatives may be challenged...Third, CMS's identification of therapeutic alternatives for purposes of the Drug Price Negotiation Program is nonpublic. CMS indicates in the Revised Guidance for the Medicare Drug Price Negotiation Program that the agency will not unilaterally disclose any information pertaining to its negotiations with manufacturers, including the therapeutic alternatives identified for such negotiations. As a result, Part D plans do not have access to the therapeutic alternatives that CMS identifies for selected drugs. It would be unfair and arbitrary for CMS to evaluate Part D plan formulary submissions, including the identification of therapeutic alternatives contained in the submission, on a criteria that CMS never releases to the public. Formulary guidelines like the USP Medicare Model Guidelines provide a more predictable basis for administering a prescription drug benefit than nonpublic information. ..In short, while we urge CMS to align its methodology for selecting therapeutic alternatives as much as possible with Part D plans, we also request that CMS clarify that the therapeutic alternatives considered in the Medicare Drug Price Negotiation Program are distinct from the therapeutic alternatives that Part D plans must identify for purposes of formulary submissions and the overall administration of the prescription drug benefit. This will help ensure that Medicare beneficiaries continue to have access to a broad range of affordable prescription drugs. CMS can do this via an HPMS memo to Part D plans...III. Part D plans may continue to identify therapeutic alternatives in enrollee communications consistent with existing practices, regardless of CMS's identification of therapeutic alternatives for Medicare Drug Price Negotiation Program. ..Apart from formulary development, the issue of a drug's therapeutic alternatives also has implications on communications Part D sponsors are required to provide to enrollees. The Annual Notice of Change (ANOC) describes any changes to the plan's benefits, formularies, and costs for the upcoming year. The Evidence of Coverage (EOC) document describes the plan's benefits, coverage, and exclusions. Real-time benefit tools (RTBT) provide prescribers with information at the point-of-care on formulary and benefit information (including cost, formulary alternatives, and utilization management requirements). The monthly Explanation of Benefits (EOB) must include lower cost alternatives. ..While Part D plans are not required to include information about therapeutic alternatives in the ANOC or EOC, many voluntarily do so to help enrollees make informed decisions about their prescription drug coverage. This information is especially valuable for enrollees and prospective enrollees to fully understand the different treatment options available to them based on their unique circumstances. This transparency also promotes competition among Part D plans, as enrollees can better assess which plans are best for them. ..The RTBT and EOB rules have granted plans latitude in selecting which therapeutic alternatives would be displayed. CMS has stated that the "purpose of the beneficiary RTBT is to better inform beneficiaries about alternative medications," and thus, CMS allows "part D sponsors flexibility in implementing this requirement." For the EOB, CMS requires Part D sponsors to include lower-cost therapeutic alternatives but does not impose any specific requirements on plans on how they should identify those therapeutic alternatives...In summary, while Part D plans are required to communicate certain information to enrollees about therapeutic alternatives, CMS

## Public E2 Submission

IPAY: 2026



Question	Sub-Question	Response
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	provides plans with significant flexibility in the selection of those therapeutic alternatives. As such, CMS should explicitly clarify that the information on therapeutic alternatives that Part D plans choose to communicate to enrollees in required enrollee communications to beneficiaries and other regulatory requirements is not affected by CMS's selection of therapeutic alternatives for purposes of the Medicare Drug Price Negotiation Program.
	Evidence Submitted include a cost-effectiveness measure?	
Question 29: Comparative Effectiveness on Specific Populations	What type of Evidence is shown?	
	Response to Question 29	
	Hyperlink to Citation - Additional Materials for Question 29	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	

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Question	Sub-Question	Response
Question 30: Addressing Unmet Medical Needs	Response to Question 30	
	Hyperlink to Citation - Additional Materials for Question 30	
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 31: Patient and Caregiver Experience	Response to Question 31	
Question 32: Executive Summary	Response to Question 32	





## Answers to Question #28 for Public Submission

The Pharmaceutical Care Management Association (PCMA) appreciates the opportunity to submit comments regarding the therapeutic alternatives for Rivaroxaban. Our members help administer the Part D prescription drug benefit on behalf of many Part D plan sponsors, and a central component of that function is the identification of therapeutic alternatives to develop comprehensive prescription drug formularies consistent with applicable statutory, regulatory, and clinical requirements, including ensuring formularies are not discriminatory.

