

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

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: Boehringer Ingelheim

Drug: Jardiance (Empagliflozin)

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 Basic Pre-Clinical Research Costs

"Research and Development costs:

[Redacted]

The costs reported as Basic Pre-Clinical Research Direct Costs for All FDA-Approved Indications of the Selected Drug are all project costs as defined above related to Jardiance that were incurred from [REDACTED] for indications for Type 2 Diabetes Mellitus (T2DM), Heart Failure (HF), and Chronic Kidney Disease (CKD) and costs for [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

This document includes trade secret and confidential commercial information and is exempt from public disclosure under 5 U.S.C. § 552(b)(4)."

Explanation of Post-IND Costs

"The costs reported in response to Question 3 refer to clinical development activities for Jardiance. Costs related to clinical development activities for combination products that include Jardiance (fixed dosed combinations, e.g., Synjardy) are excluded.

[REDACTED]

Costs related to indications that currently do not have FDA approval were not considered.

The costs reported in response to Question 3 are driven by clinical development (post-IND) activities throughout the entire BI Organization (including all OPUs).

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

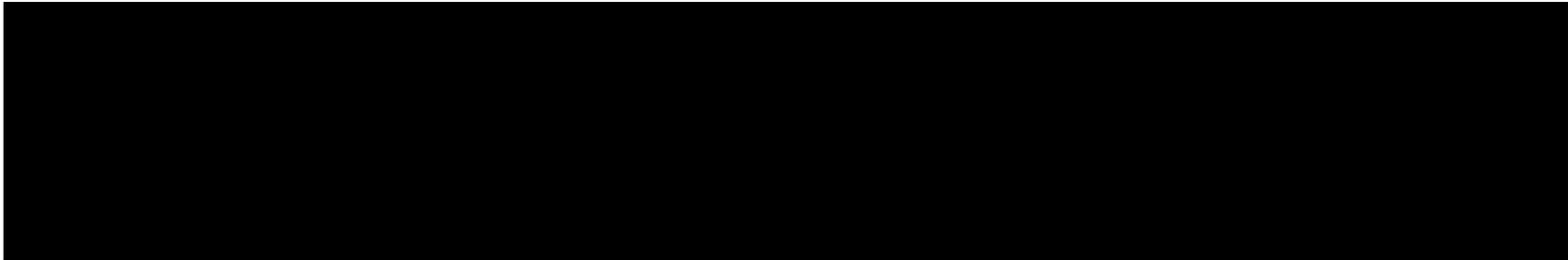
[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

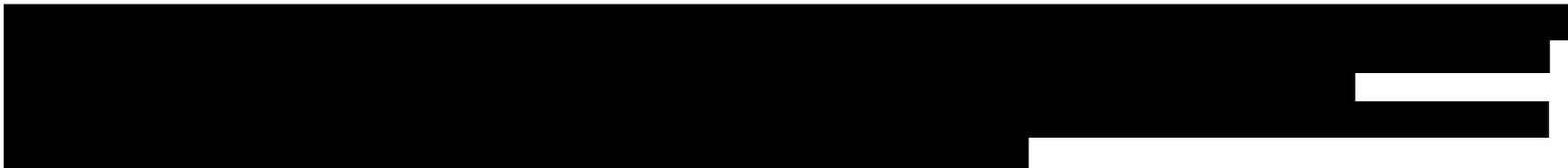
[REDACTED]



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Explanation of Costs on Allowable

"Pharmaceutical drug discovery involves extensive experimentation across a variety of targets and mechanisms of action. Accordingly, revenue from a product like Jardiance is not limited to supporting only research and development costs for its own FDA-approved indications or R&D costs for products in the same therapeutic class or having the same active moiety. Rather, revenue from Jardiance supports BI's broader research and development efforts in pursuit of innovative medicines for patients.



CMS states Question 4 should include "a sum of the portion of direct basic pre-clinical research costs on drugs with the same active moiety/active ingredient or mechanism of action as the selected drug that did not make it to clinical trials and a portion of direct post-IND costs for drugs in the same therapeutic class as the selected drug that did not achieve FDA approval." [REDACTED]

[REDACTED]

[REDACTED]

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Explanation of Costs of Other R&D

[REDACTED]

Early Exploratory Research Cost:

[REDACTED]

Impairment and amortization cost:

[REDACTED]

[Redacted]

[Redacted]

Other Basic Pre-Clinical Research Costs for failed and abandoned cost for the CRM Therapeutic class not reflected in Question 4

[Redacted]

“Other Basic POST-IND Costs for failed and abandoned projects for the CRM therapeutic class” not reflected in Question 4.

[Redacted]

[Redacted]

Other Basic Post-IND Costs not reflected in Question 3

[Redacted]

[Redacted]

[Redacted]

Other Global Costs:

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

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Explanation of Global

[Redacted]

[Redacted]

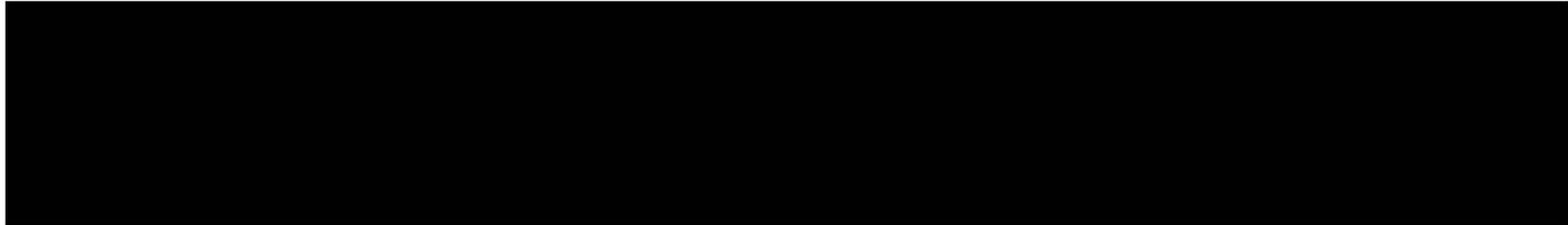
[Redacted]

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Explanation of U.S. Lifetime Net Revenue

[Redacted]

[Redacted]



Boehringer Ingelheim Pharmaceuticals, Inc., a US company, originates Total Lifetime Revenue and reports such revenue in US Dollars. A currency conversion was not necessary.

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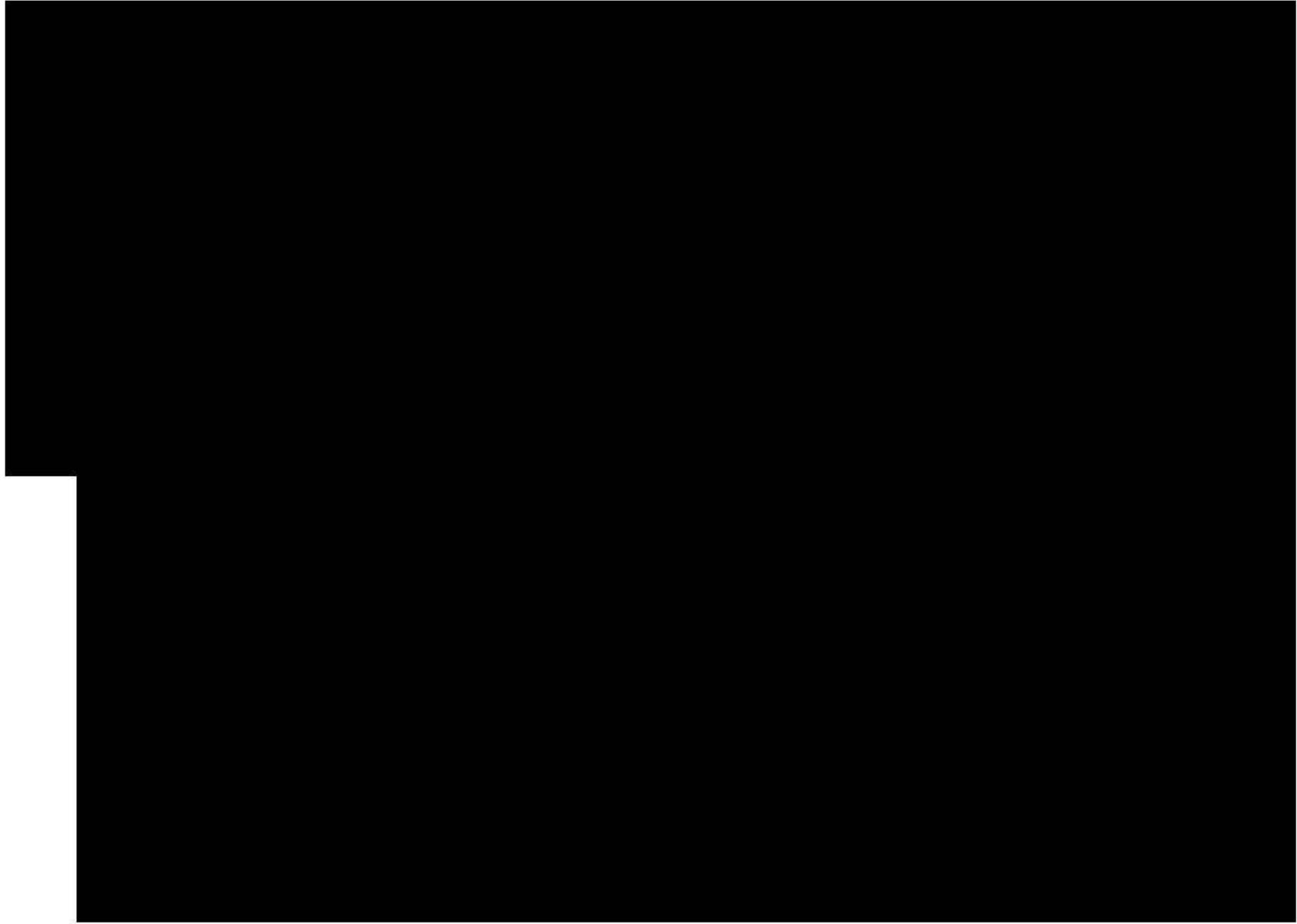
D. Current Unit Costs of Production and Distribution				
Background: Manufacturers were required to report production and distribution unit costs separately for each NDC-11 of the selected drug, including any NDC-11 of the selected drug marketed by a Secondary Manufacturer. A free response field was 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
00597-0152-07			EA	
00597-0152-30			EA	
00597-0152-37			EA	
00597-0152-90			EA	
00597-0153-07			EA	
00597-0153-30			EA	
00597-0153-37			EA	
00597-0153-90			EA	

Explanations: "Boehringer Ingelheim (BI) Methodology for Calculating Per Unit Production and Distribution Costs:

[Redacted]

[Redacted]

[Redacted]



[REDACTED]

[REDACTED]

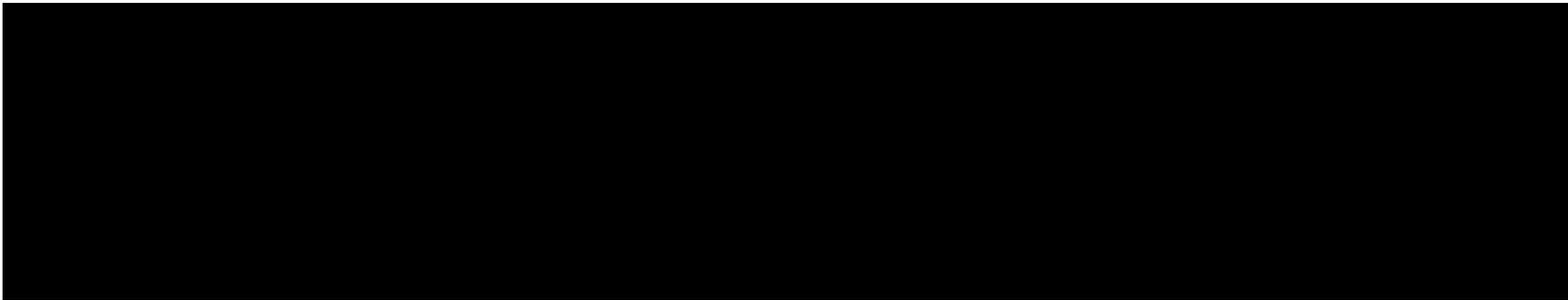
[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



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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
[REDACTED]	<p>"The only Federal Financial Support received by Boehringer Ingelheim is the US Federal Credit for Increasing Research Activities under section 41 of the Internal Revenue Code ("US Research Tax Credit"). Any computation that attempts to allocate portions of the US Research Tax Credit to a specific product is a "best estimate" due to the manner the credit is calculated as required by the US Internal Revenue Code. The US Research Tax Credit is fundamentally based on increasing levels of a limited class of direct research costs incurred year-over-year to qualify for the credit. This credit is not allocated to specific products and may also relate to research associated with products not commercialized. As such, it is not possible to reasonably allocate a portion of this tax credit to research for Jardiance.</p>	[REDACTED]		

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
7579449	2005-03-15	2028-08-01	N	Y	N	N	UTL	Y
7713938	2006-04-19	2027-04-15	Y	Y	N	N	UTL	Y
8551957	2010-04-15	2029-10-14	N	N	Y	N	UTL	Y
9949997	2015-10-21	2034-05-17	N	N	Y	N	UTL	Y
9949998	2015-10-21	2034-06-11	N	N	Y	N	UTL	Y
10258637	2018-03-12	2034-04-03	N	N	Y	N	UTL	Y
11090323	2019-02-28	2034-04-03	N	N	Y	N	UTL	Y
11666590	2020-11-10	2034-04-03	N	N	Y	N	UTL	N

Explanations: "The Orange Book currently lists the following patents for Jardiance: U.S. Pat. Nos. 7,579,449; 7,713,938; 8,551,957; 9,949,997; 9,949,998; 10,258,637; and 11,090,323.

For U.S. Pat. No. 8,551,957, the Patent Use Code listed in the Orange Book for both the 10 mg and 25 mg tablets is U-1651. A description of this and other use codes can be found on FDA's website: https://www.accessdata.fda.gov/scripts/cder/ob/results_patent.cfm.

For U.S. Pat. No. 9,949,997, the Patent Use Codes listed in the Orange Book for the 10 mg tablet are U-2292, U-3199, and U-3325.

For U.S. Pat. No. 9,949,997, the Patent Use Code listed in the Orange Book for the 25 mg tablet is U-2292.

For U.S. Pat. No. 9,949,998, the Patent Use Code listed in the Orange Book for both the 10 mg and 25 mg tablets is U-2290.

For U.S. Pat. No. 10,258,637, the Patent Use Code listed in the Orange Book for both the 10 mg and 25 mg tablets is U-2290.

For U.S. Pat. No. 11,090,323, the Patent Use Code listed in the Orange Book for both the 10 mg and 25 mg tablets is U-3191.

For U.S. Pat. No. 11,666,590, the patent will be listed in the Orange Book for the 10 mg tablets and a Use Code describing the reduction of risk in adults with chronic kidney disease at risk of progression.

[REDACTED]

U.S. Pat. No. 10,406,172 was previously listed in the 2020 Orange Book with Patent Use Code U-1652, but this patent was removed from the Orange Book in 2021.

[REDACTED] it is instead listed in association with Trijardy XR.

[REDACTED] Abandoned patent

applications have not been included in the Question 12 response given the HHS/CMS directive to not include patent applications that have been denied.

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F. Patents, Exclusivities, and Approvals

Regulatory Exclusivity Periods

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

Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
CEE	2019-08-01	204629	00597-0152; 00597-0153	New chemical entity exclusivity. The following statements about NDCs apply to all listed exclusivities in this submission. The Orange Book and FDA do not identify NDC-9s that are covered by regulatory exclusivities. The listed NDCs in Question 14 are not intended to address the scope of any exclusivity period. The submission does not include NDCs from other labelers (e.g. repackagers). We consider these NDCs to be covered by the listed exclusivities to the same extent as our corresponding NDC for the relevant strength.
CIE	2018-06-26	204629	00597-0152; 00597-0153	New Clinical Investigation Exclusivity with Use Code M-160: UPDATED LABELING WITH DATA FROM A RANDOMIZED, DOUBLE-BLIND ACTIVE-CONTROLLED STUDY COMPARING EMPAGLIFLOZIN TO GLIMEPIRIDE IN PATIENTS WITH TYPE 2 DIABETES AND INSUFFICIENT GLYCEMIC CONTROL DESPITE METFORMIN TREATMENT
CIE	2018-06-26	204629	00597-0152; 00597-0153	New Clinical Investigation Exclusivity with Use Code M-161: UPDATED LABELING WITH DATA FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF EMPAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND INSUFFICIENT GLYCEMIC CONTROL ON A MULTIPLE DAILY INJECTION INSULIN REGIMEN ALONE OR WITH METFORMIN

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Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
CIE	2019-03-18	204629	00597-0152; 00597-0153	New Clinical Investigation Exclusivity with Use Code M-174: INFORMATION ADDED TO CLINICAL STUDIES SECTION OF THE LABELING REGARDING INITIAL COMBINATION THERAPY OF EMPAGLIFLOZIN WITH METFORMIN
CIE	2019-12-02	204629	00597-0152; 00597-0153	New Clinical Investigation Exclusivity with Use Code I-739: TO REDUCE THE RISK OF CARDIOVASCULAR DEATH IN ADULT PATIENTS WITH TYPE 2 DIABETES MELLITUS AND ESTABLISHED CARDIOVASCULAR DISEASE
CIE	2024-08-18	204629	00597-0152	New Clinical Investigation Exclusivity with Use Code I-869: REDUCE THE RISK OF CARDIOVASCULAR DEATH AND HOSPITALIZATION FOR HEART FAILURE IN ADULTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION
PED	2024-02-18	204629	00597-0152	Pediatric Exclusivity extension of New Clinical Investigation Exclusivity "I-869": REDUCE THE RISK OF CARDIOVASCULAR DEATH AND HOSPITALIZATION FOR HEART FAILURE IN ADULTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION
CIE	2025-02-24	204629	00597-0152	New Clinical Investigation Exclusivity with Use Code M-82: LABELING REVISIONS RELATED TO CLINICAL STUDIES
PED	2025-08-24	204629	00597-0152; 00597-0153	Pediatric Exclusivity extension of New Clinical Investigation Exclusivity "M-82": LABELING REVISIONS RELATED TO CLINICAL STUDIES
CIE	2026-06-20	204629	00597-0152; 00597-0153	New Clinical Investigation Exclusivity with Code NPP (New Patient Population)
PED	2026-12-20	204629	00597-0152; 00597-0153	Pediatric Exclusivity extension of New Clinical Investigation Exclusivity "NPP" (New Patient Population)

F. Patents, Exclusivities, and Approvals

Regulatory Exclusivity Periods

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Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
PED	2027-10-15	204629	00597-0152; 00597-0153	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 7,713,938, which expires 4/15/2027 (and related 6 months PED exclusivity expires on 10/15/2027)
PED	2029-02-01	204629	00597-0152; 00597-0153	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 7,579,449, which expires 8/1/2028 (and related 6 months PED exclusivity expires on 2/1/2029)
PED	2030-04-14	204629	00597-0152; 00597-0153	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 8,551,957, which expires 10/14/2029 (and related 6 months PED exclusivity expires on 4/14/2030)
PED	2034-11-17	204629	00597-0152; 00597-0153	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 9,949,997, which expires 5/17/2034 (and related 6 months PED exclusivity expires on 11/17/2034)
PED	2034-12-11	204629	00597-0152; 00597-0153	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 9,949,998, which expires 6/11/2034 (and related 6 months PED exclusivity expires on 12/11/2034)
PED	2034-10-03	204629	00597-0152; 00597-0153	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 10,258,637, which expires 4/3/2034 (and related 6 months PED exclusivity expires on 10/3/2034)
PED	2034-10-03	204629	00597-0152; 00597-0153	Pediatric exclusivity extension applicable with respect to U.S. Pat. No. 11,090,323, which expires 4/3/2034 (and related 6 months PED exclusivity expires on 10/3/2034)

F. Patents, Exclusivities, and Approvals

Regulatory Exclusivity Periods

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Type of Exclusivity	Exclusivity Expiration Date	Application (NDA/BLA) Number	NDC-9s Covered by Exclusivity	Comments
CIE	2026-09-21	204629	00597-0152	New Clinical Investigation Exclusivity for Empa-Kidney study (not yet published in the Orange Book).

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
204629	NDA	1	2014-08-01	JARDIANCE is indicated as an	tablets, 10 mg, 25 mg	Boehringer Ingelheim	APP	Consistent with CMS's instructions for

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
				adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus		Pharmaceuticals Inc.		Question 15, we have included information about efficacy supplements (as classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements. Supplements do not have Classification Codes listed on the Drugs@FDA website, so the Classification Code from the original NDA 204629 being supplemented is listed for all listed supplements.
204629	NDA	1	2015-06-26	JARDIANCE is indicated as an	tablets, 10 mg, 25 mg	Boehringer Ingelheim	APP	Associated with Supplement-001.

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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
				adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus		Pharmaceuticals Inc.		Consistent with CMS's instructions for Question 15, we have included information about efficacy supplements (as classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements. Supplements do not have Classification Codes listed on the Drugs@FDA website, so the Classification Code from the original NDA 204629 being supplemented is listed for all listed supplements.

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
204629	NDA	1	2015-06-26	JARDIANCE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	tablets, 10 mg, 25 mg	Boehringer Ingelheim Pharmaceuticals Inc.	APP	Associated with Supplement-002. Consistent with CMS's instructions for Question 15, we have included information about efficacy supplements (as classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements. Supplements do not have Classification Codes listed on the Drugs@FDA website, so the Classification Code from the original NDA 204629 being supplemented is listed

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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
								for all listed supplements.
204629	NDA	1	2015-06-26	JARDIANCE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	tablets, 10 mg, 25 mg	Boehringer Ingelheim Pharmaceuticals Inc.	APP	Associated with Supplement-003. Consistent with CMS's instructions for Question 15, we have included information about efficacy supplements (as classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements. Supplements do not have Classification Codes listed on the Drugs@FDA website, so the Classification Code from the original

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
								NDA 204629 being supplemented is listed for all listed supplements.
204629	NDA	1	2016-03-18	JARDIANCE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	tablets, 10 mg, 25 mg	Boehringer Ingelheim Pharmaceuticals Inc.	APP	Associated with Supplement-005. Consistent with CMS's instructions for Question 15, we have included information about efficacy supplements (as classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements. Supplements do not have Classification Codes listed on the Drugs@FDA website,

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
								so the Classification Code from the original NDA 204629 being supplemented is listed for all listed supplements.
204629	NDA	1	2016-12-02	JARDIANCE is indicated: <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 cardiovascular death in adult patients with type 2 diabetes mellitus and 	tablets, 10 mg, 25 mg	Boehringer Ingelheim Pharmaceuticals Inc.	APP	Associated with Supplement-008. Consistent with CMS's instructions for Question 15, we have included information about efficacy supplements (as classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements. Supplements do not have Classification

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
				established cardiovascular disease				Codes listed on the Drugs@FDA website, so the Classification Code from the original NDA 204629 being supplemented is listed for all listed supplements.
204629	NDA	1	2021-08-18	JARDIANCE is indicated: <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 cardiovascular death in adults with type 2 	tablets, 10 mg, 25 mg	Boehringer Ingelheim Pharmaceuticals Inc.	APP	Associated with Supplement-026. Consistent with CMS's instructions for Question 15, we have included information about efficacy supplements (as classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements.

