



Maximum Fair Price (MFP) Explanation for Jardiance

Introduction

In August 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA) (P.L. 117-169) into law. For the first time, the law provides Medicare with the ability to directly negotiate the prices of certain high expenditure, single source drugs without generic or biosimilar competition. On March 15, 2023, the Centers for Medicare & Medicaid Services (CMS) issued [initial guidance](#) for the Medicare Drug Price Negotiation Program (the “Negotiation Program”), including requests for public comment on key elements. On June 30, 2023, CMS issued [revised guidance](#) detailing the requirements and parameters of the Negotiation Program for the first cycle of negotiations.¹ CMS engaged in negotiations with participating manufacturers between October 1, 2023 and August 1, 2024. These negotiations resulted in agreements establishing prices (which the IRA refers to as “maximum fair prices” or “MFPs”) that will be effective beginning in 2026 (the first cycle of negotiations is referred to as negotiations for “initial price applicability year 2026” because any agreed-upon prices will be effective in 2026). CMS published the agreed-upon MFPs on August 15, 2024.

The MFP explanation for Jardiance for the agreed-upon MFP that resulted from the negotiations for initial price applicability year 2026 with Boehringer Ingelheim, the manufacturer of Jardiance (the “Primary Manufacturer”), provides information about the negotiations for Jardiance. This information includes CMS’ perspective on the data considered that had the greatest impact in CMS’ determination of offers and consideration of counteroffers during the negotiation process through which the parties reached agreement on an MFP.² In some respects, the Primary Manufacturer had a different perspective on the relevant data. The parties to the negotiation had productive exchanges during the negotiation meetings described below in which they discussed their respective views, and these exchanges resulted in the exchange of offer(s) and counteroffer(s) among the parties and, ultimately, an agreed-upon MFP for Jardiance.

On the basis of the factors described below and the related considerations and evidence, CMS negotiated with the Primary Manufacturer in good faith and consistent with the requirements of the law on behalf of people with Medicare and the Medicare program. Throughout the negotiation process and in accordance with the IRA, CMS’ goal was to achieve agreement with the Primary Manufacturer on the lowest possible MFP for Jardiance that would be consistent with the process defined in the IRA for these price negotiations. CMS believes that the agreed-upon MFP achieves this aim. The negotiation process

¹ The [Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026](#), is referred to throughout this document as the revised guidance.

² Section 1195(a)(2) of the Social Security Act (the “Act”) requires CMS to publish an explanation for the MFP with respect to the factors as applied under section 1194(e) for each selected drug. The MFP explanation is discussed in section 60.6.1 of the [revised guidance](#).

ended in both parties agreeing to an MFP of \$197.00 for Jardiance by the conclusion of the negotiation period on August 1, 2024.³ The agreed-upon MFP is set to take effect on January 1, 2026.

The MFP explanation contains the following components:

- MFP Explanation Narrative for Jardiance
 - Summary of the Negotiation Process
 - Indications for Jardiance
 - Factors Applied
 - Manufacturer-Specific Data
 - Evidence about Jardiance and Therapeutic Alternatives to Jardiance
 - Therapeutic Alternatives
 - Outcomes and Additional Considerations
 - Citations to Data Reviewed during the Negotiation Process for Jardiance
- Redacted Negotiation Meeting Summaries for Jardiance
- Redacted Data Submitted by the Primary Manufacturer and Other Interested Parties for Jardiance

MFP Explanation Narrative for Jardiance

Summary of the Negotiation Process

CMS followed the negotiation process laid out in the IRA and in the revised guidance. On August 29, 2023, CMS announced the 10 selected drugs for the first cycle of negotiations, which included Jardiance. The Primary Manufacturers of the selected drugs signed agreements to participate in the Negotiation Program by the deadline in the IRA of October 1, 2023 and submitted information on the selected drugs by the deadline in the IRA of October 2, 2023.

CMS collected relevant data from numerous sources, such as written submissions from the Primary Manufacturers and other interested parties in response to an information collection request issued for the Negotiation Program (referred to as the “Negotiation Program information collection request” throughout this document), feedback from patient-focused listening sessions, meetings between CMS and the Primary Manufacturers to discuss the information submitted, and CMS’ literature review.⁴

Using the information collected, CMS then developed initial offers for the selected drugs, which were based on the factors outlined in the IRA for CMS’ determination of offers and which CMS developed in accordance with the process described in the revised guidance.⁵ As required by the IRA, CMS’ initial offers each included a concise justification on the range of evidence and other information within the negotiation factors that CMS found compelling during the development of the initial offer. The Primary

³ The MFP is expressed as the price per 30-days equivalent supply. See section 60.1 of the [revised guidance](#) and the [Negotiated Prices for Initial Price Applicability Year 2026 Fact Sheet](#) for additional information.

⁴ 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.

⁵ Section 1194(e) of the Act requires CMS to consider certain data as the basis for all offers and counteroffers in the negotiation. These data, which are referred to in this document as the “negotiation factors,” are discussed in more detail later in this document. More information on the negotiation factors is also available in sections 50, 60.3 and 60.4 of the [revised guidance](#). CMS’ process for developing the initial offers is described in section 60.3 of the revised guidance.

Manufacturers each responded by declining CMS' initial offer and providing a written counteroffer and justification for such offer, including considerations based on the negotiation factors.

CMS considered each counteroffer proposed by the Primary Manufacturers and declined each counteroffer. CMS and each Primary Manufacturer then held three negotiation meetings. These meetings included extensive discussion of the negotiation factors, including any new information consistent with the factors that may have become available about the selected drugs or therapeutic alternatives, CMS' initial offer and the Primary Manufacturer's written counteroffer, and, in some cases, additional proposals for an MFP.

Across the first cycle of negotiations for all ten selected drugs, more than 50 revised offers or counteroffers were proposed by CMS or a Primary Manufacturer, not including the ten initial offers CMS made and the ten written counteroffers provided by Primary Manufacturers. During the negotiation meetings, CMS revised its initial offer for each selected drug upwards at least once in response to the discussions with the Primary Manufacturer. While many of the details of the negotiations are confidential between CMS and each Primary Manufacturer, the frequency of revised offers and counteroffers in the first cycle of negotiations indicates the robustness of the negotiations that occurred for each of the ten drugs. CMS' approach to its negotiations with each Primary Manufacturer turned on the particular details relevant to each selected drug and was sensitive to the issues raised during the course of CMS' conversations with the Primary Manufacturer. CMS anticipates this drug-specific approach will continue to inform CMS' negotiations with participating manufacturers in future cycles of negotiation.

Overall, in six of ten negotiations CMS moved more than the Primary Manufacturer during the meetings and for the final offer (if applicable) prior to reaching agreement, and in four of ten negotiations the Primary Manufacturer moved more than CMS prior to reaching agreement. For five of the selected drugs, this process of exchanging revised offers and counteroffers resulted in CMS and the Primary Manufacturer reaching an agreement on a negotiated price for the selected drug in association with a negotiation meeting. In four of these cases, CMS accepted a revised counteroffer proposed by the Primary Manufacturer. For the remaining five selected drugs, CMS sent a written final offer to the Primary Manufacturer, consistent with the process described in the revised guidance, and in each instance, the Primary Manufacturer accepted CMS' offer on or before the statutory deadline. Throughout the negotiation process, CMS and the Primary Manufacturers exchanged perspectives about a range of topics related to the negotiation factors, and while the parties did not always agree, CMS appreciated the Primary Manufacturers' engagement.

A detailed timeline of the negotiation process for Jardiance is below.

- August 29, 2023: CMS announced the 10 selected drugs for initial price applicability year 2026
- October 1, 2023: Deadline for the Primary Manufacturer to sign an agreement to participate in the Negotiation Program
- October 2, 2023: Deadline for the Primary Manufacturer and the public to submit information related to Jardiance in response to the Negotiation Program information collection request
- October 24, 2023: CMS met with the Primary Manufacturer regarding its response to the Negotiation Program information collection request
- November 8, 2023: CMS held a patient-focused listening session for Jardiance
- February 1, 2024: CMS provided the Primary Manufacturer with CMS' initial offer
- March 1, 2024: The Primary Manufacturer rejected CMS' initial offer and provided CMS with a counteroffer

- March 29, 2024: CMS rejected the Primary Manufacturer’s counteroffer and invited the Primary Manufacturer to a negotiation meeting
- April 24, 2024: CMS and the Primary Manufacturer met for the first negotiation meeting
- May 20, 2024: CMS and the Primary Manufacturer met for the second negotiation meeting
- June 21, 2024: CMS and the Primary Manufacturer met for the third negotiation meeting
- August 1, 2024: The negotiation period ended
- August 15, 2024: MFP of \$197.00 was published

Indications for Jardiance

Jardiance is a sodium-glucose cotransporter 2 inhibitor that works by helping the kidneys remove glucose (sugar) and sodium from the bloodstream. Jardiance is used to treat conditions like type 2 diabetes mellitus (T2DM), chronic kidney disease (CKD), and heart failure (HF). It may be combined with other medications or lifestyle modifications, like diet and exercise, to treat these conditions.⁶

For Jardiance, CMS included the following indications in its assessment⁷:

Description of indication	Terminology used in this document
<ul style="list-style-type: none"> • To reduce the risk of cardiovascular (CV) death and hospitalization for heart failure (HF) in adults with HF. 	HF
<ul style="list-style-type: none"> • To reduce the risk of sustained decline in eGFR, end-stage kidney disease, CV death, and hospitalization in adults with chronic kidney disease at risk of progression. 	CKD
<ul style="list-style-type: none"> • To reduce the risk of CV death in adults with type 2 diabetes mellitus and established CV disease. 	T2DM with CVD
<ul style="list-style-type: none"> • 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. 	T2DM

Table 1. CKD=chronic kidney disease; CVD=cardiovascular disease; T2DM=type 2 diabetes mellitus. For purposes of CMS’ consideration of indications for Jardiance, CMS grouped certain indications using the terminology as shown in this table. CMS’ use of the terms listed here does not alter the FDA-approved indications for Jardiance.

⁶ To compose this brief description, CMS used various sources, including MedlinePlus, a free online health information resource for patients and the general public. MedlinePlus is a service of the National Library of Medicine (NLM), a part of the U.S. National Institutes of Health (NIH). For more information about any drugs or conditions mentioned in this document, MedlinePlus can be accessed at: <https://medlineplus.gov/>.

⁷ CMS’ process for identifying indications for a selected drug was to identify the FDA-approved indication(s) not otherwise excluded from coverage or otherwise restricted under section 1860D-2(e)(2) of the Act, using prescribing information approved by the FDA for the selected drug, in accordance with section 1194(e)(2)(B) of the Act. CMS considered off-label use when identifying indications if such use was included in nationally recognized, evidence-based guidelines and recognized in CMS-approved Part D compendia. CMS included indications that met these criteria during the negotiation period. Indications newly approved by FDA or included in nationally recognized, evidence-based guidelines and recognized in CMS-approved Part D compendia after the end of the negotiation period were not included.

