

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

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.¹ 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.

¹ 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 and described in section 50 of revised guidance.

Section 1194(e)(1) Data Factors

IPAY Year: 2026

Manufacturer: Astrazeneca AB

Drug: Farxiga (Dapagliflozin)

Background: 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 & 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:

- C: Research and Development Costs and Recoupment,
- D: Current Unit Costs of Production and Distribution,
- E: Prior Federal Financial Support,
- F: Patents, Exclusivities, and Approvals, and
- G: Market Data and Revenue and Sales Volume Data.

The Primary Manufacturer is responsible for aggregating and reporting all necessary data on its selected drug(s) from other parties, as applicable.

Disclaimers: 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.

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							
<p>Description: 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.</p>							
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

This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

AstraZeneca’s interest in FARXIGA was acquired in two stages:

- AstraZeneca entered into a collaboration with Bristol-Myers Squibb (“BMS”) to develop and commercialize FARXIGA in January 2007, at which time FARXIGA was in Phase II clinical trials.
- In February 2014 AstraZeneca acquired BMS’ remaining interest in FARXIGA in an agreement acquiring rights to a portfolio of products with BMS.

[REDACTED]

[REDACTED]

[REDACTED]

Explanation of Basic Pre-Clinical Research Costs

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As detailed in Question 1, AstraZeneca first acquired an interest in FARXIGA in 2007 when FARXIGA was in Phase II clinical trials. AstraZeneca thus did not incur any costs for basic pre-clinical research for FARXIGA as defined by CMS’s instructions.

Explanation of Post-IND Costs

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[REDACTED]

Type of Approval Pathway:

FARXIGA did not receive early approval for any of its three indications. The approval pathway was section 505(b)(1) of the Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)(1)).

Applicable Direct Costs:

Costs include costs associated with dosing and preparing FARXIGA for clinical trials and FARXIGA's Phase I, Phase II, and Phase III clinical trials for all currently approved indications [REDACTED]

Costs exclude (1) R&D costs related to studies that did not progress to an approved indication, such as Type 1 Diabetes; (2) trials run specifically to support non-U.S. approvals; (3) costs associated with developing fixed-dose combinations of dapagliflozin with other active ingredients [REDACTED]; (4) costs associated with ongoing basic pre-clinical research, clinical trials, and pending approvals; and (5) acquisition payments to BMS (see below for a description of the applicable allocation methodology). As noted in our response to Section E, no federal support payments have been identified for FARXIGA.

Calculation and Conversion Methodology

[REDACTED] These data sets are prepared using IFRS accounting principles, with all costs reported within the AstraZeneca Group Financial Statements as R&D costs. [REDACTED]

[REDACTED]

Costs are expressed in US dollars ("USD"). Consistent with the consolidation accounting principles applied in the AstraZeneca Group Financial Statements and GAAP, where costs are incurred in currencies other than USD, the amounts are translated into USD at average exchange rates, which approximate to actual rates, for the relevant accounting periods.

Length of Post-IND Period

The post-IND period began on December 20, 2003, which was the effective date for the IND for FARXIGA's T2D indication. [REDACTED]

[REDACTED] the post-IND period for FARXIGA runs from December 20, 2003, through August 29, 2023.

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

This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

[REDACTED]

Explanation of Costs of Other R&D

"This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

[REDACTED]

[REDACTED]

In accordance with the CMS ICR instructions, R&D costs reported in Section C are only included where they can be allocated to the development of FARXIGA. AstraZeneca policy is typically to not disclose research and development costs associated with a specific product, as this can lead to wrong conclusions and decisions. Research is a non-linear, iterative process where “failure” in a certain time may or may not generate benefits to later innovation efforts.”

Explanation of Global Lifetime Net Revenue

This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

Relevant Currency Conversions

In accordance with CMS instructions, the global, total lifetime net revenue is reported in nominal USD. Consistent with the consolidation accounting principles applied in the AstraZeneca Group Financial Statements and GAAP, where costs are incurred in currencies other than USD, the amounts are translated into US dollars at average exchange rates, which approximate to actual rates, for the relevant accounting periods.

Date Ranges for the Global, Total Lifetime Net Revenue Period

The global, total lifetime net revenue period begins on the date AstraZeneca first sold FARXIGA anywhere globally (2013) and runs through June 30, 2023, which is the end of the last full quarter prior to the selected drug publication date for FARXIGA.

How the Final Amount was Calculated:

The global, total lifetime net revenue for FARXIGA represents net invoice value less estimated rebates, cash discounts, returns, distribution service agreement fees, excise fees, patient affordability programs, chargebacks across all purchasers, [REDACTED]

[REDACTED] Many of these inputs are considered to be variable consideration and include significant estimates.

Sales are recognized when the control of the goods has been transferred to a third party. This is usually when title passes to the customer, either on shipment or on receipt of goods by the customer, depending on local trading terms. In markets where returns are significant, estimates of the quantity and value of goods which may ultimately be returned are accounted for at the point revenue is recognized. Revenue is not recognized in full until it is highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur.

Rebates are amounts payable or credited to a customer, usually based on the quantity or value of Product Sales to the customer for specific products in a certain period. Product sales rebates, which relate to product sales that occur over a period of time, are normally issued retrospectively. At the time product sales are invoiced, rebates and deductions that AstraZeneca expects to pay are estimated based upon assumptions developed using contractual terms, historical experience and market-related information. The rebates and deductions are recognized as variable consideration and recorded as a reduction to revenue with an accrual recorded. [REDACTED]

[REDACTED]

[REDACTED]

Explanation of U.S. Lifetime Net Revenue

This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

Methodology for currency conversions and calculations aligns to the details in the response to Question 6a, with only revenue from the United States and Territories included in the value reported for 6b.

Date Ranges for the U.S., Total Lifetime Net Revenue Period

The U.S., total lifetime net revenue period begins on the date AstraZeneca first sold FARXIGA in the U.S., which was January 1, 2014, and runs through June 30, 2023, which is the end of the last full quarter prior to the selected drug publication date for FARXIGA.

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
00310-6210-30	[REDACTED]	[REDACTED]	EA	[REDACTED]
00310-6210-39	[REDACTED]	[REDACTED]	EA	[REDACTED]
00310-6205-30	[REDACTED]	[REDACTED]	EA	[REDACTED]
00310-6210-95	[REDACTED]	[REDACTED]	EA	[REDACTED]

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
00310-6205-95	[REDACTED]	[REDACTED]	EA	[REDACTED]

Explanations: This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

Average Per Unit Production and Distribution Costs for FARXIGA were determined by calculating the total direct and indirect Production and Distribution costs allocatable to FARXIGA between June 1, 2022 and May 31, 2023 and dividing this sum by the Total Unit Volume at the NDC-11 level.

[REDACTED] Production costs included: (1) purchase of raw ingredients (including active pharmaceutical ingredients) [REDACTED]; (3) the direct cost incurred in formulating and preparing the finished product, including packaging, machine run-time, and product storage; (4) relevant site structure activities; (5) allocated central overhead costs; and [REDACTED]

Distribution Costs: Direct and indirect Distribution costs included: (1) packaging and packaging materials; (2) transportation costs; (3) warehousing; and (4) regional distribution center (RDC) fees. Transportation fees were inclusive of both primary and secondary distribution points.

E. Federal Financial Support

Description: 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
\$ -	No such federal funding support programs have been identified for FARXIGA.	OTH		No such federal funding support programs have been identified for FARXIGA.

Explanations: None.

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
6414126	2000-10-04	2020-10-04	Y	Y	Y	N	UTL	N
6515117	2002-05-20	2025-10-04	Y	Y	Y	N	UTL	Y
6936590	2002-10-04	2020-10-04	N	N	Y	N	UTL	N
7456254	2005-04-13	2025-06-30	N	N	Y	N	UTL	Y
7851502	2008-03-21	2028-08-19	Y	N	N	N	UTL	Y
7919598	2007-06-20	2029-12-16	N	Y	N	N	UTL	Y
8221786	2010-11-18	2028-03-21	Y	N	N	N	UTL	Y
8329648	2011-04-12	2026-08-18	N	N	Y	N	UTL	Y
8361972	2012-06-21	2028-03-21	N	N	Y	N	UTL	Y
8431685	2010-02-25	2025-04-13	N	N	Y	N	UTL	Y
8461105	2009-09-17	2025-04-13	N	N	Y	N	UTL	Y
8501698	2011-03-16	2027-06-20	Y	N	Y	N	UTL	Y
8685934	2010-05-26	2030-05-26	N	N	Y	N	UTL	Y
8716251	2013-01-04	2028-03-21	Y	N	N	N	UTL	Y
8906851	2012-12-07	2026-08-18	N	N	Y	N	UTL	Y
9198925	2014-05-02	2020-10-04	N	N	Y	N	UTL	N

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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
9238076	2013-01-16	2024-04-15	N	N	Y	N	UTL	Y
10973836	2020-03-09	2040-03-09	N	N	Y	N	UTL	Y
2020/0078382	2019-07-18	2039-07-18	N	N	Y	Y	UTL	N
2021/0260083	2021-02-25	2040-03-09	N	N	Y	Y	UTL	N

Explanations:

- Expired patent relates to the drug method of use: 6936590, 9198925
- Expired patent relates to the drug product, drug substance, and drug method of use: 6414126

- Granted patent relates to the drug method of use: 7456254, 8329648, 8361972, 8431685, 8461105, 8685934, 8906851, 9238076, 10973836
- Granted patent relates to the drug product: 7851502, 8221786, 8716251
- Granted patent relates to the drug product and drug method of use: 8501698
- Granted patent relates to the drug product, drug substance, and drug method of use: 6515117

- Granted patent relates to the drug substance: 7919598
- Pending application relates to the drug method of use: 2020/0078382, 2021/0260083 [REDACTED]

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	2023-05-05	202293	00310-6210; 00310-6205	S-020: To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure (NYHA class II-IV) with reduced ejection fraction
CIE	2024-04-30	202293	00310-6210; 00310-6205	S-024: To reduce the risk of sustained eGFR decline, end stage renal disease, CV death, hospitalization for heart failure in adults with chronic kidney disease at risk of progression
CIE	2026-05-08	202293	00310-6210; 00310-6205	S-026: Labeling revisions related to study D1699CC00001

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
202293	NDA	1	2014-01-08	New indication: An adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	TABLET: 5mg, 10mg	Bristol-Myers Squibb and AstraZeneca	APP	Orig-1: Initial FDA approval of FARXIGA for marketing
202293	NDA	10	2019-10-18	Added new indication: as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. • to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple	TABLET: 5mg, 10mg	AstraZeneca	APP	S-018: Provides revisions to labeling based on the results of Study D1693C0001, Dapagliflozin Effect on Cardiovascular Events (DECLARE), which was conducted to assess cardiovascular outcomes and to assess the risk of bladder cancer associated with dapagliflozin

F. Patents, Exclusivities, and Approvals

All Active and Pending FDA Applications and Approvals

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Application (NDA / BLA) Number	Application Type (NDA; BLA)	Class Code	Approval Date	Indication	Dosage Form and Strength	Sponsor	Application Status	Comments
				cardiovascular risk factors.				
202293	NDA	10	2020-05-05	Added new indication (and added disease headers) Type 2 Diabetes Mellitus: • as an adjunct to diet and exercise to improve glycemic control. • to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors. Heart Failure: • to reduce the risk of cardiovascular death	TABLET: 5mg, 10mg	AstraZeneca	APP	S-020: Efficacy-New Indication (Heart Failure)

F. Patents, Exclusivities, and Approvals

All Active and Pending FDA Applications and Approvals

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Application (NDA / BLA) Number	Application Type (NDA; BLA)	Class Code	Approval Date	Indication	Dosage Form and Strength	Sponsor	Application Status	Comments
				and hospitalization for heart failure in adults with heart failure with reduced ejection fraction (NYHA class II-IV).				
202293	NDA	10	2021-04-30	Added new indication: <ul style="list-style-type: none"> • as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. • to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple 	TABLET: 5mg, 10mg	AstraZeneca	APP	S-024: Efficacy-New Indication for kidney disease

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All Active and Pending FDA Applications and Approvals

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Application (NDA / BLA) Number	Application Type (NDA; BLA)	Class Code	Approval Date	Indication	Dosage Form and Strength	Sponsor	Application Status	Comments
				cardiovascular risk factors. • to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure with reduced ejection fraction (NYHA class II-IV). • to reduce the risk of sustained eGFR decline, end stage kidney disease cardiovascular death and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.				