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
				diabetes mellitus and established cardiovascular disease. • to reduce the risk of cardiovascular death plus hospitalization for heart failure in adults with heart failure and reduced ejection fraction.				Supplements do not have Classification Codes listed on the Drugs@FDA website, so the Classification Code from the original NDA 204629 being supplemented is listed for all listed supplements.
204629	NDA	1	2022-02-24	JARDIANCE is indicated: • to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart	tablets, 10 mg, 25 mg	Boehringer Ingelheim Pharmaceuticals Inc.	APP	Associated with Supplement-033. Consistent with CMS's instructions for Question 15, we have included information about efficacy supplements (as

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
				failure. • to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease. • as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.				classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements. Supplements do not have Classification Codes listed on the Drugs@FDA website, so the Classification Code from the original NDA 204629 being supplemented is listed for all listed supplements.
204629	NDA	1	2023-06-20	JARDIANCE is indicated: to reduce the risk of cardiovascular death and hospitalization for	tablets, 10 mg, 25 mg	Boehringer Ingelheim Pharmaceuticals Inc.	APP	Associated with Supplement-042. Consistent with CMS's instructions for Question 15, we have included information

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 heart failure.; to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.; as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.				about efficacy supplements (as classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements. Supplements do not have Classification Codes listed on the Drugs@FDA website, so the Classification Code from the original NDA 204629 being supplemented is listed for all listed supplements.

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
204629	NDA	1	2023-09-21	JARDIANCE is indicated: To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure. To reduce the risk of sustained decline in eGFR, end-stage kidney disease, cardiovascular death, and hospitalization in adults with chronic kidney disease at risk of progression. To	tablets, 10 mg, 25 mg	Boehringer Ingelheim Pharmaceuticals Inc.	APP	Associated with Supplement-040. Consistent with CMS's instructions for Question 15, we have included information about efficacy supplements (as classified by FDA on Drugs@FDA per 21 C.F.R. 314.3) and not included other supplements. Supplements do not have Classification Codes listed on the Drugs@FDA website, so the Classification Code from the original NDA 204629 being supplemented is listed

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
				reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease. As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.				for all listed supplements.

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
00597-0153-37	2018-Q1	\$15.50	EA	
00597-0153-37	2018-Q2	\$15.50	EA	
00597-0153-37	2018-Q3	\$15.50	EA	
00597-0153-37	2018-Q4	\$15.50	EA	
00597-0153-37	2019-Q1	\$16.43	EA	
00597-0153-37	2019-Q2	\$16.43	EA	
00597-0153-37	2019-Q3	\$16.43	EA	
00597-0153-37	2019-Q4	\$16.43	EA	
00597-0153-37	2020-Q1	\$17.41	EA	
00597-0153-37	2020-Q2	\$17.41	EA	
00597-0153-37	2020-Q3	\$17.41	EA	
00597-0153-37	2020-Q4	\$17.41	EA	
00597-0153-37	2021-Q1	\$18.28	EA	
00597-0153-37	2021-Q2	\$18.28	EA	
00597-0153-37	2021-Q3	\$18.28	EA	
00597-0153-37	2021-Q4	\$18.28	EA	
00597-0153-37	2022-Q1	\$19.02	EA	
00597-0153-37	2022-Q2	\$19.02	EA	
00597-0153-37	2022-Q3	\$19.02	EA	
00597-0153-37	2022-Q4	\$19.02	EA	
00597-0152-37	2018-Q1	\$15.50	EA	
00597-0152-37	2018-Q2	\$15.50	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
00597-0152-37	2018-Q3	\$15.50	EA	
00597-0152-37	2018-Q4	\$15.50	EA	
00597-0152-37	2019-Q1	\$16.43	EA	
00597-0152-37	2019-Q2	\$16.43	EA	
00597-0152-37	2019-Q3	\$16.43	EA	
00597-0152-37	2019-Q4	\$16.43	EA	
00597-0152-37	2020-Q1	\$17.41	EA	
00597-0152-37	2020-Q2	\$17.41	EA	
00597-0152-37	2020-Q3	\$17.41	EA	
00597-0152-37	2020-Q4	\$17.41	EA	
00597-0152-37	2021-Q1	\$18.28	EA	
00597-0152-37	2021-Q2	\$18.28	EA	
00597-0152-37	2021-Q3	\$18.28	EA	
00597-0152-37	2021-Q4	\$18.28	EA	
00597-0152-37	2022-Q1	\$19.02	EA	
00597-0152-37	2022-Q2	\$19.02	EA	
00597-0152-37	2022-Q3	\$19.02	EA	
00597-0152-37	2022-Q4	\$19.02	EA	
00597-0152-30	2018-Q1	\$15.50	EA	
00597-0152-30	2018-Q2	\$15.50	EA	
00597-0152-30	2018-Q3	\$15.50	EA	
00597-0152-30	2018-Q4	\$15.50	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
00597-0152-30	2019-Q1	\$16.43	EA	
00597-0152-30	2019-Q2	\$16.43	EA	
00597-0152-30	2019-Q3	\$16.43	EA	
00597-0152-30	2019-Q4	\$16.43	EA	
00597-0152-30	2020-Q1	\$17.41	EA	
00597-0152-30	2020-Q2	\$17.41	EA	
00597-0152-30	2020-Q3	\$17.41	EA	
00597-0152-30	2020-Q4	\$17.41	EA	
00597-0152-30	2021-Q1	\$18.28	EA	
00597-0152-30	2021-Q2	\$18.28	EA	
00597-0152-30	2021-Q3	\$18.28	EA	
00597-0152-30	2021-Q4	\$18.28	EA	
00597-0152-30	2022-Q1	\$19.02	EA	
00597-0152-30	2022-Q2	\$19.02	EA	
00597-0152-30	2022-Q3	\$19.02	EA	
00597-0152-30	2022-Q4	\$19.02	EA	
00597-0153-90	2018-Q1	\$15.50	EA	
00597-0153-90	2018-Q2	\$15.50	EA	
00597-0153-90	2018-Q3	\$15.50	EA	
00597-0153-90	2018-Q4	\$15.50	EA	
00597-0153-90	2019-Q1	\$16.43	EA	
00597-0153-90	2019-Q2	\$16.43	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
00597-0153-90	2019-Q3	\$16.43	EA	
00597-0153-90	2019-Q4	\$16.43	EA	
00597-0153-90	2020-Q1	\$17.41	EA	
00597-0153-90	2020-Q2	\$17.41	EA	
00597-0153-90	2020-Q3	\$17.41	EA	
00597-0153-90	2020-Q4	\$17.41	EA	
00597-0153-90	2021-Q1	\$18.28	EA	
00597-0153-90	2021-Q2	\$18.28	EA	
00597-0153-90	2021-Q3	\$18.28	EA	
00597-0153-90	2021-Q4	\$18.28	EA	
00597-0153-90	2022-Q1	\$19.02	EA	
00597-0153-90	2022-Q2	\$19.02	EA	
00597-0153-90	2022-Q3	\$19.02	EA	
00597-0153-90	2022-Q4	\$19.02	EA	
00597-0153-30	2018-Q1	\$15.50	EA	
00597-0153-30	2018-Q2	\$15.50	EA	
00597-0153-30	2018-Q3	\$15.50	EA	
00597-0153-30	2018-Q4	\$15.50	EA	
00597-0153-30	2019-Q1	\$16.43	EA	
00597-0153-30	2019-Q2	\$16.43	EA	
00597-0153-30	2019-Q3	\$16.43	EA	
00597-0153-30	2019-Q4	\$16.43	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
00597-0153-30	2020-Q1	\$17.41	EA	
00597-0153-30	2020-Q2	\$17.41	EA	
00597-0153-30	2020-Q3	\$17.41	EA	
00597-0153-30	2020-Q4	\$17.41	EA	
00597-0153-30	2021-Q1	\$18.28	EA	
00597-0153-30	2021-Q2	\$18.28	EA	
00597-0153-30	2021-Q3	\$18.28	EA	
00597-0153-30	2021-Q4	\$18.28	EA	
00597-0153-30	2022-Q1	\$19.02	EA	
00597-0153-30	2022-Q2	\$19.02	EA	
00597-0153-30	2022-Q3	\$19.02	EA	
00597-0153-30	2022-Q4	\$19.02	EA	
00597-0152-90	2018-Q1	\$15.50	EA	
00597-0152-90	2018-Q2	\$15.50	EA	
00597-0152-90	2018-Q3	\$15.50	EA	
00597-0152-90	2018-Q4	\$15.50	EA	
00597-0152-90	2019-Q1	\$16.43	EA	
00597-0152-90	2019-Q2	\$16.43	EA	
00597-0152-90	2019-Q3	\$16.43	EA	
00597-0152-90	2019-Q4	\$16.43	EA	
00597-0152-90	2020-Q1	\$17.41	EA	
00597-0152-90	2020-Q2	\$17.41	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
00597-0152-90	2020-Q3	\$17.41	EA	
00597-0152-90	2020-Q4	\$17.41	EA	
00597-0152-90	2021-Q1	\$18.28	EA	
00597-0152-90	2021-Q2	\$18.28	EA	
00597-0152-90	2021-Q3	\$18.28	EA	
00597-0152-90	2021-Q4	\$18.28	EA	
00597-0152-90	2022-Q1	\$19.02	EA	
00597-0152-90	2022-Q2	\$19.02	EA	
00597-0152-90	2022-Q3	\$19.02	EA	
00597-0152-90	2022-Q4	\$19.02	EA	

Explanations: "NDC 0597-0152-07, NDC 0597-0152-70, NDC 0597-0153-07, and NDC 0597-0153-70 are associated with free samples. Therefore, there is no data reported for these NDCs.

Assumption: "Most recent 5 years" = January 1, 2018 through December 31, 2022. The data for this 5 year time period was compiled, analyzed and reviewed prior to the September 21, 2023 FAQ release.

There are no deviations between the WAC unit price data provided in response to Question 16. Boehringer Ingelheim Pharmaceuticals Inc. consulted Analysource and confirmed that there are no deviations between the WAC unit price data provided in response to Question 16 and that provided in Analysource."

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	00597-0152	2018-Q1		EA	
Y	00597-0152	2018-Q2		EA	
Y	00597-0152	2018-Q3		EA	
Y	00597-0152	2018-Q4		EA	
Y	00597-0152	2019-Q1		EA	
Y	00597-0152	2019-Q2		EA	
Y	00597-0152	2019-Q3		EA	
Y	00597-0152	2019-Q4		EA	
Y	00597-0152	2020-Q1		EA	
Y	00597-0152	2020-Q2		EA	
Y	00597-0152	2020-Q3		EA	
Y	00597-0152	2020-Q4		EA	
Y	00597-0152	2021-Q1		EA	
Y	00597-0152	2021-Q2		EA	
Y	00597-0152	2021-Q3		EA	
Y	00597-0152	2021-Q4		EA	
Y	00597-0152	2022-Q1		EA	
Y	00597-0152	2022-Q2		EA	
Y	00597-0152	2022-Q3		EA	
Y	00597-0152	2022-Q4		EA	

G. Market Data and Revenue and Sales Volume Data

Medicaid Best Price

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

Medicaid Best Price	National Drug Code (NDC-9)	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
Y	00597-0153	2018-Q1		EA	
Y	00597-0153	2018-Q2		EA	
Y	00597-0153	2018-Q3		EA	
Y	00597-0153	2018-Q4		EA	
Y	00597-0153	2019-Q1		EA	
Y	00597-0153	2019-Q2		EA	
Y	00597-0153	2019-Q3		EA	
Y	00597-0153	2019-Q4		EA	
Y	00597-0153	2020-Q1		EA	
Y	00597-0153	2020-Q2		EA	
Y	00597-0153	2020-Q3		EA	
Y	00597-0153	2020-Q4		EA	
Y	00597-0153	2021-Q1		EA	
Y	00597-0153	2021-Q2		EA	
Y	00597-0153	2021-Q3		EA	
Y	00597-0153	2021-Q4		EA	
Y	00597-0153	2022-Q1		EA	
Y	00597-0153	2022-Q2		EA	
Y	00597-0153	2022-Q3		EA	
Y	00597-0153	2022-Q4		EA	

Explanations: "NDC 0597-0152-07, NDC 0597-0152-70, NDC 0597-0153-07, and NDC 0597-0153-70 are samples and not sold commercially. Therefore, there is no data reported for these NDCs.

Assumption: "Most recent 5 years" = January 1, 2018 through December 31, 2022. The data for this 5 year time period was compiled, analyzed and reviewed prior to the September 21, 2023 FAQ release.



This document includes trade secret and confidential commercial information and is exempt from public disclosure under 5 U.S.C. § 552(b)(4)."

G. Market Data and Revenue and Sales Volume Data					
Federal Supply Schedule 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. 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.</p>					
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	00597-0152-30	2018-01-01 - 2018-12-31	\$230.74	EA	
Y	00597-0152-37	2018-01-01 - 2018-12-31	\$230.74	EA	
Y	00597-0152-90	2018-01-01 - 2018-12-31	\$670.50	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	00597-0153-30	2018-01-01 - 2018-12-31	\$233.76	EA	
Y	00597-0153-37	2018-01-01 - 2018-12-31	\$233.76	EA	
Y	00597-0153-90	2018-01-01 - 2018-12-31	\$679.77	EA	
Y	00597-0152-30	2019-01-01 - 2019-12-31	\$317.15	EA	
Y	00597-0152-37	2019-01-01 - 2019-12-31	\$317.25	EA	
Y	00597-0152-90	2019-01-01 - 2019-12-31	\$948.52	EA	
Y	00597-0153-30	2019-01-01 - 2019-12-31	\$316.65	EA	
Y	00597-0153-37	2019-01-01 - 2019-12-31	\$318.47	EA	
Y	00597-0153-90	2019-01-01 - 2019-12-31	\$938.07	EA	
Y	00597-0152-30	2020-01-01 - 2020-12-31	\$322.57	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	00597-0152-37	2020-01-01 - 2020-12-31	\$322.67	EA	
Y	00597-0152-90	2020-01-01 - 2020-12-31	\$964.74	EA	
Y	00597-0153-30	2020-01-01 - 2020-12-31	\$322.07	EA	
Y	00597-0153-37	2020-01-01 - 2020-12-31	\$323.92	EA	
Y	00597-0153-90	2020-01-01 - 2020-12-31	\$954.11	EA	
Y	00597-0152-30	2021-01-01 - 2021-12-31	\$326.99	EA	
Y	00597-0152-37	2021-01-01 - 2021-12-31	\$327.10	EA	
Y	00597-0152-90	2021-01-01 - 2021-12-31	\$977.96	EA	
Y	00597-0153-30	2021-01-01 - 2021-12-31	\$326.48	EA	
Y	00597-0153-37	2021-01-01 - 2021-12-31	\$328.36	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	00597-0153-90	2021-01-01 - 2021-12-31	\$967.19	EA	
Y	00597-0152-30	2022-01-01 - 2022-09-14	\$344.62	EA	
Y	00597-0152-37	2022-01-01 - 2022-09-14	\$344.72	EA	
Y	00597-0152-90	2022-01-01 - 2022-09-14	\$1,030.67	EA	
Y	00597-0153-30	2022-01-01 - 2022-09-14	\$344.08	EA	
Y	00597-0153-37	2022-01-01 - 2022-09-14	\$346.06	EA	
Y	00597-0153-90	2022-01-01 - 2022-09-14	\$1,019.32	EA	
Y	00597-0152-30	2022-09-15 - 2022-12-31	\$434.34	EA	
Y	00597-0152-37	2022-09-15 - 2022-12-31	\$434.34	EA	
Y	00597-0152-90	2022-09-15 - 2022-12-31	\$1,303.02	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	00597-0153-30	2022-09-15 - 2022-12-31	\$434.34	EA	
Y	00597-0153-37	2022-09-15 - 2022-12-31	\$434.34	EA	
Y	00597-0153-90	2022-09-15 - 2022-12-31	\$1,303.02	EA	

Explanations: "NDC 0597-0152-07, NDC 0597-0152-70, NDC 0597-0153-07, and NDC 0597-0153-70 are samples and not sold commercially. Therefore, there is no data reported for these NDCs.

The Federal Supply Schedule (FSS) Price information reported in Question 20 reflects the information submitted annually by Boehringer Ingelheim Pharmaceuticals Inc. to the Department of Veterans Affairs (VA) for January 1, 2018 through December 31, 2022. The data for this 5 year time period was compiled, analyzed and reviewed prior to the September 21, 2023 FAQ release.

The FSS price is calculated based on the prior non-federal average manufacturer price (and the current non-FAMP, consumer price inflation index (CPI-U), and the statutory discount rate.

FSS eligible sales were identified through chargeback transactions from wholesalers and distributors on the FSS contracts received. Packages were aggregated by product by quarter for all chargeback transactions using invoice date. Package quantity was then converted to units using the Medicaid conversion factor for each product.

FSS prices are reported at the package level. The units reported are eaches (EA) at the single unit level.

This document includes trade secret and confidential commercial information and is exempt from public disclosure under 5 U.S.C. § 552(b)(4)."

G. Market Data and Revenue and Sales Volume Data					
Big Four 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 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.</p>					
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	00597-0152-30	2022-09-15 - 2022-12-31	\$344.62	EA	
Y	00597-0152-37	2022-09-15 - 2022-12-31	\$344.72	EA	
Y	00597-0152-90	2022-09-15 - 2022-12-31	\$1,030.67	EA	
Y	00597-0153-30	2022-09-15 - 2022-12-31	\$344.08	EA	
Y	00597-0153-37	2022-09-15 - 2022-12-31	\$346.06	EA	
Y	00597-0153-90	2022-09-15 - 2022-12-31	\$1,019.32	EA	
Y	00597-0152-30	2022-09-15 - 2022-12-31	\$344.62	EA	

Explanations: "NDC 0597-0152-07, NDC 0597-0152-70, NDC 0597-0153-07, and NDC 0597-0153-70 are samples and not sold commercially. Therefore, there is no data reported for these NDCs.

The Big Four price information reported in Question 22 reflects the information that Boehringer Ingelheim Pharmaceuticals Inc. submitted to the Department of Veterans Affairs for January 1, 2018 through December 31, 2022. The data for this 5 year time period was compiled, analyzed and reviewed prior to the September 21, 2023 FAQ release.

Big Four sales were identified through chargeback transactions received from wholesalers and distributors on the Big 4 contract. Packages were aggregated by product by quarter for all chargeback transactions using invoice date. Package quantity was then converted to units using the Medicaid conversion factor for each product.

This document includes trade secret and confidential commercial information and is exempt from public disclosure under 5 U.S.C. § 552(b)(4)."

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
00597-0153-37	2018-Q1				EA	
00597-0152-37	2018-Q1				EA	
00597-0152-30	2018-Q1				EA	
00597-0153-90	2018-Q1				EA	
00597-0153-30	2018-Q1				EA	
00597-0152-90	2018-Q1				EA	
00597-0153-37	2018-Q2				EA	
00597-0152-37	2018-Q2				EA	
00597-0152-30	2018-Q2				EA	
00597-0153-90	2018-Q2				EA	
00597-0153-30	2018-Q2				EA	
00597-0152-90	2018-Q2				EA	

G. Market Data and Revenue and Sales Volume Data

U.S. Commercial Average Net Unit Price

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

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
00597-0153-37	2018-Q3				EA	
00597-0152-37	2018-Q3				EA	
00597-0152-30	2018-Q3				EA	
00597-0153-90	2018-Q3				EA	
00597-0153-30	2018-Q3				EA	
00597-0152-90	2018-Q3				EA	
00597-0153-37	2018-Q4				EA	
00597-0152-37	2018-Q4				EA	
00597-0152-30	2018-Q4				EA	
00597-0153-90	2018-Q4				EA	
00597-0153-30	2018-Q4				EA	
00597-0152-90	2018-Q4				EA	
00597-0153-37	2019-Q1				EA	
00597-0152-37	2019-Q1				EA	
00597-0152-30	2019-Q1				EA	
00597-0153-90	2019-Q1				EA	
00597-0153-30	2019-Q1				EA	
00597-0152-90	2019-Q1				EA	
00597-0153-37	2019-Q2				EA	
00597-0152-37	2019-Q2				EA	

G. Market Data and Revenue and Sales Volume Data

U.S. Commercial Average Net Unit Price

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

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
00597-0152-30	2019-Q2				EA	
00597-0153-90	2019-Q2				EA	
00597-0153-30	2019-Q2				EA	
00597-0152-90	2019-Q2				EA	
00597-0153-37	2019-Q3				EA	
00597-0152-37	2019-Q3				EA	
00597-0152-30	2019-Q3				EA	
00597-0153-90	2019-Q3				EA	
00597-0153-30	2019-Q3				EA	
00597-0152-90	2019-Q3				EA	
00597-0153-37	2019-Q4				EA	
00597-0152-37	2019-Q4				EA	
00597-0152-30	2019-Q4				EA	
00597-0153-90	2019-Q4				EA	
00597-0153-30	2019-Q4				EA	
00597-0152-90	2019-Q4				EA	
00597-0153-37	2020-Q1				EA	
00597-0152-37	2020-Q1				EA	
00597-0152-30	2020-Q1				EA	
00597-0153-90	2020-Q1				EA	

G. Market Data and Revenue and Sales Volume Data

U.S. Commercial Average Net Unit Price

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

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
00597-0153-30	2020-Q1				EA	
00597-0152-90	2020-Q1				EA	
00597-0153-37	2020-Q2				EA	
00597-0152-37	2020-Q2				EA	
00597-0152-30	2020-Q2				EA	
00597-0153-90	2020-Q2				EA	
00597-0153-30	2020-Q2				EA	
00597-0152-90	2020-Q2				EA	
00597-0153-37	2020-Q3				EA	
00597-0152-37	2020-Q3				EA	
00597-0152-30	2020-Q3				EA	
00597-0153-90	2020-Q3				EA	
00597-0153-30	2020-Q3				EA	
00597-0152-90	2020-Q3				EA	
00597-0153-37	2020-Q4				EA	
00597-0152-37	2020-Q4				EA	
00597-0152-30	2020-Q4				EA	
00597-0153-90	2020-Q4				EA	
00597-0153-30	2020-Q4				EA	
00597-0152-90	2020-Q4				EA	