Factors Applied

Consistent with the IRA, CMS considered certain negotiation factors as the basis for determining all offers and counteroffers during the negotiation process.

The following negotiation factors are referred to in this document as “manufacturer-specific data”⁸:

- Research and development (R&D) costs of the Primary Manufacturer for Jardiance and the extent to which the Primary Manufacturer has recouped R&D costs;
- Current unit costs of production and distribution of Jardiance;
- Prior Federal financial support for novel therapeutic discovery and development with respect to Jardiance;
- Data on pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals for New Drug Applications and Biologics License Applications for Jardiance;⁹ and
- Market data and revenue and sales volume data for Jardiance in the United States (U.S.).

The following negotiation factors are referred to in this document as “evidence about Jardiance and therapeutic alternatives to Jardiance”¹⁰:

- The extent to which Jardiance represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives;
- Prescribing information approved by the FDA for Jardiance and therapeutic alternatives to Jardiance;
- Comparative effectiveness of Jardiance and therapeutic alternatives to Jardiance, taking into consideration the effects of Jardiance and therapeutic alternatives to Jardiance on specific populations, such as individuals with disabilities, the elderly, the terminally ill, children, and other patient populations; and
- The extent to which Jardiance and therapeutic alternatives to Jardiance address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy.

The below sections describe how CMS considered and applied these factors during the negotiation process. CMS considered these factors, taking into account all data in totality during the negotiation process.

CMS and the Primary Manufacturer did not always agree on the information presented below, and the Primary Manufacturer was not restricted to consideration of these factors during the negotiation process but was free to discuss any topics with CMS it deemed relevant to its consideration of offer(s) and counteroffer(s) for Jardiance.

⁸ These factors are listed at section 1194(e)(1) of the Act.

⁹ New Drug Applications are approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act and Biologics License Applications are approved under section 351(a) of the Public Health Service Act.

¹⁰ These factors are listed at section 1194(e)(2) of the Act. In accordance with section 1194(e)(2) and section 1182(e) of Title XI of the Act, CMS did not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, non-disabled, or not terminally ill, and, consistent with section 1182(e) of Title XI of the Act, did not use quality adjusted life years (QALYs).

Manufacturer-Specific Data

CMS considered the information submitted by the Primary Manufacturer related to the manufacturer-specific data factors. These factors include R&D costs and the extent to which the Primary Manufacturer has recouped R&D costs, current unit costs of production and distribution, prior Federal financial support, data on pending and approved patents and exclusivities recognized by the FDA, and market data, including revenue and sales volume data for the drug in the United States. CMS considered these factors in totality, as part of its application of the negotiation factors during the negotiation process.

The Primary Manufacturer provided CMS with information for each of these factors in response to the Negotiation Program information collection request.¹¹ For R&D costs, CMS requested information separated into various categories of costs related to R&D, including acquisition costs, pre-clinical research costs, post-Investigational New Drug costs, costs of failed or abandoned products related to Jardiance, and other allowable direct costs. CMS also requested the global and U.S. total lifetime net revenue for Jardiance to provide insight into the extent to which the Primary Manufacturer has recouped R&D costs. CMS requested current average unit costs of production for Jardiance and current average unit costs of distribution for Jardiance separately, as well as a description of the methodology the Primary Manufacturer used to estimate such costs. For information related to prior Federal financial support, CMS requested the total amount of Federal financial support received, as well as a breakdown by various types of financial support, like tax credits and National Institutes of Health funding. CMS requested information on patents, both expired and unexpired, issued by the U.S. Patent and Trademark Office, patent applications, regulatory exclusivity periods, and active and pending FDA applications and approvals. For market data, CMS requested information about the prices for Jardiance and volume dispensed for other payers in the U.S. market, including commercial payers (e.g., the U.S. commercial average net price), Medicaid (Medicaid Best Price), and other Federal payers (the Federal supply schedule price and the Big Four price).

Throughout the negotiation process, CMS holistically considered the information submitted by the Primary Manufacturer related to the manufacturer-specific data negotiation factors for the purpose of negotiating an MFP for Jardiance. For example, CMS applied information on prices for Jardiance available to other payers in the U.S. market and how they compared to any offers or counteroffers when considering whether a potential price was consistent with CMS' aim to arrive at an agreement on the lowest possible MFP. The totality of CMS' application of these factors, in conjunction with application of the factors described below, informed CMS' negotiation of the MFP with the Primary Manufacturer.

Evidence about Jardiance and Therapeutic Alternatives to Jardiance

CMS considered information related to the negotiation factors regarding evidence about Jardiance and therapeutic alternatives to Jardiance. CMS' holistic consideration of clinical benefit included evidence from sources such as: pivotal clinical trials, pre-specified subgroup analyses, clinical practice guidelines, expert consensus statements, comparative clinical evidence, published literature reviews, real-world evidence, and FDA prescription drug labeling, among others. CMS evaluated the evidence based on a variety of considerations, including relevance and credibility, giving priority to well-designed and well-

¹¹ In accordance with the revised guidance, CMS treats R&D costs and the extent to which they are recouped, unit costs of production and distribution, pending patent applications, and market, revenue, and sales volume data as proprietary, unless the information that is provided to CMS is already publicly available. For more information, see section 40.2.1 of the [revised guidance](#).

conducted studies, as stated in the revised guidance.¹² In general, CMS prioritized direct comparative evidence (e.g., head-to-head randomized controlled trials) when available. CMS also reviewed mixed and/or indirect treatment comparisons (e.g., network meta-analyses) when available and real-world evidence (e.g., observational studies) when available as part of its holistic assessment of comparative evidence.

In addition to information from the Primary Manufacturer, CMS received information from the public, including from patients during the patient-focused listening session held by CMS on November 8, 2023.¹³ Patient input was important to CMS' consideration of the evidence about Jardiance and therapeutic alternatives to Jardiance, including to help identify outcomes of interest for patients and to understand additional considerations such as the drug's impact on patients' day-to-day lives. For example, speakers during the patient-focused listening sessions described the positive impact Jardiance had on the symptoms they experienced following a cardiovascular event. This was one consideration among the many that informed CMS' understanding of the factors regarding evidence about Jardiance and its therapeutic alternatives. Throughout all of the patient-focused listening sessions for the first cycle of negotiations, speakers provided insight on the importance of affordability and access, which provided CMS helpful context for the speakers' described experiences.

Therapeutic Alternatives

The IRA directs CMS to compare Jardiance to therapeutic alternatives in its determination of offers and consideration of counteroffers for Jardiance.¹⁴ In the revised guidance, CMS defines a therapeutic alternative for the first cycle of negotiations as a pharmaceutical product that is clinically comparable to the selected drug.¹⁵

Importantly, use of the term "therapeutic alternative" in this MFP explanation is limited to the purposes and definition outlined in the IRA and the revised guidance. Use of this term does not suggest that CMS believes such drugs are interchangeable or otherwise universally appropriate to prescribe for an individual in place of Jardiance or that these are the only pharmaceutical treatments that might be used by a person with one of the indications treated by Jardiance. CMS trusts that patients and health care providers will continue to choose the therapy that best suits a given patient's needs based on the patient's health, history, experience, and preferences, the provider's expertise, FDA-approved prescribing information, and relevant clinical guidelines, as applicable.

During the negotiation process, CMS identified therapeutic alternatives to Jardiance based on a holistic consideration of the available evidence from a range of sources. In addition to the sources listed above,

¹² In section 50.2 of the [revised guidance](#), CMS stated, "When reviewing the literature from the public and manufacturer submissions as well as literature from CMS' review, CMS will consider the source, rigor of the study methodology, current relevance to the selected drug and its therapeutic alternative(s), whether the study has been through peer review, study limitations, degree of certainty of conclusions, risk of bias, study time horizons, generalizability, study population, and relevance to the negotiation factors listed in section 1194(e)(2) of the Act to ensure the integrity of the contributing data within the negotiation process. CMS will prioritize research, including both observational research and research based on randomized samples, that is methodologically rigorous, appropriately powered (i.e., has sufficient sample size) to answer the primary question of the research, and structured to avoid potential false positive findings due to multiple subgroup analyses."

¹³ The redacted transcript for this patient-focused listening session is available at the following link: <https://www.cms.gov/files/document/jardiance-transcript-110823.pdf>.

¹⁴ See section 1194(e)(2) of the Act and sections 50, 60.3 and 60.4 of the [revised guidance](#) for additional information.

¹⁵ This definition appears in Appendix C of the [revised guidance](#).

such as data submitted by the Primary Manufacturer and the public and widely accepted clinical guidelines, other examples of data sources used include the following: drug classification systems commonly used in the public and commercial sector for formulary development, indications included in CMS-approved Part D compendia, and drug or drug class reviews.

The following table lists the therapeutic alternatives, among all clinically comparable alternatives that CMS reviewed, which were particularly relevant to CMS’ consideration, due to guideline recommendations, utilization in the Medicare population, and other considerations.

Indication	Therapeutic Alternatives
HF	<ul style="list-style-type: none"> • Dapagliflozin
CKD	<ul style="list-style-type: none"> • Dapagliflozin
T2DM with CVD	<ul style="list-style-type: none"> • Canagliflozin • Dapagliflozin • Dulaglutide • Liraglutide • Semaglutide
T2DM	<ul style="list-style-type: none"> • Canagliflozin • Dapagliflozin • Dulaglutide • Glimepiride • Glipizide • Metformin • Pioglitazone • Semaglutide • Sitagliptin

Table 2. CKD=chronic kidney disease; CVD=cardiovascular disease; HF=heart failure; T2DM=type 2 diabetes mellitus. Use of the term “therapeutic alternative” in this MFP explanation is limited to the purposes and definition outlined in the IRA and the revised guidance. Use of this term does not suggest that CMS believes such drugs are interchangeable or otherwise universally appropriate to prescribe for an individual in place of Jardiance or that these are the only pharmaceutical treatments that might be used by a person with one of the indications treated by Jardiance. CMS trusts that patients and health care providers will continue to choose the therapy that best suits a given patient’s needs based on the patient’s health, history, experience, and preferences, the provider’s expertise, FDA-approved prescribing information, and relevant clinical guidelines, as applicable.

CMS considered utilization for Jardiance and its therapeutic alternatives by indication as one part of its application of the negotiation factors.