In general, while we understand that CMS cannot disclose the specifics of their negotiations with manufacturers of selected drugs, we believe the public is best served by CMS disclosing as much about this process as possible, and otherwise aligning its methodology for selecting therapeutic alternatives with how Part D plans select therapeutic alternatives. Our comments focus on emphasizing the differences between identifying therapeutic alternatives for purposes of the Medicare Drug Price Negotiation Program, and the role that the identification of therapeutic alternatives plays under the Medicare Part D program's formulary standards and enrollee communication requirements. PCMA has three main points:

1. As a general principle, CMS should identify therapeutic alternatives under the Medicare Drug Price Negotiation Program consistent with the guardrails that apply to Part D plan sponsors when identifying therapeutic alternatives for the Part D program.
2. CMS should clarify in an HPMS memo to Part D plans that CMS's identification of therapeutic alternatives for the Medicare Drug Price Negotiation Program will not impact the agency's existing approach towards evaluating Part D formulary design for compliance with Part D formulary requirements.
3. CMS should clarify in an HPMS memo that Part D plans retain discretion on how to communicate therapeutic alternatives to enrollees, and that CMS's identification of therapeutic alternatives for purposes of the Medicare Drug Price Negotiation Program will not affect these enrollee communications.

We discuss these issues in more detail below.

### **I. CMS should identify therapeutic alternatives under the Medicare Drug Price Negotiation Program consistent with the guardrails that apply to Part D plan sponsors when identifying therapeutic alternatives for their formulary submissions.**

Currently, Part D plan sponsors consider a variety of factors when identifying therapeutic alternatives for their formulary submissions, including but not limited to (i) clinical effectiveness, (ii) safety, (iii) price, (iv) availability, and (v) patient preferences. Importantly, these factors are considered within a regulatory framework that imposes certain overarching formulary requirements.

First, Part D plans must ensure that their formulary designs are nondiscriminatory.<sup>1</sup> CMS considers several criteria when assessing whether a formulary is nondiscriminatory. CMS may presumptively approve formulary designs which align with the United States Pharmacopoeia's (USP) Medicare Model Guidelines (MMGs) based on the view that the MMGs reflect a

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<sup>1</sup> See 42 C.F.R. § 423.272(b)(2).

scientifically and-clinically-based taxonomy developed by an independent expert body without a vested financial interest in the Part D program. The MMGs are also important because they provide a guiding framework for Part D plans to use when determining therapeutic alternatives. The MMGs group drugs into categories and classes. These categories and classes generally encompass the universe of potential therapeutic alternatives for a given medical condition. This means that Part D plans can use the MMGs to identify the range of therapeutic alternatives to consider when developing their formularies.

Second, Part D plans must provide an adequate formulary, which among other things, means including at least two Part D drugs within a particular category or class of Part D drugs.<sup>2</sup> This minimum formulary standard helps ensure a wide range of treatment options for enrollees, even if they have complex or rare medical conditions. Additionally, this requirement promotes patient choice and competition among drug manufacturers because the ability for patients to access alternative treatments incentivizes drug manufacturers to lower prices and innovate. The requirement to include at least two drugs per category or class helps to ensure that patients with a given medical condition have at least two formulary treatment options available to them, even if there are few therapeutic alternatives. This requirement is important because it prevents Part D plans from excluding entire categories or classes of drugs from their formularies.

Third, Part D plans must consider cost sharing in the development of formularies. For example, CMS could raise concerns about formularies that place drugs on high cost-sharing tiers without placing therapeutic alternatives in preferable positions.<sup>3</sup> CMS has also expressed concerns about "adverse tiering" where a plan sponsor assigns most or all drugs in the same therapeutic class needed to treat a specific chronic, high-cost medical condition to a high cost-sharing tier.<sup>4</sup> In short, Part D plans must consider the enrollee's share of costs for a particular drug when considering therapeutic alternatives.