G. Market Data and Revenue and Sales Volume Data

U.S. Commercial Average Net Unit Price

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

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
00597-0153-37	2021-Q1				EA	
00597-0152-37	2021-Q1				EA	
00597-0152-30	2021-Q1				EA	
00597-0153-90	2021-Q1				EA	
00597-0153-30	2021-Q1				EA	
00597-0152-90	2021-Q1				EA	
00597-0153-37	2021-Q2				EA	
00597-0152-37	2021-Q2				EA	
00597-0152-30	2021-Q2				EA	
00597-0153-90	2021-Q2				EA	
00597-0153-30	2021-Q2				EA	
00597-0152-90	2021-Q2				EA	
00597-0153-37	2021-Q3				EA	
00597-0152-37	2021-Q3				EA	
00597-0152-30	2021-Q3				EA	
00597-0153-90	2021-Q3				EA	
00597-0153-30	2021-Q3				EA	
00597-0152-90	2021-Q3				EA	
00597-0153-37	2021-Q4				EA	
00597-0152-37	2021-Q4				EA	

G. Market Data and Revenue and Sales Volume Data

U.S. Commercial Average Net Unit Price

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

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
00597-0152-30	2021-Q4				EA	
00597-0153-90	2021-Q4				EA	
00597-0153-30	2021-Q4				EA	
00597-0152-90	2021-Q4				EA	
00597-0153-37	2022-Q1				EA	
00597-0152-37	2022-Q1				EA	
00597-0152-30	2022-Q1				EA	
00597-0153-90	2022-Q1				EA	
00597-0153-30	2022-Q1				EA	
00597-0152-90	2022-Q1				EA	
00597-0153-37	2022-Q2				EA	
00597-0152-37	2022-Q2				EA	
00597-0152-30	2022-Q2				EA	
00597-0153-90	2022-Q2				EA	
00597-0153-30	2022-Q2				EA	
00597-0152-90	2022-Q2				EA	
00597-0153-37	2022-Q3				EA	
00597-0152-37	2022-Q3				EA	
00597-0152-30	2022-Q3				EA	
00597-0153-90	2022-Q3				EA	

G. Market Data and Revenue and Sales Volume Data

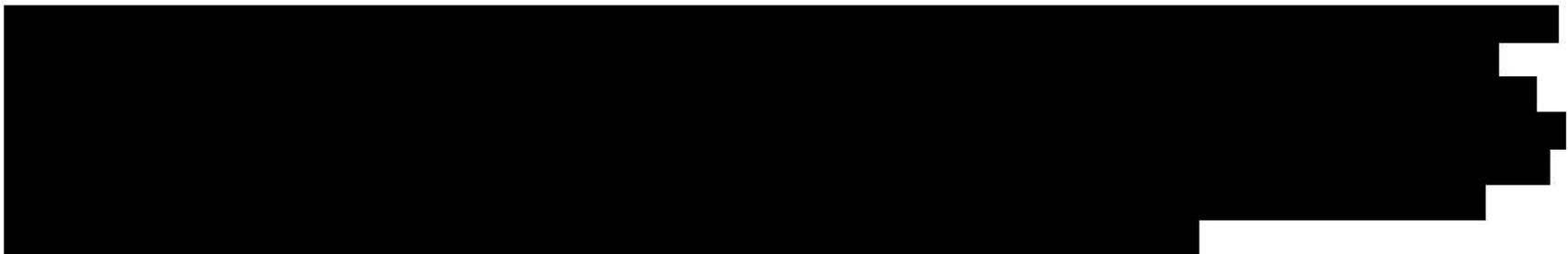
U.S. Commercial Average Net Unit Price

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

National Drug Code (NDC-11)	Quarter	U.S. Commercial Average Unit Net Price	U.S. Commercial Average Net Unit Price - Without Patient Assistance Programs	U.S. Commercial Average Net Unit Price- Best	Unit type (EA, ML, GM)	Total Unit Volume
00597-0153-30	2022-Q3				EA	
00597-0152-90	2022-Q3				EA	
00597-0153-37	2022-Q4				EA	
00597-0152-37	2022-Q4				EA	
00597-0152-30	2022-Q4				EA	
00597-0153-90	2022-Q4				EA	
00597-0153-30	2022-Q4				EA	
00597-0152-90	2022-Q4				EA	

Explanations: "NDC 0597-0152-07, NDC 0597-0152-70, NDC 0597-0153-07, and NDC 0597-0153-70 are samples and not sold commercially. Therefore, there is no data reported for these NDCs.

Assumption: "Most recent 5 years" = January 1, 2018 through December 31, 2022. The data for this 5 year time period was compiled, analyzed and reviewed prior to the September 21, 2023 FAQ release.



[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

This document includes trade secret and confidential commercial information and is exempt from public disclosure under 5 U.S.C. § 552(b)(4)."



Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	EMPAGLIFLOZIN
	Respondent Name	[REDACTED]
	Organization Name (if applicable)	Boehringer Ingelheim Pharm
	Respondent Email	[REDACTED]
	Who is completing this form?	
Question 27: Prescribing Information	Prescribing Information	<p>JARDIANCE® (empagliflozin) Indications Empagliflozin is a sodium-glucose co-transporter 2 (SGLT2) inhibitor (SGLT2i) that is approved by the US Food and Drug Administration (FDA) for the following indications: -To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure; -To reduce the risk of sustained decline in eGFR, end-stage kidney disease, cardiovascular death, and hospitalization in adults with chronic kidney disease at risk of progression; -To reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease; and -As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.</p> <p>Introduction</p> <p>Empagliflozin demonstrates significant efficacy in the treatment of cardiovascular (CV), renal, and metabolic (CRM) conditions and provides a range of benefits that extend beyond its original indication of glycemic control. Studies investigating empagliflozin have evaluated its benefit in populations with a high prevalence of these disorders, especially in people ≥65 years of age. Empagliflozin reduces the risk of CV death, hospitalization for heart failure (HHF), and progression of renal disease, independent of its effects on glycemic control. [REDACTED]</p> <p>[REDACTED]</p> <p>Empagliflozin lowers blood glucose by inhibiting SGLT2 in the kidneys, which is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into circulation. SGLT2 inhibition reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, thereby increasing urinary glucose</p>



Question	Sub-Question	Response
		<p>excretion. Empagliflozin also goes beyond lowering blood glucose to reduce sodium reabsorption and increasing the delivery of sodium to the distal tubule, a mechanism that likely accounts for empagliflozin’s CV and renal benefits. This may influence several physiologic functions, such as lowering both preload and afterload of the heart and downregulating sympathetic activity. In addition, empagliflozin provides renoprotection by lowering intraglomerular hypertension via modulation of pre- and post-glomerular vascular tone.</p> <p>Unmet Need in Cardio-Renal-Metabolic Disease</p> <p>CRM conditions are progressive, overlapping, and exacerbate one another resulting in substantial morbidity, mortality, and increased healthcare costs to Medicare. Among Americans ≥65 years of age, 56% and 22% are estimated to have ≥1 and ≥2 CRM conditions, respectively. CV disease (CVD) is the leading cause of mortality in people with diabetes, accounting for two-thirds of deaths, and a significant driver of healthcare costs. In people >65 years of age, HF is the most common reason for hospitalization and the primary cause of 30-day readmission. Approximately 50% of people die within 5 years of HF diagnosis. The annual direct costs for HF hospitalizations are estimated at \$18 billion. CKD is highly prevalent in the Medicare population, affecting one of every three people ≥65 years of age, and accounts for \$85 billion of Medicare spend (without ESRD), driven primarily by medical costs. People with CKD make up 47% of all hospitalizations and the annual hospital readmission rate is approximately 20%. Empagliflozin is a therapeutic advance for the treatment of CRM conditions, provides substantial clinical benefit to people with these conditions, and adds value to Medicare in achieving its population health and budgetary goals.</p> <p>Clinical Guidelines and Therapeutic Alternatives to Empagliflozin for People with Type 2 Diabetes Mellitus (T2DM)</p> <div data-bbox="632 1073 1961 1219" style="background-color: black; width: 100%; height: 90px; margin: 10px 0;"></div> <p>It is estimated that nearly 80% of beneficiaries with T2DM have ≥1 CRM condition. People with T2DM are at a high risk of developing CV and renal disease, which are the leading causes of death and morbidity in this population. The American Diabetes Association (ADA) 2023 Standards reflect a shift in focus from glycemic control to protecting people with T2DM from cardiorenal risks.</p> <p>The 2023 ADA Standards state that an HbA1c goal of <7.0% is appropriate for most adults; however, less aggressive HbA1c goals (<8.0%) are recommended for older adults to avoid adverse outcomes (hypoglycemia, morbidity from falls, and death) associated with tight glycemic control.</p>



Question	Sub-Question	Response
		<p>The 2023 ADA Standards recommend an SGLT2i or GLP-1RA with proven CV and/or renal benefit for people with T2DM who have established atherosclerotic CVD or indicators of high CV risk, HF, and/or established CKD, as part of the glucose-lowering regimen and comprehensive cardiorenal risk-reduction strategy, independent of HbA1c ('level A' evidence).</p> <p>Empagliflozin is indicated in people with T2DM for glycemic control as well as to reduce the risk of CV death, HHF, and progression of CKD. [REDACTED]</p> <p>[REDACTED] per ADA guidelines [REDACTED].</p> <p>It is important to note that empagliflozin is the only SGLT2i with an FDA indication for glycemic control in children with T2DM ≥ 10 years of age. The GLP-1RAs dulaglutide and liraglutide are also FDA indicated for pediatric patients ≥ 10 years of age.</p> <p>Clinical Guidelines and Therapeutic Alternatives to Empagliflozin for People with T2DM and CVD</p> <p>Among people with T2DM who have established CVD or indicators of high CV risk, the 2023 ADA Standards recommend an SGLT2i and/or GLP-1RA with proven CVD benefit as part of a glucose-lowering regimen and comprehensive CV risk-reduction strategy independent of glycemic control, with consideration of a person's individual characteristics.</p> <p>[REDACTED]</p> <p>Empagliflozin is the only agent FDA approved to reduce the risk of CV death in people with T2DM and CVD. CV death was studied as an outcome for dapagliflozin and canagliflozin, but these agents failed to demonstrate a reduction in the risk of CV death in people with T2DM and CVD.</p> <p>Clinical Guidelines and Therapeutic Alternatives to Empagliflozin for HF With and Without T2DM</p> <p>Based on FDA indications and guideline recommendations, [REDACTED]</p>



Question	Sub-Question	Response
		<p>[REDACTED]</p> <p>HF classification and treatment are based on left ventricular ejection fraction (LVEF). People with LVEF $\geq 50\%$ have HF with preserved ejection fraction (HFpEF), people with LVEF $\leq 40\%$ have HF with reduced ejection fraction (HFrEF), and those with LVEF $>40\%$ and $<50\%$ have midrange ejection fraction. Empagliflozin is FDA-indicated to reduce the risk of CV death and HFrEF in adults with HF, regardless of LVEF and T2DM status.</p> <p>For people with HFrEF, the 2022 American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America (HFSA) Guideline for the Management of Heart Failure recommends initiation of 4 classes of medical therapies for first-line treatment, in no particular order: a renin-angiotensin system (RAS) inhibitor, a beta-blocker, a mineralocorticoid receptor antagonist (MRA), and an SGLT2i. Importantly in patients with symptomatic chronic HFrEF, the guidelines recommend SGLT2is with evidence of benefit to reduce HFrEF and CV mortality, irrespective of the presence of T2DM.</p> <p>For people with HFpEF, the 2022 AHA/ACC/HFSA guidance, along with the 2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction, now recommend initiation of SGLT2is with evidence of benefit in all individuals with HFpEF without contraindications, with the goal of reducing CV death and HFrEF and improving health status. Treatment with diuretics, RAS inhibitors, or MRAs can then be added as required; however, the level of evidence supporting the use of these agents is lower.</p> <p>[REDACTED]</p> <p>Clinical Guidelines and Therapeutic Alternatives to Empagliflozin for CKD With and Without T2DM</p> <p>The 2023 Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease recommends SGLT2is as first-line therapy for most people, including the following CKD populations:</p> <ul style="list-style-type: none"> -Patients with T2DM, CKD, and an estimated glomerular filtration rate (eGFR) ≥ 20 mL/min/1.73 m²; -Adults with CKD and HF or eGFR ≥ 20 mL/min/1.73 m² with urine albumin-to-creatinine ratio (ACR) ≥ 200 mg/g; and -Adults with eGFR ≥ 20 to 45 mL/min/1.73 m² with urine ACR <200 mg/g. <p>The 2023 KDIGO guidelines place high value on the large relative risk reductions for kidney disease progression shown in large, randomized, placebo-controlled trials of SGLT2is. The guidelines place moderate value on the</p>



Question	Sub-Question	Response
		<p>Therapeutic guidelines for T2DM recommend a shift in focus from glycemic control to protecting people with T2DM from the risks of CVD, HF, and CKD, which affect nearly 80% of the Medicare population with T2DM. Empagliflozin is the only agent indicated to reduce the risk of CV death in people with T2DM and CVD. Additionally, empagliflozin is used to treat people with HF and CKD with or without T2DM. The broad range of clinical benefits from the use of a single agent across CV, renal, and metabolic outcomes, and the resulting reduction in costly hospitalizations and slowing of kidney disease progression, highlight the unique value of empagliflozin.</p> <p>In summary, when considering alternatives to empagliflozin for the Medicare population, it is crucial to assess their applicability and functionality. This involves examining labelled uses, guidelines, health outcomes and their costs, clinical trial generalizability, as well as determining the best choice for Medicare recipients. Empagliflozin is a one-product, comprehensive treatment that fills unmet needs across individual CRM conditions, reducing risks of morbidity, mortality, hospitalization, and costs.</p> <p>This document includes trade secret and confidential commercial information and is exempt from public disclosure under 5 U.S.C. § 552(b)(4).</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>Introduction</p> <p>JARDIANCE® (empagliflozin) has demonstrated efficacy, established safety, and documented evidence reducing total cost of care for Medicare beneficiaries with cardiovascular (CV), renal, and metabolic (CRM) conditions. Empagliflozin addresses the unmet need for a single, comprehensive treatment that reduces risks of mortality, morbidity, hospitalization, and costs across the spectrum of CRM conditions on top of historical standard-of-care (SOC).</p> <p>Ongoing investment assessing empagliflozin in CRM conditions has thus far resulted in 4 US Food and Drug Administration (FDA)-approved indications: (1) to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure; (2) to reduce the risk of sustained decline in estimated glomerular filtration rate (eGFR), end-stage kidney disease, cardiovascular death, and hospitalization in adults with chronic kidney disease at risk of progression; (3) to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease; and (4) to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus (Tables 1 and 2) (1).</p> <p>Empagliflozin clinical trial results transformed treatment guidelines and is now recommended first-line to reduce the</p>



Question	Sub-Question	Response
		<p>risk of cardiorenal outcomes in people with CRM conditions. Post-approval comparative studies confirm empagliflozin’s clinical benefits and demonstrate cost savings versus therapeutic alternatives. The efficacy of empagliflozin compared to therapeutic alternatives (based on FDA-approved indications and treatment guidelines) is summarized in Tables 5-7.</p> <p>Type 2 Diabetes Mellitus (T2DM) People with T2DM have high risk of developing CV and renal disease, which are the leading causes of death and morbidity in this population. Nearly 80% of Americans with T2DM ≥65 years of age have ≥1 CRM condition (2). American Diabetes Association (ADA) Standards recommend pharmacotherapy that has CV and/or renal benefit in people with T2DM (3). They also recommend less stringent HbA1c goals (<8.0%) for older adults with coexisting chronic illnesses, cognitive impairment, or functional dependence (3). More intensive HbA1c lowering is associated with adverse outcomes, including increased mortality and greater risk of hypoglycemia, leading to less emphasis on glycemic control and prioritization of reducing cardiorenal complications (4).</p> <p>[REDACTED]</p> <p>Key Outcomes in T2DM Clinical trials evaluating glycemic control use the surrogate endpoint HbA1c to assess efficacy.</p> <p>Efficacy of Empagliflozin Versus Therapeutic Alternatives in T2DM Empagliflozin and Other SGLT2is Empagliflozin demonstrates effective glycemic control across T2DM populations, including patients ≥65 years of age and those with hypertension or renal impairment, and is the only SGLT2i approved for pediatric patients ≥10 years of age (1, 10-12). Pivotal trials of SGLT2i monotherapy in adults with T2DM indicate similar efficacy in reducing HbA1c (Table 3) (1, 6, 7).</p> <p>Empagliflozin and GLP-1RAs Pivotal trials indicate GLP-1RAs generally attain greater HbA1c lowering than SGLT2is (Table 3) (5, 8, 9). However, greater potency of GLP-1RAs may not be relevant for older people with chronic conditions as less stringent HbA1c goals are recommended for this population (3).</p> <p>CV Disease (CVD) in T2DM ADA Standards [REDACTED]</p>



Question	Sub-Question	Response
		<p>[REDACTED]</p> <p>Key Outcomes in Patients with T2DM and CVD All pivotal trials of empagliflozin and therapeutic alternatives utilized 3-point major adverse cardiovascular events (MACE; composite of nonfatal myocardial infarction, nonfatal stroke, or CV death) as the primary outcome, supported by the FDA (1, 5-9, 13).</p> <p>Efficacy of Empagliflozin Versus Therapeutic Alternatives in T2DM and CVD Empagliflozin and Other SGLT2is</p> <p>[REDACTED]</p> <p>Empagliflozin and GLP-1RAs</p> <p>[REDACTED]</p> <p>HF For people with HF with reduced ejection fraction (HFrEF), the 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America Guideline (18) recommends initiation of 4 classes of therapies for first-line treatment: a renin-angiotensin system inhibitor, a beta-blocker, a mineralocorticoid receptor antagonist, and an SGLT2i. This guideline was updated with the 2023 American College of Cardiology Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction, which recommends SGLT2is with</p>



Question	Sub-Question	Response
		<p>evidence of benefit as first-line treatment in people with HF with preserved ejection fraction (HFpEF) (19).</p> <p>[REDACTED]</p> <p>Key Outcomes in HF Endpoints commonly used to evaluate efficacy in HF include CV death, HHF, and renal function; HHF and CV death have the greatest impact on morbidity, mortality, and cost of care (22, 23).</p> <p>Efficacy of Empagliflozin Versus Therapeutic Alternatives in HF</p> <p>[REDACTED]</p>



Question	Sub-Question	Response
		<p>CKD</p> <p>The 2023 Kidney Disease Improving Global Outcomes (KDIGO) guideline recommends SGLT2is with evidence as first-line therapy for most patients with CKD (31).</p> <p>[REDACTED]</p> <p>Key Outcomes in CKD</p> <p>In the pivotal trials of SGLT2is in CKD, decline of eGFR, progression to end-stage disease, hospitalizations, and death are among the key endpoints (32, 33).</p> <p>Efficacy of Empagliflozin Versus Therapeutic Alternatives in CKD</p> <p>Empagliflozin was studied in a broad CKD population, including patients ≥ 65 years of age, and demonstrated risk reduction in kidney disease progression and CV death (Table 7). Empagliflozin was the first SGLT2i to demonstrate a RRR in first and recurrent all-cause hospitalizations in patients with CKD, by 14% versus placebo (11).</p> <p>[REDACTED]</p> <p>[REDACTED] stated in the 2022 Annual report of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), [REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p>



Question	Sub-Question	Response
		<p>Real-World Comparative Effectiveness and Costs Versus Therapeutic Alternatives EMPagliflozin compaRative effectiveness and SafEty (EMPRISE) Program EMPRISE is a large, real-world study program assessing comparative effectiveness, safety, impact on healthcare resource utilization (HCRU) impact, and cost of empagliflozin in routine care. Real-world data were collected from Medicare fee-for-service (FFS) and 2 commercial databases containing Medicare Advantage (Optum Clinformatics and MarketScan) participants from 2014 to 2019. To minimize confounding, sequentially built new users of empagliflozin were 1:1 propensity-score-matched with initiators of the comparator agents (38).</p> <p>[REDACTED]</p> <p>In a pre-specified analysis of only people with T2DM and CVD, empagliflozin was associated with significant reduction of \$2,110 PMPY compared to the GLP-1RA cohort (Table 8, row C). In people with T2DM and CKD, empagliflozin and GLP-1RA cohorts were compared on cardiorenal outcomes. Compared to GLP-1RAs, empagliflozin was associated with reduced risk of HHF by 32% (0.68 [0.55-0.85]) and reduced risk of ESRD by 30% (0.70 [0.56-0.87]) (Table 8, row D) (41). The robust EMPRISE program demonstrates that empagliflozin reduces risk of cardiorenal events, and lowers HCRU and total cost, compared to GLP-1RAs in a diverse T2DM population, including those with and without CVD, those with T2DM and HF, and those with T2DM and advanced CVD.</p> <p>Comparative effectiveness and cost analysis in HF</p> <p>[REDACTED]</p>



Question	Sub-Question	Response
		<div style="background-color: black; width: 100%; height: 80px; margin-bottom: 10px;"></div> <p>Evidence from Outcomes Based Agreements (OBAs) OBAs comparing empagliflozin to other antidiabetics were implemented by several US payers, in which empagliflozin demonstrated up to 20% total cost savings. One published OBA comparing people with T2DM showed cost neutrality; higher pharmacy costs for empagliflozin were offset by lower medical costs (Table 8, row H) (43). Pharmacy costs did not include rebates.</p> <p>Other Comparative Effectiveness and Cost Analysis in T2DM with CVD The effect of empagliflozin on hospitalization among older adults with T2DM was examined using Medicare FFS claims. Empagliflozin was associated with near significant 12% reduced risk of total CV hospitalizations (0.88 [0.77-1.00]) and a nonsignificant 24% reduction in total HHF (0.76 [0.56-1.03]) compared to GLP-1RAs (Table 8, row E) (44). Raju et al. used the IQVIA PharMetrics® Plus Claims Database to compare direct costs and HCRU in cohorts with T2DM and CVD (adjusted for baseline characteristics) receiving empagliflozin versus other branded anti-hyperglycemic agents (AHAs). Compared to the AHA cohort, the empagliflozin cohort was observed to have mean total all-cause per-patient-per-month (PPPM) costs that were \$412 lower (Table 8, row I) (45).</p> <p>Real-world Evidence Summary Real-world evidence demonstrates consistency with empagliflozin clinical trial results and provides important information on empagliflozin’s comparative effectiveness in routine practice and its effect in reducing HCRU and cost. Empagliflozin provides incremental clinical and economic value versus therapeutic alternatives in people ≥65 years of age with T2DM and CRM conditions, which account for most Medicare beneficiaries (2).</p> <p>Safety of Empagliflozin Versus Therapeutic Alternatives Safety profiles for empagliflozin and therapeutic alternatives are presented in Table 9. Although SGLT2is may be associated with moderately increased risk of diabetic ketoacidosis (1, 6, 7, 20), they demonstrate lower rates of hypoglycemia versus GLP-1RAs (1, 5-9, 20), a common side effect of antihyperglycemic agents, particularly in the elderly, that can result in treatment discontinuation and costly complications (46). Based on clinical study findings, SGLT2is have labelled warnings regarding incidences of lower limb amputation, particularly in patients with peripheral artery disease, and diabetic foot infection (including osteomyelitis) (1, 6). Observed incidences vary by agent (Table 5).</p>