Outcomes and Additional Considerations

Outcomes are measurable effects or impacts of a treatment or intervention. Outcomes can be used to measure differences in the safety or effectiveness of different treatments. Patient-centered outcomes are outcomes identified by patients that are important to how they feel, function, or survive. To consider comparative effectiveness between Jardiance and therapeutic alternatives to Jardiance, CMS identified clinically relevant and patient-centered outcomes of interest from the body of available literature to evaluate for each indication of Jardiance. CMS then identified evidence comparing Jardiance to therapeutic alternatives based on these outcomes. The following table includes a non-exhaustive list of outcomes that were of interest to CMS in its consideration of Jardiance:

Indication	Effectiveness Outcomes	Safety Outcomes
HF	<ul style="list-style-type: none"> • Hospitalization for HF • Cardiovascular death • Patient-reported health status (e.g., KCCQ) 	<ul style="list-style-type: none"> • Serious adverse events • Tolerability (e.g., discontinuation due to adverse events) • Urinary tract infection • Genital mycotic infection
CKD	<ul style="list-style-type: none"> • Progression of kidney disease (e.g., renal composite outcome) • Cardiovascular death • Hospitalization for HF 	<ul style="list-style-type: none"> • Serious adverse events • Tolerability (e.g., discontinuation due to adverse events) • Urinary tract infection • Genital mycotic infection
T2DM with CVD	<ul style="list-style-type: none"> • Cardiovascular death • Hospitalization for HF • Stroke • Myocardial infarction • Glycemic control (e.g., hemoglobin A1c) 	<ul style="list-style-type: none"> • Serious adverse events • Tolerability (e.g., discontinuation due to adverse events) • Urinary tract infection • Genital mycotic infection
T2DM	<ul style="list-style-type: none"> • Glycemic control (e.g., hemoglobin A1c) 	<ul style="list-style-type: none"> • Serious adverse events • Tolerability (e.g., discontinuation due to adverse events) • Urinary tract infection • Genital mycotic infection • Hypoglycemia

Table 3. CKD=chronic kidney disease; CVD=cardiovascular disease; HF=heart failure; KCCQ = Kansas City Cardiomyopathy Questionnaire; T2DM=type 2 diabetes mellitus. Outcomes identified in this table were of interest to CMS in its evaluation of Jardiance. Evidence to support an assessment may not have been available for every outcome of interest.

Outcomes, like those listed above, were identified as being of interest to CMS based on their importance to patients and their ability to measure how effective and safe a drug is when used to treat these indications. For example, major adverse cardiovascular events, like myocardial infarction (i.e., heart attack), stroke, hospitalization for HF, and death from cardiovascular causes, are key outcomes that are often used to evaluate the effectiveness of treatments for patients with T2DM with CVD. In addition, across indications, the risk of serious adverse events and tolerability, or the degree to which patients can tolerate adverse events associated with taking a drug, are outcomes that reflect important safety considerations when evaluating drugs for these indications.

Additionally, CMS considered the extent to which Jardiance represents a therapeutic advance as compared to existing therapeutic alternatives, and the extent to which Jardiance and its therapeutic alternatives address an unmet medical need. CMS also evaluated access, equity, and health outcomes for specific populations (including individuals with disabilities, the elderly, individuals who are terminally ill, children, and other patient populations).

For the purpose of negotiating the MFP for Jardiance, CMS holistically considered the negotiation factors regarding evidence about Jardiance and its therapeutic alternatives, including consideration of the clinical benefit of Jardiance in the context of its therapeutic alternatives. For example, CMS applied its understanding of the comparative effectiveness of Jardiance and its therapeutic alternatives for each of the identified indications, including for the management of glycemic control in patients with T2DM and reduction of cardiovascular risk for patients with T2DM with CVD, when negotiating with the Primary Manufacturer. CMS' holistic assessment was informed by additional contextual considerations, such as use in patients with certain common co-occurring conditions treated by Jardiance, complexity of treatment regimens, FDA safety labeling, and patients' preferences regarding treatment.

Throughout the negotiation process, including the development of the initial offer and in the consideration of any offers and counteroffers, CMS applied these and other factors regarding evidence about Jardiance and therapeutic alternatives. The totality of CMS' application of these factors, in conjunction with application of the manufacturer-submitted data negotiation factors described above, informed CMS' negotiation of the MFP with the Primary Manufacturer.

Citations to Data Reviewed during the Negotiation Process for Jardiance

CMS provides below a list of citations representative of evidence that CMS reviewed during the negotiation process, including citations provided by the Primary Manufacturer and the public in response to the Negotiation Program information collection request, those included in CMS' initial offer concise justification, and other citations which were considered during the evaluation of the Primary Manufacturer's counteroffer and during negotiation meetings.

Consistent with the IRA and section 1182(e) of Title XI of the Act, CMS did not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill, and, consistent with section 1182(e) of Title XI of the Act, did not use quality adjusted life years (QALYs). Inclusion on this list of a citation that contains such evidence does not mean that CMS used such evidence in the course of the negotiation.

This list is intended to provide insight into the range of evidence that various parties, including CMS and the Primary Manufacturer, identified as being relevant to the negotiation. This list does not represent the totality of evidence that CMS reviewed and considered as part of its holistic consideration of the negotiation factors in the determination of any offers and consideration of any counteroffers.

1. Aïdoud A, Gana W, Poitau F, Debacq C, Leroy V, Nkodo JA, et al. High Prevalence of Geriatric Conditions Among Older Adults With Cardiovascular Disease. *J Am Heart Assoc.* 2023;12(2):e026850. Epub 20230111. doi: 10.1161/jaha.122.026850. PubMed PMID: 36628962; PubMed Central PMCID: PMC9939057.
2. Alfaddagh A, Welty FK. Management of Stable Coronary Artery Disease in Patients with Diabetes Mellitus. *American College of Cardiology.* 2020. Available from: <https://www.acc.org/Latest-in-Cardiology/Articles/2020/08/18/07/41/Management-of-Stable-Coronary-Artery-Disease-in-Patients-with-DM>.
3. American Diabetes Association Professional Practice Committee. 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2024. *Diabetes Care.* 2024;47(Suppl 1):S179-S218. doi: 10.2337/dc24-S010. PubMed PMID: 38078592; PubMed Central PMCID: PMC10725811.
4. American Diabetes Association Professional Practice Committee. 11. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes-2024. *Diabetes Care.* 2024;47(Suppl 1):S219-S30. doi: 10.2337/dc24-S011. PubMed PMID: 38078574; PubMed Central PMCID: PMC10725805.
5. American Diabetes Association Professional Practice Committee. 13. Older Adults: Standards of Care in Diabetes-2024. *Diabetes Care.* 2024;47(Suppl 1):S244-S57. doi: 10.2337/dc24-S013. PubMed PMID: 38078580; PubMed Central PMCID: PMC10725804.
6. American Diabetes Association Professional Practice Committee. 14. Children and Adolescents: Standards of Care in Diabetes-2024. *Diabetes Care.* 2024;47(Suppl 1):S258-S81. doi: 10.2337/dc24-S014. PubMed PMID: 38078582; PubMed Central PMCID: PMC10725814.
7. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. *Diabetes Care.* 2024;47(Suppl 1):S20-S42. doi: 10.2337/dc24-S002. PubMed PMID: 38078589; PubMed Central PMCID: PMC10725812.
8. American Diabetes Association Professional Practice Committee. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2024. *Diabetes Care.*

- 2024;47(Suppl 1):S158-S78. doi: 10.2337/dc24-S009. PubMed PMID: 38078590; PubMed Central PMCID: PMC10725810.
9. American Geriatrics Society 2023 updated AGS Beers Criteria[®] for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-81. Epub 20230504. doi: 10.1111/jgs.18372. PubMed PMID: 37139824.
 10. Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, Bohm M, et al. Empagliflozin in Heart Failure with a Preserved Ejection Fraction. *N Engl J Med.* 2021;385(16):1451-61. Epub 20210827. doi: 10.1056/NEJMoa2107038. PubMed PMID: 34449189.
 11. Arnott C, Li Q, Kang A, Neuen BL, Bompont S, Lam CSP, et al. Sodium-Glucose Cotransporter 2 Inhibition for the Prevention of Cardiovascular Events in Patients With Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. *J Am Heart Assoc.* 2020;9(3):e014908. Epub 20200129. doi: 10.1161/JAHA.119.014908. PubMed PMID: 31992158; PubMed Central PMCID: PMC7033896.
 12. Arslanian SA, Hannon T, Zeitler P, Chao LC, Boucher-Berry C, Barrientos-Pérez M, et al. Once-Weekly Dulaglutide for the Treatment of Youths with Type 2 Diabetes. *N Engl J Med.* 2022;387(5):433-43. Epub 20220604. doi: 10.1056/NEJMoa2204601. PubMed PMID: 35658022.
 13. AstraZeneca. Farxiga (dapagliflozin) [package insert]. U.S. Food and Drug Administration. Revised 2023 Sep. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/202293s030lbl.pdf.
 14. Azad N, Lemay G. Management of chronic heart failure in the older population. *J Geriatr Cardiol.* 2014;11(4):329-37. doi: 10.11909/j.issn.1671-5411.2014.04.008. PubMed PMID: 25593582; PubMed Central PMCID: PMC4292097.
 15. Bhatt DL, Szarek M, Steg PG, Cannon CP, Leiter LA, McGuire DK, et al. Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure. *N Engl J Med.* 2021;384(2):117-28. Epub 20201116. doi: 10.1056/NEJMoa2030183. PubMed PMID: 33200892.
 16. Blonde L, Umpierrez GE, Reddy SS, McGill JB, Berga SL, Bush M, et al. American Association of Clinical Endocrinology Clinical Practice Guideline: Developing a Diabetes Mellitus Comprehensive Care Plan-2022 Update. *Endocr Pract.* 2022;28(10):923-1049. Epub 20220811. doi: 10.1016/j.eprac.2022.08.002. PubMed PMID: 35963508; PubMed Central PMCID: PMC10200071.
 17. Boehringer Ingelheim Pharmaceuticals, Inc. Jardiance (empagliflozin) [package insert]. U.S. Food and Drug Administration. 2023 Sep. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/204629s040lbl.pdf.
 18. Boehringer Ingelheim. A Phase III Randomised, Double-blind Trial to Evaluate the Effect of 12 Weeks Treatment of Once Daily EMPagliflozin 10 mg Compared With Placebo on Exercise Ability and Heart Failure Symptoms, In Patients With Chronic Heart Failure With Reduced Ejection Fraction (HFREF) (EMPERIAL-reduced); NCT03448419. 2020 Nov 27. Available from: <https://www.clinicaltrials.gov/study/NCT03448419>.
 19. Boehringer Ingelheim. A Phase III Randomised, Double-blind Trial to Evaluate the Effect of 12 Weeks Treatment of Once Daily EMPagliflozin 10 mg Compared With Placebo on Exercise Ability and Heart Failure Symptoms, In Patients With Chronic Heart Failure With Preserved Ejection Fraction (HFpEF) (EMPERIAL - Preserved); NCT03448406. 2020 Dec 08. Available from: <https://www.clinicaltrials.gov/study/NCT03448406#collaborators-and-investigators>.
 20. Boehringer Ingelheim. EMPACT-MI: A Streamlined, Multicentre, Randomised, Parallel Group, Double-blind Placebo-controlled Superiority Trial to Evaluate the Effect of EMPagliflozin on Hospitalisation for Heart Failure and Mortality in Patients With aCuTe Myocardial Infarction;