PCMA encourages CMS to identify therapeutic alternatives for the Medicare Drug Price Negotiation Program in the same way that Part D plans do for their formularies. This would ensure consistency in process across two closely related programs and avoid introducing multiple, confusing standards for the same underlying definitional term. At the very least, aligning the selection of therapeutic alternatives under the Medicare Drug Price Negotiation Program with Part D formulary submissions would give Part D plans some assurance that CMS's assessment of their formulary submissions will not be affected by CMS's own process of selecting therapeutic alternatives.

**II. CMS's identification of therapeutic alternatives for the Medicare Drug Price Negotiation Program should not compromise the agency's evaluation of the adequacy of Part D plan formulary design, ensuring that Medicare beneficiaries continue to have access to a broad range of affordable prescription drugs.**

PCMA acknowledges that CMS's identification of therapeutic alternatives under the Medicare Drug Price Negotiation Program is required by law and essential for successful drug pricing

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<sup>2</sup> *Id.* at §

<sup>3</sup> § 30.2.7, Chapter 6, Medicare Prescription Drug Manual ("The CMS review will focus on identifying drug categories that may substantially discourage enrollment of certain beneficiaries by placing drugs in non-preferred tiers in the absence of commonly used therapeutically similar drugs in more preferred positions.").

<sup>4</sup> 87 Fed. Reg. 27208, 27303 (May 6, 2022).

negotiations. As stated above, we urge CMS to attempt to align its selection of therapeutic alternatives with how Part D plans select therapeutic alternatives.

That being said, it is important to recognize that the exercise of selecting therapeutic alternatives for the Medicare Drug Price Negotiation Program and the Part D program, while overlapping in some areas, are ultimately distinct. Selecting therapeutic alternatives for the Medicare Drug Price Negotiation Program requires unique considerations that are not fully applicable to how Part D plans identify and leverage therapeutic alternatives for formulary development.<sup>5</sup> Accordingly, we do not expect CMS to perfectly align itself with Part D plan sponsor methodologies for selecting therapeutic alternatives.

First, therapeutic alternatives are a statutory feature of the Medicare Drug Price Negotiation Program. CMS selects therapeutic alternatives when negotiating pricing for selected drugs because the statute *requires* the agency to do so. Even if the statute did not require CMS to identify therapeutic alternatives, CMS would likely need to do so because it supports the agency in carrying out its statutory mandate to negotiate a "maximum fair price" (MFP) with manufacturers. Importantly, the MFP applies in a vacuum without regards to affordability and relative competitiveness with other drugs that a beneficiary may access.

By contrast, while Part D plans are required to select therapeutic alternatives for formulary submissions, Part D plans select therapeutic alternatives based on a delicate balance between clinical comparability, cost-effectiveness, and beneficiary access. Unlike CMS, which is required to focus on a single drug in isolation when assessing therapeutic alternatives, Part D plans, PBMs, and their pharmacy and therapeutics (P&T) committees are tasked with developing comprehensive formularies that holistically meet the complex needs of their enrollees. Part D plans must, already, cover selected drugs on their formularies under the statute,<sup>6</sup> and CMS's interpretation worryingly suggests that such coverage may also involve a preferred status designation.<sup>7</sup> Additional indirect restrictions on formulary design stemming from CMS's evaluation criteria under the Medicare Drug Price Negotiation Program could significantly hamper Part D plans' ability to offer competitive plan designs. In light of the comprehensive considerations that Part D plans must consider in developing formularies, CMS must ensure plans retain flexibility to adequately weigh all of these factors when developing formularies, including identifying therapeutic alternatives.

Second, CMS's selection of therapeutic alternatives is a one-time event, done solely to determine the MFP for a selected drug. Once the MFP is determined, the drug's therapeutic alternatives play no further role in how Medicare beneficiaries access the selected drug.

In contrast, a Part D plan sponsor's selection of therapeutic alternatives is used in multiple ways, including formulary design, coverage determination, tiering exceptions, and Part D appeals. This means that Part D plans must carefully consider all potential scenarios in which their selection of therapeutic alternatives may be challenged.

Third, CMS's identification of therapeutic alternatives for purposes of the Drug Price Negotiation Program is nonpublic. CMS indicates in the Revised Guidance for the Medicare Drug Price

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<sup>5</sup> See 42 C.F.R. § 423.128(d)(4)(ii).

<sup>6</sup> Social Security Act § 1860D-4(b)(3)(I).

<sup>7</sup> See § 110, Medicare Drug Price Negotiation Program: Revised Guidance (June 30, 2023), <https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf>.



Negotiation Program that the agency will not unilaterally disclose any information pertaining to its negotiations with manufacturers, including the therapeutic alternatives identified for such negotiations. As a result, Part D plans do not have access to the therapeutic alternatives that CMS identifies for selected drugs. It would be unfair and arbitrary for CMS to evaluate Part D plan formulary submissions, including the identification of therapeutic alternatives contained in the submission, on a criteria that CMS never releases to the public. Formulary guidelines like the USP Medicare Model Guidelines provide a more predictable basis for administering a prescription drug benefit than nonpublic information.

In short, while we urge CMS to align its methodology for selecting therapeutic alternatives as much as possible with Part D plans, we also request that CMS clarify that the therapeutic alternatives considered in the Medicare Drug Price Negotiation Program are distinct from the therapeutic alternatives that Part D plans must identify for purposes of formulary submissions and the overall administration of the prescription drug benefit. This will help ensure that Medicare beneficiaries continue to have access to a broad range of affordable prescription drugs. CMS can do this via an HPMS memo to Part D plans.

**III. Part D plans may continue to identify therapeutic alternatives in enrollee communications consistent with existing practices, regardless of CMS's identification of therapeutic alternatives for Medicare Drug Price Negotiation Program.**

Apart from formulary development, the issue of a drug's therapeutic alternatives also has implications on communications Part D sponsors are required to provide to enrollees. The Annual Notice of Change (ANOC) describes any changes to the plan's benefits, formularies, and costs for the upcoming year. The Evidence of Coverage (EOC) document describes the plan's benefits, coverage, and exclusions. Real-time benefit tools (RTBT) provide prescribers with information at the point-of-care on formulary and benefit information (including cost, formulary alternatives, and utilization management requirements).<sup>8</sup> The monthly Explanation of Benefits (EOB) must include lower cost alternatives.<sup>9</sup>

While Part D plans are not required to include information about therapeutic alternatives in the ANOC or EOC, many voluntarily do so to help enrollees make informed decisions about their prescription drug coverage. This information is especially valuable for enrollees and prospective enrollees to fully understand the different treatment options available to them based on their unique circumstances. This transparency also promotes competition among Part D plans, as enrollees can better assess which plans are best for them.

The RTBT and EOB rules have granted plans latitude in selecting which therapeutic alternatives would be displayed. CMS has stated that the "purpose of the beneficiary RTBT is to better inform beneficiaries about alternative medications," and thus, CMS allows "part D sponsors flexibility in implementing this requirement."<sup>10</sup> For the EOB, CMS requires Part D sponsors to include lower-cost therapeutic alternatives but does not impose any specific requirements on plans on how they should identify those therapeutic alternatives.

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<sup>8</sup> § 119, Title I, Division CC, Consolidated Appropriations Act, 2021, Pub. L. No. 117-328 (amending section 1860D-4); *see also* 86 Fed. Reg. 5864, 5868 (Jan. 19, 2021).

<sup>9</sup> 42 C.F.R. 423.138(e)(5).

<sup>10</sup> 86 Fed. Reg. 5864, (May 6, 2022).

In summary, while Part D plans are required to communicate certain information to enrollees about therapeutic alternatives, CMS provides plans with significant flexibility in the selection of those therapeutic alternatives. As such, CMS should explicitly clarify that the information on therapeutic alternatives that Part D plans choose to communicate to enrollees in required enrollee communications to beneficiaries and other regulatory requirements is not affected by CMS's selection of therapeutic alternatives for purposes of the Medicare Drug Price Negotiation Program.