Question	Sub-Question	Response
		<p>[REDACTED]</p> <p>Empagliflozin generally demonstrated safety in a wider population than comparators. For example, in people with CKD and moderate renal impairment (eGFR \geq30-60 mL/min/1.73 m²), there was no increase in serious hyperkalemia or acute kidney injury compared with placebo and in those with eGFR down to \geq20 mL/min/1.73 m² (11, 24). In contrast, dapagliflozin is not recommended for use in people with CKD or HF and an eGFR <25 mL/min/1.73 m², or eGFR <45 mL/min/1.73 m² in those with T2DM (7). The ability of empagliflozin to be used in people with lower eGFR is particularly beneficial for older adults as renal function declines with age. All GLP-1RA therapeutic alternatives carry a Boxed Warning for increased risk of thyroid c-cell tumors (5, 8, 9). Additionally, common gastrointestinal side effects associated with GLP-1RAs may negatively impact adherence (48).</p> <p>Summary Empagliflozin addresses critical unmet needs in the Medicare population by reducing risk of death, disease progression, hospitalization, and reducing costs across CRM conditions. Empagliflozin is the only treatment with an FDA indication to reduce the risk of CV death in people with T2DM and CVD. [REDACTED]</p>
	Hyperlink to Citation - Additional Materials for Question 28	[REDACTED]
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28	[REDACTED]
	Evidence Submitted include a cost-effectiveness measure?	N



Question	Sub-Question	Response
	What type of Evidence is shown?	
Question 29: Comparative Effectiveness on Specific Populations	Response to Question 29	<p>Introduction Results of the JARDIANCE® (empagliflozin) clinical trial program, supported by real-world evidence, demonstrate strong clinical and economic value across specific populations impacted by cardiovascular, renal, and metabolic (CRM) conditions. These populations include people ≥65 years of age, minorities experiencing health inequities, and pediatric patients with type 2 diabetes mellitus (T2DM). In people ≥65 years of age, approximately 56% have ≥1 CRM condition, 22% have ≥2, and 5% have 3 CRM conditions (1). Cardiovascular (CV) events are the most common cause of death in people with T2DM and an estimated 70% of people ≥70 years of age have cardiovascular disease (CVD) (2, 3). Heart failure (HF) is the leading cause of hospitalization for people ≥65 years of age (4). HF is often associated with chronic kidney disease (CKD) development (5), the latter of which significantly increases the risk of CV complications and progression to end-stage renal disease (ESRD), leading to further risk of hospitalization (6). Vulnerable populations such as Black/African Americans are at increased risk for hospitalization, ESRD, and death (7). Empagliflozin provides cardiac, renal, and glucose-lowering benefits as a single, once-daily oral medication with established safety profile for these specific populations.</p> <p>People ≥65 Years of Age People ≥65 Years of Age with T2DM Approximately 75% of people with T2DM ≥65 years of age suffer from either CVD, HF, and/or CKD, which increases to 90% for those ≥75 years of age (8). Delaying consequences of the increased risks that come with cardiorenal conditions is an important treatment goal. The American Diabetes Association (ADA) Standards of Care in Diabetes recommend treating people with T2DM and CVD (or high risk of CVD), HF, and/or CKD with agents that have proven CV and/or renal benefit independent of HbA1c. The guidelines also recommend a less stringent HbA1c goal of <8.0% for older adults with multiple coexisting chronic illnesses (3). Although minimizing hyperglycemia is important, stringent glycemic control can be associated with adverse outcomes in elderly people with T2DM (hypoglycemia, morbidity from falls, and death) (9, 10). Greater reductions in morbidity and mortality are likely to result from a clinical focus on comprehensive cardiorenal risk reduction (3, 8).</p> <p>[REDACTED]</p> <p>Empagliflozin reduces HbA1c as well as other SGLT2is (11, 12, 16). GLP-1RAs demonstrate a greater HbA1c lowering effect than the SGLT2is (Table 1) (13-15). However, the level of HbA1c reductions seen with empagliflozin align with</p>



Question	Sub-Question	Response
		<p>ADA guideline recommendations for older patients with CRM conditions (17). Renal impairment is more prevalent in people ≥65 years of age (18). CKD is often underdiagnosed, as approximately 40% of people with severely decreased kidney function are not aware they have CKD (19). In a study evaluating labs (not diagnoses) in people with T2DM ≥65 years of age, the prevalence of CKD was 35% (8). As previously noted, managing cardiorenal outcomes in T2DM is an important treatment goal. Empagliflozin is approved for glycemic control in people with an estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73 m² (Table 1), expanding available treatment options for those ≥65 years of age and providing benefit to those with undiagnosed CKD (16).</p> <p>[REDACTED]</p> <p>The use of empagliflozin versus therapeutic alternatives to treat T2DM has been shown to yield substantial annual cost savings in the Medicare population. In a large, retrospective, comparative, cost analysis using the 100% Medicare fee-for-service (FFS) claims dataset from the EMPRISE study (20), propensity-score-matched cohorts of 63,512 patients with T2DM initiating empagliflozin or GLP-1RAs were assessed. [REDACTED]</p> <p>[REDACTED]</p> <p>Desai, et al. assessed the comparative effectiveness of empagliflozin versus GLP-1RAs in reducing recurrent CV hospitalization in Medicare FFS beneficiaries with T2DM. In this retrospective, claims-based, propensity-score-matched cohort analysis, compared to GLP-1RAs, researchers observed a trend of 12% (HR 0.88 [0.77-1.00]) reduced risk of total CV hospitalizations favoring the empagliflozin cohort (22).</p> <p>People ≥65 Years of Age with CVD and T2DM CV events are the most common cause of death in T2DM, and approximately 50% of people with T2DM have CVD (3, 23). An estimated 70% of people ≥70 years of age will develop CVD, and nearly 70% of older adults with CVD have multiple CRM conditions (2). In people with T2DM and CVD, empagliflozin is the only agent FDA approved to reduce the risk of CV death (16). Empagliflozin is also the only agent to significantly reduce the risk of CV death and the composite of CV death or hospitalization for heart failure (HHF) versus placebo in patients ≥65 years of age with T2DM and established CVD (Table 3). These benefits were more pronounced in those ≥65 years of age (17). Benefits of reduction in the risk of 3-point major adverse cardiovascular events (MACE; composite of CV death, non-fatal myocardial infarction [MI], and non-fatal stroke), HHF, all-cause hospitalization, and all-cause mortality in patients ≥65 years of age were consistent with findings from the overall study population (17). None of the GLP-1RAs demonstrated statistically significant benefit in 3-point MACE in patients ≥60 years of age with T2DM and CVD (24-26). Empagliflozin was shown to add years of life to older patients in an actuarial analysis. The analysis projected a mean</p>



Question	Sub-Question	Response
		<p>survival benefit of an additional 2.5 years, 2 years, and 1 year, in patients 60, 70 and 80 years of age, respectively, with empagliflozin compared with standard of care (SOC) at that time (27).</p> <p>[REDACTED]</p> <p>People ≥65 Years of Age with HF</p> <p>HF is a leading cause of hospitalization for people ≥65 years of age, accounting for more than 80% of HF-related costs (29). Between 2009 and 2019, HHF in Medicare beneficiaries more than doubled, and approximately 20% of patients admitted for HF were readmitted within 30 days (30, 31).</p> <p>Empagliflozin has been shown to reduce the risk of CV death and HHF (composite outcome) in patients ≥65 years of age with HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF; Table 4) (32, 33). In dedicated clinical trials, empagliflozin reduced the risk of the primary composite outcome versus placebo by 22% in patients ≥65 years of age with HFrEF and by 25% in patients ≥70 years of age with HFpEF (32, 33).</p> <p>[REDACTED]</p>



Question	Sub-Question	Response
		<p>[REDACTED]</p> <p>People ≥65 Years of Age with CKD CKD and HF are interconnected, and having 1 of these conditions increases the risk of developing the other. CKD significantly increases the risk of CV complications and the development of ESRD, doubling the risk for hospitalization (6, 18). Total Medicare FFS spending for all beneficiaries (both older and younger than age 66) with CKD was \$85 billion in 2020, representing 23.5% of total Medicare FFS expenditures (18). Empagliflozin demonstrated a reduction in the risk of kidney disease progression or CV death in patients ≥65 years of age, with and without T2DM, and with severely decreased eGFR (Table 5) (36). [REDACTED]</p> <p>[REDACTED]</p> <p>In a subgroup analysis of the EMPA-KIDNEY trial, the significant risk reduction for the composite primary endpoint, first occurrence of progression of kidney disease or CV death, was consistent for patients ≥70 years of age (1300 patients comprising 40% of study population) with the overall trial population (36). [REDACTED]</p> <p>[REDACTED]</p> <p>In the EMPRISE study, the effect of empagliflozin compared to GLP-1RAs on cardiorenal outcomes has been demonstrated in patients with T2DM and advanced CKD. In a propensity-matched subgroup analysis using Medicare, Optum, and Marketscan data, empagliflozin (n=10,930) was associated with a reduced risk of HHF (HR 0.68 [0.55, 0.85]) and a reduced risk of ESRD (HR 0.70 [0.56, 0.87]) versus GLP-1RAs (n=10,930) (39).</p> <p>Safety and Administration in People ≥65 Across Indications The safety profile of empagliflozin in people ≥65 years of age is consistent with its safety profile in the general population (Table 1) (17). In a study of empagliflozin added to SOC in patients with T2DM, the frequency of adverse events was generally similar in adults <65 and ≥65 years of age, except for urinary tract infections, volume depletion, and acute kidney injury, which were more common in those ≥65 years of age (17). Empagliflozin may provide a more tolerable safety profile in older adults compared with GLP-1RAs. [REDACTED]</p> <p>[REDACTED]</p>



Question	Sub-Question	Response
		<p>[REDACTED]</p> <p>When determining treatment options for older adults, potential side effects is a critical consideration (44). Empagliflozin has consistently demonstrated a tolerable safety profile in this population (17).</p> <p>Pediatrics (≥10 to <18 Years of Age) with T2DM There has been an increase in the prevalence and incidence of T2DM in children and adolescents in recent years (45). [REDACTED]</p> <p>[REDACTED]</p> <p>Patients Experiencing Health Disparities Racial and ethnic minorities, especially Black/African Americans, have higher rates of T2DM, CV and kidney disease (7). [REDACTED] These groups are more prone to diabetes diagnosis, hospitalization, mortality, and rapid progression to ESRD (Black/African Americans to White ratio: diabetes diagnosis 1.8; hospitalization 3.8; diabetes death 2.0; ESRD 3.2). A larger percentage of minority populations suffer from CVD and related risk factors, such as hypertension, which is the leading cause of adverse CV outcomes (Table 7) (7). Empagliflozin has been evaluated in a randomized trial specific to hypertensive Black/African American adults with T2DM, and showed significant improvements in HbA1c, blood pressure (BP; 24-hr mean ambulatory systolic BP), and body weight. The reductions in BP were similar to those observed in products with an indication for lowering BP</p>



Question	Sub-Question	Response
		<p>(49). In addition, empagliflozin reduced the risk of CV death or first HFrEF in Black/African American patients with HFrEF (32).</p> <p>[REDACTED]</p> <p>CRM conditions are more likely to coexist and are more prevalent in populations with health disparities, such as Black/African Americans. Empagliflozin provides benefits for multiple CRM conditions with 1 pill compared to medications that treat only 1 condition.</p> <p>Summary</p> <p>CRM conditions are more likely to coexist and are more prevalent in specific populations. Empagliflozin is a therapeutic advance that demonstrates significant benefit across CRM conditions in specific populations:</p> <ul style="list-style-type: none"> • People ≥65 years of age with T2DM and established CVD, empagliflozin is the only agent that has shown significant reduction in the risk of CV death and hospitalization for HF (17); • People ≥65 years of age with HF, empagliflozin reduced the risk of CV death and hospitalization for HF (in HFpEF ≥70) (32, 33); • People ≥65 years of age with CKD, empagliflozin reduced the risk of kidney disease progression and CV death including those with eGFR down to 30 mL/min/1.73 m² (36); • [REDACTED] • Pediatric patients with T2DM (46); and • Black/African Americans, empagliflozin reduces the risk of CV death and hospitalization for HF by 54% (50). <p>This document includes trade secret and confidential commercial information and is exempt from public disclosure under 5 U.S.C. § 552(b)(4).</p>
	<p>Hyperlink to Citation - Additional Materials for Question 29</p>	<p>[REDACTED]</p>



Question	Sub-Question	Response
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29	[REDACTED]
	Evidence Submitted include a cost-effectiveness measure?	N
	What type of Evidence is shown?	
Question 30: Addressing Unmet Medical Needs	Response to Question 30	<p>Cardiovascular (CV), renal, and metabolic (CRM) conditions are progressive, overlap, and exacerbate one another, resulting in substantial morbidity, mortality, and increased healthcare costs (1-3). Among people ≥65 years of age, 14 million (26%) have type 2 diabetes mellitus (T2DM), 13 million (24%) have cardiovascular disease (CVD; including heart failure [HF]), and 17 million (33%) have chronic kidney disease (CKD; Figure 1) (2). Moreover, 56% have ≥1 CRM condition, 22% have ≥2, and 5% have 3 CRM conditions (2). Clinical unmet needs across CRM conditions include reducing the risks of death, hospitalization, and disease progression.</p> <p>JARDIANCE® (empagliflozin) addresses unmet needs, as a single treatment, by reducing the residual risks of mortality, hospitalization, and disease progression following the use of previous standard-of-care (SOC) treatments. Empagliflozin clinical trial results have transformed treatment guidelines and is recommended as first-line treatment in people with CRM conditions (4-7).</p> <p>Proven Benefits in T2DM and T2DM with CVD The primary treatment goals for people with T2DM are to lower blood glucose and reduce the risk of cardiorenal events. Accordingly, American Diabetes Association (ADA) Standards recommend the use of agents with proven cardiorenal benefit in people with T2DM and cardiorenal conditions (4).</p> <p>CVD is the leading cause of mortality, accounting for 80% of deaths, in people with diabetes, and is a significant driver of healthcare costs (4, 8, 9). Empagliflozin is a therapeutic advancement as it is the only agent with an FDA indication to reduce the risk of CV death in people with T2DM and established CVD (10). [REDACTED]</p>



Question	Sub-Question	Response
		<p>[REDACTED]</p> <p>In a large, real-world, comparative effectiveness analysis of matched Medicare cohorts with T2DM, empagliflozin reduced the risk of HFrEF compared to a glucagon-like peptide-1 receptor agonist (GLP-1RA) (16).</p> <p>[REDACTED]</p> <p>Reducing Death and Costly Hospitalization in HF HF is the leading cause for hospitalization and 30-day readmission in people ≥65 years of age, and hospitalizations account for most healthcare expenditures in HF (19-22). The American Heart Association, American College of Cardiology, and Heart Failure Society of America (AHA/ACC/HFSA) guidelines recommend sodium-glucose co-transporter 2 inhibitors (SGLT2is) with proven benefit as first-line treatments for HF with reduced ejection fraction (HFrEF; ejection fraction ≤40%) (5). ACC 2023 guidelines recommend SGLT2is as first-line treatment for HF with preserved ejection fraction (HFpEF; ejection fraction ≥50%) (6).</p> <p>Empagliflozin received Breakthrough Therapy status by the FDA for HF (23). In pivotal trials, empagliflozin reduced the combined risk of CV death or HFrEF versus placebo by 25% in patients with HFrEF and by 21% in patients with HFpEF (24, 25). Empagliflozin also significantly reduced the risk of first and recurrent hospitalizations by 30% and 27%, respectively, and slowed the rate of estimated glomerular filtration rate (eGFR) decline (24, 25).</p> <p>[REDACTED]</p> <p>Reducing Death, Disease Progression, and Hospitalizations in CKD CKD is highly prevalent in the Medicare population, affecting 1 in 3 people ≥65 years of age, and is a major driver of healthcare costs (30, 31). Medicare spend for CKD (without end-stage renal disease [ESRD]) was \$85 billion in 2020 (31). CKD healthcare costs are driven mainly by medical, not prescription drug, costs (Figures 2 and 3) (3, 31). The CKD hospitalization rate is high, 47%, with an annual readmission rate of ~20% (31).</p>



Question	Sub-Question	Response
		<p>The FDA granted empagliflozin Fast Track designation for CKD (32), and the Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend empagliflozin as first-line therapy, along with other SGLT2is with proven renal benefit (7).</p> <p>Empagliflozin demonstrated a 28% reduced risk of kidney disease progression or death from CV causes on top of SOC and without major safety concerns (33). This benefit was independent of diabetes status and glycemic control. The risk of hospitalization for any cause was 14% lower with empagliflozin versus placebo (33). Empagliflozin addresses critical unmet needs in the CKD population by reducing the risk of death, disease progression, and hospitalization.</p> <p>Empagliflozin was studied in patients with/without T2DM, with/without albuminuria, with an eGFR down to ≥ 20 mL/min/1.73 m², and in a range of CKD etiologies, including glomerular disease (33). [REDACTED]</p> <p>[REDACTED]</p> <p>Comparative Effectiveness and Costs Versus Therapeutic Alternatives Empagliflozin’s benefits from clinical trials are consistent with observations in large, real-world comparative effectiveness and cost studies. Empagliflozin has an extensive and robust real-world evidence program. The EMPagliflozin compaRative effectiveness and SafEty (EMPRISE) program has been assessing the comparative effectiveness, safety, healthcare utilization, and cost of empagliflozin over 5 years in people with T2DM in routine care using matched Medicare cohorts (37). [REDACTED]</p> <p>[REDACTED]</p> <p>Conclusion Empagliflozin helps to address CMS’ goals of improving outcomes, lowering total cost of care, and addressing unmet needs as a single comprehensive treatment for CRM conditions, which affect a large percentage of the Medicare population.</p>
	<p>Hyperlink to Citation - Additional Materials for Question 30</p>	<p>[REDACTED]</p>



Question	Sub-Question	Response
	Hyperlink to Table/Charts/Graphs - Additional Materials for Question 30	[REDACTED]
	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		[REDACTED]
	Response to Question 32	[REDACTED]



Question	Sub-Question	Response
		[REDACTED]
[REDACTED]		
[REDACTED]		



Question	Sub-Question	Response
		[Redacted]

Question 28: Therapeutic Impact and Comparative Effectiveness

Introduction

JARDIANCE® (empagliflozin) has demonstrated efficacy, established safety, and documented evidence reducing total cost of care for Medicare beneficiaries with cardiovascular (CV), renal, and metabolic (CRM) conditions. Empagliflozin addresses the unmet need for a single, comprehensive treatment that reduces risks of mortality, morbidity, hospitalization, and costs across the spectrum of CRM conditions on top of historical standard-of-care (SOC).

Ongoing investment assessing empagliflozin in CRM conditions has thus far resulted in 4 US Food and Drug Administration (FDA)-approved indications: (1) to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure; (2) to reduce the risk of sustained decline in estimated glomerular filtration rate (eGFR), end-stage kidney disease, cardiovascular death, and hospitalization in adults with chronic kidney disease at risk of progression; (3) to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease; and (4) to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus (**Tables 1 and 2**) (1).

Empagliflozin clinical trial results transformed treatment guidelines and is now recommended first-line to reduce the risk of cardiorenal outcomes in people with CRM conditions. Post-approval comparative studies confirm empagliflozin's clinical benefits and demonstrate cost savings versus therapeutic alternatives.

The efficacy of empagliflozin compared to therapeutic alternatives (based on FDA-approved indications and treatment guidelines) is summarized in **Tables 5-7**.

Type 2 Diabetes Mellitus (T2DM)

People with T2DM have high risk of developing CV and renal disease, which are the leading causes of death and morbidity in this population. Nearly 80% of Americans with T2DM ≥65 years of age have ≥1 CRM condition (2). American Diabetes Association (ADA) *Standards* recommend pharmacotherapy that has CV and/or renal benefit in people with T2DM (3). They also recommend less stringent HbA1c goals (<8.0%) for older adults with coexisting chronic illnesses, cognitive impairment, or functional dependence (3). More intensive HbA1c lowering is associated with adverse outcomes, including increased mortality and greater risk of hypoglycemia, leading to less emphasis on glycemic control and prioritization of reducing cardiorenal complications (4).



[REDACTED]

Key Outcomes in T2DM

Clinical trials evaluating glycemic control use the surrogate endpoint HbA1c to assess efficacy.

Efficacy of Empagliflozin Versus Therapeutic Alternatives in T2DM

Empagliflozin and Other SGLT2is

Empagliflozin demonstrates effective glycemic control across T2DM populations, including patients ≥ 65 years of age and those with hypertension or renal impairment, and is the only SGLT2i approved for pediatric patients ≥ 10 years of age (1, 10-12). Pivotal trials of SGLT2i monotherapy in adults with T2DM indicate similar efficacy in reducing HbA1c (**Table 3**) (1, 6, 7).

Empagliflozin and GLP-1RAs

Pivotal trials indicate GLP-1RAs generally attain greater HbA1c lowering than SGLT2is (**Table 3**) (5, 8, 9). However, greater potency of GLP-1RAs may not be relevant for older people with chronic conditions as less stringent HbA1c goals are recommended for this population (3).

CV Disease (CVD) in T2DM

ADA Standards

[REDACTED]

Key Outcomes in Patients with T2DM and CVD

All pivotal trials of empagliflozin and therapeutic alternatives utilized 3-point major adverse cardiovascular events (MACE; composite of nonfatal myocardial infarction, nonfatal stroke, or CV death) as the primary outcome, supported by the FDA (1, 5-9, 13).

Efficacy of Empagliflozin Versus Therapeutic Alternatives in T2DM and CVD

[REDACTED]



[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Empagliflozin and GLP-1RAs

[REDACTED]

HF

For people with HF with reduced ejection fraction (HFrEF), the 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America Guideline (18) recommends initiation of 4 classes of therapies for first-line treatment: a renin-angiotensin system inhibitor, a beta-blocker, a mineralocorticoid receptor antagonist, and an SGLT2i. This guideline was updated with the 2023 American College of Cardiology Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction, which recommends SGLT2is with evidence of benefit as first-line treatment in people with HF with preserved ejection fraction (HFpEF) (19).

[REDACTED]



CKD

The 2023 Kidney Disease Improving Global Outcomes (KDIGO) guideline recommends SGLT2is with evidence as first-line therapy for most patients with CKD (31).

[REDACTED]

Key Outcomes in CKD

In the pivotal trials of SGLT2is in CKD, decline of eGFR, progression to end-stage disease, hospitalizations, and death are among the key endpoints (32, 33).

Efficacy of Empagliflozin Versus Therapeutic Alternatives in CKD

Empagliflozin was studied in a broad CKD population, including patients ≥ 65 years of age, and demonstrated risk reduction in kidney disease progression and CV death (**Table 7**).

Empagliflozin was the first SGLT2i to demonstrate a RRR in first and recurrent all-cause hospitalizations in patients with CKD, by 14% versus placebo (11).