- NCT04509674. 2023 Nov 14. Available from:
<https://www.clinicaltrials.gov/study/NCT04509674>.
21. Bron M, Marynchenko M, Yang H, Yu AP, Wu EQ. Hypoglycemia, treatment discontinuation, and costs in patients with type 2 diabetes mellitus on oral antidiabetic drugs. *Postgrad Med*. 2012;124(1):124-32. doi: 10.3810/pgm.2012.01.2525. PubMed PMID: 22314122.
 22. Butler J, Filippatos G, Jamal Siddiqi T, Brueckmann M, Böhm M, Chopra VK, et al. Empagliflozin, Health Status, and Quality of Life in Patients With Heart Failure and Preserved Ejection Fraction: The EMPEROR-Preserved Trial. *Circulation*. 2022;145(3):184-93. Epub 20211115. doi: 10.1161/circulationaha.121.057812. PubMed PMID: 34779658; PubMed Central PMCID: PMC8763045.
 23. Cahn A, Mosenzon O, Wiviott SD, Rozenberg A, Yanuv I, Goodrich EL, et al. Efficacy and Safety of Dapagliflozin in the Elderly: Analysis From the DECLARE-TIMI 58 Study. *Diabetes Care*. 2020;43(2):468-75. Epub 20191216. doi: 10.2337/dc19-1476. PubMed PMID: 31843945.
 24. Carvalho PEP, Veiga TMA, Simões ESAC, Gewehr DM, Dagostin CS, Fernandes A, et al. Cardiovascular and renal effects of SGLT2 inhibitor initiation in acute heart failure: a meta-analysis of randomized controlled trials. *Clin Res Cardiol*. 2023;112(8):1044-55. Epub 20230102. doi: 10.1007/s00392-022-02148-2. PubMed PMID: 36592186; PubMed Central PMCID: PMC9807098.
 25. Chen HB, Yang YL, Meng RS, Liu XW. Indirect comparison of SGLT2 inhibitors in patients with established heart failure: evidence based on Bayesian methods. *ESC Heart Fail*. 2023;10(2):1231-41. Epub 20230126. doi: 10.1002/ehf2.14297. PubMed PMID: 36702979; PubMed Central PMCID: PMC10053258.
 26. Chen X, Wang J, Lin Y, Yao K, Xie Y, Zhou T. Cardiovascular outcomes and safety of SGLT2 inhibitors in chronic kidney disease patients. *Front Endocrinol (Lausanne)*. 2023;14:1236404. Epub 20231116. doi: 10.3389/fendo.2023.1236404. PubMed PMID: 38047108; PubMed Central PMCID: PMC10690412.
 27. Christopher C, Kc B, Shrestha S, Blebil AQ, Alex D, Mohamed Ibrahim MI, et al. Medication use problems among older adults at a primary care: A narrative of literature review. *Aging Med (Milton)*. 2022;5(2):126-37. Epub 20220315. doi: 10.1002/ags2.12203. PubMed PMID: 35783113; PubMed Central PMCID: PMC9245166.
 28. Chronic Kidney Disease Basics [Internet]. Georgia: U.S. Centers for Disease Control and Prevention; [cited 2023 Oct 2]. Available from: https://www.cdc.gov/kidney-disease/about/?CDC_AAref_Val=https://www.cdc.gov/kidneydisease/basics.html.
 29. Chronic Kidney Disease in the United States, 2023 [Internet]. Georgia: U.S. Centers for Disease Control and Prevention [cited 2023 Oct 2]. Available from: https://www.cdc.gov/kidney-disease/php/data-research/?CDC_AAref_Val=https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html.
 30. Claggett B, Lachin JM, Hantel S, Fitchett D, Inzucchi SE, Woerle HJ, et al. Long-Term Benefit of Empagliflozin on Life Expectancy in Patients With Type 2 Diabetes Mellitus and Established Cardiovascular Disease. *Circulation*. 2018;138(15):1599-601. doi: 10.1161/circulationaha.118.033810. PubMed PMID: 30354516.
 31. Cox Z. DICTATE-AHF - Efficacy and Safety of Dapagliflozin in Acute Heart Failure NCT04298229. ESC Congress 2023; 2023 August 28. Available from: <https://www.acc.org/-/media/Clinical/PDF-Files/Approved-PDFs/2023/03/04/ESC23/28Aug/DICTATE-AHF-esc-2023.pdf>.
 32. Desai RJ, Glynn RJ, Everett BM, Schneeweiss S, Wexler DJ, Bessette LG, et al. Comparative effectiveness of Empagliflozin in reducing the burden of recurrent cardiovascular

- hospitalizations among older adults with diabetes in routine clinical care. *Am Heart J.* 2022;254:203-15. Epub 20220921. doi: 10.1016/j.ahj.2022.09.008. PubMed PMID: 36150454.
33. Doshi S, Wish JB. Strategies to Reduce Rehospitalization in Patients with CKD and Kidney Failure. *Clin J Am Soc Nephrol.* 2021;16(2):328-34. Epub 20200713. doi: 10.2215/CJN.02300220. PubMed PMID: 32660962; PubMed Central PMCID: PMC7863646.
 34. Duan XY, Liu SY, Yin DG. Comparative efficacy of 5 sodium glucose cotransporter 2 inhibitor and 7 glucagon-like peptide 1 receptor agonists interventions on cardiorenal outcomes in type 2 diabetes patients: A network meta-analysis based on cardiovascular or renal outcome trials. *Medicine (Baltimore).* 2021;100(30):e26431. doi: 10.1097/MD.00000000000026431. PubMed PMID: 34397684; PubMed Central PMCID: PMC8322563.
 35. Eli Lilly and Company. Trulicity (dulaglutide) [package insert]. U.S. Food and Drug Administration. Revised 2022 Nov. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125469s051lbl.pdf.
 36. FDA Grants Jardiance Breakthrough Therapy Designation for Heart Failure with Preserved Ejection Fraction [Internet]. Connecticut, Indiana: Boehringer Ingelheim; 2021 Sep 9 [cited 2023 Aug 17]. Available from: <https://www.boehringer-ingelheim.com/us/media/press-releases/jardiance-empagliflozin-granted-designation-heart-failure-boehringer-ingelheim-us>.
 37. Ferdinand KC, Izzo JL, Lee J, Meng L, George J, Salsali A, et al. Antihyperglycemic and Blood Pressure Effects of Empagliflozin in Black Patients With Type 2 Diabetes Mellitus and Hypertension. *Circulation.* 2019;139(18):2098-109. doi: 10.1161/CIRCULATIONAHA.118.036568. PubMed PMID: 30786754.
 38. Fernandez-Fernandez B, Sarafidis P, Soler MJ, Ortiz A. EMPA-KIDNEY: expanding the range of kidney protection by SGLT2 inhibitors. *Clin Kidney J.* 2023;16(8):1187-98. Epub 20230616. doi: 10.1093/ckj/sfad082. PubMed PMID: 37529652; PubMed Central PMCID: PMC10387399.
 39. Ferrannini E, Ramos SJ, Salsali A, Tang W, List JF. Dapagliflozin monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: a randomized, double-blind, placebo-controlled, phase 3 trial. *Diabetes Care.* 2010;33(10):2217-24. Epub 20100621. doi: 10.2337/dc10-0612. PubMed PMID: 20566676; PubMed Central PMCID: PMC2945163.
 40. Fitchett D, Inzucchi SE, Cannon CP, McGuire DK, Scirica BM, Johansen OE, et al. Empagliflozin Reduced Mortality and Hospitalization for Heart Failure Across the Spectrum of Cardiovascular Risk in the EMPA-REG OUTCOME Trial. *Circulation.* 2019;139(11):1384-95. doi: 10.1161/CIRCULATIONAHA.118.037778. PubMed PMID: 30586757; PubMed Central PMCID: PMC6416009.
 41. Fiuzat M, Lowy N, Stockbridge N, Sbolli M, Latta F, Lindenfeld J, et al. Endpoints in Heart Failure Drug Development: History and Future. *JACC Heart Fail.* 2020;8(6):429-40. Epub 20200408. doi: 10.1016/j.jchf.2019.12.011. PubMed PMID: 32278679.
 42. Garber A, Henry R, Ratner R, Garcia-Hernandez PA, Rodriguez-Pattzi H, Olvera-Alvarez I, et al. Liraglutide versus glimepiride monotherapy for type 2 diabetes (LEAD-3 Mono): a randomised, 52-week, phase III, double-blind, parallel-treatment trial. *Lancet.* 2009;373(9662):473-81. Epub 20080924. doi: 10.1016/s0140-6736(08)61246-5. PubMed PMID: 18819705.
 43. Gerstein HC, Colhoun HM, Dagenais GR, Diaz R, Lakshmanan M, Pais P, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. *Lancet.* 2019;394(10193):121-30. Epub 20190609. doi: 10.1016/S0140-6736(19)31149-3. PubMed PMID: 31189511.

44. Gerstein HC, Miller ME, Byington RP, Goff DC, Jr., Bigger JT, Buse JB, et al. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med.* 2008;358(24):2545-59. Epub 20080606. doi: 10.1056/NEJMoa0802743. PubMed PMID: 18539917; PubMed Central PMCID: PMC4551392.
45. Ghosal S, Ghosal S, Ghosal A. The Renal Composite Benefit of Sodium Glucose Co-Transporter 2 Inhibitors Should Ideally Be Assessed Based on a Standardised Definition: A Meta-Analysis of Randomised Controlled Trials. *J Clin Med.* 2023;12(20). Epub 20231011. doi: 10.3390/jcm12206462. PubMed PMID: 37892600; PubMed Central PMCID: PMC10607004.
46. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med.* 2004;351(13):1296-305. doi: 10.1056/NEJMoa041031. PubMed PMID: 15385656.
47. Golestaneh L, Alvarez PJ, Reaven NL, Funk SE, McGaughey KJ, Romero A, et al. All-cause costs increase exponentially with increased chronic kidney disease stage. *Am J Manag Care.* 2017;23(10 Suppl):S163-S72. PubMed PMID: 28978205.
48. Green JB, Bethel MA, Armstrong PW, Buse JB, Engel SS, Garg J, et al. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med.* 2015;373(3):232-42. Epub 20150608. doi: 10.1056/NEJMoa1501352. PubMed PMID: 26052984.
49. Gross DJ, Ratner J, Perez J, Glavin SL. International pharmaceutical spending controls: France, Germany, Sweden, and the United Kingdom. *Health Care Financ Rev.* 1994;15(3):127-40. PubMed PMID: 10137794; PubMed Central PMCID: PMC4193451.
50. Haring HU, Merker L, Seewaldt-Becker E, Weimer M, Meinicke T, Broedl UC, et al. Empagliflozin as add-on to metformin in patients with type 2 diabetes: a 24-week, randomized, double-blind, placebo-controlled trial. *Diabetes Care.* 2014;37(6):1650-9. Epub 20140410. doi: 10.2337/dc13-2105. PubMed PMID: 24722494.
51. Harrington J, Sun JL, Fonarow GC, Heitner SB, Divanji PH, Binder G, et al. Clinical Profile, Health Care Costs, and Outcomes of Patients Hospitalized for Heart Failure With Severely Reduced Ejection Fraction. *J Am Heart Assoc.* 2023;12(10):e028820. Epub 20230509. doi: 10.1161/jaha.122.028820. PubMed PMID: 37158118; PubMed Central PMCID: PMC10227282.
52. Harrington J, Udell JA, Jones WS, Anker SD, Bhatt DL, Petrie MC, et al. Empagliflozin in patients post myocardial infarction rationale and design of the EMPACT-MI trial. *Am Heart J.* 2022;253:86-98. Epub 20220517. doi: 10.1016/j.ahj.2022.05.010. PubMed PMID: 35595091.
53. Hashmi MF, Benjamin O, Lappin SL. End-Stage Renal Disease. [Updated 2023 Aug 28]. In: StatPearls [Internet]. Florida: StatPearls Publishing; 2023 Aug 28. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK499861/>.
54. 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 20200924. doi: 10.1056/NEJMoa2024816. PubMed PMID: 32970396.
55. Heidenreich PA, Albert NM, Allen LA, Blumke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. *Circ Heart Fail.* 2013;6(3):606-19. Epub 20130424. doi: 10.1161/HHF.0b013e318291329a. PubMed PMID: 23616602; PubMed Central PMCID: PMC3908895.
56. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee

- on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2022;79(17):1757-80. Epub 20220401. doi: 10.1016/j.jacc.2021.12.011. PubMed PMID: 35379504.
57. Herrington WG, Staplin N, Wanner C, Green JB, Hauske SJ, Emberson JR, et al. Empagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med.* 2023;388(2):117-27. Epub 20221104. doi: 10.1056/NEJMoa2204233. PubMed PMID: 36331190; PubMed Central PMCID: PMC7614055.
 58. Hines A, Barrett M, Jiang H, and Steiner C. Conditions With the Largest Number of Adult Hospital Readmissions by Payer, 2011. HCUP Statistical Brief #172. Agency for Healthcare Research and Quality; April 2014. Available from: <http://www.hcup-us.ahrq.gov/reports/statbriefs/sb172-Conditions-Readmissions-Payer.pdf>.
 59. Htoo PT, Patorno E, Tesfaye H, Wexler DJ, Glynn R, Schmedt N, et al. 1227-P: Cardiorenal Effectiveness of Empagliflozin vs. GLP-1 Receptor Agonists in Patients with Advanced Chronic Kidney Disease—Results from the EMPRISE Study. *Diabetes.* 2023;72(Supplement_1):1227-P. doi: 10.2337/db23-1227-P.
 60. Htoo PT, Tesfaye H, Paik JM, Wexler DJ, Najafzadeh M, Glynn R, et al. 1079-P: Effectiveness and Safety of Empagliflozin in Routine Care: Results from the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) Study. *Diabetes.* 2022;71(Supplement_1):1079-P. doi: 10.2337/db22-1079-P.
 61. Htoo PT, Tesfaye H, Paik JM, Wexler DJ, Najafzadeh M, Glynn R, et al. 179-OR: Cardiovascular Effectiveness of Empagliflozin vs. Glucagon-Like Peptide-1 Receptor Agonists or Liraglutide in the EMPRISE Study. *Diabetes.* 2022;71(Supplement_1):179-OR. doi: 10.2337/db22-179-OR.
 62. Htoo PT, Tesfaye H, Schneeweiss S, Wexler DJ, Everett BM, Glynn RJ, et al. Comparative Effectiveness of Empagliflozin vs Liraglutide or Sitagliptin in Older Adults With Diverse Patient Characteristics. *JAMA Netw Open.* 2022;5(10):e2237606. Epub 20221003. doi: 10.1001/jamanetworkopen.2022.37606. PubMed PMID: 36264574; PubMed Central PMCID: PMC9585433.
 63. Htoo PT, Tesfaye H, Schneeweiss S, Wexler DJ, Everett BM, Glynn RJ, et al. Cardiorenal effectiveness of empagliflozin vs. glucagon-like peptide-1 receptor agonists: final-year results from the EMPRISE study. *Cardiovasc Diabetol.* 2024;23(1):57. Epub 20240208. doi: 10.1186/s12933-024-02150-0. PubMed PMID: 38331813; PubMed Central PMCID: PMC10854040.
 64. Htoo PT, Tesfaye H, Schneeweiss S, Wexler DJ, Everett BM, Glynn RJ, et al. Effectiveness and safety of empagliflozin: final results from the EMPRISE study. *Diabetologia.* 2024;67(7):1328-42. Epub 20240321. doi: 10.1007/s00125-024-06126-3. PubMed PMID: 38509341.
 65. Htoo PT, Tesfaye H, Schneeweiss S, Wexler DJ, Glynn R, Schmedt N, et al. 270-OR: Health Care Utilization and Cost Associated with Empagliflozin in Older Adults with Type 2 Diabetes—Results from the EMPRISE study. *Diabetes.* 2023;72(Supplement_1):270-OR. doi: 10.2337/db23-270-OR.
 66. Hussain A, Misra A, Bozkurt B. Endpoints in Heart Failure Drug Development. *Card Fail Rev.* 2022;8:e01. Epub 20220118. doi: 10.15420/cfr.2021.13. PubMed PMID: 35111335; PubMed Central PMCID: PMC8790723.
 67. Hussein H, Zaccardi F, Khunti K, Davies MJ, Patsko E, Dhalwani NN, et al. Efficacy and tolerability of sodium-glucose co-transporter-2 inhibitors and glucagon-like peptide-1 receptor agonists: A systematic review and network meta-analysis. *Diabetes Obes Metab.* 2020;22(7):1035-46. Epub 20200318. doi: 10.1111/dom.14008. PubMed PMID: 32077218.
 68. Iglay K, Hannachi H, Joseph Howie P, Xu J, Li X, Engel SS, et al. Prevalence and co-prevalence of comorbidities among patients with type 2 diabetes mellitus. *Curr Med Res Opin.*

- 2016;32(7):1243-52. Epub 20160404. doi: 10.1185/03007995.2016.1168291. PubMed PMID: 26986190.
69. Inzucchi SE, Iliev H, Pfarr E, Zinman B. Empagliflozin and Assessment of Lower-Limb Amputations in the EMPA-REG OUTCOME Trial. *Diabetes Care*. 2018;41(1):e4-e5. Epub 20171113. doi: 10.2337/dc17-1551. PubMed PMID: 29133344.
 70. Inzucchi SE, Kosiborod M, Fitchett D, Wanner C, Hehnke U, Kaspers S, et al. Improvement in Cardiovascular Outcomes With Empagliflozin Is Independent of Glycemic Control. *Circulation*. 2018;138(17):1904-7. doi: 10.1161/circulationaha.118.035759. PubMed PMID: 30354665.
 71. Janssen Pharmaceuticals, Inc. Invokana (canagliflozin) [package insert]. U.S. Food and Drug Administration. Revised 2023 Jul. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/204042s040lbl.pdf.
 72. Jenca D, Melenovsky V, Stehlik J, Stanek V, Kettner J, Kautzner J, et al. Heart failure after myocardial infarction: incidence and predictors. *ESC Heart Fail*. 2021;8(1):222-37. Epub 20201214. doi: 10.1002/ehf2.13144. PubMed PMID: 33319509; PubMed Central PMCID: PMC7835562.
 73. Kandelaki K, Marrone G, Lundborg CS, Schmidt I, Björkman I. Patient-centredness as a quality domain in Swedish healthcare: results from the first national surveys in different Swedish healthcare settings. *BMJ Open*. 2016;6(1):e009056. Epub 20160108. doi: 10.1136/bmjopen-2015-009056. PubMed PMID: 26747031; PubMed Central PMCID: PMC4716147.
 74. KDIGO 2023 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease: Public Review Draft. *Kidney Disease Improving Global Outcomes (KDIGO)*; 2023 Jul. Available from: https://web.archive.org/web/20231109104442/https://kdigo.org/wp-content/uploads/2017/02/KDIGO-2023-CKD-Guideline-Public-Review-Draft_5-July-2023.pdf.
 75. Khan MS, Sreenivasan J, Lateef N, Abougergi MS, Greene SJ, Ahmad T, et al. Trends in 30- and 90-Day Readmission Rates for Heart Failure. *Circ Heart Fail*. 2021;14(4):e008335. Epub 20210419. doi: 10.1161/circheartfailure.121.008335. PubMed PMID: 33866827.
 76. Kidney Disease: Improving Global Outcomes Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int*. 2022;102(5S):S1-S127. doi: 10.1016/j.kint.2022.06.008. PubMed PMID: 36272764.
 77. Kittleson MM, Panjrath GS, Amancherla K, Davis LL, Deswal A, Dixon DL, et al. 2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2023;81(18):1835-78. Epub 20230419. doi: 10.1016/j.jacc.2023.03.393. PubMed PMID: 37137593.
 78. 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 20230201. doi: 10.1016/s2213-8587(22)00387-4. PubMed PMID: 36738751; PubMed Central PMCID: PMC10851109.
 79. Lee AK, Juraschek SP, Windham BG, Lee CJ, Sharrett AR, Coresh J, et al. Severe Hypoglycemia and Risk of Falls in Type 2 Diabetes: The Atherosclerosis Risk in Communities (ARIC) Study. *Diabetes Care*. 2020;43(9):2060-5. Epub 20200701. doi: 10.2337/dc20-0316. PubMed PMID: 32611607; PubMed Central PMCID: PMC7440903.
 80. Levey AS, Inker LA, Matsushita K, Greene T, Willis K, Lewis E, et al. GFR decline as an end point for clinical trials in CKD: a scientific workshop sponsored by the National Kidney