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
202293	NDA	10	2023-05-08	Modified indication and re-ordered others: • To reduce the risk of sustained eGFR decline, end stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression. • To reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure. • To reduce the risk of hospitalization for	TABLET: 5mg, 10mg	AstraZeneca	APP	S-026: Efficacy-New Indication for broadened Heart Failure

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
				heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors. • As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus				

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
00310-6205-30	2023-Q2	\$ 18.84	EA	
00310-6205-30	2023-Q1	\$ 18.84	EA	
00310-6205-30	2022-Q4	\$ 18.29	EA	
00310-6205-30	2022-Q3	\$ 18.29	EA	
00310-6205-30	2022-Q2	\$ 18.29	EA	
00310-6205-30	2022-Q1	\$ 18.29	EA	
00310-6205-30	2021-Q4	\$ 17.76	EA	
00310-6205-30	2021-Q3	\$ 17.76	EA	
00310-6205-30	2021-Q2	\$ 17.76	EA	
00310-6205-30	2021-Q1	\$ 17.76	EA	
00310-6205-30	2020-Q4	\$ 17.24	EA	
00310-6205-30	2020-Q3	\$ 17.24	EA	
00310-6205-30	2020-Q2	\$ 16.91	EA	
00310-6205-30	2020-Q1	\$ 16.91	EA	
00310-6205-30	2019-Q4	\$ 16.41	EA	
00310-6205-30	2019-Q3	\$ 16.41	EA	
00310-6205-30	2019-Q2	\$ 16.41	EA	
00310-6205-30	2019-Q1	\$ 16.41	EA	
00310-6205-30	2018-Q4	\$ 15.48	EA	
00310-6205-30	2018-Q3	\$ 15.48	EA	
00310-6210-30	2023-Q2	\$ 18.84	EA	
00310-6210-30	2023-Q1	\$ 18.84	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
00310-6210-30	2022-Q4	\$ 18.29	EA	
00310-6210-30	2022-Q3	\$ 18.29	EA	
00310-6210-30	2022-Q2	\$ 18.29	EA	
00310-6210-30	2022-Q1	\$ 18.29	EA	
00310-6210-30	2021-Q4	\$ 17.76	EA	
00310-6210-30	2021-Q3	\$ 17.76	EA	
00310-6210-30	2021-Q2	\$ 17.76	EA	
00310-6210-30	2021-Q1	\$ 17.76	EA	
00310-6210-30	2020-Q4	\$ 17.24	EA	
00310-6210-30	2020-Q3	\$ 17.24	EA	
00310-6210-30	2020-Q2	\$ 16.91	EA	
00310-6210-30	2020-Q1	\$ 16.91	EA	
00310-6210-30	2019-Q4	\$ 16.41	EA	
00310-6210-30	2019-Q3	\$ 16.41	EA	
00310-6210-30	2019-Q2	\$ 16.41	EA	
00310-6210-30	2019-Q1	\$ 16.41	EA	
00310-6210-30	2018-Q4	\$ 15.48	EA	
00310-6210-30	2018-Q3	\$ 15.48	EA	
00310-6210-39	2023-Q2	\$ 18.84	EA	
00310-6210-39	2023-Q1	\$ 18.84	EA	
00310-6210-39	2022-Q4	\$ 18.29	EA	
00310-6210-39	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
00310-6210-39	2022-Q2		EA	
00310-6210-39	2022-Q1		EA	
00310-6210-39	2021-Q4		EA	
00310-6210-39	2021-Q3		EA	
00310-6210-39	2021-Q2		EA	
00310-6210-39	2021-Q1		EA	
00310-6210-39	2020-Q4		EA	
00310-6210-39	2020-Q3		EA	
00310-6210-39	2020-Q2		EA	
00310-6210-39	2020-Q1		EA	
00310-6210-39	2019-Q4		EA	
00310-6210-39	2019-Q3		EA	
00310-6210-39	2019-Q2		EA	
00310-6210-39	2019-Q1		EA	
00310-6210-39	2018-Q4		EA	
00310-6210-39	2018-Q3		EA	

Explanations: This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

WAC pricing is established by AstraZeneca Pharmaceuticals, LP. WAC pricing does not exist for sample packs 00310-6210-95 and 00310-6205-95.

WAC unit prices provided align to those found in available drug databases (e.g. Medi-Span, First Databank, Red Book). 00310-6210-39 launched

in 4Q22 and prior quarters are accordingly reported as 0. Total units reflect standard and emergency orders net of returns and credit/debit adjustments.

G. Market Data and Revenue and Sales Volume Data					
Medicaid Best Price					
<p>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.</p>					
Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	00310-6205	2023-Q2		EA	
Y	00310-6205	2023-Q1		EA	
Y	00310-6205	2022-Q4		EA	
Y	00310-6205	2022-Q3		EA	
Y	00310-6205	2022-Q2		EA	
Y	00310-6205	2022-Q1		EA	
Y	00310-6205	2021-Q4		EA	
Y	00310-6205	2021-Q3		EA	
Y	00310-6205	2021-Q2		EA	
Y	00310-6205	2021-Q1		EA	
Y	00310-6205	2020-Q4		EA	
Y	00310-6205	2020-Q3		EA	
Y	00310-6205	2020-Q2		EA	
Y	00310-6205	2020-Q1		EA	
Y	00310-6205	2019-Q4		EA	
Y	00310-6205	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	00310-6205	2019-Q2		EA	
Y	00310-6205	2019-Q1		EA	
Y	00310-6205	2018-Q4		EA	
Y	00310-6205	2018-Q3		EA	
Y	00310-6210	2023-Q2		EA	
Y	00310-6210	2023-Q1		EA	
Y	00310-6210	2022-Q4		EA	
Y	00310-6210	2022-Q3		EA	
Y	00310-6210	2022-Q2		EA	
Y	00310-6210	2022-Q1		EA	
Y	00310-6210	2021-Q4		EA	
Y	00310-6210	2021-Q3		EA	
Y	00310-6210	2021-Q2		EA	
Y	00310-6210	2021-Q1		EA	
Y	00310-6210	2020-Q4		EA	
Y	00310-6210	2020-Q3		EA	
Y	00310-6210	2020-Q2		EA	
Y	00310-6210	2020-Q1		EA	
Y	00310-6210	2019-Q4		EA	
Y	00310-6210	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	00310-6210	2019-Q2		EA	
Y	00310-6210	2019-Q1		EA	
Y	00310-6210	2018-Q4		EA	
Y	00310-6210	2018-Q3		EA	

Explanations: This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

Best Price is based on sales and contracted discounts from AstraZeneca Pharmaceuticals, LP.

Best Price data provided aligns to CMS Medicaid Drug Programs system filings, rounded to the second decimal place. The Medicaid Best Price Unit Type for FARXIGA is a tablet.

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	00310-6205-30	2022-01-01 - 2022-12-31	\$452.30	EA	
Y	00310-6205-30	2021-01-01 - 2021-12-31	\$486.61	EA	
Y	00310-6205-30	2020-01-01 - 2020-12-31	\$480.04	EA	
Y	00310-6205-30	2019-09-30 - 2019-12-31	\$480.04	EA	
Y	00310-6205-30	2019-01-01 - 2019-09-29	\$415.52	EA	
Y	00310-6205-30	2018-01-01 - 2018-12-31	\$304.94	EA	
Y	00310-6210-30	2021-01-01 - 2021-12-31	\$486.61	EA	
Y	00310-6210-30	2020-01-01 - 2020-12-31	\$480.04	EA	
Y	00310-6210-30	2019-09-30 - 2019-12-31	\$480.04	EA	
Y	00310-6210-30	2019-01-01 - 2019-09-29	\$415.52	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	00310-6210-30	2018-01-01 - 2018-12-31	\$304.94	EA	
Y	00310-6210-39	2023-01-18 - 2023-06-30	\$394.16	EA	
Y	00310-6210-30	2022-01-01 - 2022-12-31	\$452.30	EA	

Explanations: This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

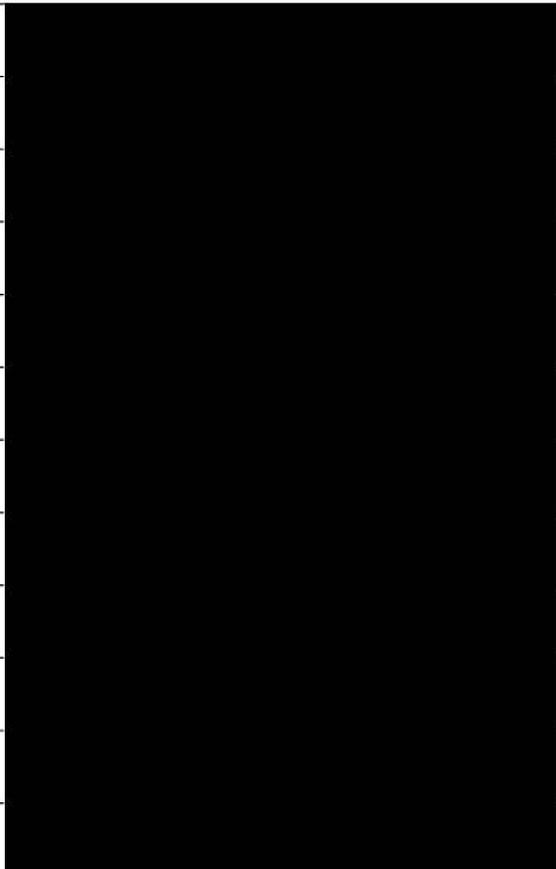
FSS Price is based on sales and contracted discounts from AstraZeneca Pharmaceuticals, LP. FSS Price does not exist for sample packs 00310-6210-95 and 00310-6205-95.

FSS Price is reported at the package level, aligned to what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs. Total unit volume is reported at the EA (30 tablets = 1 package). Pricing for 00310-6210-39 was not active on FSS contract until 01/18/2023.

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	00310-6205-30	2022-01-01 - 2022-12-31	\$395.98	EA	
Y	00310-6205-30	2021-01-01 - 2021-12-31	\$361.76	EA	
Y	00310-6205-30	2020-01-01 - 2020-12-31	\$343.58	EA	
Y	00310-6205-30	2019-09-30 - 2019-12-31	\$319.16	EA	
Y	00310-6205-30	2019-01-01 - 2019-09-29	\$319.16	EA	
Y	00310-6205-30	2018-01-01 - 2018-12-31	\$286.65	EA	
Y	00310-6210-30	2022-01-01 - 2022-12-31	\$396.14	EA	
Y	00310-6210-30	2021-01-01 - 2021-12-31	\$361.83	EA	
Y	00310-6210-30	2020-01-01 - 2020-12-31	\$344.34	EA	
Y	00310-6210-30	2019-09-30 - 2019-12-31	\$318.67	EA	
Y	00310-6210-30	2019-01-01 - 2019-09-29	\$318.67	EA	
Y	00310-6210-30	2018-01-01 - 2018-12-31	\$286.49	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	00310-6210-39	2023-05-16 - 2023-06-30		EA	
Y	00310-6210-39	2023-01-18 - 2023-05-15		EA	

Explanations: This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

Big4 Price is based on sales and contracted discounts from AstraZeneca Pharmaceuticals, LP. Big4 Price does not exist for sample packs 00310-6210-95 and 00310-6205-95.

Big4 Price is reported at the package level, aligned to what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs. Total unit volume is reported at the EA (30 tablets = 1 package). Pricing for 00310-6210-39 was not active on FSS contract until 01/18/2023.

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
00310-6205-30	2023-Q2				EA	
00310-6205-30	2023-Q1				EA	
00310-6205-30	2022-Q4				EA	
00310-6205-30	2022-Q3				EA	
00310-6205-30	2022-Q2				EA	
00310-6205-30	2022-Q1				EA	
00310-6205-30	2021-Q4				EA	
00310-6205-30	2021-Q3				EA	
00310-6205-30	2021-Q2				EA	
00310-6205-30	2021-Q1				EA	
00310-6205-30	2020-Q4				EA	
00310-6205-30	2020-Q3				EA	
00310-6205-30	2020-Q2				EA	
00310-6205-30	2020-Q1				EA	
00310-6205-30	2019-Q4				EA	
00310-6205-30	2019-Q3				EA	
00310-6205-30	2019-Q2				EA	
00310-6205-30	2019-Q1				EA	
00310-6205-30	2018-Q4				EA	
00310-6205-30	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
00310-6210-30	2023-Q2				EA	
00310-6210-30	2023-Q1				EA	
00310-6210-30	2022-Q4				EA	
00310-6210-30	2022-Q3				EA	
00310-6210-30	2022-Q2				EA	
00310-6210-30	2022-Q1				EA	
00310-6210-30	2021-Q4				EA	
00310-6210-30	2021-Q3				EA	
00310-6210-30	2021-Q2				EA	
00310-6210-30	2021-Q1				EA	
00310-6210-30	2020-Q4				EA	
00310-6210-30	2020-Q3				EA	
00310-6210-30	2020-Q2				EA	
00310-6210-30	2020-Q1				EA	
00310-6210-30	2019-Q4				EA	
00310-6210-30	2019-Q3				EA	
00310-6210-30	2019-Q2				EA	
00310-6210-30	2019-Q1				EA	
00310-6210-30	2018-Q4				EA	
00310-6210-30	2018-Q3				EA	

Explanations: This narrative and the data reported should be treated as proprietary and trade secret and otherwise protected from disclosure under the Trade Secrets Act or Exemption 4 under the Freedom of Information Act.

U.S. Commercial Average Net Unit Price is based on sales and contracted discounts from AstraZeneca Pharmaceuticals, LP.