[REDACTED]

[REDACTED] stated in the 2022 Annual report of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), [REDACTED]

[REDACTED]

[REDACTED]



[REDACTED]

Real-World Comparative Effectiveness and Costs Versus Therapeutic Alternatives

EMPagliflozin compaRative effectIveness and SafEty (EMPRISE) Program

EMPRISE is a large, real-world study program assessing comparative effectiveness, safety, impact on healthcare resource utilization (HCRU) impact, and cost of empagliflozin in routine care. Real-world data were collected from Medicare fee-for-service (FFS) and 2 commercial databases containing Medicare Advantage (Optum Clinformatics and MarketScan) participants from 2014 to 2019. To minimize confounding, sequentially built new users of empagliflozin were 1:1 propensity-score-matched with initiators of the comparator agents (38).

[REDACTED]

[REDACTED]

[REDACTED] In a pre-specified analysis of only people with T2DM and CVD, empagliflozin was associated with significant reduction of \$2,110 PMPY compared to the GLP-1RA cohort (**Table 8, row C**).

In people with T2DM and CKD, empagliflozin and GLP-1RA cohorts were compared on cardiorenal outcomes. Compared to GLP-1RAs, empagliflozin was associated with reduced risk of HHF by 32% (0.68 [0.55-0.85]) and reduced risk of ESRD by 30% (0.70 [0.56-0.87]) (**Table 8, row D**) (41).

The robust EMPRISE program demonstrates that empagliflozin reduces risk of cardiorenal events, and lowers HCRU and total cost, compared to GLP-1RAs in a diverse T2DM population, including those with and without CVD, those with T2DM and HF, and those with T2DM and advanced CVD.

Comparative effectiveness and cost analysis in HF

[REDACTED]



[REDACTED]

Evidence from Outcomes Based Agreements (OBAs)

OBAs comparing empagliflozin to other antidiabetics were implemented by several US payers, in which empagliflozin demonstrated up to 20% total cost savings. One published OBA comparing people with T2DM showed cost neutrality; higher pharmacy costs for empagliflozin were offset by lower medical costs (**Table 8, row H**) (43). Pharmacy costs did not include rebates.

Other Comparative Effectiveness and Cost Analysis in T2DM with CVD

The effect of empagliflozin on hospitalization among older adults with T2DM was examined using Medicare FFS claims. Empagliflozin was associated with near significant 12% reduced risk of total CV hospitalizations (0.88 [0.77-1.00]) and a nonsignificant 24% reduction in total HHF (0.76 [0.56-1.03]) compared to GLP-1RAs (**Table 8, row E**) (44).

Raju et al. used the IQVIA PharMetrics® Plus Claims Database to compare direct costs and HCRU in cohorts with T2DM and CVD (adjusted for baseline characteristics) receiving empagliflozin versus other branded anti-hyperglycemic agents (AHAs). Compared to the AHA cohort, the empagliflozin cohort was observed to have mean total all-cause per-patient-per-month (PPPM) costs that were \$412 lower (**Table 8, row I**) (45).

Real-world Evidence Summary

Real-world evidence demonstrates consistency with empagliflozin clinical trial results and provides important information on empagliflozin's comparative effectiveness in routine practice and its effect in reducing HCRU and cost. Empagliflozin provides incremental clinical and economic value versus therapeutic alternatives in people ≥65 years of age with T2DM and CRM conditions, which account for most Medicare beneficiaries (2).

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Safety of Empagliflozin Versus Therapeutic Alternatives

Safety profiles for empagliflozin and therapeutic alternatives are presented in **Table 9**.

Although SGLT2is may be associated with moderately increased risk of diabetic ketoacidosis (1, 6, 7, 20), they demonstrate lower rates of hypoglycemia versus GLP-1RAs (1, 5-9, 20), a common side effect of antihyperglycemic agents, particularly in the elderly, that can result in treatment discontinuation and costly complications (46).

Based on clinical study findings, SGLT2is have labelled warnings regarding incidences of lower limb amputation, particularly in patients with peripheral artery disease, and diabetic foot infection (including osteomyelitis) (1, 6). Observed incidences vary by agent (**Table 5**).

[REDACTED]

Empagliflozin generally demonstrated safety in a wider population than comparators. For example, in people with CKD and moderate renal impairment (eGFR ≥ 30 -60 mL/min/1.73 m²), there was no increase in serious hyperkalemia or acute kidney injury compared with placebo and in those with eGFR down to ≥ 20 mL/min/1.73 m² (11, 24). In contrast, dapagliflozin is not recommended for use in people with CKD or HF and an eGFR < 25 mL/min/1.73 m², or eGFR < 45 mL/min/1.73 m² in those with T2DM (7). The ability of empagliflozin to be used in people with lower eGFR is particularly beneficial for older adults as renal function declines with age.

All GLP-1RA therapeutic alternatives carry a Boxed Warning for increased risk of thyroid c-cell tumors (5, 8, 9). Additionally, common gastrointestinal side effects associated with GLP-1RAs may negatively impact adherence (48).

Summary

Empagliflozin addresses critical unmet needs in the Medicare population by reducing risk of death, disease progression, hospitalization, and reducing costs across CRM conditions. Empagliflozin is the only treatment with an FDA indication to reduce the risk of CV death in people with T2DM and CVD. [REDACTED]

[REDACTED]

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[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

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Table 1. Indications and WAC for Empagliflozin and Therapeutic Alternatives

Brand Name	Generic Name	Therapeutic Class	Disease	Indication(s)	WAC: Cost/30 days ^{a,1}
SGLT2is					
JARDIANCE ^{®2}	Empagliflozin	SGLT2i	HF	To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure	\$593.30
			CKD	To reduce the risk of sustained decline in eGFR, end-stage kidney disease, cardiovascular death, and hospitalization in adults with chronic kidney disease at risk of progression	
			T2DM + CVD	To reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease	
			T2DM	As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus	

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GLP-1RAs

CKD, chronic kidney disease; CVD, cardiovascular disease; GLP-1RAs, glucagon-like peptide-1 receptor agonists; HF, heart failure; SGLT2i, sodium-glucose cotransporter-2 inhibitor; WAC, wholesale acquisition cost.

^aWACs are current as of September 26, 2023.

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■ [REDACTED]

■ [REDACTED]



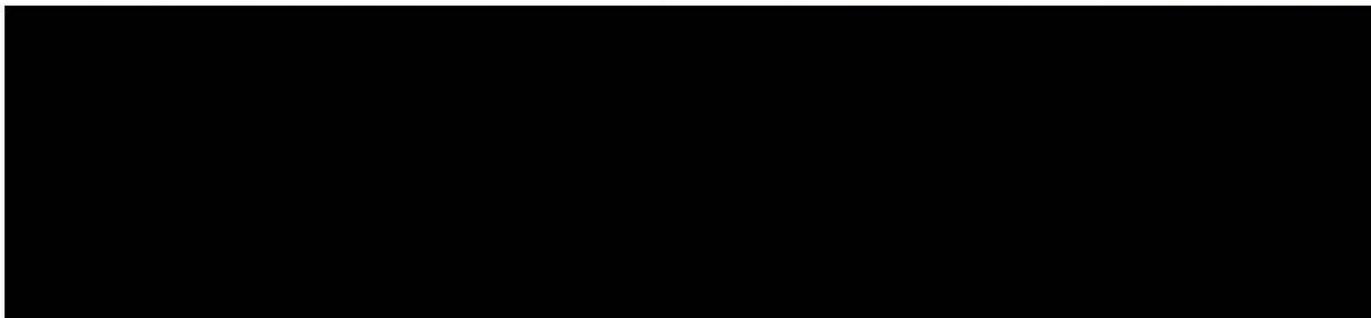
Table 2. Indications for Empagliflozin and Therapeutic Alternatives

Indications	SGLT2is		GLP-1RAs
	Empagliflozin ¹		
T2DM	✓		
T2DM + CVD	✓		
HF	✓		
CKD	✓		

CKD, chronic kidney disease; CVD, cardiovascular disease; GLP-1RAs, glucagon-like peptide-1 receptor agonists; HF, heart failure; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

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1. JARDIANCE® (empagliflozin tablets), for oral use [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2023.



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Table 3. Key Baseline/Outcomes Data in T2DM for Empagliflozin and Therapeutic Alternatives^a

Product (trial) ^b	Population	Age, mean (SD)	Baseline HbA1c	Primary outcome	Safety outcomes of interest
Empagliflozin ¹ (EMPA-REG MONO) N = 986	Adults with T2DM and inadequate glycemic control (HbA1c 7.0-10%)	55 (11)	7.9	CIB in HbA1c: -0.78% Difference from placebo -0.9% (p <0.0001) 44% of patients achieving HbA1c <7%	Higher incidence of genital infections vs placebo No difference in incidence of hypoglycemia and UTI vs placebo
SGLT2i Alternatives					
GLP-1RA Alternatives					

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Product (trial) ^b	Population	Age, mean (SD)	Baseline HbA1c	Primary outcome	Safety outcomes of interest
[REDACTED]					

AEs, adverse events; AHA, antihyperglycemic agent; CIB, change in baseline; GI, genital infection; GLP-1RAs, glucagon-like peptide-1 receptor agonists; T2DM, type 2 diabetes mellitus; UTI, urinary tract infection, hx, history; pts, patients; MEN, multiple endocrine neoplasia; MTC, medullary thyroid carcinoma.

^aData reported for highest dose studied.

[REDACTED]

Note that indirect treatment comparisons should be interpreted with caution due to differences in study design and populations.

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Table 4. American Diabetes Association Standards of Care in Diabetes—2023¹

Overall goal	Cardiorenal risk reduction in high-risk patients with T2DM (in addition to comprehensive CV risk management)
Overall treatment recommendation	In patients with HF, CKD, established CVD, or multiple risk factors for CVD, SGLT2i or GLP-1RA with proven benefit should be used independent of HbA1c
Comorbidity	Treatment recommendation
CVD or indicators of high risk	SGLT2i or GLP-1RAs with proven CVD benefit
HF	SGLT2i with proven HF benefit
CKD	SGLT2i with primary evidence of reducing CKD progression

CKD, chronic kidney disease; CVD, cardiovascular disease; GLP-1RAs, glucagon-like peptide-1 receptor agonists; HF, heart failure; SGLT2i, sodium-glucose cotransporter-2 inhibitor; T2DM, type 2 diabetes mellitus.

References:

1. American Diabetes Association. Standards of Care in Diabetes—2023. *Diabetes Care*. 2023;46(suppl 1):S1-S291.

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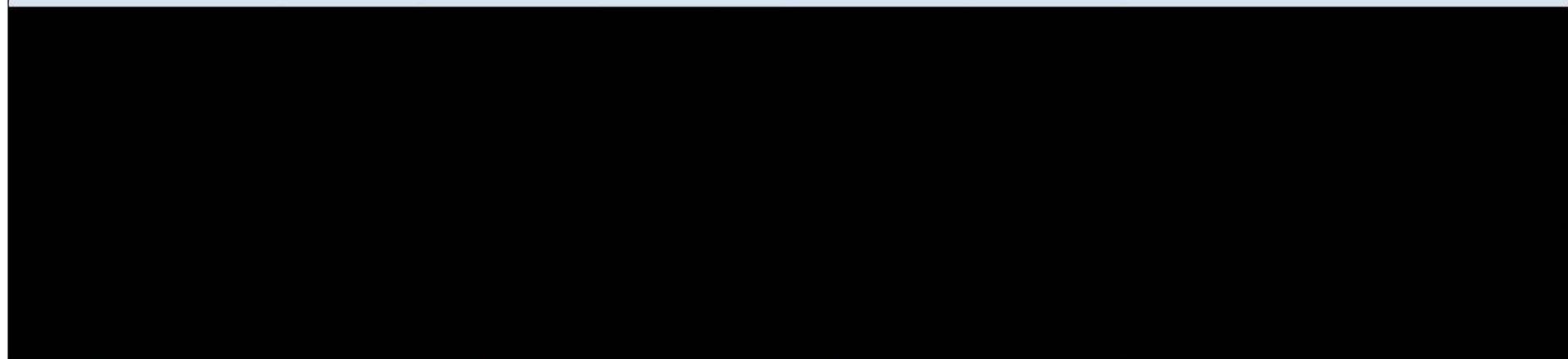
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Table 5. Key Baseline/Outcomes Data in T2DM with CVD for Empagliflozin and Therapeutic Alternatives^a

Product (trial) ^b	Mean (SD) age, years	3P-MACE definition	3P-MACE outcome ^c	CV death outcome ^c	HHF outcome ^c	Safety (serious AEs)
Empagliflozin ¹ (EMPA-REG OUTCOME) N = 7020	63.1 (8.6)	CV death, nonfatal MI, or nonfatal stroke	HR 0.86 (0.74, 0.99) p = 0.04	HR 0.62 (0.49, 0.77) p <0.001	HR 0.65 (0.50, 0.85) p = 0.002	39.0% empagliflozin vs 42.3% placebo
						Amputation: empagliflozin 1.9%; placebo 1.8% ² Bone fracture: empagliflozin 3.8%; placebo 3.9%
SGLT2i Alternatives						
Dapagliflozin ³ (DECLARE-TIMI 58) N = 17,160	63.9 (6.8)	CV death, MI, or ischemic stroke	HR 0.93 (0.84, 1.03) p = 0.17	HR 0.98 (0.82, 1.17) p-value NR	HR 0.73 (0.61, 0.88) p-value NR	34.1% dapagliflozin vs 36.2% placebo
						Amputation: dapagliflozin: 1.4%; placebo: 1.3% Bone fracture: dapagliflozin: 5.3%; placebo: 5.1%
Canagliflozin ⁴ (CANVAS Program) N = 10,142	63.2 (8.3)	CV death, nonfatal MI or nonfatal stroke	HR 0.86 (0.75, 0.97) p = 0.02	HR 0.87 (0.72, 1.06) p-value NR	HR 0.67 (0.52, 0.87) p-value NR	104.3 canagliflozin vs 120.0 placebo events/1000 PY (p = 0.04)
						Amputation: events per 1000 PY: canagliflozin: 6.3; placebo: 3.4 (p <0.001) Bone fracture: event rate per 1000 PY: canagliflozin: 15.4; placebo: 11.9 (p = 0.02)
GLP-1RA Alternatives						



³P-MACE, 3-point major cardiovascular event; AEs, adverse events; CV, cardiovascular; GLP-1RAs, glucagon-like peptide-1 receptor agonists; HHF, hospitalization for heart failure; HR, hazard ratio; NR, not reported; PY, patient-years; SGLT2i, sodium-glucose cotransporter-2 inhibitor; T2DM, type 2 diabetes mellitus.

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^aData are reported for active treatment arm where available.

^bPlacebo comparator for all trials.

^cHazard ratios are shown with 95% confidence intervals.

Note that indirect treatment comparisons should be interpreted with caution due to differences in study design and populations.

References:

1. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*. 2015;373(22):2117-28. Epub 2015/09/17. doi: 10.1056/NEJMoa1504720. PubMed PMID: 26378978.
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Table 6. Key Baseline/Outcomes Data in HF for Empagliflozin and Therapeutic Alternatives^a

	Product (trial)	Mean (SD) age, years	T2DM status	Mean (SD) baseline eGFR, mL/min/1.73 m ²	Composite CV death and HHF ^b	Total HHF ^b	eGFR decline ^c	Safety	PROs
HF _r EF	Empagliflozin ¹ (EMPEROR-Reduced) N = 3730	67.2 (10.8)	With and without T2DM	61.8 (21.7)	HR 0.75 (0.65, 0.86) p <0.001	HR 0.70 (0.58, 0.85) p <0.001	Absolute difference in eGFR 1.73 (1.10, 2.37) p <0.001	Similar AE rates between empagliflozin vs placebo (76.2% vs 78.5%)	Change in QoL score on KCCQ at 52 wks: HR 1.7 (0.5, 3.0) p-value NR
	Dapagliflozin ² (DAPA-HF) N = 4744	66.2 (11.0)	With and without T2DM	66.0 (19.6)	HR 0.74 (0.65, 0.85) p <0.001	HR 0.70 (0.59, 0.83) p-value NR	HR 0.71 (0.44, 1.16) p-value NR	Similar SAE rates between dapagliflozin vs placebo (35.7% vs 40.2%) 4.7% vs 4.9% of patients discontinued due to AEs	Change in KCCQ TSS at 8 mo: HR 1.18 (1.11, 1.26) p <0.001
	Sotagliflozin ³ (SOLOIST-WHF) Overall: N = 1222 LVEF <40%: N = 725	Median (IQR) 69 (63-76)	With T2DM only	Median (IQR) 49.2 (39.5-61.2)	LVEF <40%: HR 0.69 (0.51, 0.92) p-value NR	0.64 (0.49, 0.83) P <0.001	-0.16 (-1.30, 0.98)	Similar serious TEAE rates between sotagliflozin vs placebo (38.8% vs 41.1%); 4.8% vs 3.8% of patients discontinued due to TEAEs	Change in KCCQ-12 score at 4 mo: absolute difference 4.1 (1.3, 7.0)
LVEF 40 to <50%: N = 230	LVEF 40 to <50%: HR 0.74 (0.40, 1.39) p-value NR								
HF _p EF	Empagliflozin ⁴ (EMPEROR-Preserved) N = 5988	71.8 (9.3)	With and without T2DM	60.6 (19.8)	HR 0.79 (0.69, 0.90) p <0.001	HR 0.73 ^d (0.61, 0.88) p <0.001	Absolute difference in eGFR 1.36 (1.06, 1.66) p <0.001	Similar SAE rates between empagliflozin vs placebo (47.9% vs 51.6%); 19.1% vs 18.4% of patients discontinued due to AEs	Significant improvements (adj. mean diff) vs placebo across KCCQ domains at Wk 52: ⁵ CSS 1.50; TSS 2.07; OSS 1.60 (all p <0.01)

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AE, adverse event; CSS clinical summary score; CV, cardiovascular; ED, emergency department; eGFR, estimated glomerular filtration rate; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; HR, hazard ratio; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; NR, not reported; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; NYHA, New York Heart Association; OSS, overall summary score; PRO, patient-reported outcome; RAAS, renin-angiotensin-aldosterone system; SAE, serious adverse event; SD, standard deviation; TEAE, treatment-emergent adverse event; T2DM, type 2 diabetes mellitus; TSS, total symptom score; WR, win ratio.

^aData are reported for active treatment arm where available.

^bHazard ratios are shown with 95% confidence intervals.

^cThe eGFR (Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula) slope is analyzed on the basis of on-treatment data, using a random intercept–random slope model including age, baseline eGFR, and baseline left ventricular ejection fraction as linear covariates and sex, geographic region, baseline diabetes status, and baseline-by-time and treatment-by-time interactions as fixed effects; the model allows for randomly varying slope and intercept between patients.

^dTotal number of HHF.

^eThe primary outcome was a composite of worsening heart failure (which was defined as either an unplanned hospitalization for heart failure or an urgent visit for heart failure).

Note that indirect treatment comparisons should be interpreted with caution due to differences in study design and populations.

References:

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Table 7. Key Baseline/Outcomes Data in CKD for Empagliflozin and Therapeutic Alternatives^a

		Empagliflozin¹ (EMPA-KIDNEY) N = 6609
Comorbidities, %	TD2M	46.2
	CVD	26.1
	HF	9.9
	PAD	7.1
TD2M status		With and without T2DM
Primary cause of CKD, %	Diabetic	31.2
	Glomerular	25.8
	HTN/renovascular	21.4
	Other/unknown	21.6
Mean (SD) baseline eGFR, mL/min/1.73 m²		37.4 (14.5)
eGFR categories, %	G1 eGFR ≥90	NA ^c
	G2 eGFR ≥60–<90	21.4
	G3a eGFR ≥45–<60	
	G3b eGFR ≥30–<45	44.4
	G4 eGFR ≥15–<30	34.2 ^d
	G5 eGFR <15	
Median UACR, mg/g		331
KDIGO risk category	Moderate	25.4 ^e
	High	
	Very high	74.6
Primary outcome^f <ul style="list-style-type: none"> • HR vs placebo (95% CI) • Incidence 		<ul style="list-style-type: none"> • 0.72 (0.64, 0.82) • 6.85 per 100 PY (empagliflozin) vs 8.96 per 100 PY (placebo)

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HHF or CV death		<ul style="list-style-type: none"> • 0.84 (0.67, 1.07) • 2.04 per 100 PY (empagliflozin) vs 2.37 per 100 PY (placebo)
<ul style="list-style-type: none"> • HR vs placebo (95% CI) • Incidence 		
CV death		
<ul style="list-style-type: none"> • HR vs placebo (95% CI) • Incidence 		<ul style="list-style-type: none"> • 0.84 (0.60, 1.19) • 0.91 per 100 PY (empagliflozin) vs 1.06 per 100 PY (placebo)
All-cause hospitalization		0.86 (0.78, 0.95)
HR vs placebo (95% CI)		
Adverse events, treatment vs placebo, %	Any AE	NR
	Any SAE	35.2 vs 37.7
	Drug-related AEs	NR
	Amputation	0.8 vs 0.6
	Hyperkalemia	2.8 vs 3.3 ^g
	AKI	3.2 vs 4.1 ^g

AE, adverse event; AKI, acute kidney injury; CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; ESRD, end-stage renal disease; HF, heart failure; HR, hazard ratio; HTN, hypertension; NA, not available; NR, not reported; PAD, peripheral artery disease; PY, patient-year; SAE, serious adverse event; T2DM, type 2 diabetes mellitus; UACR, urine albumin to creatinine ratio.

^aData are reported for active treatment arm where available.

^bCauses of CKD for this study were reported as “other/unknown” for 5.0% of patients and tubulointerstitial for 1.2% of patients. The value reported here includes the 4.6% for whom no reason was given.

^cInclusion criteria for eGFR was 25 to 75 mL/min/1.73 m² for DAPA-CKD and 20 to <90 mL/min/1.73 m² for EMPA-KIDNEY.

^dReported for patients with eGFR <30 mL/min/1.73 m².

^eKDIGO risk category was reported as combined low, moderate, or high.

^fDefinition of primary outcome (composite CV and renal outcome) for EMPA-KIDNEY: ESKD, a sustained decline in eGFR to <10 mL/min/1.73 m² or a ≥40% eGFR decline from randomization, or death from renal or CV causes; primary outcome for DAPA-CKD: ESRD, decline of ≥50% in eGFR, or death from renal or CV causes; primary outcome for CREDENCE: ESKD, doubling of serum creatinine level, or death from renal or CV causes.

^gSerious adverse event.

Note that indirect treatment comparisons should be interpreted with caution due to differences in study design and populations.

References:

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2. Heerspink HJL, Stefansson BV, Correa-Rotter R, Chertow GM, Greene T, Hou FF, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med.* 2020;383(15):1436-46. Epub 2020/09/25. doi: 10.1056/NEJMoa2024816. PubMed PMID: 32970396.
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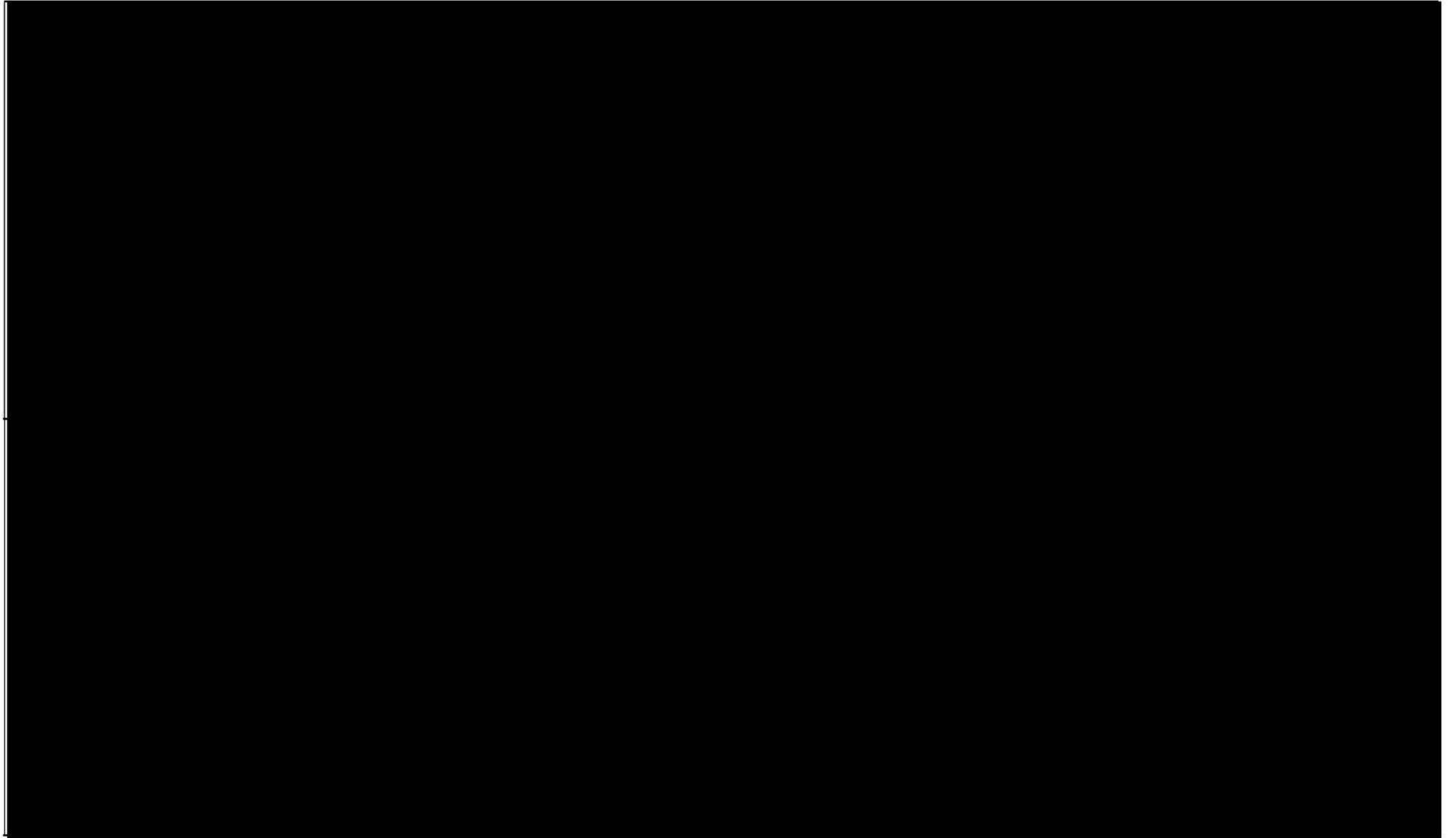
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Table 8. Summary of Real-world Comparative Effectiveness and Cost Analysis for Empagliflozin and Therapeutic Alternatives

Study	CRM populations(s)	Therapeutic alternative to empagliflozin	Study outcomes	Sample size and data source	Results
EMPRISE program ^a					
[Redacted content]					

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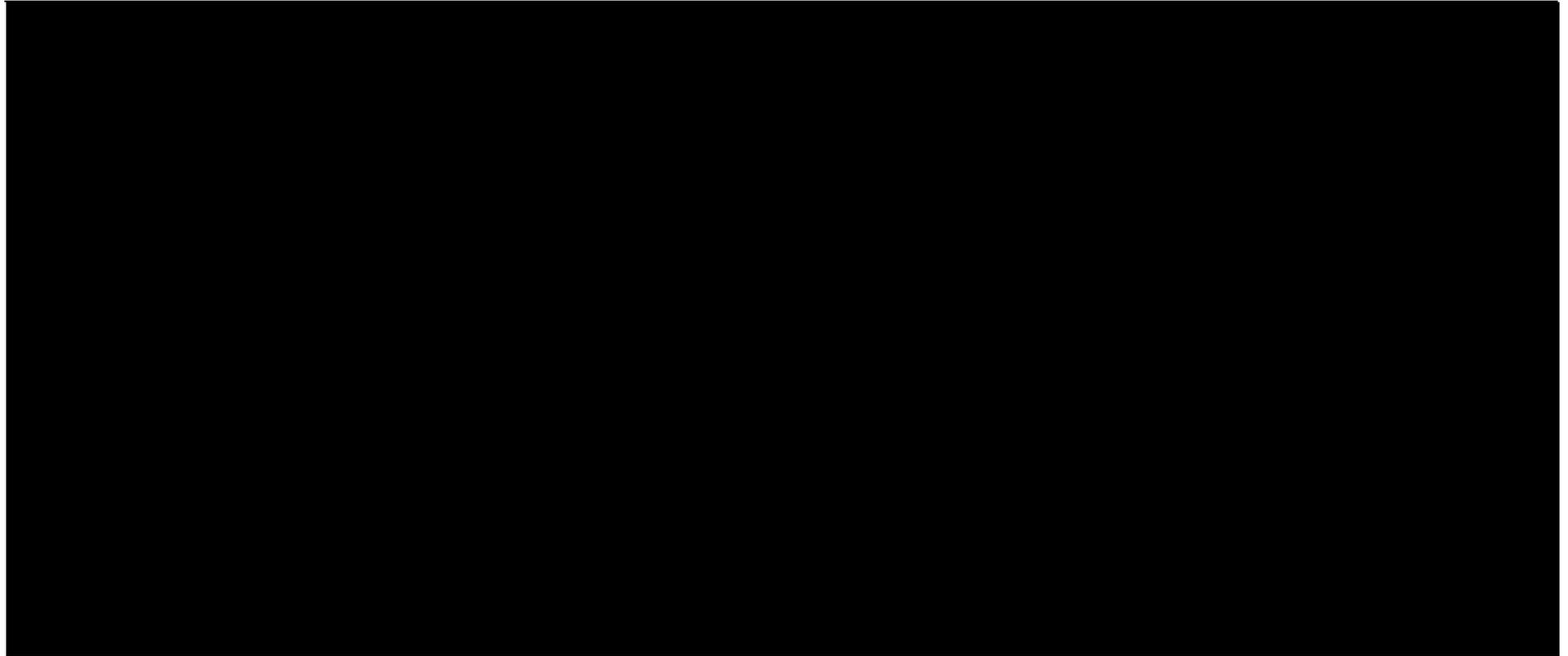
D ³	T2DM + CKD	GLP-1RAs	HHF ESRD	Empagliflozin: 10,930 GLP-1RAs: 10,930 Data source: Medicare FFS, Optum, and MarketScan claims datasets in EMPRISE	<ul style="list-style-type: none">• Empagliflozin vs GLP-1RAs: HR (95% CI):<ul style="list-style-type: none">○ HHF: 0.68 (0.55, 0.85)○ ESRD: 0.70 (0.56, 0.87)
Other real-world data studies					
E ⁴	T2DM	GLP-1RAs	CV hospitalizations HHF	Empagliflozin: 17,502 GLP-1RAs: 17,502 Data source: Medicare FFS claims dataset in EMPRISE ^b	<ul style="list-style-type: none">• Empagliflozin vs GLP-1RAs: HR (95% CI):<ul style="list-style-type: none">○ CV hospitalizations: 0.88 (0.77, 1.00)○ HHF: 0.76 (0.56, 1.03)

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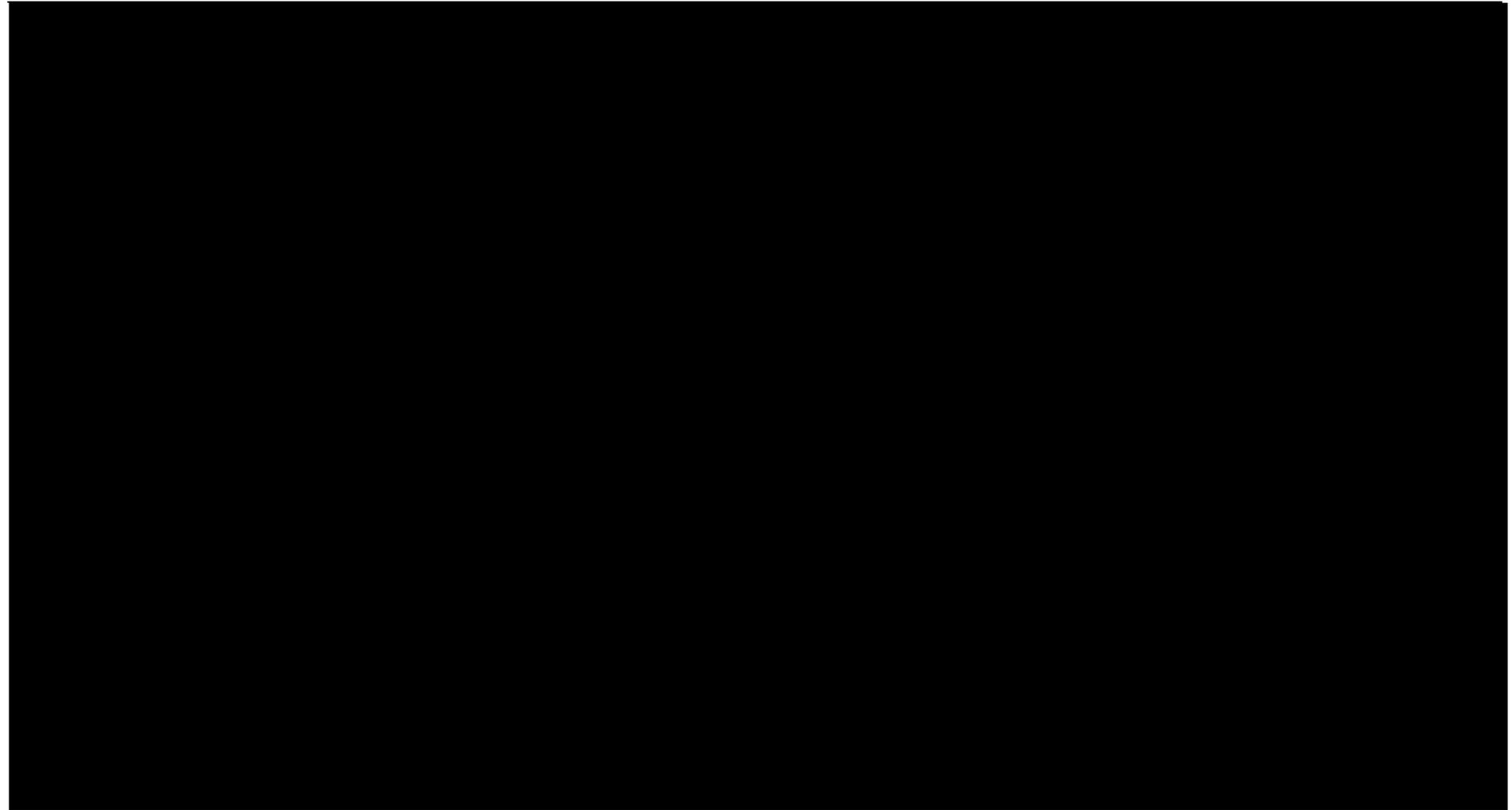


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AHAs, antihyperglycemic agents; CI, confidence interval; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; DPP-4is; dipeptidyl peptidase-4 inhibitors; ESRD, end-stage renal disease; FFS, fee-for-service; GLP-1RAs, glucagon-like peptide-1 receptor agonists; HF, heart failure; HHF, hospitalization for heart failure; HR, hazard ratio; MACE, major adverse cardiovascular events; PMPY, per-member-per-year; PPPM, per-patient-per-month; PPPY, per-patient-per-year; PY, patient-year; SU, sulfonylurea; T2DM, type 2 diabetes mellitus; TZD, thiazolidinediones.

^aPMPY values calculated for EMPRISE participants meeting criteria for the analysis.

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^bStudy was not part of the EMPRISE analysis plan, but leveraged infrastructure of the EMPRISE study.

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Table 9. Key Safety Data for Empagliflozin and Therapeutic Alternatives

Agent	Boxed warning	Contraindications	Limitations of use	Warnings and Precautions	Most common AEs
Empagliflozin ¹	None	Hypersensitivity to empagliflozin or any of the excipients in JARDIANCE	<p>JARDIANCE is not recommended for use to improve glycemic control in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.</p> <p>JARDIANCE is not recommended for use to improve glycemic control in patients with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73 m². JARDIANCE is likely to be ineffective in this setting based upon its mechanism of action.</p> <p>JARDIANCE is not recommended for the treatment of chronic kidney disease in patients with polycystic kidney disease or patients requiring or with a recent history of intravenous immunosuppressive therapy or greater than 45 mg of prednisone or equivalent for kidney disease. JARDIANCE is not expected to be effective in these populations.</p>	<p>Diabetic Ketoacidosis in Patients with Type 1 Diabetes Mellitus and Other Ketoacidosis: Consider ketone monitoring in patients with type 1 diabetes mellitus and consider ketone monitoring in others at risk for ketoacidosis, as indicated. Assess for ketoacidosis regardless of presenting blood glucose levels and discontinue JARDIANCE if ketoacidosis is suspected. Monitor patients for resolution of ketoacidosis before restarting.</p> <p>Volume Depletion: Before initiating JARDIANCE, assess volume status and renal function in patients with impaired renal function, elderly patients, or patients on loop diuretics. Monitor for signs and symptoms during therapy.</p> <p>Urosepsis and Pyelonephritis: Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated.</p> <p>Hypoglycemia: Adult patients taking an insulin secretagogue or insulin may have an increased risk of hypoglycemia. In pediatric patients 10 years of age and older, the risk of hypoglycemia was higher regardless of insulin use. Consider lowering the dosage of insulin secretagogue or insulin to reduce the risk of hypoglycemia when initiating JARDIANCE.</p> <p>Necrotizing Fasciitis of the Perineum (Fournier's Gangrene): Serious, life-threatening cases have</p>	Most common adverse reactions (5% or greater incidence) were urinary tract infections and female genital mycotic infections.

CORRECTED

Section I; Question 28: Full Answer

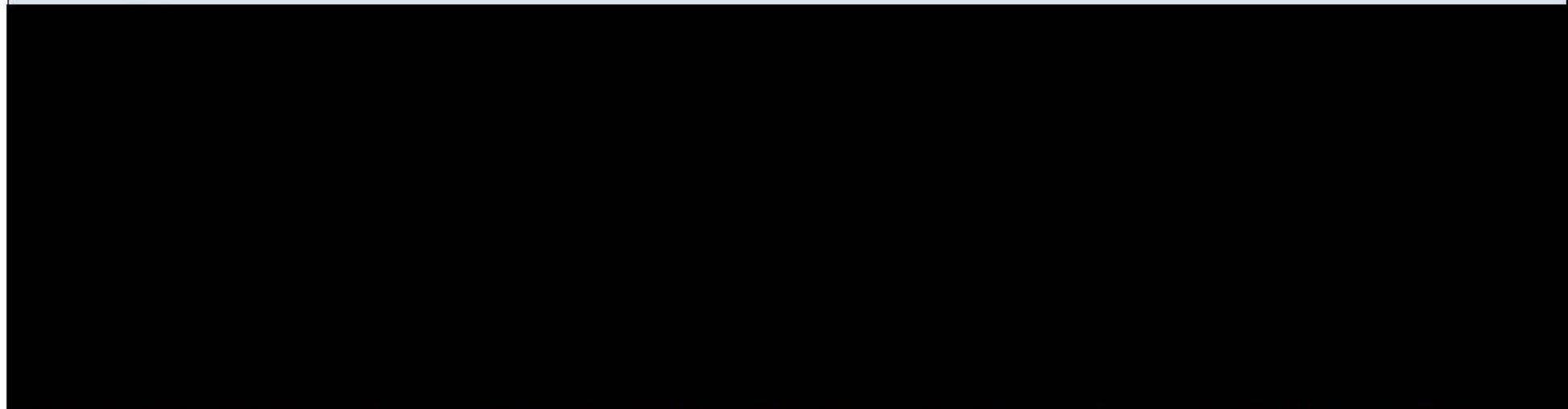
Boehringer Ingelheim P1125

October 12, 2023



Agent	Boxed warning	Contraindications	Limitations of use	Warnings and Precautions	Most common AEs
				<p>occurred in both females and males. Assess patients presenting with pain or tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise. If suspected, institute prompt treatment.</p> <p>Genital Mycotic Infections: Monitor and treat as appropriate.</p> <p>Lower Limb Amputation: Monitor patients for infections or ulcers of lower limbs, and institute appropriate treatment</p> <p>Hypersensitivity Reactions: Serious hypersensitivity reactions (e.g., angioedema) have occurred with JARDIANCE. If hypersensitivity reactions occur, discontinue JARDIANCE, treat promptly, and monitor until signs and symptoms resolve.</p>	

SGLT2i Alternatives



CORRECTED

Section I; Question 28: Full Answer

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October 12, 2023



Agent	Boxed warning	Contraindications	Limitations of use	Warnings and Precautions	Most common AEs
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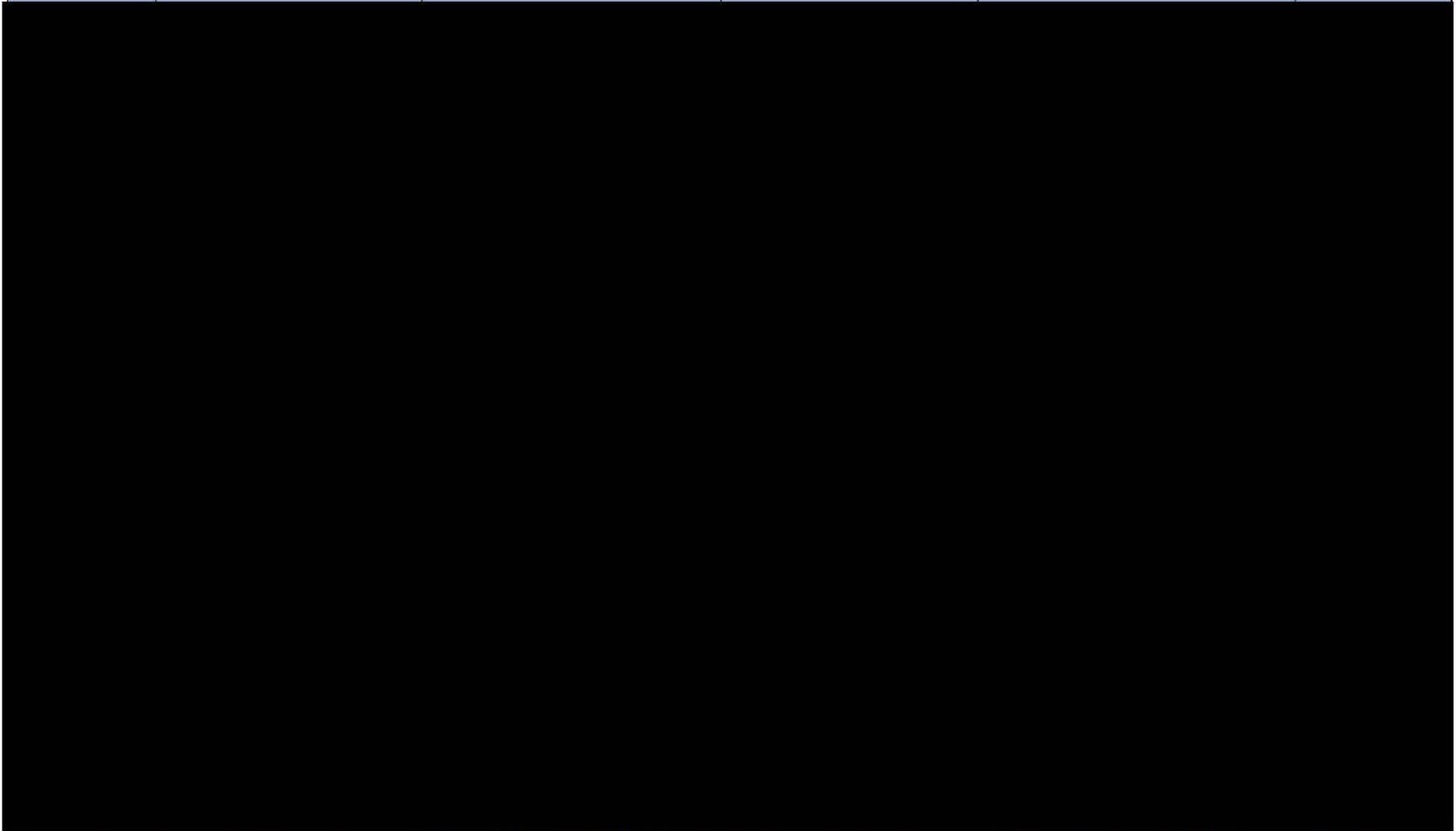
Section I; Question 28: Full Answer