- Foundation and the US Food and Drug Administration. *Am J Kidney Dis.* 2014;64(6):821-35. Epub 20141016. doi: 10.1053/j.ajkd.2014.07.030. PubMed PMID: 25441437.
81. Lexicon. Inpefa (sotagliflozin) [package insert]. U.S. Food and Drug Administration. Revised 2023 May. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216203s000lbl.pdf.
 82. Longino K. Testimony of the National Kidney Foundation, Kevin Longino, CEO, Before the House Committee on Appropriations, Subcommittee on Labor, HHS, Education, and Related Agencies in Support of FY 2024 Funding for CDC and NIDDK. 2023. Available from: <https://www.congress.gov/118/meeting/house/115507/witnesses/HHRG-118-AP07-Wstate-LonginoK-20230323.pdf>.
 83. Marassi M, Fadini GP. The cardio-renal-metabolic connection: a review of the evidence. *Cardiovasc Diabetol.* 2023;22(1):195. Epub 20230731. doi: 10.1186/s12933-023-01937-x. PubMed PMID: 37525273; PubMed Central PMCID: PMC10391899.
 84. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jodar E, Leiter LA, et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. *N Engl J Med.* 2016;375(19):1834-44. Epub 20160915. doi: 10.1056/NEJMoa1607141. PubMed PMID: 27633186.
 85. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med.* 2016;375(4):311-22. Epub 20160613. doi: 10.1056/NEJMoa1603827. PubMed PMID: 27295427; PubMed Central PMCID: PMC4985288.
 86. McMurray JJV, Solomon SD, Inzucchi SE, Kober L, Kosiborod MN, Martinez FA, et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. *N Engl J Med.* 2019;381(21):1995-2008. Epub 20190919. doi: 10.1056/NEJMoa1911303. PubMed PMID: 31535829.
 87. McNulty R. How Potential Unintended Impacts of the IRA May Affect Patients: Dr Julie Patterson. *The American Journal of Managed Care*; 2024 Apr 24. Available from: <https://www.ajmc.com/view/how-potential-unintended-impacts-of-the-ira-may-affect-patients-dr-julie-patterson>.
 88. Medicare Part D: CMS Should Monitor Effects of Rebates on Plan Formularies and Beneficiary Spending. Washington D.C.: U.S. Government Accountability Office; 2023 Sep 5. Report No: GAO-23-105270. Available from: <https://www.gao.gov/products/gao-23-105270>.
 89. Monteiro P, Bergenstal RM, Tournal E, Inzucchi SE, Zinman B, Hantel S, et al. Efficacy and safety of empagliflozin in older patients in the EMPA-REG OUTCOME® trial. *Age Ageing.* 2019;48(6):859-66. doi: 10.1093/ageing/afz096. PubMed PMID: 31579904; PubMed Central PMCID: PMC7963112.
 90. Morris AA, Testani JM, Butler J. Sodium-Glucose Cotransporter-2 Inhibitors in Heart Failure: Racial Differences and a Potential for Reducing Disparities. *Circulation.* 2021;143(24):2329-31. Epub 20210614. doi: 10.1161/circulationaha.120.052821. PubMed PMID: 34125562; PubMed Central PMCID: PMC8210466.
 91. National Committee for Quality Assurance. Medication Management in Older Adults (DDE/DAE) [Internet]. Washington, D.C. [cited 2024 Mar 1]. Available from: <https://www.ncqa.org/hedis/measures/medication-management-in-older-adults>.
 92. National Institute of Diabetes and Digestive and Kidney Diseases. Overview of the Immune System [Internet]. National Institutes of Health; 2022 [cited 2023 Oct 2]. Available from: <https://usrds-adr.niddk.nih.gov/2022/chronic-kidney-disease/1-ckd-in-the-general-population>.

93. National Institute of Diabetes and Digestive and Kidney Health. United States Renal Data System: 2022 Annual Data Report. National Institutes of Health; 2022. Available from: <https://usrds-adr.niddk.nih.gov/2022>.
94. Navaneethan SD, Zoungas S, Caramori ML, Chan JCN, Heerspink HJL, Hurst C, et al. Diabetes Management in Chronic Kidney Disease: Synopsis of the KDIGO 2022 Clinical Practice Guideline Update. *Ann Intern Med.* 2023;176(3):381-7. Epub 20230110. doi: 10.7326/M22-2904. PubMed PMID: 36623286.
95. Ndumele CE, Neeland IJ, Tuttle KR, Chow SL, Mathew RO, Khan SS, et al. A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association. *Circulation.* 2023;148(20):1636-64. Epub 20231009. doi: 10.1161/CIR.0000000000001186. PubMed PMID: 37807920.
96. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondou N, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. *N Engl J Med.* 2017;377(7):644-57. Epub 20170612. doi: 10.1056/NEJMoa1611925. PubMed PMID: 28605608.
97. Nichols GA, Ustyugova A, Deruaz-Luyet A, O'Keefe-Rosetti M, Brodovicz KG. Health Care Costs by Type of Expenditure across eGFR Stages among Patients with and without Diabetes, Cardiovascular Disease, and Heart Failure. *J Am Soc Nephrol.* 2020;31(7):1594-601. Epub 20200602. doi: 10.1681/ASN.2019121308. PubMed PMID: 32487562; PubMed Central PMCID: PMC7350988.
98. Novo Nordisk Inc. Ozempic (semaglutide) [package insert]. U.S. Food and Drug Administration. Revised 2023 Sep. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/209637s020s021lbl.pdf.
99. Novo Nordisk Inc. Ozempic (semaglutide) [package insert]. U.S. Food and Drug Administration. Revised 2022 Oct. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/209637s012lbl.pdf.
100. Novo Nordisk Inc. Victoza (liraglutide) [package insert]. U.S. Food and Drug Administration. Revised 2023 Jul. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/022341s039lbl.pdf.
101. Office of Minority Health. Black/African American Health [Internet]. Washington, D.C.: U.S. Department of Health and Human Services. [cited 2024 Mar 1]. Available from: <https://minorityhealth.hhs.gov/blackafrican-american-health>.
102. Onstad K, Hart A, Hwee T. Chronic Kidney Disease Disparities: Educational Guide for Primary Care. Centers for Medicare & Medicaid Services; 2021 Apr. Available from: <https://www.cms.gov/files/document/chronic-kidney-disease-disparities-educational-guide-primary-care.pdf>.
103. Osenenko KM, Kuti E, Deighton AM, Pimple P, Szabo SM. Burden of hospitalization for heart failure in the United States: a systematic literature review. *J Manag Care Spec Pharm.* 2022;28(2):157-67. doi: 10.18553/jmcp.2022.28.2.157. PubMed PMID: 35098748; PubMed Central PMCID: PMC10373049.
104. Oseran AS, Dong H, Wadhwa RK. Cardiovascular hospitalizations for Medicare advantage beneficiaries in the United States, 2009 to 2019. *Am Heart J.* 2023;265:77-82. Epub 20230713. doi: 10.1016/j.ahj.2023.07.002. PubMed PMID: 37451356.
105. Ostrominski JW, Arnold SV, Butler J, Fonarow GC, Hirsch JS, Palli SR, et al. Prevalence and Overlap of Cardiac, Renal, and Metabolic Conditions in US Adults, 1999-2020. *JAMA Cardiol.* 2023;8(11):1050-60. doi: 10.1001/jamacardio.2023.3241. PubMed PMID: 37755728; PubMed Central PMCID: PMC10535010.

106. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. *N Engl J Med.* 2020;383(15):1413-24. Epub 20200828. doi: 10.1056/NEJMoa2022190. PubMed PMID: 32865377.
107. Packer M, Butler J, Zannad F, Filippatos G, Ferreira JP, Pocock SJ, et al. Effect of Empagliflozin on Worsening Heart Failure Events in Patients With Heart Failure and Preserved Ejection Fraction: EMPEROR-Preserved Trial. *Circulation.* 2021;144(16):1284-94. Epub 20210829. doi: 10.1161/CIRCULATIONAHA.121.056824. PubMed PMID: 34459213; PubMed Central PMCID: PMC8522627.
108. Packer M, Butler J, Zeller C, Pocock SJ, Brueckmann M, Ferreira JP, et al. Blinded Withdrawal of Long-Term Randomized Treatment With Empagliflozin or Placebo in Patients With Heart Failure. *Circulation.* 2023;148(13):1011-22. Epub 20230824. doi: 10.1161/circulationaha.123.065748. PubMed PMID: 37621153; PubMed Central PMCID: PMC10516173.
109. Parliamentary Office of Science & Technology. Postnote: Drug pricing. Houses of Parliament; 2010 Oct. Report No. 364. Available from: https://www.parliament.uk/globalassets/documents/post/postpn_364_Drug_Pricing.pdf.
110. Patorno E, Najafzadeh M, Pawar A, Franklin JM, Deruaz-Luyet A, Brodovicz KG, et al. The EMPagliflozin compaRative effectiveness and SafEty (EMPRISE) study programme: Design and exposure accrual for an evaluation of empagliflozin in routine clinical care. *Endocrinol Diabetes Metab.* 2020;3(1):e00103. Epub 20191126. doi: 10.1002/edm2.103. PubMed PMID: 31922030; PubMed Central PMCID: PMC6947693.
111. Peasah SK, Huang Y, Palli SR, Swart EC, Donato BM, Pimple P, et al. Real-world impact of empagliflozin on total cost of care in adults with type 2 diabetes: Results from an outcomes-based agreement. *J Manag Care Spec Pharm.* 2023;29(2):152-60. doi: 10.18553/jmcp.2023.29.2.152. PubMed PMID: 36705285; PubMed Central PMCID: PMC10387982.
112. Perkovic V, Jardine MJ, Neal B, Bompoin S, Heerspink HJL, Charytan DM, et al. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. *N Engl J Med.* 2019;380(24):2295-306. Epub 20190414. doi: 10.1056/NEJMoa1811744. PubMed PMID: 30990260.
113. Raghavan S, Vassy JL, Ho YL, Song RJ, Gagnon DR, Cho K, et al. Diabetes Mellitus-Related All-Cause and Cardiovascular Mortality in a National Cohort of Adults. *J Am Heart Assoc.* 2019;8(4):e011295. doi: 10.1161/jaha.118.011295. PubMed PMID: 30776949; PubMed Central PMCID: PMC6405678.
114. Raju A, Pimple P, Stafkey-Mailey D, Farrelly E, Shetty S. Healthcare Costs and Resource Utilization Associated with the Use of Empagliflozin Versus Other Antihyperglycemic Agents Among Patients with Type 2 Diabetes Mellitus and Cardiovascular Disease: A Real-World Retrospective Cohort Analysis. *Diabetes Ther.* 2022;13(1):25-42. Epub 20211102. doi: 10.1007/s13300-021-01173-0. PubMed PMID: 34727356; PubMed Central PMCID: PMC8776959.
115. Riaz M, Smith SM, Dietrich EA, Winchester DE, Guo J, Park H. Comparative effectiveness of sodium-glucose cotransporter-2 inhibitors among patients with heart failure with preserved ejection fraction. *Pharmacotherapy.* 2023;43(10):1024-31. Epub 20230723. doi: 10.1002/phar.2853. PubMed PMID: 37459069.
116. Roborel de Climens A, Pain E, Boss A, Shaunik A. Understanding Reasons for Treatment Discontinuation, Attitudes and Education Needs Among People Who Discontinue Type 2 Diabetes Treatment: Results from an Online Patient Survey in the USA and UK. *Diabetes Ther.* 2020;11(8):1873-81. Epub 20200612. doi: 10.1007/s13300-020-00843-9. PubMed PMID: 32533547; PubMed Central PMCID: PMC7376801.