[Redacted]

[Redacted]

Manufacturer E2 Submission - AstraZeneca



Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	DAPAGLIFLOZIN
	Respondent Name	Emery Melville
	Organization Name (if applicable)	AstraZeneca
	Respondent Email	emery.melville1@astrazeneca.com
	Who is completing this form?	
Question 27: Prescribing Information	Prescribing Information	<p>I. Overview FARXIGA® is approved to treat three interrelated and often comorbid diseases: chronic kidney disease (CKD), heart failure (HF), and type 2 diabetes mellitus (T2DM), each of which imposes a significant and growing burden on the Medicare patient population and increases overall medical expenditures.[1] FARXIGA is representative of AstraZeneca’s commitment to developing innovative, lifesaving medicines and making these medicines accessible to patients, aligning with CMS’ goals for the Medicare Drug Price Negotiation Program.</p> <p>It is well recognized that patients with one of CKD, HF, or T2DM comorbid diseases are at high risk for developing two or more of these conditions.[2][3][4] Indeed, approximately 31% of the Medicare Part D population with one of the three comorbid conditions treated by FARXIGA—CKD, HF, and T2DM—suffers from two or more of them.[5]</p> <p>[REDACTED] Indeed, patients with each of these conditions present significantly disproportionate costs for Medicare. Patients with one condition of CKD, HF, or T2DM account for almost double the average healthcare spending per capita, while the average cost for a patient with all three conditions is nearly \$50,000 per year—approximately four times that of the average American.[6] Medicare enrollees experience 11 million costly and life-changing clinical events—hospitalization or death—annually related to CKD and HF alone.[7]</p> <p>[REDACTED]</p> <p>As described herein, current clinical treatment guidelines recognize the value of the SGLT2i class as a foundational treatment for these critical Medicare patient populations. However, FARXIGA [REDACTED] demonstrating significant reductions in clinical outcomes across the metabolic, cardiovascular, and renal continuum</p>



Question	Sub-Question	Response
		<p>for patients with and without T2DM.[8][9][10][11] Notably, FARXIGA obtained a Breakthrough Therapy Designation for patients with CKD and was the first SGLT2i approved for the treatment of CKD irrespective of T2DM status.[12][13] It is the only SGLT2i where clinical trials have shown a reduction in all-cause mortality in patients with CKD.[1][14][15][16][17][18][19][20] In HF, FARXIGA is the only SGLT2i that has been proven to reduce the risk of cardiovascular (CV) death in patients with HF with reduced ejection fraction (HFrEF).[8] FARXIGA is also the only SGLT2i that has demonstrated a reduction in the risk of hospitalization for heart failure (hHF) in patients with T2DM without established CV diseases.[21]</p> <p>FARXIGA delivers these benefits across these three prevalent disease areas [REDACTED] [REDACTED] [REDACTED] [22][23][24] Notably, these therapies are not SGLT2i and have no evidence to support a therapeutic impact across the metabolic, cardiovascular, and renal spectrum thus cannot be considered therapeutic alternatives to FARXIGA.</p> <p>II. Mechanism of Action By inhibiting SGLT2, FARXIGA reduces reabsorption of filtered glucose and thereby promotes urinary glucose excretion.[1] FARXIGA also reduces sodium reabsorption and increases the delivery of sodium to the distal tubule. This may influence several physiological functions including, but not restricted to, lowering both pre- and afterload of the heart and downregulation of sympathetic activity, and decreased intraglomerular pressure which is believed to be mediated by increased tubuloglomerular feedback. The mechanism of action leads to both glycemic and non-glycemic effects, as outlined herein.</p> <p>III. Prescribing Information by Indication for Selected Drug and Therapeutic Alternatives Below we provide the approved prescribing information for the selected drug, FARXIGA, and its therapeutic alternatives, by indication. [REDACTED] [REDACTED]</p> <p>A. Chronic Kidney Disease Selected Drug: FARXIGA is indicated to reduce the risk of sustained eGFR decline, ESKD, CV death, and hHF in adults with CKD at risk of progression.[1] FARXIGA is also likely to be effective in patients with less advanced CKD.[1]</p> <p>Therapeutic Alternatives: As of the date of drafting, FARXIGA is the only SGLT2i indicated for the treatment of CKD</p>



Question	Sub-Question	Response
		with and without T2DM with benefits across the metabolic, cardiovascular, and renal spectrum.[1][14][15][16][17][18]
		[19]
		[15]
		[16][17][18] [1][17]
		[25]



Question	Sub-Question	Response
		<p>[REDACTED]</p> <p>[26][27][1][28][29][30]</p>
		<p>B. Heart Failure</p> <p>Selected Drug: FARXIGA is indicated to reduce the risk of CV death, hHF, and urgent HF visits in adults with HF.[1]</p> <p>[REDACTED]</p> <p>[14]</p> <p>[REDACTED]</p> <p>[1]</p> <p>[REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p> <p>C. Type 2 Diabetes</p> <p>Selected Drug: FARXIGA is indicated: (1) as an adjunct to diet and exercise to improve glycemic control in adults with T2DM; and (2) to reduce the risk of hHF in adults with T2DM and either established CV disease or multiple CV risk factors.[1]</p> <p>[REDACTED]</p>



Question	Sub-Question	Response
		<p>[REDACTED]</p>
		<p>[REDACTED]</p>
		<p>[REDACTED]</p>
		<p>In general, other glucose-lowering drugs—several of which come at a higher cost—are not therapeutic alternatives to FARXIGA for T2DM because these products are not in the same therapeutic class and are not clinically comparable because they do not provide comparable benefits across CKD, HF, and T2DM.</p> <p>The 2023 American Diabetes Association/European Association for the Study of Diabetes (ADA/EASD) guidelines[37] include metformin, DPP4i, thiazolidinediones, sulfonylureas, insulin (human and analogs), GLP1 RAs, GIP/GLP1 RAs, and SGLT2i. [REDACTED] CV effects of GIP/GLP-1 RAs are under investigation and their use is not emphasized in the guidelines. That is, SGLT2i, [REDACTED], uniquely provide cardiovascular and renal protection to patients with T2DM who are likely to have or to develop cardiorenal comorbidities, while also reducing HbA1c, SBP, and body weight.[1][14]</p> <p>[REDACTED], as ADA guidelines recommend use in different populations compared with SGLT2i.[37]</p>



Question	Sub-Question	Response
		<p>[REDACTED] is generally introduced later in a patient’s treatment pathway after other therapies, [REDACTED]</p> <p>IV. Use in Course of Care FARXIGA, as part of the SGLT2i class, is now included in numerous national and international treatment guidelines across CKD; HF, for which it is a “foundational” therapy; and T2DM, where SGLT2i offer unique cardiorenal benefits in addition to glycemic control.[38][39][40][37]</p> <p>A. Chronic Kidney Disease The public preview draft of the Kidney Disease: Improving Global Outcome (KDIGO) guidelines (published July 2023)[41] considered the demonstrated benefits of SGLT2i (reduced risk of kidney failure, AKI, HFrEF, CV death and MI) to outweigh the low risk of any harm and recommends the use of SGLT2i in adults:</p> <ul style="list-style-type: none"> • With CKD and HF or an eGFR ≥ 20 ml/min/1.73 m² with urine albumin-to-creatinine ratio (UACR) ≥ 200 mg/g (1A); and • With eGFR ≥ 20 to 45 ml/min/1.73 m² with UACR <200 mg/g (2B). <p>These guidelines capture the majority of CKD patients, and the KDIGO guidelines describe SGLT2i use as a “first line drug therapy for most patients,” continued until dialysis or transplant, as part of a recommended holistic approach to CKD treatment and risk modification.[41]</p> <p>A commentary on a previous (2020) version of KDIGO guidelines from the U.S. Kidney Disease Outcomes Quality Initiative (KDOQI)[42] specifically discussed SGLT2i use in the context of how to optimize care for patients with T2DM and CKD. They describe the cardiorenal benefits associated with SGLT2i therapies as “a turning point” for the treatment and prognosis of patients with T2DM and CKD, and the “magnitude of their mitigating effect on cardiorenal end points and general consistency of findings” as “a rarity.”[42]</p> <p>B. Heart Failure Guidelines for HF treatment have historically been segregated on the basis of ejection fraction (EF): heart failure with reduced ejection fraction (HFrEF), heart failure with mildly reduced ejection fraction (HFmrEF), and heart failure with preserved ejection fraction (HFpEF) because no class of drug had demonstrated efficacy across the spectrum of ejection fraction. This has changed in recent years as the SGLT2i class has shown efficacy across the EF spectrum. [38][39][40]</p>



Question	Sub-Question	Response
		<p>In the 2022 American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America (HFSA) Guideline for the Management of Heart Failure, SGLT2i are recommended across the EF spectrum as part of guideline-directed medical therapy for all three categories of ejection fractions.[38]</p> <p>Heart Failure with Reduced Ejection Fraction: The term “foundational” therapy refers to key life-saving pharmacological treatments that form the foundations of drug and device management of patients with HFrEF. As such, “foundational” therapy is strongly recommended in the major clinical guidelines for all patients who can tolerate it. Currently, “foundational” therapy for HFrEF consists of distinct effects, administered by four medication classes: renin-angiotensin system inhibitors (ARNi, ACEi or ARB), beta blockers, MRAs, and SGLT2i, including FARXIGA.[32] The therapies are complementary, acting on distinct patho-physiological pathways, with independent and additive mechanisms of action.</p> <p>In patients with symptomatic and chronic HFrEF, SGLT2i are recommended to reduce hHF and CV mortality irrespective of T2DM status, based on the hHF, CV death, and all-cause mortality results in the DAPA-HF and EMPEROR-Reduced trials.[32]</p> <p>Guideline-directed medical therapy for HFrEF includes SGLT2i together with ARNi/ACEi/ARB, beta-blockers and MRAs (including spironolactone). Starting a patient on all four therapies as quickly as possible, even at a low dose, is the primary treatment goal, reflecting SGLT2i’s key role as a foundational therapy.[32]</p> <p>Heart Failure with Mildly Reduced Ejection Fraction: As there are no prospective RCTs specifically for patients with HFmrEF, recommendations are based on post-hoc and subset analyses of other HF trials. SGLT2i are recommended in HFmrEF as being beneficial in decreasing hHF and CV mortality.[38][40] Other classes of medication which are part of the guideline-directed medical therapy (ARNi, ACEi, ARB, MRAs, beta blockers) have lower levels of evidence supporting their use than SGLT2i.[38][40]</p> <p>Heart Failure with Preserved Ejection Fraction: HFpEF is highly prevalent, accounting for up to 50% of all patients with HF, and is associated with significant morbidity and mortality. Until the emergence of SGLT2i, there was a large unmet need for patients with HF and HFpEF due to the paucity of specifically indicated treatments and suboptimal management.</p> <p>Currently, guidelines recommend SGLT2i for HFpEF patients to reduce HF hospitalizations and CV mortality.[38][40] ARB, ARNi, and MRAs have weaker evidence underlying their recommendations than SGLT2i.[38]</p> <p>C. Type 2 Diabetes</p>



Question	Sub-Question	Response
		<p>SGLT2i is recommended within specific populations with T2DM, while delivering broad benefits at a lower cost than many clinical alternatives.</p> <p>The 2022 Consensus Report by the ADA and the EASD[43] represents a major guideline of best practice.</p> <ul style="list-style-type: none"> • It recommends to preferentially use SGLT2i or ██████████ GLP-1 RAs for glycemic management in patients who are at risk or have established atherosclerotic cardiovascular disease (ASCVD) ahead of other oral therapy classes (e.g., metformin, TZD) or insulin. • For patients with HF, SGLT2i with a proven benefit in this population are preferred (FARXIGA and empagliflozin). • For patients with CKD, SGLT2i with a proven benefit in this population are preferred over ██████████ priced GLP-1 RAs and other medications. • For patients with T2DM with established atherosclerotic CV disease or kidney disease, an SGLT2i or a (generally higher-priced) GLP-1 RA is recommended as part of a CV risk reduction and/or glycemic management regimen ahead of other oral therapy classes (including metformin, TZD) or insulin. <p>In the U.S., the ADA more recently published “Standards of Care in Diabetes – 2023,” which largely mirror the 2022 Consensus Report recommendations in their recommendations of SGLT2i use.[37]</p> <p>Note: References for this questions can be found in the .zip file attached to question I-30.</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>I. Therapeutic Advance FARXIGA, and sodium-glucose cotransporter 2 inhibitors (SGLT2i) as a class, represent an important, unique therapeutic advance that addresses three separate but frequently coexisting disease states: chronic kidney disease (CKD), heart failure (HF), and type 2 diabetes mellitus (T2DM). FARXIGA is representative of AstraZeneca’s commitment to developing innovative, lifesaving medicines and making these medicines accessible to patients, aligning with CMS’ goals for the Medicare Drug Price Negotiation Program.</p> <p>As illustrated in Figure 2, CKD, HF, and T2DM combine to place substantial clinical burdens on Medicare Part D</p>



Question	Sub-Question	Response
		<p>beneficiaries and substantial costs on the Medicare program. Of the 16 million Medicare Part D beneficiaries who have at least one of these diseases, approximately 31% suffer from two or more. [1].</p> <p>FARXIGA provides a particular advance in treating CKD, HF, and T2DM because it, [REDACTED] [REDACTED] can lower blood glucose while also providing cardiorenal benefits, such as reducing the progression of CKD and lowering the rate of cardiovascular (CV) death and hospitalization for heart failure (hHF).[2][3][4][5][6][7][8] Given these benefits, and taking into account the 799,000 Medicare Part D enrollees prescribed FARXIGA in the most recent 12 months of data, Medicare would expect medical cost reductions of [REDACTED] [REDACTED] due to the avoidance of clinical events, [REDACTED] [REDACTED]</p> <p>As described herein, FARXIGA has demonstrated unique benefits in comparison to its therapeutic alternatives within the SGLT2i class: It is the only SGLT2i where clinical trials have shown a reduction in all-cause mortality in patients with CKD. [10][11][12][13][14][15][16][5][17] In HF, FARXIGA is the only SGLT2i that has been proven to reduce the risk of cardiovascular death in patients with HFrEF and is the only SGLT2i that has shown benefit across the full ejection fraction range, without attenuation of benefit.[10][18] FARXIGA is the only SGLT2i that has demonstrated a significant reduction in the risk of hHF in both non-T2DM patients and a broad T2DM patient population, including those with either CV risk factors or established CV disease.[2]</p> <p>II. Comparative Effectiveness</p> <p>While the following sections compare FARXIGA with its therapeutic alternatives on key outcomes across CKD, HF, and T2DM, FARXIGA’s comparative effectiveness cannot fully be summarized for any single indication. Instead, by providing clinical benefits across all three co-occurring disease states in a way no other class of drugs does, FARXIGA and certain other SGLT2i inherently represent a therapeutic advance over other products.</p> <p>Because there have been no head-to-head randomized controlled trials (RCTs) among SGLT2i, the highest quality of evidence for comparative effectiveness are meta-analyses and network meta-analyses (making indirect comparison using common comparators), which are cited throughout. The use of such analyses is a standard methodology used by technology assessment bodies, such as ICER in the U.S., to assess comparative clinical effectiveness.[19]</p> <p>FARXIGA specifically, and SGLT2i generally, stand out versus therapeutic alternatives and [REDACTED] [REDACTED]—products for delivering proven benefits across key outcomes for CKD, HF, and T2DM. Figure 4 represents</p>



Question	Sub-Question	Response
		<p>this by summarizing the below evidence on key outcomes.</p> <p>A. Chronic Kidney Disease In 2020, approximately one in seven Medicare FFS beneficiaries had CKD, with spending exceeding \$75 billion, representing about 25% of fee-for-service total spending.[20] Each year, about one in ten Medicare beneficiaries with CKD will die.[20] FARXIGA was the first SGLT2i approved to treat CKD for patients with and without T2DM and was designated a Breakthrough Therapy by the FDA. FARXIGA delivers [REDACTED] versus therapeutic alternatives and other products on three key outcomes for CKD, including: (1) kidney disease progression; (2) cardiovascular death or hHF; and (3) acute kidney injury. These key outcomes were selected because they are the most impactful clinical outcomes and have been studied widely in CKD across SGLT2i in peer-reviewed meta-analyses, reflecting the clinical relevance to CKD patients and the substantial amount of randomized, high-quality data available in the published literature. This evidence is outlined below for each of the key outcomes.</p> <p>The clinical benefits of FARXIGA across these key outcomes in CKD translate into significantly fewer deaths and lower medical costs, hHF, initiation of kidney replacement due to ESKD, and dramatic declines in kidney function [21][47][22] These improvements translate into a 6.6-year delay in the onset of ESKD and a [REDACTED] delay in all-cause mortality, while producing projected total medical cost-offsets (savings) versus the standard of care of [REDACTED] in the over-65 population in one year.[47][22] Modeling suggests these benefits can generate a cost savings of approximately [REDACTED] per patient in medical costs avoided for CKD [REDACTED]</p> <p>These significant benefits are not typically seen outside of the SGLT2i class, where [REDACTED] products in other classes do not deliver benefits on these key outcomes. For instance, in a meta-analysis involving over 50,000 patients, Zhang et al. found that glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and finerenone failed to reduce the risk of kidney disease progression, renal death, hHF, cardiovascular death, or all-cause death for patients with CKD and T2DM, relative to SGLT2i as a class.[23]</p> <p>Kidney Disease Progression: SGLT2i deliver immensely valuable benefits in delaying kidney disease progression. One meta-analysis involving more than 90,000 patients demonstrated SGLT2i reduce the risk of kidney disease progression, with similar reductions in risk achieved in patients with and without T2DM.[24] Further, a meta-analysis across three SGLT2i found that SGLT2i substantially reduced the risk of dialysis, transplantation, and death due to kidney disease—with clear, separate evidence across all subgroups with declining levels of kidney function.[25]</p> <p>Across the entire class, the meta-analysis found that there was a 35% reduction in the risk of end-stage kidney</p>



Question	Sub-Question	Response
		<p>As discussed at greater length in Question 27, SGLT2i have been described as a “foundational therapy” for HF patients.[28] The most recent AHA Guidelines for the Management of Heart Failure recommend SGLT2i as a first-line therapy for patients, as part of standard of care, regardless of EF.[29] SGLT2i significantly reduce hHF and CV death across the full spectrum of age and EF subgroups, as shown in a meta-analysis including more than 12,000 HF patients.[30]</p> <p>Because SGLT2i are a foundational therapy for HF, other therapies may be used as part of the standard of care, but these products are less favorable on the key outcomes without the use of SGLT2i.[29][31][32] Within SGLT2i, the only other products indicated for HF are [REDACTED]. [REDACTED] pivotal clinical trials for HF included only patients with T2DM, and the drug is thus not clinically comparable [REDACTED]. Against [REDACTED] [REDACTED] 2]</p> <p>Underscoring the value delivered by FARXIGA, [REDACTED], with a net price estimated at [REDACTED] [REDACTED],[33] may offer benefits for HF patients in addition to standard of care, but two meta-analyses found that SGLT2i deliver similar or superior (trending but not statistically significant) outcomes versus [REDACTED] on HF hospitalization or CV death for patients with reduced EF.[34][35] Notably, in comparison with [REDACTED] has been shown to be cost-effective: a study found that the cost needed to treat to avoid one HF event with FARXIGA was approximately one-third of the cost needed to treat for [REDACTED] [36]</p> <p>C. Type 2 Diabetes FARXIGA and SGLT2i generally deliver significant benefits on key outcomes for T2DM, including reductions in: (1) HF hospitalizations or CV death; (2) CKD progression; and (3) renal death in T2DM. These key outcomes were selected because they reflect the substantial risk patients with T2DM face with respect to CKD and HF complications and comorbidities. Other outcomes warranting discussion are more narrowly focused solely on glycemic control, including HbA1c, Fasting Plasma Glucose (FPG), Post Prandial Glucose (PPG), and weight loss, which many products may deliver, but typically without the cardiorenal benefits of SGLT2i.</p> <p>As with the first two indications discussed, the ability of FARXIGA to reduce costly and serious cardiorenal outcomes such as CKD progression and hHF or CV death means that the use of FARXIGA can produce significant medical cost offsets. [REDACTED]</p>



Question	Sub-Question	Response
		<p>[REDACTED]</p> <p>In general, there are eight major categories of drugs for lowering and controlling blood glucose that are referenced in the ADA guidelines: SGLT2i, GLP-1 RAs, GIP/GLP-1 RAs, DPP4i, thiazolidinedione, sulfonylureas, insulin, and metformin.[37] Most of the drugs in these categories— [REDACTED] do not produce the kind of cardiorenal protective effects, essential for many patients with T2DM who suffer from or who are at risk of comorbidities.[38]</p> <p>SGLT2i are uniquely protective against cardiorenal outcomes, which is why, for high-risk T2DM patients with a need for cardiovascular risk management, ADA guidelines recommend SGLT2i as a first-line agent in patients with CKD or HF in addition to T2DM.[39] Within the SGLT2i class, only FARXIGA has an indication to reduce hHF in a broad spectrum of patients with T2DM with established CV disease or multiple CV risk factors.[10][11][12][13][14][15]</p> <p>For patients with T2DM and diabetic kidney disease (DKD), SGLT2i are recommended by guidelines both to reduce CKD progression and reduce CV events, regardless of urine albumin-to-creatinine ratio (UACR), reflecting their comparative effectiveness for these patients.[40]</p> <p>Other classes of medicines for T2DM lack demonstrated outcomes on common cardiorenal risk factors. For instance, in considering GLP-1 RAs, [REDACTED] a meta-analysis of more than 32,000 patients found that GLP-1 RAs did not reduce the risk of cardiovascular or renal adverse events versus placebo, while SGLT2i demonstrated improvements versus placebo on both outcomes.[41] Similarly, a network meta-analysis found that DPP4i do not lower the risk of any cardiorenal outcome when compared with placebo, and were associated with higher risks of major adverse CV events, hHF, and renal outcomes when compared with either SGLT2i.[38]</p> <p>Other products that are effective for lowering blood glucose, such as metformin and SU, similarly have no evidence to demonstrate benefits on HF and CKD. Further, direct and indirect treatment comparisons support a benefit for SGLT2i over metformin, DPP4i, and sulfonylurea. [42][43][44]</p> <p>III. Relative Risks, Harms, and Side Effects As a class of drugs, SGLT2i have a proven safety profile.[45] Trials have shown that, in all three indications, there was no notable increase in overall adverse events for FARXIGA (see Figure 5 for adverse events in DAPA-CKD; Figure 6 for pooled data of FARXIGA T2DM trials).</p>



Question	Sub-Question	Response
		<p>Similarly, the DAPA-HF study showed no notable excess of any adverse events or serious adverse events in patients receiving FARXIGA.[3]</p> <p>While patients with CKD may face an elevated risk of ketoacidosis, the Nuffield meta-analysis concluded that “in all the trial populations studied to date, the absolute benefits of SGLT2i considerably outweighed any serious hazards.”[24]</p> <p>IV. Cost of Therapeutic Alternatives FARXIGA delivers benefits similar to other SGLT2i, in addition to unique positive outcomes such as protection from all-cause death in CKD, at a lower wholesale acquisition cost (WAC) price than its therapeutic alternatives as indicated in Figure 7.</p> <p>As Figure 8 demonstrates, FARXIGA’s WAC is also lower than that of other branded products that treat CKD, HF, or T2DM, [REDACTED]</p> <p>Further, evidence from databases that track net prices suggests that the discounts, rebates, and price concessions offered for FARXIGA drive its cost down even further relative to its therapeutic competitors and other commonly prescribed products that do not deliver the benefits of FARXIGA across the cardiorenal spectrum, such as the widely prescribed GLP1-RAs, semaglutide and dulaglutide.[33] When comparing FARXIGA with therapeutic alternatives specifically, its net price according to these third-party databases, is comparable to or lower than empagliflozin.[33]</p>
	<p>Hyperlink to Citation - Additional Materials for Question 28</p>	<p>[REDACTED]</p>
	<p>Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28</p>	<p>[REDACTED]</p>
	<p>Evidence Submitted include a cost-effectiveness measure?</p>	<p>N</p>



Question	Sub-Question	Response
	What type of Evidence is shown?	
Question 29: Comparative Effectiveness on Specific Populations	Response to Question 29	<p>I. Overview FARXIGA has unique effectiveness as compared with therapeutic alternatives and other products among specific populations that CMS has emphasized are of particular importance to the Medicare program: the elderly, frail individuals, individuals suffering from multiple chronic conditions (MCC), and individuals from racial and ethnic minority groups, including Black Americans. Each of these populations are a frequent focus for efforts by CMS to improve care quality and reduce Medicare program costs, and each benefit from FARXIGA's clinical utility across the three interrelated and often comorbid diseases of chronic kidney disease (CKD), heart failure (HF), and type 2 diabetes mellitus (T2DM).</p> <p>FARXIGA has demonstrated proven benefits in these specific populations—the elderly, frail individuals, individuals with MCC, and Black Americans—across all of its indications, diseases from which these populations often disproportionately suffer. By avoiding serious patient outcomes and delivering medical cost offsets for populations like frail patients and those with MCC, who are often especially costly, FARXIGA delivers savings and improved outcomes for the Medicare program. Further, by providing value to populations, such as Black Americans, who are frequently underserved by healthcare providers, FARXIGA reduces the Medicare program's medical expenditures and helps promote health equity.</p> <p>I. Impact on Specific Populations</p> <p>A. Elderly CMS has expressed concerns that data from pivotal trials on therapies “may not be generalizable to the Medicare population if Medicare beneficiaries are insufficiently represented.”[1] The Food and Drug Administration (FDA) has also noted that “[g]eriatric patients,” defined by the FDA as patients 65 and older, “often have comorbidities and concomitant therapies that could interact with [a drug] and make patients more likely to have undesirable effects and interaction,” making it “important to assess the safety and efficacy of a drug in such patients.”[2] It is therefore notable that data from analysis of the pivotal FARXIGA trials shows that the product reduces the risk of all three disease states of CKD, HF, and T2DM among elderly patients. FARXIGA has demonstrated it can improve health outcomes in the elderly, thus reducing ineffective spending.</p> <p>1. Chronic Kidney Disease The incidence of CKD increases with age and is especially common in the Medicare population.[3] For elderly</p>



Question	Sub-Question	Response
		<p>patients with CKD, FARXIGA has demonstrated similar efficacy on the primary outcome in the DAPA-CKD trial in the subgroup of patients >65 years of age than in the group 65 years of age or below (see Table 1).[4] Further, FARXIGA’s relative risk reduction in the primary composite outcomes was consistent across age groups.</p> <p>In elderly patients who may have short life expectancies, delivery of clinical benefits in a shorter time frame can provide more value by improving patient health as soon as possible. The data from the heart failure outcomes trial (DAPA-HF) and the renal outcomes trial (DAPA-CKD), demonstrated that FARXIGA’s outcome benefits may occur within a relatively short timeframe: DAPA-HF reported a reduced risk of cardiovascular (CV) death and hospitalization for HF (hHF) as early as 28 days post-randomization; for DAPA-CKD, the event horizon for outcome benefits was 13 months.[5][6][7] On safety, DAPA-HF and DELIVER showed similar differences in rates of adverse events between the treatment and placebo arms across all age categories.[8][9]</p> <p>2. Heart Failure HF is disproportionately common among the elderly and is a significant burden for this population. The prevalence of HF in men and women aged 60-79 is 6.9% and 4.8%, respectively, and increases to 12.8% and 12% for those over the age of 80.[10] FARXIGA has been shown to reduce the risk of the primary composite endpoint of worsening HF or CV death, CV death, worsening HF and all-cause death across all age categories. As illustrated in Table 2 and Table 3, in both the DAPA-HF and DELIVER trials, there was significant benefit of FARXIGA across age groups, with FARXIGA demonstrating statistically significant reductions in the primary endpoint in patients aged 65-74 and patients aged >=75.[8][9]</p> <p>FARXIGA’s efficacy and safety in elderly patients has been recognized, with a review of safety and efficacy considerations of among elderly for the treatment of HF concluding that, as SGLT2i are well tolerated in the older population, the class offers significant therapy advancements for the elderly in managing heart failure.[8][9][11] On safety, DAPA-HF and DELIVER showed similar differences in rates of adverse events between the treatment and placebo arms across all age categories.</p> <p>Real-world evidence also supports the efficacy of SGLT2i for elderly patients with HF. In a Medicare claims observational study for elderly patients with comorbid T2DM and HFpEF, SGLT2i were associated with a significant reduction in hHF versus DPP4i (HR: 0.67; 95% CI: 0.63 to 0.72) and GLP-1 (HR: 0.86; 95% CI: 0.79 to 0.93). In patients with HFpEF, SGLT2i demonstrated further significant reductions for HHF versus DPP4i (HR: 0.65; 95% CI: 0.61 to 0.69).[12]</p> <p>3. Type 2 Diabetes FARXIGA’s proven efficacy for T2DM in the elderly population are especially important given that, as CMS has</p>



Question	Sub-Question	Response
		<p>described, “few diseases in the United States can match the health and economic toll wrought by diabetes, especially in the older population.”[13] An estimated 29.2% of Americans over 65 have T2DM,[14] and approximately 50% of older people have prediabetes.[15] According to CMS, 32% of Medicare enrollees are diagnosed with T2DM, as compared with 11% of the general population.[13] In addition, having T2DM places a person at increased risk of developing CKD and HF.</p> <p>Evidence confirms that the beneficial effects of SGLT2i, including FARXIGA, persist in T2DM patients over the age of 65. A network meta-analysis of cardiovascular outcome trials indicated that the effect of SGLT2i on CV outcomes among older people (>=65 years) with T2DM was consistent across all age groups.[16] Further, for blood glucose control, patients taking FARXIGA monotherapy or in combination with other glucose lowering drugs, saw rates of hypoglycemia that were comparable between treatment groups in all the age groups, while episodes of severe hypoglycemia were rare in all treatment groups regardless of age.[17]</p> <p>A review of overall evidence for the SGLT2i class found that the products are “well tolerated in frail older adults with or without diabetes, with a low risk of serious adverse effects that should not overshadow the significant cardioprotective benefits.” The review suggested that “increased use of [SGLT2i] in frail older adults with or without diabetes has the potential to provide early clinical benefits and improve symptoms and outcomes for this population.”[7]</p> <p>The DECLARE TIMI-58 trial found that FARXIGA reduced the composite of CV death or hHF consistently, in age-groups <65, >=65 to <75, and >=75 years, respectively (interaction P value 0.5277).[18]</p> <p>In terms of safety profile, the DECLARE-TIMI 58 study demonstrated no heterogeneity across safety outcomes by age groups,[18] while a network meta-analysis of randomized control trials with safety outcomes in elderly patients with T2DM and DKD indicated that SGLT2i are considered relatively safe.[18][19]</p> <p>SGLT2i have shown equal or favorable results in cardiovascular outcomes when compared with GLP-1s in the elderly population. In a network meta-analysis, GLP-1 RAs in adults aged >= 65 years were associated with a 15.3% (OR 0.847 (95% CI 0.788 to 0.910)) reduction in MACE events, compared with a reduction by SGLT2i in older participants by 16.9% (OR 0.831 (95% CI 0.699 to 0.989)).[20]</p> <p>Real-world evidence also supports positive outcomes from FARXIGA in CKD patients over the age of 65. Several studies reported significant reductions in a composite renal outcome or progression to end-stage kidney disease (ESKD) with SGLT2i compared with other glucose-lowering drugs, DPP-4 and GLP-1s. Hence, observational studies in real-life conditions confirm previous results reported in placebo-controlled trials and support a positive risk-benefit</p>



Question	Sub-Question	Response
		<p>balance in elderly patients with T2DM at risk of HF and chronic kidney disease.</p> <p>B. Frail Patients Data from analysis of the pivotal FARXIGA trials shows that the product reduces the risk of CKD, HF, and T2DM among frail patients. FARXIGA has demonstrated it can improve health outcomes in the frail, thus reducing ineffective spending.</p> <p>1. Chronic Kidney Disease Frail Medicare beneficiaries have been estimated to cost Medicare as much as five times more than non-frail beneficiaries,[21] and CKD is disproportionately common among frail patients.[22] A recent analysis of the DAPA-CKD trial evaluated outcomes by degree of frailty according to the Rockwood cumulative deficit approach. FARXIGA reduced the risk of the primary composite endpoint across all frailty categories.[23] Results were similar for secondary outcomes, including kidney composite outcome (sustained $\geq 50\%$ eGFR decline, ESKD, or death from kidney cause), CV endpoint (hHF or CV death), and all-cause mortality. Occurrence of serious adverse events was numerically lower in patients receiving FARXIGA vs. placebo in all frailty categories (16.9% vs. 20.1% [not-to-mildly frail], 26.3% vs. 30.7% [moderately frail], and 42.9% vs 47.8% [severely frail]).</p> <p>2. Heart Failure HF is also more common in patients with frailty.[24] A post-hoc subgroup analysis of the DAPA-HF trial evaluated the effects of FARXIGA according to frailty status. FARXIGA reduced the risk of worsening HF, CV death, and all-cause death, with improvement in KCCQ scores regardless of frailty class. The absolute risk reductions in clinical outcomes evaluated and improvements in health status were generally larger in patients with Frailty Index class 3 (most frail).[25] Similarly, a subgroup analysis of the DELIVER trial found no attenuation of treatment effect by frailty.[26] These outcomes indicate that offering FARXIGA to patients irrespective of their degree of frailty provides a safe and efficacious treatment option.</p> <p>C. Patients with Multiple Chronic Conditions MCC are both common for patients in the Medicare program and a population that the Department of Health and Human Services has specifically identified as a major driver of high costs to be addressed.[27] Data show that FARXIGA remains efficacious even in populations facing MCC, including CKD, HF, and T2DM, and other comorbidities: DELIVER showed similar results in the MCC population as the general patient population when evaluating patients with higher numbers of unique background medications and of cardiorenal metabolic comorbidities.[28][29] Given the high rate of occurrence of comorbidities among HF patients especially, FARXIGA provides a unique and vital treatment option for HF patients.[28]</p>



Question	Sub-Question	Response
		<p>D. Black Americans</p> <p>Data from analysis of the pivotal FARXIGA trials shows a statistically significant reduction in the risk of CKD, HF, and T2DM among Black patients, demonstrating FARXIGA’s ability to improve health outcomes in Black patients, reduce unnecessary spending, and advance health equity.</p> <p>1. Chronic Kidney Disease</p> <p>FARXIGA has demonstrated efficacy in the Black population for CKD, which is especially notable given that CMS has identified particular health disparities in this disease area,[30] and CKD is disproportionately common among Black patients.[31] In the DAPA-CKD trial, across Black and White patients, FARXIGA reduced the risk of the primary composite outcome (composed of $\geq 50\%$ sustained eGFR decline, ESKD, or CV or renal death) as well as the secondary outcomes of composite of eGFR decline $\geq 50\%$, ESKD, or renal death (kidney outcomes), CV death or hHF, and all-cause mortality, with no heterogeneity of benefit between the subgroups.[32]</p> <p>2. Heart Failure</p> <p>FARXIGA has demonstrated efficacy for HF in Black patients, among whom HF is more common.[28][33] Racial and ethnic inequities in incidence, prevalence, mortality and readmission rates for patients with HF in the U.S. have been widely documented, and the mortality disparity gap in black patients has widened over time.[33] A pooled HF analysis across DAPA-HF and DELIVER demonstrated efficacy in Black patients was comparable to that observed in white patients.[34] Separately, the effect of FARXIGA on the primary composite endpoint of DELIVER was consistent across Black patients (HR: 0.69; 95% CI: 0.47 to 1.02) and white patients (HR: 0.73; 95% CI: 0.61 to 0.88). A pre-specified subgroup analysis of DAPA-HF also found FARXIGA increased the share of patients with a clinically significant improvement in symptoms, as well as reducing the proportion with a clinically meaningful deterioration irrespective of race, showing a clear and meaningful improvement in symptoms and quality of life.[35] When looking at safety, occurrence of adverse events among Black patients were similar in pooled analysis to occurrence in White patients.[35]</p> <p>3. Type 2 Diabetes</p> <p>FARXIGA has also demonstrated positive outcomes for Black patients with T2DM, a condition that is significantly more prevalent among Black Americans with higher rates of unfavorable outcomes, than among the general population.[37] Regarding HF in T2DM patients, in DECLARE FARXIGA demonstrated a significantly lower rate of the primary efficacy composite of hHF or CV death compared with the placebo, regardless of race.[38] Regarding blood glucose levels, in the FARXIGA antiglycemic clinical development program evaluating the safety and efficacy of FARXIGA in 24 Phase IIb and III studies, reductions in HbA1c were seen across all racial subgroups.[36]</p> <p>III. Underserved Populations and Health Equity</p>



Question	Sub-Question	Response
		<p>FARXIGA is also a powerful tool for promoting health equity, not only because it can improve outcomes among underserved populations, but because it can address concerns particularly prevalent among underserved populations, while reducing burdens on safety-net providers, caregivers, and the healthcare system by avoiding particularly costly health outcomes.</p> <p>One Medicine to Treat Three Conditions: FARXIGA is a single medication, taken orally at any time of day, that can provide benefits for CKD, HF and T2DM, improving health outcomes and reducing unnecessary spending. Evidence has shown that single-medication regimens can improve adherence to medication, including among HF patients.[39] The potential improvements from a one-medication regimen are especially significant when it comes to underserved populations, such as Black Americans, because these populations have greater risks of non-adherence for a variety of reasons.[40] Further, FARXIGA is a simple regimen, as a pill that can be taken at home at any time of day.</p> <p>Avoiding Polypharmacy Interactions: Importantly for patients who are often facing multiple chronic conditions or comorbidities, FARXIGA has no known significant drug interactions. Further, in a post-hoc analysis of the DAPA-HF trial, the benefit of FARXIGA was consistent regardless of background therapy for HF.[41]</p>
	<p>Hyperlink to Citation - Additional Materials for Question 29</p>	<p>[REDACTED]</p>
	<p>Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29</p>	<p>[REDACTED]</p>
	<p>Evidence Submitted include a cost-effectiveness measure?</p>	<p>N</p>



Question	Sub-Question	Response
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	<p>I. Overview FARXIGA addresses a critical unmet medical need for Medicare patients with chronic kidney disease (CKD), heart failure (HF), and type 2 diabetes mellitus (T2DM), which are costly, serious diseases common across Medicare patients that drive high medical costs. FARXIGA is a single medication that treats CKD, HF, and T2DM and improves health outcomes and thus reduces ineffective spending. “Cardiorenal diseases” generally describes a bidirectional effect between the heart and kidneys in which a dysfunction in one organ promotes a dysfunction in the other. These dysfunctions manifest themselves along a continuum of interrelated diseases that include CKD, HF, and T2DM. Of the 16 million Medicare Part D beneficiaries impacted by at least one of these conditions, approximately 31% suffer from two or more.[1]</p> <p>Only certain SGLT2i, including FARXIGA, have demonstrated the ability to reduce adverse health outcomes across CKD, HF, and T2DM, which is why these products are recommended as foundational therapies for cardiorenal diseases, as discussed in question 27. FARXIGA also uniquely addresses unmet medical needs within its class, as the only SGLT2i to have demonstrated a statistically significant reduction of all-cause mortality in CKD patients. FARXIGA is also the only SGLT2i proven to reduce the risk of cardiovascular (CV) death in patients with HF with reduced ejection fraction (HFrEF), and the only SGLT2i to reduce CV death and hospitalization for HF (hHF) across the spectrum of LVEF without attenuation of benefit at higher ejection fraction (EF).[2][3]</p> <p>FARXIGA’s ability to meet these widespread, critical unmet needs can deliver significant savings for the Medicare program. Modeling demonstrates that, for 799,000 Medicare Part D patients taking FARXIGA, CMS would expect medical cost reductions of [REDACTED]</p> <p>II. Benefits of SGLT2i Across Cardiorenal Spectrum SGLT2i are the only class of drugs demonstrated to reduce adverse health outcomes across the range of cardiorenal diseases, from CKD to HF to T2DM, including reduced and preserved EF. Accordingly, as discussed in responses to questions 27 and 28, SGLT2i are recommended by clinical guidelines for patients suffering from CKD, HF, and T2DM. Untreated patients with just one or more of these comorbidities represent a significant unmet need as they experience a higher risk of hospitalization, kidney failure, and mortality.[5][6][7][8] This unmet need is amplified in older populations for whom the prevalence of all three diseases is higher and who are more likely to present with comorbid conditions.[9]</p>



Question	Sub-Question	Response
		<p>III. Unique Benefits of FARXIGA to Address Unmet Medical Need</p> <p>FARXIGA further addresses critical unmet medical needs by standing above its therapeutic alternatives and other clinical options on several key outcome measures.</p> <p>First, FARXIGA is the only SGLT2i to have demonstrated a statistically significant reduction of all-cause mortality in patients with CKD.[2][10][11][12][13][14][15][16][17] CKD is a serious progressive condition associated with CV disease and increasing risk of adverse outcomes, including HF and premature death.[18][19][20][21] The most common causes of CKD are diabetes and hypertension.[22]</p> <p>FARXIGA was the first SGLT2i approved to treat CKD in patients with and without T2DM and was designated a Breakthrough Therapy by FDA.[23][24] During the technology appraisal of FARXIGA in CKD by the National Institute of Health and Care Excellence,[25] patient experts felt that FARXIGA offered a step change for treating CKD, and clinical experts highlighted that the benefits of FARXIGA were distinct from a blood glucose reduction alone, and that reducing progression to end-stage renal disease would increase quality of life.</p> <p>Second, FARXIGA is the only SGLT2i demonstrating a consistent treatment effect for worsening HF and CV death without attenuation across the range of LVEF.[2][3][26] In the U.S., the prevalence of HF in men and women aged 60-79 is 6.9% and 4.8%, respectively, increasing to 12.8% and 12% over age 80.[28] Patients diagnosed with HF have a poor prognosis, with frequent hospitalizations related to HF and comorbidities, high mortality, and poor quality of life. Inter-related comorbidities and risk factors, particularly T2DM, CKD and obesity, can all negatively impact each other.[6][29] In the U.S., the total cost of care for HF in 2020 was estimated at \$43.6 billion, with at least 70% attributed to medical costs.[30] There is significant unmet need in terms of both disease prevalence/poor outcomes and high costs for Medicare and the health system.[31]</p> <p>The AHA/ACC/HFSA guidelines for the management of patients with HFrEF consists of four pillars: ACEi/ARB/ARNI, beta blockers, MRAs and SGLT2i.[32][33] SGLT2i are a foundational therapy within these guidelines, meaning the product delivers benefits in addition to, not in place of, the other treatment pillars. Jardiance® (empagliflozin), another SGLT2i, demonstrated a significant reduction in the worsening of HF or CV death, but an attenuated treatment effect at a higher EF.[34] Only FARXIGA has demonstrated a consistent treatment across the broad range of LVEF for worsening HF and mortality without attenuation, especially among higher LVEF ranges.[3] FARXIGA has also been specifically recognized by guidelines for demonstrating a significant reduction in CV death in a HFrEF clinical trial.[32]</p> <p>Third, FARXIGA can lower HbA1c while also mitigating the risks associated with the damage that high blood glucose can cause to the kidneys and heart in ways that no other T2DM products have demonstrated. FARXIGA’s clinical data in T2DM are more comprehensive than other products, providing [REDACTED] demonstrating how FARXIGA</p>



Question	Sub-Question	Response
		<p>addresses unmet cardiorenal need associated with T2DM. The FARXIGA DECLARE-TIMI 58 trial remains the largest, longest, and broadest trial for T2DM, demonstrating both cardiovascular and renal protective effects, including the reduction of hHF, regardless of history of established CVD or HF. FARXIGA was also associated with a significantly lower risk compared to placebo of the cardiorenal composite of at least a 40% decrease in eGFR to less than 60 mL/min/1.73 m², ESKD, or death from renal or CV cause, and of the renal specific composite of at least a 40% decrease in eGFR to less than 60 mL/min/1.73 m², ESKD, or death from renal cause.[29]</p> <p>Note: The attached .zip file below contains supporting references for question I-27, NOT I-30.</p>
	<p>Hyperlink to Citation - Additional Materials for Question 30</p>	<p>[REDACTED]</p>
	<p>Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30</p>	<p>[REDACTED]</p>
	<p>Evidence Submitted include a cost-effectiveness measure?</p>	<p>N</p>
	<p>What type of Evidence is shown?</p>	



Question	Sub-Question	Response
Question 31: Patient and Caregiver Experience	Response to Question 31	
Question 32: Executive Summary	Response to Question 32	<p>AstraZeneca is committed to developing innovative, lifesaving medicines and making these medicines accessible to patients, aligning with CMS’ goals for the Medicare Drug Price Negotiation Program. AstraZeneca demonstrates its commitment to patients through our collaboration with Medicare payers, providing [REDACTED] discounts to ensure FARXIGA (dapagliflozin) formulary positions provide the lowest possible out-of-pocket cost for Medicare patients. This translates into savings for beneficiaries: the average FARXIGA Medicare copay is \$42; and for those who cannot afford this co-pay, AstraZeneca also makes a significant investment in our AZ&Me Prescription Savings Program to support access to FARXIGA for all qualified Medicare enrollees.</p> <p>CKD, HF, and T2DM are Critical Areas of Patient Unmet Need. FARXIGA represents an important therapeutic advance addressing three separate but frequently coexisting disease states. These disease states—chronic kidney disease (CKD), heart failure (HF), and type 2 diabetes mellitus (T2DM)—combine to place clinical burdens on 16 million Medicare enrollees, as well as avoidable costs on the Medicare program. Medicare enrollees experience 11 million costly and life-changing clinical events—hospitalization or death—annually related to CKD and HF alone.</p> <p>There is a disproportionate economic burden imposed on the Medicare program by these diseases.</p> <ul style="list-style-type: none"> · In 2020, 14% of Medicare beneficiaries had CKD, with spending exceeding \$75 billion, representing about 25% of fee-for-service total spending. · Roughly 10% of Medicare beneficiaries have HF, with spending exceeding \$65 billion, representing about 28% of fee-for-service total spending. · Approximately 24% of Medicare beneficiaries have T2DM, with annual Medicare spending exceeding \$106 billion, representing about 36% of fee-for-service total spending each year. <p>FARXIGA Uniquely Treats CKD, HF, and T2DM Patients with a Single Therapy. There is no comparable class to SGLT2i, which addresses the unique challenges of multimorbidity across CKD, HF, and T2DM. Of the 16 million Medicare Part D beneficiaries impacted by at least one of these conditions, approximately 31% suffer from two of more. Through continued R&D investment of more than [REDACTED], FARXIGA has proven life-saving benefits beyond its original T2DM indication. And, AstraZeneca is committed to further improving patient care, investing [REDACTED] of our annual revenue in research and development, with a significant focus on developing improved therapies for CKD, HF, and metabolism.</p>



Question	Sub-Question	Response
		<p>Current clinical treatment guidelines recognize the SGLT2i class as a foundational treatment for these patient populations. In 2022, KDIGO modified its Clinical Practice Guideline for Diabetes Management in CKD to recognize SGLT2i as a foundation of pharmacologic therapy and first-line agents for patients with T2DM and CKD. The most recent AHA/ACC/HFSA Guideline for the Management of Heart Failure recommends SGLT2i for patients with HF, regardless of ejection fraction (EF). Lastly, the ADA recognizes SGLT2i as a first-line therapy in patients with CKD or HF, and a foundational therapy in patients with ASCVD, and those ≥ 55 years of age with risk factors for ASCVD.</p> <p>Among this remarkable class, FARXIGA is unique as the only such therapy with indications across CKD, HF, and T2DM.</p> <ul style="list-style-type: none"> · In CKD, FARXIGA is the only SGLT2i where clinical trials have shown a reduction in all-cause mortality in patients with CKD. · In HF, FARXIGA is the only SGLT2i that has been proven to reduce the risk of cardiovascular (CV) death in patients with HFrEF, and FARXIGA is proven to reduce the risk of CV death or hospitalization for HF (hHF) in patients with HF across the full EF range. · FARXIGA is the only SGLT2i that has demonstrated a reduction in the risk of hHF in a broad T2DM population, with either CV risk factors or established CV disease. <p>FARXIGA Provides Growing Value to a Growing Medicare Population: FARXIGA reduces the incidence of high-cost events among Medicare enrollees. Cost offset modeling demonstrates that, among the 799,000 Medicare Part D enrollees taking FARXIGA, CMS would expect annualized medical cost reductions of [REDACTED] due to decreased clinical events. The benefit of FARXIGA grows over time as the risk of clinical events increases; [REDACTED] the estimated medical cost reduction to CMS of FARXIGA is \$6 billion due to the avoidance of clinical events. Assuming a continuation of the [REDACTED], FARXIGA would create [REDACTED] or more in net savings (including net drug costs) to CMS over the next [REDACTED] through the avoidance of these high-cost events. Based on the projected rise in utilization of FARXIGA among Part D enrollees with CKD, HF and T2DM, FARXIGA's value to CMS is expected to increase year-over-year.</p> <p>By delivering significant medical cost offsets for some of the most costly and serious conditions faced by Medicare beneficiaries, FARXIGA delivers tremendous value for the Medicare program and the patients it serves.</p> <p>[REDACTED]</p>

[REDACTED]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[REDACTED]

[REDACTED]

[REDACTED]

Figure 4. Comparison of Outcomes from FDA-Approved Labeling Across Select CKD/HF/T2DM Products (As of 9/20/23).

Available FDA approved indications	CKD				HF		T2D			
	Kidney function decline and ESKD	CV death & hHF	All cause mortality	All cause hospitalization	CV death & hHF	Urgent HF visit	A1C reduction	MACE	CV Death	hHF
Dapagliflozin			Data in PI	Demonstrated in post-hoc analysis						



Sources: Farxiga® (dapagliflozin) [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP, 2023.; [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



Figure 5: DAPA-CKD Trial Adverse Events

Outcome	Dapagliflozin	Placebo	HR (95%CI)
Serious urinary tract infection	52 (1.6)	54 (1.6)	0.94 (0.64–1.37)
Serious genital infection	1 (<0.1)	1 (<0.1)	-
<i>Serious hyperkalemia</i>	92 (2.8)	109 (3.3)	0.83 (0.63–1.09)
<i>Serious acute kidney injury</i>	107 (3.2)	135 (4.1)	0.78 (0.60–1.00)
<i>Serious dehydration</i>	30 (0.9)	24 (0.7)	1.25 (0.73–2.14)
<i>Liver injury</i>	13 (0.4)	12 (0.4)	1.09 (0.50–2.38)
<i>Ketoacidosis</i>	6 (0.2)	1 (<0.1)	-
<i>Lower-limb amputation</i>	28 (0.8)	19 (0.6)	1.43 (0.80–2.57)
<i>Bone fracture</i>	133 (4.0)	123 (3.7)	1.08 (0.84–1.38)
<i>Severe hypoglycemia</i>	77 (2.3)	77 (2.3)	1.00 (0.73–1.37)
<i>Symptomatic dehydration</i>	83 (2.5)	76 (2.3)	1.10 (0.81–1.51)

Note: Similar adverse events were reported with use of empagliflozin for EMPA-Kidney trial.

Source: Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2020;383(15):1436-46.

Figure 6: Summary of Overall Adverse Events in FARXIGA T2DM Trials

	Placebo group (N = 2295; 957.9 patient-years) n (%)	Dapagliflozin 10 mg group (N = 2360; 997.6 patient-years) n (%)
≥1 AE	1279 (55.7)	1416 (60.0)
AE leading to discontinuation	82 (3.6)	102 (4.3)
≥1 SAE	123 (5.4)	120 (5.1)
SAE leading to discontinuation	24 (1.0)	16 (0.7)
Deaths	4 (0.2)	7 (0.3)
Most common adverse events (≥3% in either treatment group)		
Nasopharyngitis	133 (5.8)	126 (5.3)
Diarrhoea	87 (3.8)	79 (3.3)
Headache	83 (3.6)	81 (3.4)
Upper respiratory tract infection	91 (4.0)	72 (3.1)
UTI	61 (2.7)	91 (3.9)
Back pain	56 (2.4)	83 (3.5)

Source: Jabbour S, Seufert J, Scheen A, et al. Dapagliflozin in patients with type 2 diabetes mellitus: A pooled analysis of safety data from phase IIb/III clinical trials. Diabetes Obes Metab. 2018 Mar;20(3):620-8.

Figure 7. WAC Prices of FARXIGA and Therapeutic Alternatives

		Therapeutic Alternative by Indication		
	WAC	CKD	HF	T2DM
FARXIGA	\$565.29	X	X	X
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

**Current prices as of 8/29/2023; price based on WAC for a 30-count bottle.*

[REDACTED]

[REDACTED]

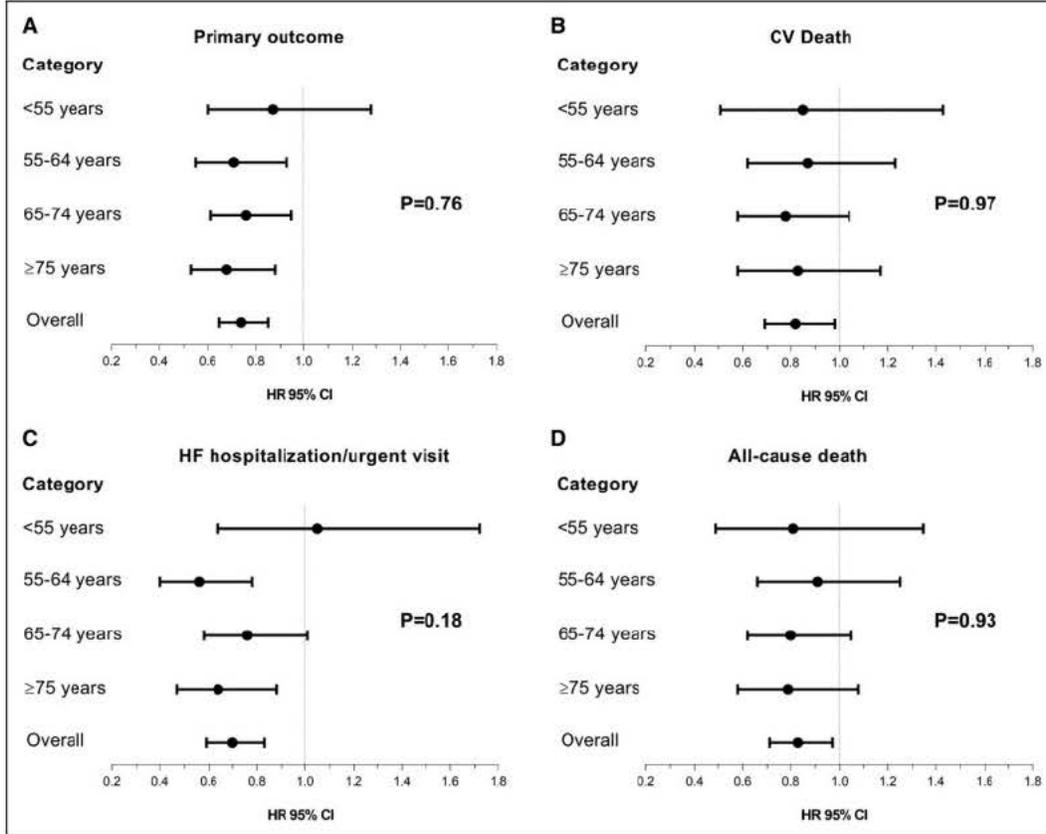
Table 1: Effect of dapagliflozin by age categories in DAPA-CKD trial

Subgroup	Dapagliflozin	Placebo	Hazard Ratio (95% CI)	
	<i>no. of participants/total no.</i>			
All participants	197/2152	312/2152		0.61 (0.51–0.72)
Age				
≤65 yr	122/1247	191/1239		0.64 (0.51–0.80)
>65 yr	75/905	121/913		0.58 (0.43–0.77)

(outcome: composite of sustained decline in eGFR of at least 50%, ESKD, or death from renal or CV causes)

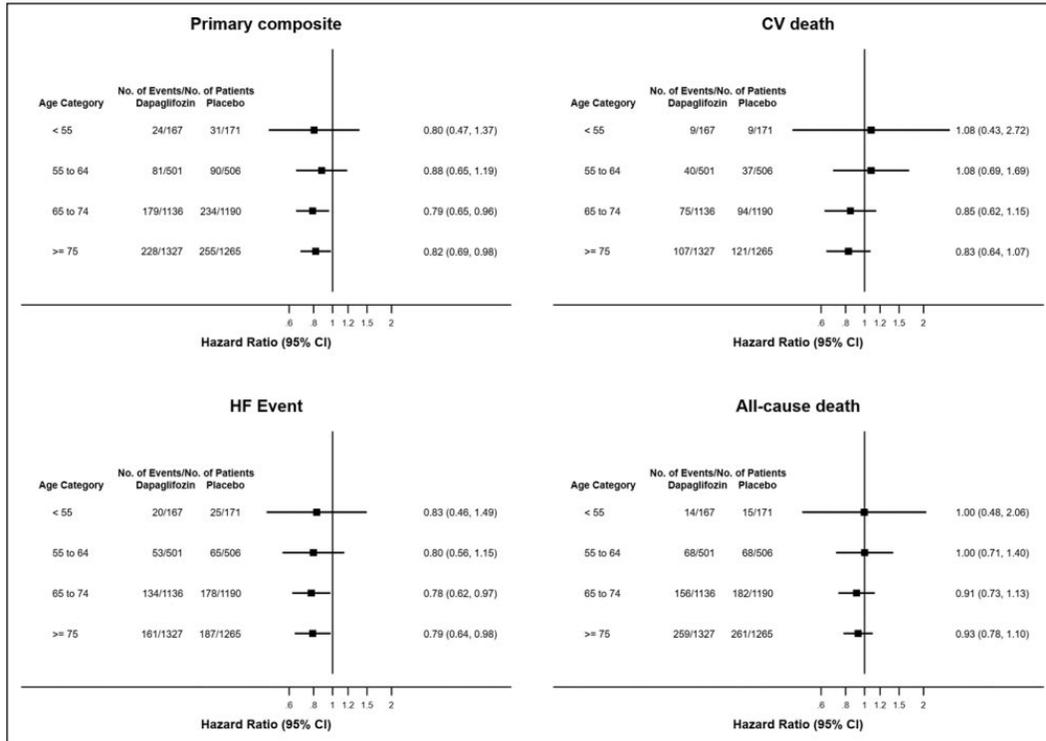
Source: Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med.* 2020;383(15):1436-46.

Table 2. Effect of dapagliflozin by age categories in the DAPA-HF trial



Source: Martinez FA, et al. Efficacy and Safety of Dapagliflozin in Heart Failure With Reduced Ejection Fraction According to Age: Insights From DAPA-HF. *Circulation*. 2020;141(2):100-111.

Table 3. Effect of dapagliflozin by age categories in the DELIVER trial



Source: Peikert A, et al. Efficacy and Safety of Dapagliflozin in Heart Failure With Mildly Reduced or Preserved Ejection Fraction According to Age: The DELIVER Trial. *Circ Heart Fail.* 2022 Oct;15(10):e010080.

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[REDACTED]

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[REDACTED]

[REDACTED]

[REDACTED]

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Question 29

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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	DAPAGLIFLOZIN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	AAHFN
	Respondent Email	
Question 27: Prescribing Information	Who is completing this form?	PAO
	Prescribing Information	<p>The medication Farxiga is prescribed for the treatment of chronic heart failure. Farxiga is recommended by the American Heart Association, American College of Cardiology, and Heart Failure Society of America with a Class 1a indication to be used in patients with symptomatic chronic heart failure with reduced ejection fraction to reduce hospitalizations for heart failure and cardiovascular mortality regardless of the presence of type 2 diabetes. Farxiga has been shown in trials to reduce the risk of cardiovascular death for heart failure patients by 25% and reduce heart failure hospitalization by 30%. Furthermore, Farxiga is associated with slowing the rate of kidney function decline which also can reduce cardiovascular death and heart failure hospitalizations (AHA/ACC, 2022)..Farxiga is also recommended with a Class 2a indication by the American Heart Association, American College of Cardiology, and Heart Failure Society of America in the treatment of heart failure with preserved ejection fraction. In this population, Farxiga is found to reduce heart failure hospitalization and cardiovascular mortality (AHA/ACC, 2022). .Farxiga is an essential medication in the treatment of heart failure patients and is a cornerstone of guideline directed medical therapy for these patients. We urge this committee to consider the benefit Farxiga has shown for the heart failure population and lower the price of this important and necessary medication so that the benefits can be reaped for all patients.</p>
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and	Therapeutic Impact and Comparative Effectiveness	Farxiga (dapagliflozin) is a medication used to treat type 2 diabetes mellitus. It is also now used to help treat patients with heart failure. It belongs to the class of drugs known as sodium-glucose co-transporter 2 (SGLT2) inhibitors. Farxiga works by reducing the reabsorption of glucose in the kidneys, leading to increased glucose excretion in the urine.

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Question Sub-Question

Comparative Effectiveness

Response

- **Cardiovascular Benefits:** Farxiga has shown cardiovascular benefits in clinical trials. The DECLARE-TIMI 58 trial demonstrated a reduction in major adverse cardiovascular events (MACE) in patients with type 2 diabetes and established cardiovascular disease.
- **Heart Failure Benefits:** Farxiga has demonstrated benefits in reducing the risk of hospitalization for heart failure, even in patients without diabetes, as shown in the DAPA-HF trial.
- **Blood Sugar Control:** Farxiga effectively lowers blood sugar levels in people with type 2 diabetes. It is often used when other oral antidiabetic medications, such as metformin or sulfonylureas, are not providing adequate control.
- **Weight Loss:** Farxiga is associated with weight loss in many patients. This can be a beneficial side effect, particularly for individuals who need to manage their weight as part of their diabetes treatment.
- **Low Risk of Hypoglycemia:** Farxiga has a relatively low risk of causing hypoglycemia (low blood sugar) compared to some other diabetes medications such as sulfonylureas or insulin.
- **Renal Protection:** Farxiga has shown renal-protective effects. It can slow the progression of kidney disease in patients with type 2 diabetes, especially those with underlying kidney issues. This was noted in the DAPA-CKD trial.
- **Urinary Tract Infections and Genital Mycotic Infections:** Like other SGLT2 inhibitors, Farxiga is associated with an increased risk of urinary tract infections and genital mycotic infections (such as yeast infections) due to its mechanism of action.

Some other common classes of medications for type 2 diabetes include:

- **Metformin:** Metformin is typically the first-line treatment for type 2 diabetes and is effective in lowering blood sugar levels. However, it may not provide the same cardiovascular, weight loss, or heart failure benefits as Farxiga.
- **Sulfonylureas:** These medications stimulate insulin secretion and can be effective in lowering blood sugar levels but are associated with a higher risk of hypoglycemia and may not offer the cardiovascular or renal benefits seen with Farxiga.
- **DPP-4 Inhibitors:** Dipeptidyl peptidase-4 (DPP-4) inhibitors increase insulin secretion and decrease glucagon production. They are generally weight-neutral and have a low risk of hypoglycemia but do not provide the same cardiovascular benefits as Farxiga.
- **GLP-1 Receptor Agonists:** Glucagon-like peptide-1 (GLP-1) receptor agonists can lower blood sugar levels, promote weight loss, and have some cardiovascular benefits. However, the cardiovascular and heart failure benefits of Farxiga may be considered stronger.

Hyperlink to
Table/Charts/Graphs -
Additional Materials for
Question 28

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Question	Sub-Question	Response
	<p>Evidence Submitted include a cost-effectiveness measure?</p> <p>What type of Evidence is shown?</p>	
<p>Question 29: Comparative Effectiveness on Specific Populations</p>	<p>Response to Question 29</p>	<p>Question 29: Questions on Comparative Effectiveness on Specific Populations:</p> <ul style="list-style-type: none">• What is known about the comparative effectiveness of the selected drug and therapeutic alternatives to the selected drug with respect to specific populations, such as individuals with disabilities, the elderly, individuals who are terminally ill, and children? <p>Not approved for children. Patients with impaired renal function (eGFR less than 60 mL/min/1.73 m²), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension.</p> <ul style="list-style-type: none">• Are there other specific populations not noted in the question above that use the selected drug that could be considered? If so, please explain. Farxiga should not be prescribed for Type 1 Diabetes or for individuals at high risk for infections or recurrent infections. Should not be prescribed for individuals with eGFR < 30.• As applicable, for other specific populations that use the selected drug, what is known about comparative effectiveness of the selected drug and its therapeutic alternative(s)? There is not an alternative for an SGLT2 for heart failure.• What health equity considerations should CMS consider related to specific populations taking the selected drugs? This may include, but is not limited to, challenges or advantages accessing the drug compared to therapeutic alternatives, differences in clinical or other outcomes, or differences in disease or condition symptoms for a specific population that the drug does or does not adequately address. A challenge for many populations is cost, depending on insurance coverage. <p>In the 2022 guidelines, SGLT2 inhibitors (Jardiance) are 1 of the 4 pillars of heart failure guideline-directed therapy, based on data from the DAPA-HF and EMPEROR-REDUCED trials showing a 15% reduction in death and 25% to 30% reduction in heart failure-related hospitalization. SGLT2 inhibition is included as step 1 for patients with stage C heart failure.</p> <ul style="list-style-type: none">• In addition to comparative effectiveness, please discuss any differences in the safety profile of the selected drug compared to its therapeutic alternative(s) for each applicable specific population. No additional information

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Question	Sub-Question	Response
	Hyperlink to Citation - Additional Materials for Question 29	
Question 30: Addressing Unmet Medical Needs	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	
	Evidence Submitted include a cost-effectiveness measure?	
	What type of Evidence is shown?	
	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>██████ was surprised. She knew that she had been feeling more tired lately, but chalked it up to a busier than normal work schedule and caring for her elderly mother after work..She had gained weight as well and her shoes did not fit from swelling, but she was always in a rush and fast food was the quickest option. It had been hot lately, and don't all women have feet swelling from running around so much? When the trouble breathing started, she stopped by the emergency room, just to check things out. It was in the neighborhood, where everyone went for their urgent care..Heart Failure. The words stuck in her throat. Five days in the hospital with daily blood tests, IV medications, echocardiogram, catheterization, and a bag full of pills she could not pronounce..Sacubitril-valsartan, dapagliflozin, metoprolol succinate, spironolactone, apixaban, and furosemide and atorvastatin. This was a new normal for her. Not the flu or even covid, but a realization that her her heart was not pumping as it should and her body was trying to make up for the dysfunction by keeping the fluid that backed up in her lungs and her legs like Black Friday traffic to the mall. She had just taken an aspirin in the past and now she had to figure this out. It was a matter of life and death..Chronic. Meaning she had to keep taking the American Heart Association “guideline directed medical therapy” for the rest of her life, hopefully longer than the 5 years given to 50% of patients admitted to the hospital for the first time. .Panic. The pharmacy told her that to renew her prescriptions, it would cost over \$1000. She did not have that kind of money. Even if she could get it together, what would she do the next month. Three of the seven meds she was taken did not come in a generic form. The nurse from the office had checked alternative options of empagliflozin or rivaroxaban but they were still too expensive. She relied on samples from the doctor's office, pharmaceutical coupons and a kind social worker who helped her apply for multiple programs. It could take 6 weeks to hear back if she met criteria for these programs..Hope. She took the medications, walked as much as she was able and went to multiple followup appointments. She started cardiac rehab and tried to cut back on her fluid and salt intake (planning her meals and avoiding fast food if possible). She started to feel better. She could live with heart failure, but the cost of the medications continued to be a concern for her and her neighbor whose Medicare plan covered prescriptions through half the year and then the cost doubled and tripled. And for her church friend who was uninsured and did not have the same options. They were all part of the over 6.5 million Americans affected by this terrible life altering illness. She had heard on the news that Congress was considering a cap on the cost of a number of the same medications she was taking. She hoped and prayed this would happen. She wanted to live her life, take care of her mother and her family. She was only 53 and had more life to live..Recommended medications were the answer. She hoped that they would be an option.</p>

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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	DAPAGLIFLOZIN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	AARP
	Respondent Email	
Question 27: Prescribing Information	Who is completing this form?	PAT
	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>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 and related out-of-pocket costs can negatively affect older adults' health and financial security. Too many seniors are being forced spend down their retirement savings or to choose between paying for their prescription drugs or other important needs like groceries or housing. It is virtually impossible to adequately prepare for your future health care costs when they include prescription drugs with prices that are set on the basis of what the market will bear. ..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 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...Sincerely, ..Nancy LeaMond.Executive Vice President and Chief Advocacy & Engagement Officer</p>

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



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.¹ 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).² 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 2006.³ Further, the median price of a new brand-name prescription drug is now approximately \$200,000 per year,⁴ 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 and related out-of-pocket costs can negatively affect older adults' health and financial security. Too many seniors are being forced spend down their retirement savings or to choose between paying for their prescription drugs or other important needs like groceries or housing. It is virtually impossible to adequately prepare for your future health care costs when they include prescription drugs with prices that are set on the basis of what the market will bear.

¹ 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>.

² *Id.*

³ *Id.*

⁴ 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/>.

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,⁵ reduce the budget deficit by \$25 billion in 2031,⁶ and save Medicare Part D enrollees \$7 billion in 2031 due to lower out-of-pocket costs and premiums.⁷

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.

Sincerely,



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

⁵ 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. Accessed September 27, 2023.

⁶ 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.

⁷ *Id.*

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



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.¹ 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.² 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.³ 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.⁴ Aimed Alliance urges CMS to ensure patient and provider lived experiences are adequately valued when considering these factors and throughout this process.

¹ 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>

² *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>

³ *Id.*

⁴ <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.⁵ Sweden further incorporates ethical considerations, prioritizing those with the greatest health care needs and ensuring the process upholds and respects individual human dignity.⁶ By valuing the needs of patients and providers, Sweden maintains an overall high health care satisfaction rate.⁷ 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.⁸ 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.⁹

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.¹⁰ Aimed Alliance urges CMS to expand the number of listening

⁵ 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>.

⁶ Global Legal Rights, *Pricing & Reimbursement Laws and Regulations 2023*,

<https://www.globallegalinsights.com/practice-areas/pricing-and-reimbursement-laws-and-regulations/sweden>

⁷ Roosa Tikkanen, et al., *Sweden Scorecard*, <https://www.commonwealthfund.org/international-health-policy-center/countries/sweden>; Ketevan 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>.

⁸ Houses of Parliament: Parliamentary Office of Science & Technology, *Drug Pricing*, https://www.parliament.uk/globalassets/documents/post/postpn_364_Drug_Pricing.pdf

⁹ *Id.*

¹⁰ 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.¹¹ While Aamed 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.¹² 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.¹³ For instance, one study found that out of 105 patients with IBD, 84 percent reported experiencing stigma associated with their condition.¹⁴ 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 if you have any additional questions.

Sincerely,
Ashira Vantrees
Counsel

¹¹ *Id.*

¹² 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/

¹³ 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/>

¹⁴ Marco Vinezco 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	DAPAGLIFLOZIN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	Chronic Care Policy Alliance
	Respondent Email Who is completing this form?	PAO
Question 27: Prescribing Information	Prescribing Information	<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. ..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.</p>
	Evidence Submitted include a cost-effectiveness measure? What type of Evidence is shown?	N
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	<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...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.</p>

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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	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.
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?	
	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.
Question 30: Addressing 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	DAPAGLIFLOZIN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	Diabetes Leadership Council
	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	<p>On behalf of the Diabetes Leadership Council (DLC), thank you for the opportunity to provide patient-focused comments on four diabetes therapies included in the first 10 Medicare Part D drugs that the Centers for Medicare & Medicaid Services (CMS) selected for price negotiation. ..DLC unites former leaders of national diabetes organizations who are dedicated to advancing patients-first policies. We are people with diabetes, parents of children with diabetes, allies and tireless volunteers dedicated to improving the lives of all people impacted by this condition. ..As advocates, we see first-hand how the diabetes community fares under an opaque and complex system that requires sick people to subsidize the healthy. Patients with chronic conditions like diabetes get stuck paying inflated costs for essential medicines under the false premise that it keeps costs lower for everyone else. People with diabetes shouldn't have to shoulder the burden for policymakers' failure to fix the dysfunctional drug pricing system. We write to urge CMS to consider the impact that its decisions will have on actual patients, and to underscore that price negotiations alone will not ensure affordable, equitable prescription drug access for Medicare beneficiaries. ..HIGH COST, HIGH UTILIZATION.Diabetes has a large and growing patient population and ranks among the top three therapy classes in terms of utilization and drug spend for both commercial insurance and Medicare. As evidenced by their overrepresentation on the initial list of drugs subject to price negotiation, diabetes therapies contribute to CMS costs not only due to price, but high volumes dispensed. The fact that four of the first ten therapies subject to negotiation are diabetes treatments also highlights the heavy toll of under-resourced and under-utilized prevention efforts in the face</p>

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Response

of the diabetes epidemic. Nearly one-third of Medicare beneficiaries have diabetes and another 26.4 million people aged 65 years or older (48.8%) have prediabetes. CMS must ensure that its efforts produce tangible improvements in prescription drug access and affordability for beneficiaries managing diabetes today and in the future. ..ACCESS TO CARE.Diabetes is a highly competitive and heavily contracted category where discounts and rebates reduce net prices to levels much lower than gross or list prices. Diabetes medications already represent 42% of the \$48.6 billion in prescription drug rebates and discounts paid annually by Part D in the US. ..Beneficiary use of highly rebated or discounted drugs has different implications for plan sponsors, Medicare and patients. It can mean lower Medicare drug spending, as its plan sponsor payments are based on net drug costs after rebates. Individual beneficiary drug payments, however, may be based on the gross cost before accounting for rebates. The General Accounting Office (GAO) recently found payments by beneficiaries exceeded plan sponsor payments, after accounting for rebates, for 79 of the 100 drugs receiving the most rebate. Three therapeutic drug classes accounted for 73% of rebates: (1) endocrine metabolic agents, including antidiabetic drugs; (2) blood modifiers, including anti-stroke drugs; and (3) respiratory agents, including anti-asthma drugs. The same GAO report found instances where plan sponsors preferred rebated brand-name drugs with higher beneficiary costs over lower-cost alternatives. ..DIRECT PATIENT BENEFIT.Patients should directly benefit from drug prices negotiated on their behalf, whether negotiations are conducted by a government agency or commercial entity...CMS's price negotiations may be successful in extracting price concessions from manufacturers. Unfortunately, the program lacks any requirement to improve affordability and access for the very patients whose lives depend on these products. Instead, the program perpetuates the existing inequities that leave patients paying more for less while intermediaries pocket the savings. Patients who rely on the diabetes medications selected for price negotiations should see all rebates or discounts reflected in the price they pay at the pharmacy counter. ..Additionally, products subject to negotiated prices should be immediately added to Medicare formularies at the lowest cost-sharing tier and without utilization management or other barriers to appropriate use. Part D plans should encourage use of lower cost, therapeutically appropriate products by eliminating prior authorization, step therapy and other access barriers. ..Thank you for your consideration.

Hyperlink to
Table/Charts/Graphs -
Additional Materials for
Question 28
Evidence Submitted include
a cost-effectiveness
measure?

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Question	Sub-Question	Response
	What type of Evidence is shown?	
Question 29: Comparative Effectiveness on Specific Populations	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?	
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	

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Question	Sub-Question	Response
	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	<p>On behalf of the Diabetes Leadership Council (DLC), thank you for the opportunity to provide patient-focused comments on four diabetes therapies included in the first 10 Medicare Part D drugs that the Centers for Medicare & Medicaid Services (CMS) selected for price negotiation. ..DLC unites former leaders of national diabetes organizations who are dedicated to advancing patients-first policies. We are people with diabetes, parents of children with diabetes, allies and tireless volunteers dedicated to improving the lives of all people impacted by this condition. ..As advocates, we see first-hand how the diabetes community fares under an opaque and complex system that requires sick people to subsidize the healthy. Patients with chronic conditions like diabetes get stuck paying inflated costs for essential medicines under the false premise that it keeps costs lower for everyone else. People with diabetes shouldn't have to shoulder the burden for policymakers' failure to fix the dysfunctional drug pricing system. We write to urge CMS to consider the impact that its decisions will have on actual patients, and to underscore that price negotiations alone will not ensure affordable, equitable prescription drug access for Medicare beneficiaries. ..HIGH COST, HIGH UTILIZATION.Diabetes has a large and growing patient population and ranks among the top three therapy classes in terms of utilization and drug spend for both commercial insurance and Medicare. As evidenced by their overrepresentation on the initial list of drugs subject to price negotiation, diabetes therapies contribute to CMS costs not only due to price, but high volumes dispensed. The fact that four of the first ten therapies subject to negotiation are diabetes treatments also highlights the heavy toll of under-resourced and under-utilized prevention efforts in the face of the diabetes epidemic. Nearly one-third of Medicare beneficiaries have diabetes and another 26.4 million people aged 65 years or older (48.8%) have prediabetes. CMS must ensure that its efforts produce tangible improvements in prescription drug access and affordability for beneficiaries managing diabetes today and in the future. ..ACCESS TO CARE.Diabetes is a highly competitive and heavily contracted category where discounts and rebates reduce net prices to levels much lower than gross or list prices. Diabetes medications already represent 42% of the \$48.6 billion in prescription drug rebates and discounts paid annually by Part D in the US.</p>

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Question Sub-Question



Response

..Beneficiary use of highly rebated or discounted drugs has different implications for plan sponsors, Medicare and patients. It can mean lower Medicare drug spending, as its plan sponsor payments are based on net drug costs after rebates. Individual beneficiary drug payments, however, may be based on the gross cost before accounting for rebates. The General Accounting Office (GAO) recently found payments by beneficiaries exceeded plan sponsor payments, after accounting for rebates, for 79 of the 100 drugs receiving the most rebate. Three therapeutic drug classes accounted for 73% of rebates: (1) endocrine metabolic agents, including antidiabetic drugs; (2) blood modifiers, including anti-stroke drugs; and (3) respiratory agents, including anti-asthma drugs. The same GAO report found instances where plan sponsors preferred rebated brand-name drugs with higher beneficiary costs over lower-cost alternatives. ..DIRECT PATIENT BENEFIT. Patients should directly benefit from drug prices negotiated on their behalf, whether negotiations are conducted by a government agency or commercial entity...CMS's price negotiations may be successful in extracting price concessions from manufacturers. Unfortunately, the program lacks any requirement to improve affordability and access for the very patients whose lives depend on these products. Instead, the program perpetuates the existing inequities that leave patients paying more for less while intermediaries pocket the savings. Patients who rely on the diabetes medications selected for price negotiations should see all rebates or discounts reflected in the price they pay at the pharmacy counter. ..Additionally, products subject to negotiated prices should be immediately added to Medicare formularies at the lowest cost-sharing tier and without utilization management or other barriers to appropriate use. Part D plans should encourage use of lower cost, therapeutically appropriate products by eliminating prior authorization, step therapy and other access barriers. ..Thank you for your consideration.

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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	DAPAGLIFLOZIN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	[REDACTED]
	Respondent Email	
Question 27: Prescribing Information	Who is completing this form?	HCW
	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>Patient PM is a newly diagnosed congestive heart patient. Within the past year, her cardiologists have started her on GDMT to treat her cardiomyopathy and prevent fluid retention. Her insurance approved coverage for her diuretic, beta blocker, aldosterone antagonist, and even her Entresto. However, when time came to add Farxiga to her heart failure medication regimen, her insurance denied it. The \$550 copay for a month's supply was too expensive for her to afford, however her household annual income was too high to apply for patient assistance. Therefore, this patient could not experience the benefits of an SGLT2i...Another patient story:..My mother was recently diagnosed with heart failure with preserved ejection fraction and the medication Farxiga was prescribed for her treatment. We were excited to start this medication as we were told it would help with her breathing, fluid, and energy. Also, the medication could extend her life and keep her out of the hospital. We were shocked when we got to the pharmacy and were told the medication would be \$634.24 for 30 pills. Our excitement and hopes regarding this medication helping my mother were dashed quickly. My mom desperately wanted to feel better, but there was no way on her limited income that she could afford Farxiga. She has Medicare A and B, and a supplemental policy. I quickly called the doctor's office hoping something could be done and they offered me a free 30-day manufacturer coupon to try. I was able to get the medication for my mother and she really did feel a difference on the medication. She said that it helped her be less short of breath when she was walking around the house, she noticed the swelling in her legs was less, and she lost several pounds of water weight. She had no side effects. However, our free pill supply ran out and Mom was left not having Farxiga anymore. She quickly became short of breath and swollen again. I was looking online with the manufacturer and found a patient assistance program through Astra Zeneca and I filled out the application for my mom and the doctor signed her portion. Thankfully Mom was approved based on her income to receive Farxiga in the mail from the manufacturer. She is back on the medication and feeling great. She states she feels like a new person. We were told we would have to reapply for patient assistance each year, so I pray my mom can continue to be on this medication. I am writing today to ask for help for our elderly parents who need these expensive medications but cannot afford them. If my mom had to pay for this medication out of her pocket, she would have to choose between groceries or utilities and her pills. We need the prices lowered for our family members on Medicare so that she can continue Farxiga and we can have her around for a long time. Thank you.</p>

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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	DAPAGLIFLOZIN
	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 Dapagliflozin. 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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Question Sub-Question

Response

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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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&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

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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

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Question	Sub-Question	Response
	<p data-bbox="262 435 609 678">Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28 Evidence Submitted include a cost-effectiveness measure?</p> <p data-bbox="262 719 609 784">What type of Evidence is shown?</p>	<p data-bbox="609 251 1967 427">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.</p>
<p data-bbox="63 1109 262 1279">Question 29: Comparative Effectiveness on Specific Populations</p>	<p data-bbox="262 849 609 881">Response to Question 29</p> <p data-bbox="262 954 609 1052">Hyperlink to Citation - Additional Materials for Question 29</p> <p data-bbox="262 1166 609 1295">Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29</p> <p data-bbox="262 1352 609 1450">Evidence Submitted include a cost-effectiveness measure?</p> <p data-bbox="262 1482 609 1547">What type of Evidence is shown?</p>	

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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 Dapagliflozin. 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.¹ 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

¹ 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.² 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.³ 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.⁴ 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

² *Id.* at §

³ § 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.").

⁴ 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.⁵ 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,⁶ and CMS's interpretation worryingly suggests that such coverage may also involve a preferred status designation.⁷ 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

⁵ See 42 C.F.R. § 423.128(d)(4)(ii).

⁶ Social Security Act § 1860D-4(b)(3)(I).

⁷ 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).⁸ The monthly Explanation of Benefits (EOB) must include lower cost alternatives.⁹

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."¹⁰ 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.

⁸ § 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).

⁹ 42 C.F.R. 423.138(e)(5).

¹⁰ 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.