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October 12, 2023



Agent	Boxed warning	Contraindications	Limitations of use	Warnings and Precautions	Most common AEs
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Section I; Question 28: Full Answer
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Agent	Boxed warning	Contraindications	Limitations of use	Warnings and Precautions	Most common AEs
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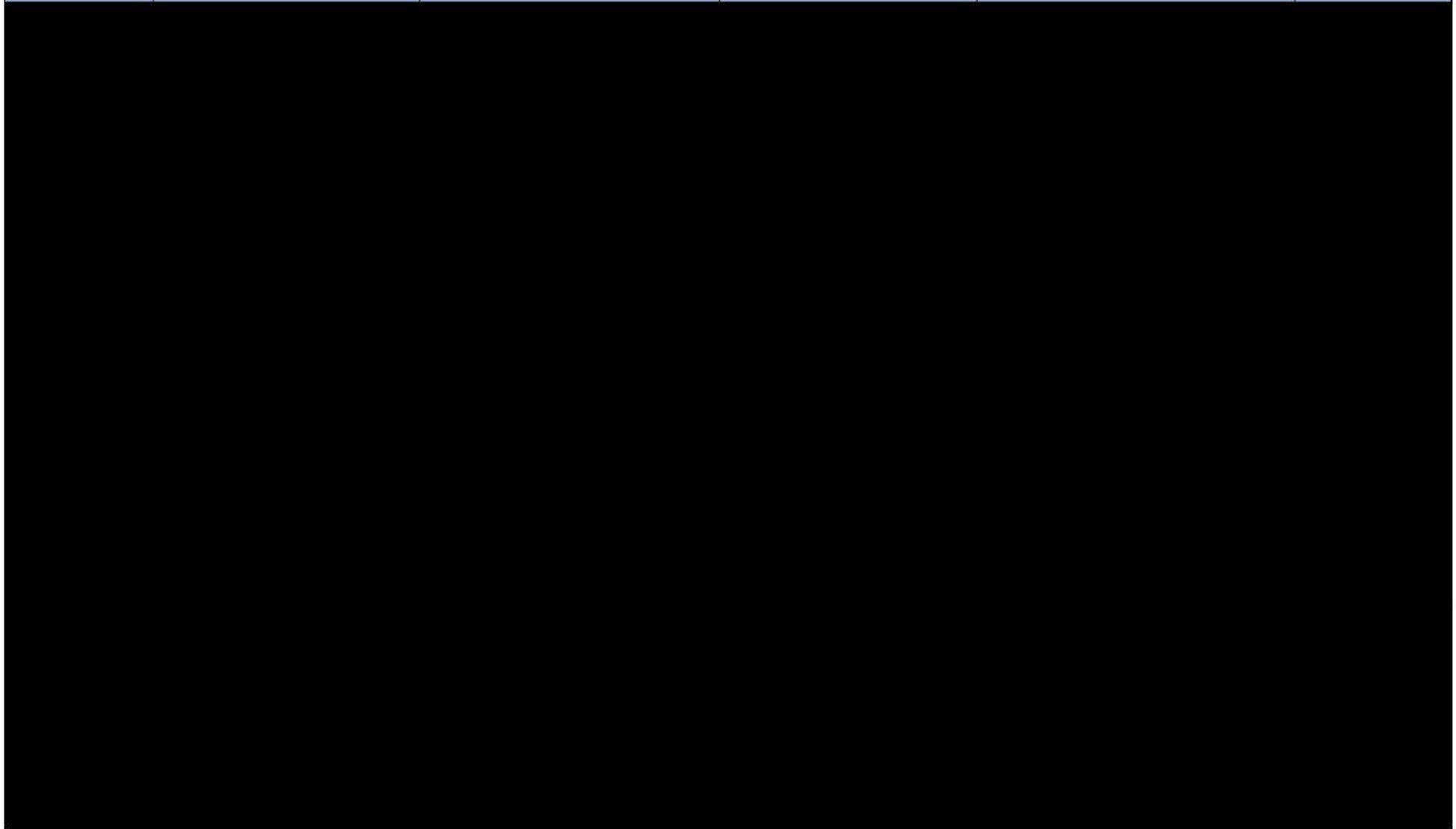
Section I; Question 28: Full Answer

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October 12, 2023



Agent	Boxed warning	Contraindications	Limitations of use	Warnings and Precautions	Most common AEs
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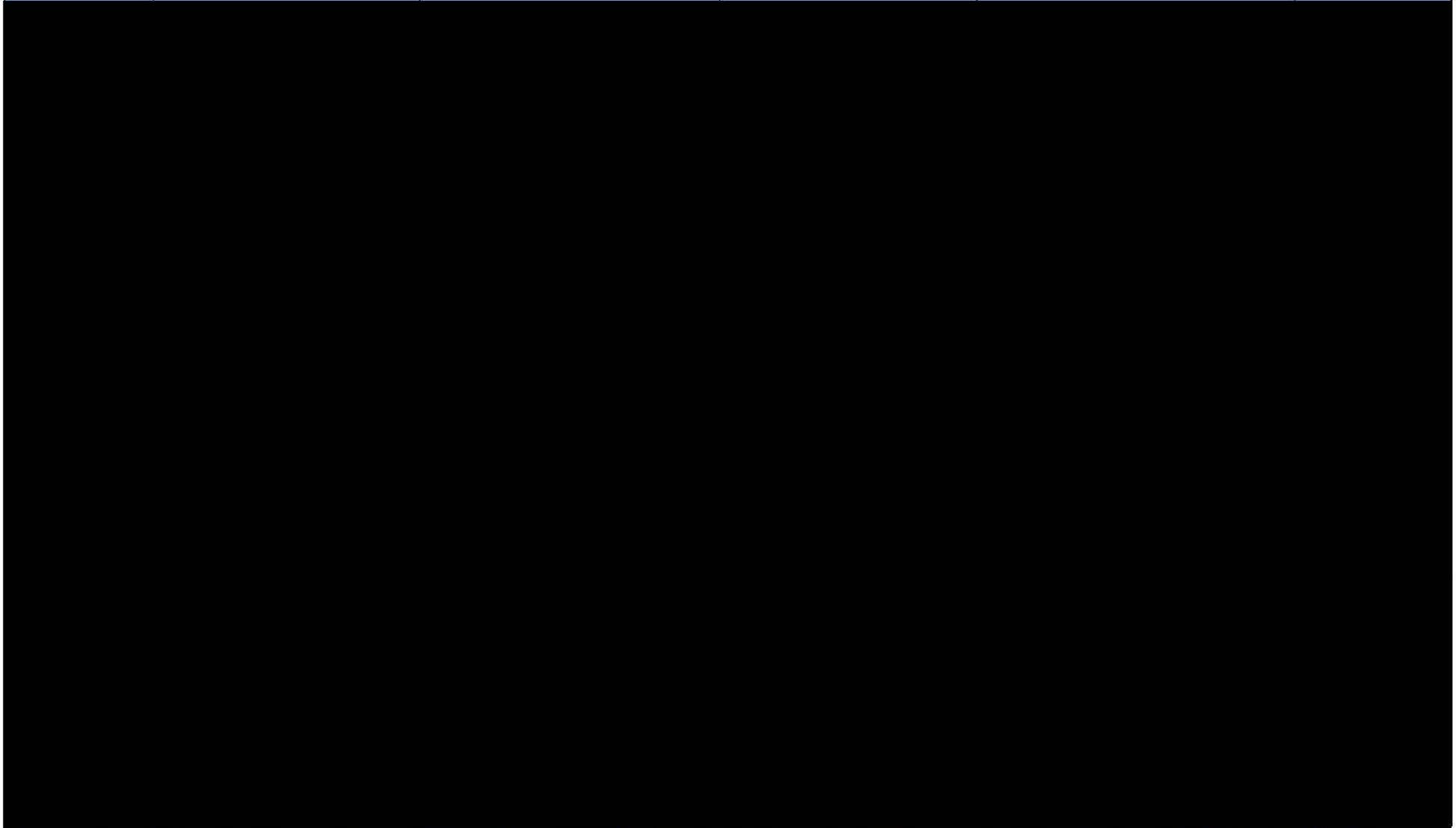
Section I; Question 28: Full Answer

Boehringer Ingelheim P1125

October 12, 2023



Agent	Boxed warning	Contraindications	Limitations of use	Warnings and Precautions	Most common AEs
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Section I; Question 28: Full Answer

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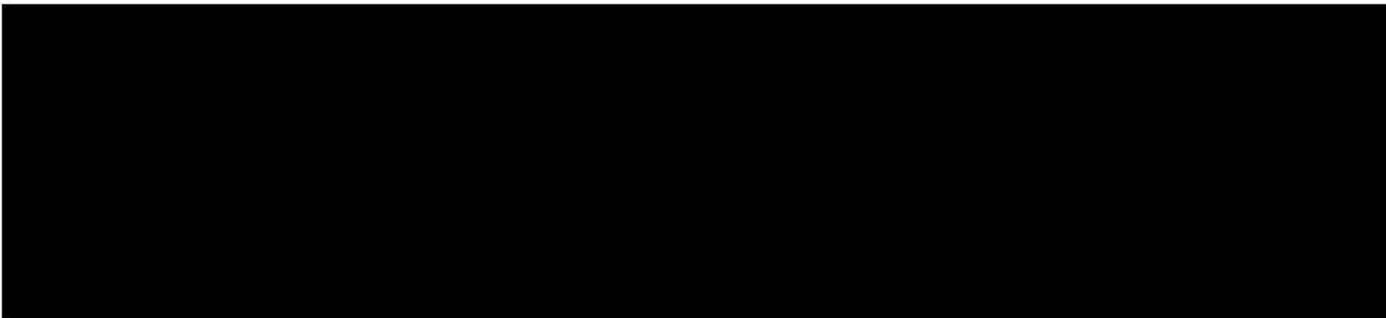
October 12, 2023



Agent	Boxed warning	Contraindications	Limitations of use	Warnings and Precautions	Most common AEs
[Redacted content]					

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Section I; Question 28: Full Answer

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Figure 1. Evaluation of empagliflozin in a Medicare-representative patient population with CKD.





Introduction

Results of the JARDIANCE® (empagliflozin) clinical trial program, supported by real-world evidence, demonstrate strong clinical and economic value across specific populations impacted by cardiovascular, renal, and metabolic (CRM) conditions. These populations include people ≥ 65 years of age, minorities experiencing health inequities, and pediatric patients with type 2 diabetes mellitus (T2DM). In people ≥ 65 years of age, approximately 56% have ≥ 1 CRM condition, 22% have ≥ 2 , and 5% have 3 CRM conditions (1). Cardiovascular (CV) events are the most common cause of death in people with T2DM and an estimated 70% of people ≥ 70 years of age have cardiovascular disease (CVD) (2, 3). Heart failure (HF) is the leading cause of hospitalization for people ≥ 65 years of age (4). HF is often associated with chronic kidney disease (CKD) development (5), the latter of which significantly increases the risk of CV complications and progression to end-stage renal disease (ESRD), leading to further risk of hospitalization (6). Vulnerable populations such as Black/African Americans are at increased risk for hospitalization, ESRD, and death (7). Empagliflozin provides cardiac, renal, and glucose-lowering benefits as a single, once-daily oral medication with established safety profile for these specific populations.

People ≥ 65 Years of Age

People ≥ 65 Years of Age with T2DM

Approximately 75% of people with T2DM ≥ 65 years of age suffer from either CVD, HF, and/or CKD, which increases to 90% for those ≥ 75 years of age (8). Delaying consequences of the increased risks that come with cardiorenal conditions is an important treatment goal. The American Diabetes Association (ADA) *Standards of Care in Diabetes* recommend treating people with T2DM and CVD (or high risk of CVD), HF, and/or CKD with agents that have proven CV and/or renal benefit independent of HbA1c. The guidelines also recommend a less stringent HbA1c goal of $< 8.0\%$ for older adults with multiple coexisting chronic illnesses (3). Although minimizing hyperglycemia is important, stringent glycemic control can be associated with adverse outcomes in elderly people with T2DM (hypoglycemia, morbidity from falls, and death) (9, 10). Greater reductions in morbidity and mortality are likely to result from a clinical focus on comprehensive cardiorenal risk reduction (3, 8).



[REDACTED]

Empagliflozin reduces HbA1c as well as other SGLT2is (11, 12, 16). GLP-1RAs demonstrate a greater HbA1c lowering effect than the SGLT2is (**Table 1**) (13-15). However, the level of HbA1c reductions seen with empagliflozin align with ADA guideline recommendations for older patients with CRM conditions (17).

Renal impairment is more prevalent in people ≥ 65 years of age (18). CKD is often underdiagnosed, as approximately 40% of people with severely decreased kidney function are not aware they have CKD (19). In a study evaluating labs (not diagnoses) in people with T2DM ≥ 65 years of age, the prevalence of CKD was 35% (8). As previously noted, managing cardiorenal outcomes in T2DM is an important treatment goal. Empagliflozin is approved for glycemic control in people with an estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m² (**Table 1**), expanding available treatment options for those ≥ 65 years of age and providing benefit to those with undiagnosed CKD (16). [REDACTED]

[REDACTED]

The use of empagliflozin versus therapeutic alternatives to treat T2DM has been shown to yield substantial annual cost savings in the Medicare population. In a large, retrospective, comparative, cost analysis using the 100% Medicare fee-for-service (FFS) claims dataset from the EMPRISE study (20), propensity-score-matched cohorts of 63,512 patients with T2DM initiating empagliflozin or GLP-1RAs were assessed. [REDACTED]

[REDACTED]

Desai, *et al.* assessed the comparative effectiveness of empagliflozin versus GLP-1RAs in reducing recurrent CV hospitalization in Medicare FFS beneficiaries with T2DM. In this retrospective, claims-based, propensity-score-matched cohort analysis, compared to GLP-1RAs, researchers observed a trend of 12% (HR 0.88 [0.77-1.00]) reduced risk of total CV hospitalizations favoring the empagliflozin cohort (22).

People ≥ 65 Years of Age with CVD and T2DM



CV events are the most common cause of death in T2DM, and approximately 50% of people with T2DM have CVD (3, 23). An estimated 70% of people ≥ 70 years of age will develop CVD, and nearly 70% of older adults with CVD have multiple CRM conditions (2).

In people with T2DM and CVD, empagliflozin is the only agent FDA approved to reduce the risk of CV death (16). Empagliflozin is also the only agent to significantly reduce the risk of CV death and the composite of CV death or hospitalization for heart failure (HHF) versus placebo in patients ≥ 65 years of age with T2DM and established CVD (**Table 3**). These benefits were more pronounced in those ≥ 65 years of age (17). Benefits of reduction in the risk of 3-point major adverse cardiovascular events (MACE; composite of CV death, non-fatal myocardial infarction [MI], and non-fatal stroke), HHF, all-cause hospitalization, and all-cause mortality in patients ≥ 65 years of age were consistent with findings from the overall study population (17). None of the GLP-1RAs demonstrated statistically significant benefit in 3-point MACE in patients ≥ 60 years of age with T2DM and CVD (24-26).

Empagliflozin was shown to add years of life to older patients in an actuarial analysis. The analysis projected a mean survival benefit of an additional 2.5 years, 2 years, and 1 year, in patients 60, 70 and 80 years of age, respectively, with empagliflozin compared with standard of care (SOC) at that time (27).

[REDACTED]

People ≥ 65 Years of Age with HF

HF is a leading cause of hospitalization for people ≥ 65 years of age, accounting for more than 80% of HF-related costs (29). Between 2009 and 2019, HHF in Medicare beneficiaries more than doubled, and approximately 20% of patients admitted for HF were readmitted within 30 days (30, 31).



Empagliflozin has been shown to reduce the risk of CV death and HHF (composite outcome) in patients ≥ 65 years of age with HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF; **Table 4**) (32, 33). In dedicated clinical trials, empagliflozin reduced the risk of the primary composite outcome versus placebo by 22% in patients ≥ 65 years of age with HFrEF and by 25% in patients ≥ 70 years of age with HFpEF (32, 33).

[REDACTED]

People ≥ 65 Years of Age with CKD

CKD and HF are interconnected, and having 1 of these conditions increases the risk of developing the other. CKD significantly increases the risk of CV complications and the development of ESRD, doubling the risk for hospitalization (6, 18). Total Medicare FFS spending for all beneficiaries (both



older and younger than age 66) with CKD was \$85 billion in 2020, representing 23.5% of total Medicare FFS expenditures (18).

Empagliflozin demonstrated a reduction in the risk of kidney disease progression or CV death in patients ≥ 65 years of age, with and without T2DM, and with severely decreased eGFR (**Table 5**) (36). [REDACTED]

In a subgroup analysis of the EMPA-KIDNEY trial, the significant risk reduction for the composite primary endpoint, first occurrence of progression of kidney disease or CV death, was consistent for patients ≥ 70 years of age (1300 patients comprising 40% of study population) with the overall trial population (36). [REDACTED]

In the EMPRISE study, the effect of empagliflozin compared to GLP-1RAs on cardiorenal outcomes has been demonstrated in patients with T2DM and advanced CKD. In a propensity-matched subgroup analysis using Medicare, Optum, and MarketScan data, empagliflozin (n=10,930) was associated with a reduced risk of HHF (HR 0.68 [0.55, 0.85]) and a reduced risk of ESRD (HR 0.70 [0.56, 0.87]) versus GLP-1RAs (n=10,930) (39).

Safety and Administration in People ≥ 65 Across Indications

The safety profile of empagliflozin in people ≥ 65 years of age is consistent with its safety profile in the general population (**Table 1**) (17). In a study of empagliflozin added to SOC in patients with T2DM, the frequency of adverse events was generally similar in adults < 65 and ≥ 65 years of age, except for urinary tract infections, volume depletion, and acute kidney injury, which were more common in those ≥ 65 years of age (17).

Empagliflozin may provide a more tolerable safety profile in older adults compared with GLP-1RAs. [REDACTED]



[REDACTED]

When determining treatment options for older adults, potential side effects is a critical consideration (44). Empagliflozin has consistently demonstrated a tolerable safety profile in this population (17).

Pediatrics (≥10 to <18 Years of Age) with T2DM

There has been an increase in the prevalence and incidence of T2DM in children and adolescents in recent years (45).

[REDACTED]

Patients Experiencing Health Disparities

Racial and ethnic minorities, especially Black/African Americans, have higher rates of T2DM, CV and kidney disease (7).

[REDACTED] These groups are more prone to diabetes diagnosis, hospitalization, mortality, and rapid progression to ESRD (Black/African Americans to White ratio: diabetes diagnosis 1.8; hospitalization 3.8; diabetes death 2.0; ESRD 3.2). A larger percentage of minority populations suffer from CVD and related risk factors, such as hypertension, which is the leading cause of adverse CV outcomes (**Table 7**) (7).

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Empagliflozin has been evaluated in a randomized trial specific to hypertensive Black/African American adults with T2DM, and showed significant improvements in HbA1c, blood pressure (BP; 24-hr mean ambulatory systolic BP), and body weight. The reductions in BP were similar to those observed in products with an indication for lowering BP (49). In addition, empagliflozin reduced the risk of CV death or first HFrEF in Black/African American patients with HFrEF (32).

[REDACTED]

CRM conditions are more likely to coexist and are more prevalent in populations with health disparities, such as Black/African Americans. Empagliflozin provides benefits for multiple CRM conditions with 1 pill compared to medications that treat only 1 condition.

Summary

CRM conditions are more likely to coexist and are more prevalent in specific populations. Empagliflozin is a therapeutic advance that demonstrates significant benefit across CRM conditions in specific populations:

- People ≥65 years of age with T2DM and established CVD, empagliflozin is the only agent that has shown significant reduction in the risk of CV death and hospitalization for HF (17);
- People ≥65 years of age with HF, empagliflozin reduced the risk of CV death and hospitalization for HF (in HFpEF ≥70) (32, 33);
- People ≥65 years of age with CKD, empagliflozin reduced the risk of kidney disease progression and CV death including those with eGFR down to 30 mL/min/1.73 m² (36);
- [REDACTED]
- Pediatric patients with T2DM (46); and
- Black/African Americans, empagliflozin reduces the risk of CV death and hospitalization for HF by 54% (50).

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[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

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Table 1. Characteristics and Outcomes in Specific Populations Studied in Pivotal Clinical Trials Measuring Glycemic Control in Patients with T2DM for Empagliflozin and SGLT2i Therapeutic Alternatives

	Empagliflozin¹	[REDACTED]	[REDACTED]
Proportion of study population in age subgroups	<ul style="list-style-type: none"> • ≥65 years: 32% (n = 2,721) • ≥75 years: 6% (n = 491) 	[REDACTED]	[REDACTED]
HbA1c by eGFR subgroups	Significant reduction in HbA1c in eGFR 30- $<$ 90 mL/min/1.73 m ²	[REDACTED]	[REDACTED]
HbA1c reductions in patients <65 versus ≥65 years of age	Greater reductions in people <65 versus ≥65 years of age ^{4,b}	[REDACTED]	[REDACTED]
Adverse reactions with higher risk in older age subgroups	≥75 years: volume depletion-related adverse reactions and UTIs	[REDACTED]	[REDACTED]
Specific populations where clinical pharmacology was studied	<ul style="list-style-type: none"> • Pediatric patients (≥10 years of age) • Hepatic impairment • Renal impairment • Demographics (age, gender, BMI, race) 	[REDACTED]	[REDACTED]
Limitations of use	Not recommended in eGFR <30 mL/min/1.73 m ²	[REDACTED]	[REDACTED]

T2DM, type 2 diabetes mellitus; SGLT2i, sodium glucose co-transporter 2 inhibitor; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; UTI, urinary tract infection; BMI, body mass index.

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^aPercentages not reported.

^bData from the EMPA-REG OUTCOME trial.

^cSimilar efficacy despite age when controlling for level of renal function.

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■ [REDACTED]
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[Redacted]

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[Redacted]

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References:

■ [REDACTED]

Table 3. Characteristics, CV Outcomes, and Safety in Older Patients (≥60 years of age) with T2DM and High CV Risk for Empagliflozin and Therapeutic Alternatives

	Empagliflozin ^{1,2} (EMPA-REG OUTCOME ≥65 years of age subpopulation) N = 7,020	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Inclusion criteria regarding high-risk CV events	History of MI, CAD, unstable angina, of stroke, or occlusive PAD	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Age in years, mean (SD) in active agent arms	<ul style="list-style-type: none"> 65-<75 years: 68.8 (2.8) ≥75 years: 77.9 (2.8) 	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Proportion of study population in older subgroups in listed agent arm	<ul style="list-style-type: none"> 65-<75 years: 35.6% (n = 1,667) ≥75 years: 9.0% (n = 424) 	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
3P-MACE definition	CV death, nonfatal MI, or nonfatal stroke	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

Primary endpoint in older subgroups, HR (95% CI)	3P-MACE² ≥65 years: 0.71 (0.59, 0.87)					
Key secondary endpoints in older subgroups, HR (95% CI)	CV death² • ≥65 years: 0.54 (0.40, 0.73) Composite HHF/CV death • 65-<75 years: 0.59 (0.44, 0.80) • ≥75 years: 0.52 (0.33, 0.82)					
Safety events in older age subgroups	Total AEs: empagliflozin versus placebo • 65-<75 years: 91.8% versus 92.8% • ≥75 years: 90.8% versus 94.3%					

CV, cardiovascular; T2DM, type 2 diabetes mellitus; MI, myocardial infarction; CAD, coronary artery disease; PAD, peripheral artery disease; CVD, cardiovascular disease; ASCVD, atherosclerotic cardiovascular disease; HDL-cholesterol, high density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; NYHA, New York Heart Association; CHF, chronic heart failure; ABI, ankle-brachial index; SD, standard deviation; NR, not reported; HR, hazard ratio; CI, confidence interval; MACE, major adverse cardiovascular event; HF, heart failure; HHF, hospitalization for heart failure; AEs, adverse events; UTI, urinary tract infection; NR, not reported.

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Table 4. Characteristics and HF Outcomes in Older Patients with HF for Empagliflozin and Therapeutic Alternatives

HF _r EF			
	Empagliflozin ¹ (EMPEROR-REDUCED) N = 3,730		
Age in years, mean (SD)	67.2 (10.8)		
Study population design	Dedicated studies for HF _r EF Enrolled with and without T2DM		
Proportion of study population in older subgroup in listed agent arm	≥65 years: 63.8% (n = 1,188)		
Primary endpoint in older subgroup, HR (95% CI)	Composite CV death/HHF ≥65 years: 0.78 (0.66, 0.93)		

HF _p EF			
	Empagliflozin ⁴ (EMPEROR-PRESERVED) N = 5988		
Age in years, mean (SD)	71.8 (9.3)		
Study population design	Dedicated studies for HF _p EF Enrolled with and without T2DM		
Proportion of study population in older subgroup in listed agent arm	≥70 years: 64.4% (n = 1,931)		



Primary endpoint in older subgroup, HR (95% CI)	Composite CV death/HHF ≥ 70 years: 0.75 (0.64, 0.87)	[REDACTED]	[REDACTED]
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*Total population sotagliflozin + placebo. Note: 966/1222 patients are HFrEF and 256/1222 patients are HFpEF (no age specific breakdown by LVEF status available).

HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; SD, standard deviation; IQR, interquartile range; T2DM, type 2 diabetes mellitus; HR, hazard ratio; CI, confidence interval; CV, cardiovascular; HHF, hospitalization for heart failure; IV, intravenous; HFpEF, heart failure with preserved ejection fraction.

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Table 5. Characteristics and Outcomes in Patients with CKD by Age, Albuminuria, and eGFR for Empagliflozin and Therapeutic Alternatives in Pivotal Clinical Trials

	Empagliflozin¹ (EMPA-KIDNEY) N = 6,609	[REDACTED]	[REDACTED]
Cause of kidney disease	<ul style="list-style-type: none"> • DKD: 31.2% (n = 1,032) • Hypertensive/renovascular disease: 21.4% (n = 706) • Glomerular disease: 25.8% (n = 853) • Other/unknown: 21.6% (n = 713) 	[REDACTED]	[REDACTED]
Age in years, mean (SD)	63.9 (13.9)	[REDACTED]	[REDACTED]
Proportion of study population in age subgroups in listed agent arm	<ul style="list-style-type: none"> • ≥60-<70 years: 25.8% (n = 853) • ≥70 years: 39.8% (n = 1,315) 	[REDACTED]	[REDACTED]
Primary outcome definition	Composite of kidney disease progression (defined as ESKD, sustained decrease in eGFR to <10 mL/min/1.73 m ² , sustained decrease in eGFR ≥40% from baseline, or death from renal causes) or CV death	[REDACTED]	[REDACTED]
Primary endpoint in age subgroups, HR (95% CI)	<ul style="list-style-type: none"> • ≥60-<70 years: 0.81 (0.64, 1.04) • ≥70 years: 0.65 (0.52, 0.81) 	[REDACTED]	[REDACTED]
Albuminuria distribution	<ul style="list-style-type: none"> • <30 mg/g: 20.1% (n = 665) • ≥30-≤300 mg/g: 28.1% (n = 927) • >300 mg/g: 51.8% (n = 1,712) 	[REDACTED]	[REDACTED]
Primary endpoint in albuminuria subgroups, HR (95% CI)	<ul style="list-style-type: none"> • <30 mg/g: 1.01 (0.66, 1.55) • ≥30-≤300 mg/g: 0.91 (0.65, 1.26) • >300 mg/g: 0.67 (0.58, 0.78) 	[REDACTED]	[REDACTED]

eGFR inclusion criteria	≥20-<90 mL/min/1.73 m ²		
eGFR distribution	<ul style="list-style-type: none"> • <30 mL/min/1.73 m²: 34.2% (n = 1,131) • ≥30-<45 mL/min/1.73 m²: 44.4% (n = 1,467) • ≥45 mL/min/1.73 m²: 21.4% (n = 706) 	  	  
Primary endpoint in eGFR subgroups, HR (95% CI)	<ul style="list-style-type: none"> • <30 mL/min/1.73 m²: 0.73 (0.62, 0.86) • ≥30-<45 mL/min/1.73 m²: 0.78 (0.62, 0.97) • ≥45 mL/min/1.73 m²: 0.64 (0.44, 0.93) 	 	 

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; DKD, diabetic kidney disease; SD, standard deviation; ESKD, end-stage kidney disease; CV, cardiovascular; HR, hazard ratio; CI, confidence interval.

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Table 6. Characteristics and Outcomes of Clinical Trials in Patients ≥10 Years of Age with T2DM for Empagliflozin and Therapeutic Alternatives

	Empagliflozin ^{1,2} N = 157	[REDACTED]	[REDACTED]
Age in years, mean (SD)	14.4 (1.9) ²	[REDACTED]	[REDACTED]
Age groups in listed agent arm	[REDACTED]	[REDACTED]	[REDACTED]
HbA1c difference versus placebo (95% CI)	-0.8 (-1.5, -0.2)	[REDACTED]	[REDACTED]
Safety events	Risk of hypoglycemia was higher in pediatric patients (19.2%) regardless of concomitant insulin use	[REDACTED]	[REDACTED]

T2DM, type 2 diabetes mellitus; SD, standard deviation; NR, not reported; HbA1c, hemoglobin A1c; CI, confidence interval.

References:

- JARDIANCE® (empagliflozin tablets), for oral use [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 2023.
- Laffel LM, Danne T, Klingensmith GJ, Tamborlane WV, Willi S, Zeitler P, et al. Efficacy and safety of the SGLT2 inhibitor empagliflozin versus placebo and the DPP-4 inhibitor linagliptin versus placebo in young people with type 2 diabetes (DINAMO): a multicentre, randomised, double-blind, parallel group, phase 3 trial. *Lancet Diabetes Endocrinol.* 2023;11(3):169-81. Epub 2023/02/05. doi: 10.1016/S2213-8587(22)00387-4. PubMed PMID: 36738751.
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Table 7. Health Inequities-statistics on Black/African American Populations

	Non-Hispanic Black	Non-Hispanic White	Non-Hispanic Black/ Non-Hispanic White Ratio
Diabetes and African Americans¹			
Age-adjusted percentage of adults aged 18 and over diagnosed with diabetes (2021)	12.7	7.0	1.8
Age-adjusted percentage of diagnosed diabetes for adults aged 18 and over (2018-2019)	12.1	7.4	1.6
Men	12.2	8.0	1.5
Women	12.1	6.9	1.7
Age-adjusted diabetes death rates per 100,000 (2019)	38.8	19.1	2.0
Men	47.1	24.9	1.9
Women	32.6	14.3	2.3
Age-adjusted percentage of visual impairment for adults with diabetes (2021)	18.4	16.0	1.2
Hospital admissions per 100,000 for uncontrolled diabetes without complications, age 18 and over (2019)	115.9	30.6	3.8
Hospital admissions with diabetes with long-term complications per 100,000, age 18 and over (2019)	231.5	94.3	2.5
Age-adjusted incidence rate per million of ESRD due to diabetes (2019)	437.5	138.2	3.2
Age-adjusted percentage of persons 40 years of age and over with diabetes who had a foot examination (2019)	67.3	66.3	1.0
Heart Disease and African Americans²			
Age-adjusted percentage of coronary heart disease among persons 18 years of age and over (2021)	5.2	5.6	0.93
Age-adjusted heart disease death rates per 100,000 (2019)	208.6	166.4	1.3



Men	267.5	210.7	1.3
Women	165.0	129.6	1.3
Age-adjusted percentage of persons 18 years of age and over who have high blood pressure (2017-2018)	57.1	43.6	1.3
Men	57.2	50.2	1.1
Women	56.7	36.7	1.5
Percentage of persons 18 years of age and over who have high blood pressure (2021)	35.2	28.3	1.2
Percentage of adults aged 18 and over with hypertension whose blood pressure is under control (2015-2016)	44.6	50.8	0.9
Men	40.1	47.7	0.8
Women	48.5	57.1	0.8

ESRD, end-stage renal disease.

Reference:

1. US Department of Health and Human Services. Minority Population Profiles [September 11, 2023]. Available from: <https://www.minorityhealth.hhs.gov/diabetes-and-african-americans>.
2. US Department of Health and Human Services. Minority Population Profiles [September 11, 2023]. Available from: <https://www.minorityhealth.hhs.gov/heart-disease-and-african-americans>

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Cardiovascular (CV), renal, and metabolic (CRM) conditions are progressive, overlap, and exacerbate one another, resulting in substantial morbidity, mortality, and increased healthcare costs (1-3). Among people ≥ 65 years of age, 14 million (26%) have type 2 diabetes mellitus (T2DM), 13 million (24%) have cardiovascular disease (CVD; including heart failure [HF]), and 17 million (33%) have chronic kidney disease (CKD; **Figure 1**) (2). Moreover, 56% have ≥ 1 CRM condition, 22% have ≥ 2 , and 5% have 3 CRM conditions (2). Clinical unmet needs across CRM conditions include reducing the risks of death, hospitalization, and disease progression.

JARDIANCE[®] (empagliflozin) addresses unmet needs, as a single treatment, by reducing the residual risks of mortality, hospitalization, and disease progression following the use of previous standard-of-care (SOC) treatments. Empagliflozin clinical trial results have transformed treatment guidelines and is recommended as first-line treatment in people with CRM conditions (4-7).

Proven Benefits in T2DM and T2DM with CVD

The primary treatment goals for people with T2DM are to lower blood glucose and reduce the risk of cardiorenal events. Accordingly, American Diabetes Association (ADA) *Standards* recommend the use of agents with proven cardiorenal benefit in people with T2DM and cardiorenal conditions (4).

CVD is the leading cause of mortality, accounting for 80% of deaths, in people with diabetes, and is a significant driver of healthcare costs (4, 8, 9). Empagliflozin is a therapeutic advancement as it is the only agent with an FDA indication to reduce the risk of CV death in people with T2DM and established CVD (10). [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



In a large, real-world, comparative effectiveness analysis of matched Medicare cohorts with T2DM, empagliflozin reduced the risk of HHF compared to a glucagon-like peptide-1 receptor agonist (GLP-1RA) (16).

[REDACTED]

Reducing Death and Costly Hospitalization in HF

HF is the leading cause for hospitalization and 30-day readmission in people ≥ 65 years of age, and hospitalizations account for most healthcare expenditures in HF (19-22). The American Heart Association, American College of Cardiology, and Heart Failure Society of America (AHA/ACC/HFSA) guidelines recommend sodium-glucose co-transporter 2 inhibitors (SGLT2is) with proven benefit as first-line treatments for HF with reduced ejection fraction (HFrEF; ejection fraction $\leq 40\%$) (5). ACC 2023 guidelines recommend SGLT2is as first-line treatment for HF with preserved ejection fraction (HFpEF; ejection fraction $\geq 50\%$) (6).

Empagliflozin received Breakthrough Therapy status by the FDA for HF (23). In pivotal trials, empagliflozin reduced the combined risk of CV death or HHF versus placebo by 25% in patients with HFrEF and by 21% in patients with HFpEF (24, 25). Empagliflozin also significantly reduced the risk of first and recurrent hospitalizations by 30% and 27%, respectively, and slowed the rate of estimated glomerular filtration rate (eGFR) decline (24, 25).

[REDACTED]

Reducing Death, Disease Progression, and Hospitalizations in CKD

CKD is highly prevalent in the Medicare population, affecting 1 in 3 people ≥ 65 years of age, and is a major driver of healthcare costs (30, 31). Medicare spend for CKD (without end-stage

renal disease [ESRD]) was \$85 billion in 2020 (31). CKD healthcare costs are driven mainly by medical, not prescription drug, costs (**Figures 2 and 3**) (3, 31). The CKD hospitalization rate is high, 47%, with an annual readmission rate of ~20% (31).

The FDA granted empagliflozin Fast Track designation for CKD (32), and the Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend empagliflozin as first-line therapy, along with other SGLT2is with proven renal benefit (7).

Empagliflozin demonstrated a 28% reduced risk of kidney disease progression or death from CV causes on top of SOC and without major safety concerns (33). This benefit was independent of diabetes status and glycemic control. The risk of hospitalization for any cause was 14% lower with empagliflozin versus placebo (33). Empagliflozin addresses critical unmet needs in the CKD population by reducing the risk of death, disease progression, and hospitalization.

Empagliflozin was studied in patients with/without T2DM, with/without albuminuria, with an eGFR down to ≥ 20 mL/min/1.73 m², and in a range of CKD etiologies, including glomerular disease (33). [REDACTED]

Comparative Effectiveness and Costs Versus Therapeutic Alternatives

Empagliflozin's benefits from clinical trials are consistent with observations in large, real-world comparative effectiveness and cost studies. Empagliflozin has an extensive and robust real-world evidence program. The EMPagliflozin compaRative effectiveness and SafEty (EMPRISE) program has been assessing the comparative effectiveness, safety, healthcare utilization, and cost of empagliflozin over 5 years in people with T2DM in routine care using matched Medicare cohorts (37). [REDACTED]

██
██

Conclusion

Empagliflozin helps to address CMS' goals of improving outcomes, lowering total cost of care, and addressing unmet needs as a single comprehensive treatment for CRM conditions, which affect a large percentage of the Medicare population.

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Section I; Question 30: Full Answer
Boehringer Ingelheim P1125
September 29, 2023



Advanced Chronic Kidney Disease—Results from the EMPRISE Study. Diabetes.
2023;72(Supp_1).



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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	EMPAGLIFLOZIN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	AAHFN
	Respondent Email Who is completing this form?	PAO
Question 27: Prescribing Information	Prescribing Information	<p>The medication Jardiance is prescribed for the treatment of chronic heart failure. Jardiance 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. Jardiance 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, Jardiance is associated with slowing the rate of kidney function decline which also can reduce cardiovascular death and heart failure hospitalizations (AHA/ACC, 2022)..Jardiance 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, Jardiance is found to reduce heart failure hospitalization and cardiovascular mortality (AHA/ACC, 2022). Jardiance 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 Jardiance 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?	D
	What type of Evidence is shown?	
Question 28: Therapeutic Impact and Comparative Effectiveness	Therapeutic Impact and Comparative Effectiveness	<p>Jardiance (empagliflozin) is a medication primarily used to treat type 2 diabetes mellitus. It recently became part of guideline therapy for the management of heart failure. It belongs to a class of drugs known as sodium-glucose co-transporter 2 (SGLT2) inhibitors. Jardiance works by reducing the reabsorption of glucose in the kidneys, thereby increasing the excretion of glucose in the urine. Jardiance has demonstrated unique therapeutic benefits:</p>

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Question	Sub-Question	Response
	<p data-bbox="262 901 619 1144">Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28 Evidence Submitted include a cost-effectiveness measure?</p> <p data-bbox="262 1185 619 1258">What type of Evidence is shown?</p>	<ul data-bbox="682 251 1967 901" style="list-style-type: none">• Cardiovascular Benefits: One of the most significant advantages of Jardiance is its cardiovascular benefits. The EMPA-REG OUTCOME trial, showed that Jardiance significantly reduces the risk of major adverse cardiovascular events (MACE), including cardiovascular death, non-fatal heart attacks, and non-fatal strokes, in patients with type 2 diabetes and established cardiovascular disease. This cardiovascular protection sets Jardiance apart from many other diabetes medications.• Heart Failure Benefits: Jardiance has also shown benefits in reducing the risk of hospitalization for heart failure in patients, especially those with a history of heart disease. The EMPEROR-Reduced and EMPEROR-Preserved trials helped demonstrate these heart failure benefits• Renal Protection: Jardiance has shown that it can slow the progression of kidney disease in patients with type 2 diabetes, especially those with underlying kidney issues. The EMPA-KIDNEY trial provided evidence of these renal benefits.• Weight Loss: Jardiance is typically weight-neutral or associated with weight loss in patients. This can be advantageous for individuals with type 2 diabetes who may benefit from weight management.• Low Risk of Hypoglycemia: Jardiance has a low risk of causing hypoglycemia (low blood sugar) compared to some other diabetes medications, such as sulfonylureas or insulin.• Urinary Tract Infections and Genital Mycotic Infections: While Jardiance is generally well-tolerated, it is associated with an increased risk of urinary tract infections and genital mycotic infections (such as yeast infections) due to its mechanism of action.
<p data-bbox="63 1315 262 1494">Question 29: Comparative Effectiveness on Specific Populations</p>	<p data-bbox="262 1388 619 1421">Response to Question 29</p>	<p data-bbox="619 1299 1396 1331">Questions on Comparative Effectiveness on Specific Populations:</p> <ul data-bbox="682 1331 1967 1511" 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?.Jardiance is approved for ages 10 and older.• Are there other specific populations not noted in the question above that use the selected drug that could be considered? If so, please explain..Jardiance should not be prescribed for Type1 Diabetes or

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Question	Sub-Question	Response
	<p data-bbox="262 958 619 1063">Hyperlink to Citation - Additional Materials for Question 29</p> <p data-bbox="262 1161 619 1307">Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29</p> <p data-bbox="262 1356 619 1469">Evidence Submitted include a cost-effectiveness measure?</p>	<p data-bbox="735 251 1934 324">for individuals at high risk for infections or recurrent infections. Should not be prescribed for individuals with eGFR<30.</p> <ul data-bbox="693 324 1934 609" style="list-style-type: none">• 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 data-bbox="630 649 1934 787">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 data-bbox="672 787 1934 901" 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
	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	American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure.
	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	



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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	EMPAGLIFLOZIN
	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?	
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?	
	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

Question 31:
Patient and
Caregiver
Experience

Response to Question 31

Response

AARP, which advocates for the more than 100 million Americans age 50 and over, is pleased to submit the following comments in response to the Centers for Medicare and Medicaid Services' (CMS) Medicare Drug Price Negotiation Program Patient-Focused Listening Sessions. AARP commends CMS for soliciting feedback from the public and appreciates its efforts to ensure that patients, caregivers, and health care providers have a voice in the negotiation process. ..Data shows that brand-name drug prices have increased dramatically faster than inflation for decades. List prices for the 25 brand-name drugs with the highest total Medicare Part D spending in 2021 have increased by an average of 226% - or more than tripled - since they first entered the market. Data also shows that all but one of the top 25 drugs' lifetime price increases greatly exceeded the corresponding annual rate of general inflation (Consumer Price Index All Urban Consumers for All Items; CPI-U) over the period that each product has been on the market (i.e., product launch date until May 2023). For example, the price of Enbrel (Etanercept), used to treat rheumatoid arthritis and psoriatic arthritis, has increased by 701% since coming to market in 1998, and the price of Januvia (Sitagliptin), used to treat diabetes, has increased by 275% since entering the market in 2006. Further, the median price of a new brand-name prescription drug is now approximately \$200,000 per year, so even relatively small percentage price increases can translate into thousands of dollars and put life-saving medications out of reach of the patients who need them...High prescription drug prices can negatively affect older adults' health and financial security. [REDACTED], a Medicare enrollee from [REDACTED], needs Januvia and Jardiance to treat a health condition. His out-of-pocket costs were upwards of \$400/month for Januvia and upwards of \$140/month for Jardiance. Within one billing cycle, [REDACTED] entered the Medicare "donut hole," and could not afford the out-of-pocket costs. "At the end of the day, I'm not going to do it. ... This issue is near and dear to me but also hacking me off."..AARP fiercely believes that the needs of Medicare beneficiaries should remain paramount as the agency implements the Negotiation Program. In 2022, about 1 in 5 adults ages 65 and up either skipped, delayed, took less medication than was prescribed, or took someone else's medication last year because of concerns about cost. It is not fair or right to ask patients and taxpayers to continue paying for high prescription drug prices that are the result of broken markets. ..Successful implementation of the new federal law will help reduce prescription drug prices and costs and ensure that millions of older Americans are better able to access the prescription drugs they need at a price they can afford. The Medicare drug price negotiation process will also finally allow CMS to push back on indiscriminately escalating drug prices and ensure that taxpayer funds are paying for value – all while saving billions for Medicare and its beneficiaries. The CBO estimates that the Negotiation Program will save Medicare and the American taxpayers nearly \$98.5 billion over 10 years, reduce the budget deficit by \$25 billion in 2031, and save Medicare Part D enrollees \$7 billion in 2031 due to lower out-of-pocket costs and premiums. ..This is about real people whose lives are on the line. For decades, older Americans have paid the highest prices in the world for prescription drugs - often three times higher than people in other countries. Now is the time to change that. Effective implementation of this Program will represent a major victory for older Americans and 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

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Question **Sub-Question**

Response

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

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 can negatively affect older adults' health and financial security. [REDACTED], a Medicare enrollee from [REDACTED], needs Januvia and Jardiance to treat a health condition. His out-of-pocket costs were upwards of \$400/month for Januvia and upwards of \$140/month for Jardiance. Within one billing cycle, [REDACTED] entered the Medicare "donut hole," and could not afford the out-of-pocket costs. "At the end of the day, I'm not going to do it. ... This issue is near and dear to me but also hacking me off."

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.*

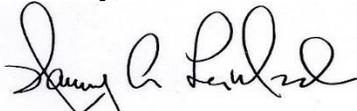
⁴ Benjamin N. Rome, Alexander C. Egilman, and Aaron S. Kesselheim, "Trends in Prescription Drug Launch Prices, 2008–2021," *Journal of the American Medical Association* 327, no. 21 (2022): 2145–47, <https://jamanetwork.com/journals/jama/fullarticle/2792986>; Deena Beasley, "U.S. New Drug Price Exceeds \$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/>.

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

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

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

⁶ 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.

⁷ 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.

⁸ *Id*

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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	EMPAGLIFLOZIN
	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	EMPAGLIFLOZIN
	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
	<p>Hyperlink to Table/Charts/Graphs - Additional Materials for Question 28</p> <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>Hyperlink to Citation - Additional Materials for Question 29</p> <p>Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29</p> <p>Evidence Submitted include a cost-effectiveness measure?</p>	<p>The Chronic Care Policy Alliance (CCPA) is a network of advocates focused on issues affecting patients living with chronic conditions. While we will let other disease-specific organizations offer their detailed perspectives on this drug, CCPA wishes to convey its views on how CMS should use the information gathered from the public...Patients with chronic diseases all have their own unique experiences – in considering comparative effectiveness, CMS should weigh equally the experiences of individuals the same as measurements of experiences of specific populations – in a way that elevates all voices, instead of letting larger voices outweigh single patients. CCPA also encourages CMS to take into account populations that may be uniquely adversely affected by negotiation, such as specific patient populations that may face new utilization or formulary restrictions. In this way, CMS can ensure that it pursues a patient-centered approach.</p>

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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? 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	EMPAGLIFLOZIN
	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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Question Sub-Question

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	EMPAGLIFLOZIN
	Q26 - Respondent Name	
	Q26 - Organization Name (if applicable)	██████████
	Respondent Email	
Question 27: Prescribing Information	Who is completing this form?	HCW
	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?	
	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 SM has been on Jardiance for almost one year. Her symptoms of heart failure have improved and there has been a decrease in her NT-proBNP numbers. Her insurance was able to cover Jardiance since first prescribed however, nearing the end of the year, the patient entered the “donut hole” and her copay increased to \$500 for a month's supply. She is not able to pay this and wouldn't qualify for patient assistance due to having active pharmacy insurance. She must remain off of her SGLT2i until she is out of the “donut hole.”</p>



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Question	Sub-Question	Response
Question 26: Respondent Information	Selected Drug	EMPAGLIFLOZIN
	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 Empagliflozin. 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="262 849 609 873">Response to Question 29</p> <p data-bbox="262 963 609 1060">Hyperlink to Citation - Additional Materials for Question 29</p> <p data-bbox="262 1166 609 1304">Hyperlink to Table/Charts/Graphs - Additional Materials for Question 29</p> <p data-bbox="262 1360 609 1458">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 Empagliflozin. 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.