117. Roden M, Weng J, Eilbracht J, Delafont B, Kim G, Woerle HJ, et al. Empagliflozin monotherapy with sitagliptin as an active comparator in patients with type 2 diabetes: a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Diabetes Endocrinol.* 2013;1(3):208-19. Epub 20130909. doi: 10.1016/s2213-8587(13)70084-6. PubMed PMID: 24622369.
118. Samson SL, Vellanki P, Blonde L, Christofides EA, Galindo RJ, Hirsch IB, et al. American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm - 2023 Update. *Endocr Pract.* 2023;29(5):305-40. doi: 10.1016/j.eprac.2023.02.001. PubMed PMID: 37150579.
119. Schrauben SJ, Chen HY, Lin E, Jepson C, Yang W, Scialla JJ, et al. Hospitalizations among adults with chronic kidney disease in the United States: A cohort study. *PLoS Med.* 2020;17(12):e1003470. Epub 20201211. doi: 10.1371/journal.pmed.1003470. PubMed PMID: 33306688; PubMed Central PMCID: PMC7732055.
120. Segall L, Nistor I, Covic A. Heart failure in patients with chronic kidney disease: a systematic integrative review. *Biomed Res Int.* 2014;2014:937398. Epub 20140515. doi: 10.1155/2014/937398. PubMed PMID: 24959595; PubMed Central PMCID: PMC4052068.
121. Shi Q, Nong K, Vandvik PO, Guyatt GH, Schnell O, Ryden L, et al. Benefits and harms of drug treatment for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. *BMJ.* 2023;381:e074068. Epub 20230406. doi: 10.1136/bmj-2022-074068. PubMed PMID: 37024129; PubMed Central PMCID: PMC10077111.
122. Sohn M, Dietrich JW, Nauck MA, Lim S. Characteristics predicting the efficacy of SGLT-2 inhibitors versus GLP-1 receptor agonists on major adverse cardiovascular events in type 2 diabetes mellitus: a meta-analysis study. *Cardiovasc Diabetol.* 2023;22(1):153. Epub 20230628. doi: 10.1186/s12933-023-01877-6. PubMed PMID: 37381019; PubMed Central PMCID: PMC10303335.
123. Solomon SD, McMurray JJV, Claggett B, de Boer RA, DeMets D, Hernandez AF, et al. Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. *N Engl J Med.* 2022;387(12):1089-98. Epub 20220827. doi: 10.1056/NEJMoa2206286. PubMed PMID: 36027570.
124. Sorli C, Harashima SI, Tsoukas GM, Unger J, Karsbøl JD, Hansen T, et al. Efficacy and safety of once-weekly semaglutide monotherapy versus placebo in patients with type 2 diabetes (SUSTAIN 1): a double-blind, randomised, placebo-controlled, parallel-group, multinational, multicentre phase 3a trial. *Lancet Diabetes Endocrinol.* 2017;5(4):251-60. Epub 20170117. doi: 10.1016/s2213-8587(17)30013-x. PubMed PMID: 28110911.
125. Standards of Medical Care in Diabetes-2016: Summary of Revisions. *Diabetes Care.* 2016;39 Suppl 1:S4-5. doi: 10.2337/dc16-S003. PubMed PMID: 26696680.
126. Stenlöf K, Cefalu WT, Kim KA, Alba M, Usiskin K, Tong C, et al. Efficacy and safety of canagliflozin monotherapy in subjects with type 2 diabetes mellitus inadequately controlled with diet and exercise. *Diabetes Obes Metab.* 2013;15(4):372-82. Epub 20130124. doi: 10.1111/dom.12054. PubMed PMID: 23279307; PubMed Central PMCID: PMC3593184.
127. Takebayashi K, Inukai T. Effect of Sodium Glucose Cotransporter 2 Inhibitors With Low SGLT2/SGLT1 Selectivity on Circulating Glucagon-Like Peptide 1 Levels in Type 2 Diabetes Mellitus. *J Clin Med Res.* 2017;9(9):745-53. Epub 20170727. doi: 10.14740/jocmr3112w. PubMed PMID: 28811850; PubMed Central PMCID: PMC5544478.
128. Tamborlane WV, Barrientos-Pérez M, Fainberg U, Frimer-Larsen H, Hafez M, Hale PM, et al. Liraglutide in Children and Adolescents with Type 2 Diabetes. *N Engl J Med.* 2019;381(7):637-46. Epub 20190428. doi: 10.1056/NEJMoa1903822. PubMed PMID: 31034184.

129. Teo YH, Yoong CSY, Syn NL, Teo YN, Cheong JYA, Lim YC, et al. Comparing the clinical outcomes across different sodium/glucose cotransporter 2 (SGLT2) inhibitors in heart failure patients: a systematic review and network meta-analysis of randomized controlled trials. *Eur J Clin Pharmacol.* 2021;77(10):1453-64. Epub 20210503. doi: 10.1007/s00228-021-03147-4. PubMed PMID: 33942132.
130. The EMPA-KIDNEY Collaborative Group, Herrington WG, Staplin N, Wanner C, Green JB, Hauske SJ, et al. Empagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med.* 2023;388(2):117-27. Epub 20221104. doi: 10.1056/NEJMoa2204233. PubMed PMID: 36331190; PubMed Central PMCID: PMC7614055.
131. Tikkanen I, Narko K, Zeller C, Green A, Salsali A, Broedl UC, et al. Empagliflozin reduces blood pressure in patients with type 2 diabetes and hypertension. *Diabetes Care.* 2015;38(3):420-8. Epub 20140930. doi: 10.2337/dc14-1096. PubMed PMID: 25271206.
132. Tsapas A, Avgerinos I, Karagiannis T, Malandris K, Manolopoulos A, Andreadis P, et al. Comparative Effectiveness of Glucose-Lowering Drugs for Type 2 Diabetes: A Systematic Review and Network Meta-analysis. *Ann Intern Med.* 2020;173(4):278-86. Epub 20200630. doi: 10.7326/M20-0864. PubMed PMID: 32598218.
133. Umpierrez G, Tofé Povedano S, Pérez Manghi F, Shurzinske L, Pechtner V. Efficacy and safety of dulaglutide monotherapy versus metformin in type 2 diabetes in a randomized controlled trial (AWARD-3). *Diabetes Care.* 2014;37(8):2168-76. Epub 20140519. doi: 10.2337/dc13-2759. PubMed PMID: 24842985.
134. Urbich M, Globe G, Pantiri K, Heisen M, Bennison C, Wirtz HS, et al. A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014-2020). *Pharmacoeconomics.* 2020;38(11):1219-36. doi: 10.1007/s40273-020-00952-0. PubMed PMID: 32812149; PubMed Central PMCID: PMC7546989.
135. US FDA Grants Fast Track Designation to Jardiance for the Treatment of Chronic Kidney Disease [Internet]. Boehringer Ingelheim; 2020 Mar 12 [cited 2023 Aug 17]. Available from: <https://www.boehringer-ingelheim.com/us/media/press-releases/fda-grants-fast-track-jardiance-empagliflozin-ckd-boehringer-ingelheim-us>.
136. Voors AA, Angermann CE, Teerlink JR, Collins SP, Kosiborod M, Biegus J, et al. The SGLT2 inhibitor empagliflozin in patients hospitalized for acute heart failure: a multinational randomized trial. *Nat Med.* 2022;28(3):568-74. Epub 20220228. doi: 10.1038/s41591-021-01659-1. PubMed PMID: 35228754; PubMed Central PMCID: PMC8938265.
137. Wang W, Shetty S, Murty S, Stafkey-Mailey D. The direct cost of cardiovascular disease-related death in patients with type 2 diabetes mellitus in a Medicare population. *J Manag Care Spec Pharm.* 2017;23(10-a Suppl):S1-S92. doi: 10.18553/jmcp.2017.23.10-a.s1.
138. Wanner C, Inzucchi SE, Lachin JM, Fitchett D, von Eynatten M, Mattheus M, et al. Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes. *N Engl J Med.* 2016;375(4):323-34. Epub 20160614. doi: 10.1056/NEJMoa1515920. PubMed PMID: 27299675.
139. Wheeler DC, Stefansson BV, Batiushin M, Bilchenko O, Cherney DZI, Chertow GM, et al. The dapagliflozin and prevention of adverse outcomes in chronic kidney disease (DAPA-CKD) trial: baseline characteristics. *Nephrol Dial Transplant.* 2020;35(10):1700-11. doi: 10.1093/ndt/gfaa234. PubMed PMID: 32862232; PubMed Central PMCID: PMC7538235.
140. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, et al. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med.* 2019;380(4):347-57. Epub 20181110. doi: 10.1056/NEJMoa1812389. PubMed PMID: 30415602.
141. Zaccardi F, Webb DR, Htike ZZ, Youssef D, Khunti K, Davies MJ. Efficacy and safety of sodium-glucose co-transporter-2 inhibitors in type 2 diabetes mellitus: systematic review and

- network meta-analysis. *Diabetes Obes Metab.* 2016;18(8):783-94. Epub 20160513. doi: 10.1111/dom.12670. PubMed PMID: 27059700.
142. 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 20150917. doi: 10.1056/NEJMoa1504720. PubMed PMID: 26378978.

Redacted Negotiation Meeting Summaries for Jardiance

Below are summaries of the negotiation meetings between CMS and the Primary Manufacturer, which include redacted information regarding the negotiation meetings and exchange of offers and counteroffers in the meetings.



SUBJECT: Meeting Summary from Negotiation Meeting between the Centers for Medicare & Medicaid Services (CMS) and Boehringer Ingelheim regarding Jardiance on April 24, 2024

Background: Sections 11001 and 11002 of the Inflation Reduction Act of 2022 (IRA) (P.L. 117-169), signed into law on August 16, 2022, established the Medicare Drug Price Negotiation Program (hereafter the “Negotiation Program”) to enable the Centers for Medicare & Medicaid Services (CMS) to negotiate maximum fair prices (MFPs) with willing manufacturers for certain high expenditure, single source drugs and biological products. Boehringer Ingelheim (hereafter “the Primary Manufacturer”) chose to enter into an agreement to participate in the Negotiation Program for Jardiance (hereafter “the Selected Drug”).

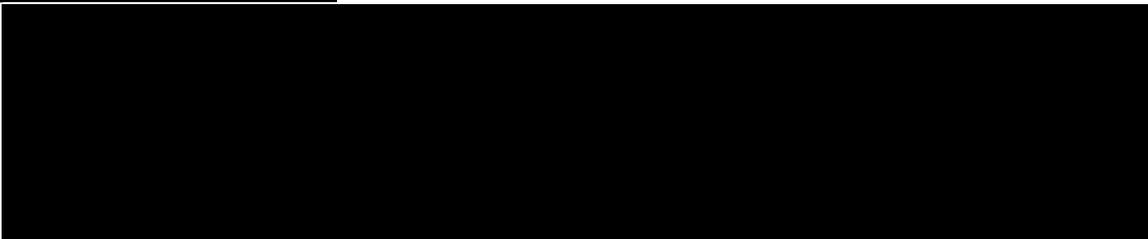
In accordance with revised guidance and in the course of negotiation for the Selected Drug, CMS invited the Primary Manufacturer to a negotiation meeting when rejecting the Primary Manufacturer’s counteroffer, and the Primary Manufacturer accepted CMS’ invitation. CMS shared a proposed meeting agenda with the Primary Manufacturer approximately two weeks before the meeting. The Primary Manufacturer had the opportunity to request additions or edits to the agenda at least one week ahead of the meeting. This document includes a summary prepared by CMS of the first negotiation meeting, which was held on April 24, 2024 between 1:00 PM ET and 3:30 PM ET.

CMS Attendees:

1. Bansri Desai, Division of Rebate Agreements and Drug Price Negotiation
2. Scott Falin, Representative from the Office of the General Counsel
3. Dan Heider, Director, Division of Rebate Agreements and Drug Price Negotiation
4. Tina Li, Medicare Drug Rebate and Negotiations Group
5. Corey Rosenberg, Deputy Director, Division of Rebate Agreements and Drug Price Negotiation
6. Lara Strawbridge, Deputy Director of Policy, Medicare Drug Rebate and Negotiations Group

Primary Manufacturer Attendees:

- 1.
- 2.
- 3.
- 4.
- 5.
- 6.



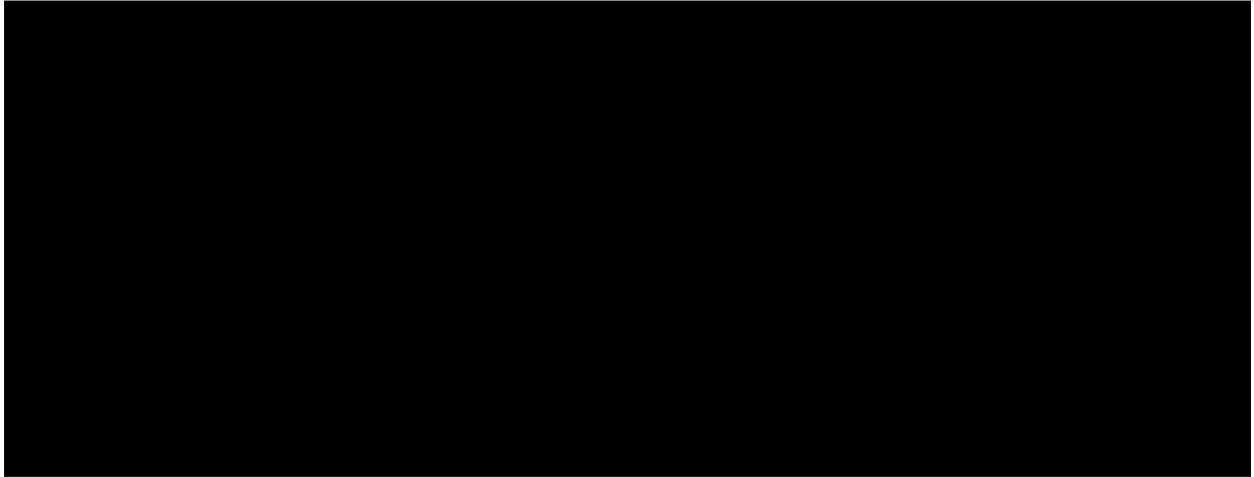
Topics: The discussion focused on topics outlined in the final agenda for the meeting, which was as follows:¹

- Welcome and opening remarks (CMS and Boehringer-Ingelheim)
- Discussion of initial offer development and any questions from the Primary Manufacturer (Boehringer-Ingelheim)

¹ Note: This agenda may be inclusive of topics proposed by the Primary Manufacturer.

- Discussion of counteroffer [REDACTED] and any questions from CMS
- Any other considerations that CMS or the Primary Manufacturer (Boehringer-Ingelheim) would like to discuss
- Next Steps and closing remarks

Offers/Counteroffers Exchanged:





SUBJECT: Meeting Summary from Negotiation Meeting between the Centers for Medicare & Medicaid Services (CMS) and Boehringer Ingelheim regarding Jardiance on May 20, 2024

Background: Sections 11001 and 11002 of the Inflation Reduction Act of 2022 (IRA) (P.L. 117-169), signed into law on August 16, 2022, established the Medicare Drug Price Negotiation Program (hereafter the “Negotiation Program”) to enable the Centers for Medicare & Medicaid Services (CMS) to negotiate maximum fair prices (MFPs) with willing manufacturers for certain high expenditure, single source drugs and biological products. Boehringer Ingelheim (hereafter “the Primary Manufacturer”) chose to enter into an agreement to participate in the Negotiation Program for Jardiance (hereafter “the Selected Drug”).

In accordance with revised guidance and in the course of negotiation for the Selected Drug, because CMS and the Primary Manufacturer did not reach agreement on an MFP in the first negotiation meeting held on April 24, 2024, each party had the opportunity to request one additional negotiation meeting, resulting in a maximum of three meetings. CMS requested a second negotiation meeting and the Primary Manufacturer accepted the invitation. CMS shared a proposed meeting agenda with the Primary Manufacturer approximately two weeks before the meeting. The Primary Manufacturer had the opportunity to request additions or edits to the agenda at least one week ahead of the meeting. This document includes a summary prepared by CMS of the second negotiation meeting, which was held on May 20, 2024 between 1:30 PM ET and 4:00 PM ET.

CMS Attendees:

1. Bansri Desai, Division of Rebate Agreements and Drug Price Negotiation
2. Scott Falin, Representative from the Office of the General Counsel
3. Dan Heider, Director, Division of Rebate Agreements and Drug Price Negotiation
4. Tina Li, Medicare Drug Rebate and Negotiations Group
5. Corey Rosenberg, Deputy Director, Division of Rebate Agreements and Drug Price Negotiation
6. Lara Strawbridge, Deputy Director of Policy, Medicare Drug Rebate and Negotiations Group

Primary Manufacturer Attendees:

1. [REDACTED]
2. [REDACTED]
3. [REDACTED]
4. [REDACTED]
5. [REDACTED]
6. [REDACTED]

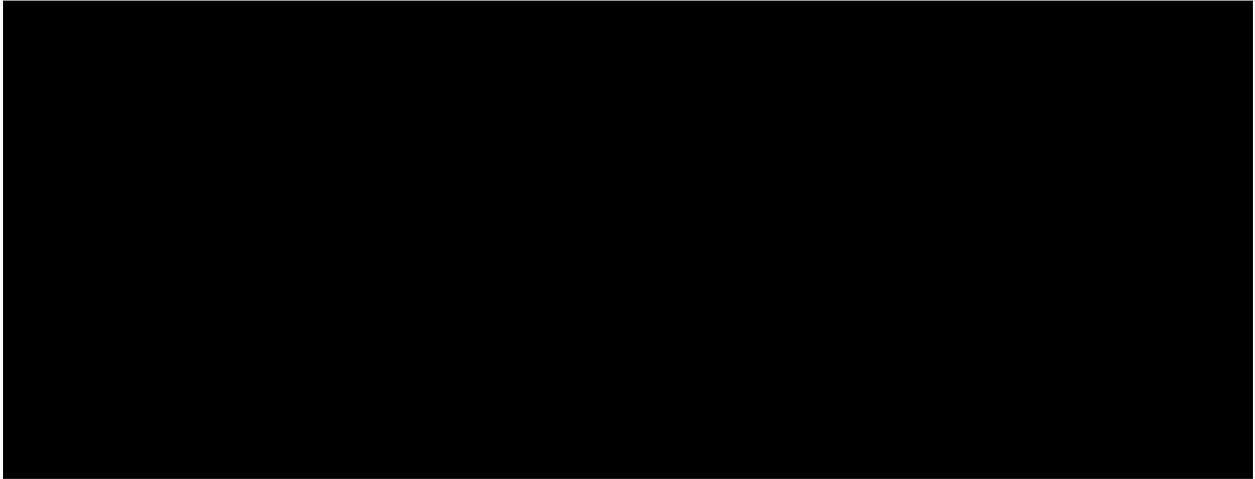
Topics: The discussion focused on topics outlined in the final agenda for the meeting, which was as follows:¹

- Introductions and meeting reminders

¹ Note: This agenda may be inclusive of topics proposed by the Primary Manufacturer.

- Discussion of Boehringer Ingelheim's request for additional information related to CMS' initial offer
- Discussion of Jardiance utilization distribution across indications
- Any additional information from the Primary Manufacturer and joint discussion [REDACTED]
- Any additional information from the Primary Manufacturer on the impact of previously discussed access concerns
- Any other considerations that CMS and the Primary Manufacturer would like to discuss
- Next steps

Offers/Counteroffers Exchanged:





SUBJECT: Meeting Summary from Negotiation Meeting between the Centers for Medicare & Medicaid Services (CMS) and Boehringer Ingelheim regarding Jardiance on June 21, 2024

Background: Sections 11001 and 11002 of the Inflation Reduction Act of 2022 (IRA) (P.L. 117-169), signed into law on August 16, 2022, established the Medicare Drug Price Negotiation Program (hereafter the “Negotiation Program”) to enable the Centers for Medicare & Medicaid Services (CMS) to negotiate maximum fair prices (MFPs) with willing manufacturers for certain high expenditure, single source drugs and biological products. Boehringer Ingelheim (hereafter “the Primary Manufacturer”) chose to enter into an agreement to participate in the Negotiation Program for Jardiance (hereafter “the Selected Drug”).

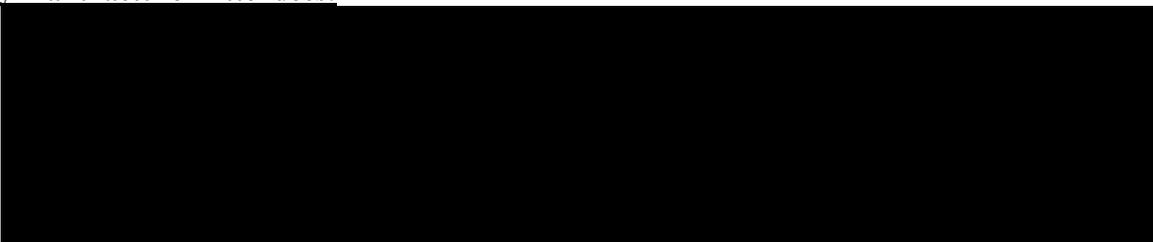
In accordance with revised guidance and in the course of negotiation for the Selected Drug, because CMS and the Primary Manufacturer did not reach agreement on an MFP in the second negotiation meeting, which was requested by CMS and held on May 20, 2024, the Primary Manufacturer had the opportunity to request one additional negotiation meeting, resulting in a maximum of three meetings. The Primary Manufacturer requested a third negotiation meeting and CMS accepted the invitation. CMS shared a proposed meeting agenda with the Primary Manufacturer approximately two weeks before the meeting. The Primary Manufacturer had the opportunity to request additions or edits to the agenda at least one week ahead of the meeting. This document includes a summary prepared by CMS of the third negotiation meeting, which was held on June 21, 2024 between 10:00 AM ET and 12:30 PM ET.

CMS Attendees:

1. Bansri Desai, Division of Rebate Agreements and Drug Price Negotiation
2. Scott Falin, Representative from the Office of the General Counsel (virtual attendance)
3. Dan Heider, Director, Division of Rebate Agreements and Drug Price Negotiation
4. Tina Li, Medicare Drug Rebate and Negotiations Group
5. Corey Rosenberg, Deputy Director, Division of Rebate Agreements and Drug Price Negotiation
6. Lara Strawbridge, Deputy Director of Policy, Medicare Drug Rebate and Negotiations Group

Primary Manufacturer Attendees:

- 1.
- 2.
- 3.
- 4.
- 5.
- 6.



Topics: The discussion focused on topics outlined in the final agenda for the meeting, which was as follows:¹

- Introductions and meeting reminders
- Revised offer/counteroffer price discussion

¹ Note: This agenda may be inclusive of topics proposed by the Primary Manufacturer.

- [REDACTED]
- Any other considerations that CMS and the Primary Manufacturer would like to discuss
- Next steps

Offers/Counteroffers Exchanged:

