Cost Review Study Dossier- Farxiga

Section 1: Background

The table below displays a list of all possible NDC-11 codes associated with Farxiga (proprietary name) and dapagliflozin (non-proprietary name). The NDC-11 codes were identified by staff through searches on the RxNorm database.

National Drug Code	Proprietary Name	Non-Proprietary Name	Dosage-Strength
00003-1428-11	Farxiga	Dapagliflozin	10 MG
00003-1428-12	Farxiga	Dapagliflozin	10 MG
00003-1428-13	Farxiga	Dapagliflozin	10 MG
00003-1428-14	Farxiga	Dapagliflozin	10 MG
00003-1428-91	Farxiga	Dapagliflozin	10 MG
00310-6210-90	Farxiga	Dapagliflozin	10 MG
00310-6210-30	Farxiga	Dapagliflozin	10 MG
00310-6210-39	Farxiga	Dapagliflozin	10 MG
00310-6210-95	Farxiga	Dapagliflozin	10 MG
50090-3481-00	Farxiga	Dapagliflozin	10 MG
50090-7057-00	Farxiga	Dapagliflozin	10 MG/1
55154-6933-08	Farxiga	Dapagliflozin	10 MG/1
63629-3253-01	Farxiga	Dapagliflozin	10 MG/1
66993-0457-30	Farxiga	Dapagliflozin	10 MG/1
00003-1427-11	Farxiga	Dapagliflozin	5 MG
00003-1427-12	Farxiga	Dapagliflozin	5 MG
00003-1427-13	Farxiga	Dapagliflozin	5 MG
00003-1427-14	Farxiga	Dapagliflozin	5 MG
00003-1427-91	Farxiga	Dapagliflozin	5 MG
00310-6205-90	Farxiga	Dapagliflozin	5 MG
00310-6205-30	Farxiga	Dapagliflozin	5 MG
00310-6205-95	Farxiga	Dapagliflozin	5 MG
50090-3482-00	Farxiga	Dapagliflozin	5 MG
50090-7056-00	Farxiga	Dapagliflozin	5 MG/1
55154-6932-08	Farxiga	Dapagliflozin	5 MG/1
66993-0456-30	Farxiga	Dapagliflozin	5 MG/1

Section 2: Clinical Information

Element 2.1: COMAR 14.01.04.05.C(1)(g)(i)—Clinical information, including FDA indications and doses and information concerning standard medical practice.

Farxiga® (dapagliflozin): FDA-approved indications and associated dosing regimen(s)[1]

Indication	*Dosing Regimen(s)*
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.	5mg (1 tablet) by mouth once daily, eGFR ≥ 45 mL/min/1.73m^2 10mg (1 tablet) by mouth once daily, eGFR ≥ 45 mL/min/1.73m^2 if further glycemic control is needed Not recommended for eGFR < 45 mL/min/1.73 m^2
To reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors	10mg (1 tablet) by mouth once daily, eGFR ≥ 25 mL/min/1.73 m^2 Not recommended for eGFR < 25 mL/min/1.73 m^2
To reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure	10mg (1 tablet) by mouth once daily, eGFR ≥ 25 mL/min/1.73 m^2 Not recommended for eGFR < 25 mL/min/1.73 m^2
To reduce the risk of sustained eGFR decline, end-stage kidney disease (ESKD), cardiovascular (CV) death, and hospitalization for heart failure (hHF) in patients with chronic kidney disease at risk of progression	10mg (1 tablet) by mouth once daily, eGFR ≥ 25 mL/min/1.73 m^2 Not recommended for eGFR < 25 mL/min/1.73 m^2

Standard Medical Practice Recommendations

Farxiga® (dapagliflozin) Placement in Therapy for Diabetes Mellitus Type 2

Diabetes mellitus (DM) describes a group of chronic metabolic disorders of blood sugar, where the body both underuses and overproduces sugar resulting in high blood sugar. Underuse of

[1] Farxiga. Wilmington (DE): AstraZeneca Pharmaceuticals LP; 2024 Jun. Package Insert. NDC 0310-6205-30.

blood sugar may be caused by either an inability of the body to make sufficient (or any) insulin, such as in Type 1 DM, or resistance to insulin as found in Type 2 DM.[2]
Farxiga, along with other medications in the SGLT2 inhibitor class, are recommended by the American Diabetes Association (ADA) and the American Association of Clinical Endocrinology (AACE) as one of the seven medication class options that may be used to lower blood sugar in patients with Type 2 DM.[3,4]

The ADA does not specify an order of use preference; choice of medication class option is based on a variety of patient specific factors such as administration preference, cost, absolute ability to lower glucose, risk of low blood sugar, dosing frequency, etc. For treatment of glycemic control only, use of Farxiga, is equal to other therapeutic options indicated for Type 2 DM (such as insulin, metformin, GLP-1, sulfonlyurea, etc).[3] The AACE similarly considers patient specific factors and explicitly prefers SGLT2 inhibitors (or GLP1 agonists) for patients who is overweight or obese or at risk of low blood sugar.[4] These guideline recommendations are in line with other major society guidelines, including the American College of Physicians and the National Kidney Foundation Kidney Disease Improving Global Outcomes.[5,6]

In adult patients with Type 2 DM and established cardiovascular disease (CVD) (including prior heart attack, stroke or revascularization procedure) or multiple risk factors for CVD (including obesity, high blood pressure, protein in urine, smoking, high cholesterol), the ADA and AACE recommend the use of SGLT2 inhibitors with proven benefit (Jardiance or Invokana [canagliflozin]) as first line therapy.[3,4]

- This recommendation is independent of the patient's use of other medications (unless specifically unable to use with a particular medication) or glycemic control.
- Farxiga is not included in either guidelines' category for reduction of major adverse cardiovascular events. This guideline distinction is based on clinical trial data that Farxiga reduces risk of hospitalization for heart failure only, not risk of cardiovascular death.

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[2] American Diabetes Association Professional Practice Committee; 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2025. *Diabetes Care* 1 January 2025; 48 (Supplement_1): S27–S49. https://doi.org/10.2337/dc25-S002.
[3] American Diabetes Association Professional Practice Committee; 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2025. *Diabetes Care* 1 January 2025; 48 (Supplement_1): S181–S206. https://doi.org/10.2337/dc25-S009.
[4] Samson, Susan L. et al. American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update. Endocrine Practice, Volume 29, Issue 5, 305 – 340.
[5] Amir Qaseem, Adam J. Obley, Tatyana Shamliyan, et al; Clinical Guidelines Committee of the American College of Physicians. Newer Pharmacologic Treatments in Adults With Type 2 Diabetes: A Clinical Guideline From the American College of Physicians. Ann Intern Med.2024;177:658-666. [Epub 19 April 2024]. https://doi.org/10.7326/M23-2788.
[6] Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2022;102 (5S):S1–S127. https://doi.org/10.1016/j.kint.2022.06.008.

Per ACC/AHA guidelines, SGLT2 inhibitors are recommended for all symptomatic chronic HFrEF patients to reduce the risk of hospitalization for heart failure and cardiovascular death. The guidelines specify the use of Jardiance, Farxiga or Inpefa (sotagliflozin) based on supporting clinical trial data for benefit.[7,8]

Per ACC/AHA guidelines, SGLT2 inhibitors, specifically Jardiance and Farxiga, are recommended for all patients with symptomatic HFpEF.[7,9] Sotagliflozin, while mentioned due to clinical trial benefits, was not recommended as it was not FDA approved at the time of the publication date.[9] It is now FDA approved and available for use.

Clinical use in HF Takeaway: SGLT2 inhibitors, specifically Jardiance, Farxiga, or Inpefa (sotagliflozin), are recommended to be taken by all symptomatic HF patients.

Farxiga® (dapagliflozin) Placement in Therapy for Chronic Kidney Disease

Chronic Kidney Disease (CKD) encompasses abnormalities of kidney function or structure that are present for at least 3 months. This carries health implications because the kidneys are unable to filter blood as well as they should.[10] Kidney function is measured through estimated glomerular filtration rate (eGFR) and the loss of protein in the form of albumin in the urine.

The Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend SGLT2 inhibitors for all adult patients with (1) Type 2 DM, CKD, and eGFR $\geq$ 20 mL/min/1.73m^2, (2) all adult patients with CKD, urinary albumin $\geq$200mg/g, and eGFR $\geq$ 20 mL/min/1.73m^2, and (3) all adult patients with CKD and HF.[10] The KDIGO guidelines also suggest to treat all adult patients with an eGFR of 20 to 45 ml/min/1.73m^2 with an SGLT2 inhibitor.[10]

The KDIGO guidelines do not recommend or specify any particular drug within the SGLT inhibitor class. The guidelines, per a review of large randomized controlled trials in support of the overall recommendations/suggestions, mention evidence for Farxiga, Jardiance, Inpefa (sotagliflozin) and Invokana (canagliflozin).[10]
Clinical use in CKD Takeaway: To lower the risk of CKD progression and acute kidney injury and improve cardiovascular outcomes, SGLT2i inhibitors (equal weight preference to Jardiance, Farxiga and canagliflozin) are recommended by major guidelines for adult CKD patients with

[8] Maddox TM, Januzzi JL Jr, et.al. 2024 ACC expert consensus decision pathway for treatment of heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2024;83(15):1444-1488.
[9] Kittleson MM, Panjrath GS, 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. Published online April 19, 2023. https://doi.org/10.1016/j.jacc.2023.03.393.
[10]Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024;105(4S): S117–S314. https://doi.org/10.1016/j.kint.2023.10.018.

DM Type 2, HF and/or albuminuria ≥200mg/g and suggested for adult CKD patients with an eGFR of 20 to 45 ml/min/1.73m^2.

Element 2.2: COMAR 14.01.04.05.C(1)(g)(ii)—The disease burden of the condition that is treated by the prescription drug product

Farxiga treats multiple conditions. The information below summarizes the disease burden of these conditions on various dimensions.

Type 2 Diabetes Mellitus (DM)

Prevalence

- In the United States (US), 38.4 million (11.6%) people have diagnosed or undiagnosed diabetes mellitus (DM).[11,12] Type 2 DM accounts for 90-95% of all diagnosed cases of diabetes.
- In Maryland, the total age-adjusted percentage of adults aged 18 years or older with diagnosed diabetes was 10.5% in 2022.[13]

Incidence

- In 2021, 1.2 million adults were diagnosed with diabetes (rate of 5.9 per 1000 people).[11,12] More than 1 in 3 people, 98 million adults, have prediabetes (38% of adult US population).[11,12] In individuals 65 years or older, 48.8% have prediabetes.[12]
- In Maryland, the age-adjusted rate of adults aged 18 years or older with newly diagnosed diabetes was 7.8 per 1000 in 2022.[13]

Disease Severity

- Diabetes is classified in categories including: Type 1 (immune destruction of insulin producing pancreatic cells); Type 2 (non-immune progressive loss of insulin secretion, frequently with an inability of the body to use available insulin); gestational (diagnosed in

[11] Centers for Disease Control and Prevention. Diabetes in the US, a US Report Card [Internet]. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2022 . Available from: https://www.cdc.gov/diabetes/images/library/socialmedia/diabetesintheus_print.pdf.
[12] Centers for Disease Control and Prevention. National Diabetes Statistics Report website [Internet]Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2024. Available from: https://www.cdc.gov/diabetes/php/data-research/index.html.
[13] United States Diabetes Surveillance System [Internet]. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention. 2000. Available from: https://gis.cdc.gov/grasp/diabetes/diabetesatlas-surveillance.html#.

2nd or 3rd trimester of pregnancy and not present pre-pregnancy); and other causes.[14] The primary tool to assess glycemic status is the A1c test as it reflects the average blood glucose value over the preceding 2-3 months and is strongly linked to diabetes complications. Higher A1c values correspond to higher complication rates of diabetes.[15]

Cost of Illness/Financial Impact

- Total direct and indirect estimated costs of diagnosed diabetes in the US were $413 billion in 2022. Excess medical costs per person associated with diabetes were $12,022 in 2022.[12]
- In Maryland for calendar year 2021, total and per patient medical costs attributable to diabetes were $6.506 billion and $11,909, respectively.[16]
- And, in the same jurisdiction and year,, diabetes-attributable total and per-person productivity losses due to morbidity were $3.4 billion and $6,224, respectively.[16]

Morbidity

- In 2020, approximately 16.8 million emergency department visits in the US were reported with diabetes as a listed diagnosis among adults aged 18 years or older. Of these, 267,000 were for hyperglycemic crisis (11.4 per 1,000 adults with diabetes) and 202,000 were for hypoglycemia (8.6 per 1,000 adults with diabetes).[12]

[14] United States Diabetes Surveillance System [Internet]. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention. 2000 - [cited 2025 Jan 4]. Available from: https://gis.cdc.gov/grasp/diabetes/diabetesatlas-surveillance.html#.
[15] American Diabetes Association Professional Practice Committee; 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes—2025. Diabetes Care 1 January 2025; 48 (Supplement_1): S128–S145. https://doi.org/10.2337/dc25-S006.
[16] A. Khavjou, Olga; Sun, Minglu; R. D'Angelo, Sophia; J. Neuwahl, Simon; J. Hoerger, Thomas; Cho, Pyone; et al. (2024). Economic Costs Attributed to Diagnosed Diabetes in Each US State and the District of Columbia, 2021. American Diabetes Association. Figure. https://doi.org/10.2337/figshare.26351743.v1.

Table 1. Number and rate of hospitalizations per 1,000 adults aged 18 years or older with diabetes for selected causes, United States, 2019-2020[12]

Risk factor	2019 Number	2019 Crude rate per 1,000 (95% CI)	2020 Number	2020 Crude Rate per 1,000 (95% CI)
Diabetes as any listed diagnosis	**8,341,000**	**356.1 (337.0–375.3)**	**7,856,000**	**335.4 (316.5–354.4)**
Major cardiovascular disease	1,920,000	82.0 (77.4–86.5)	1,677,000	71.6 (67.4–75.8)
Ischemic heart disease	443,000	18.9 (17.8–20.0)	368,000	15.7 (14.7–16.7)
Stoke	346,000	14.8 (13.9–15.6)	321,000	13.7 (12.9–14.5)
Lower-extremity amputation	162,000	6.9 (6.5–7.3)	160,000	6.8 (6.4–7.2)
Hyperglycemic crisis	231,000	9.9 (9.3–10.4)	232,000	9.9 (9.3–10.5)
Diabetic ketoacidosis	205,000	8.8 (8.3–9.2)	206,000	8.8 (8.3–9.3)
Hyperosmolar hyperglycemic syndrome	26,000	1.1 (1.0–1.2)	26,000	1.1 (1.1–1.2)
Hypoglycemia	60,000	2.5 (2.4–2.7)	51,000	2.2 (2.1–2.3)

Notes: CI = confidence interval. Numbers rounded to the nearest thousand. Data sources: 2019 and 2020 National Inpatient Sample; 2019 and 2020 National Health Interview Survey.

- Among adults aged 18 years or older with diagnosed diabetes (data from 2017-2020), 39.2% had chronic kidney disease (CKD, stages 1–4), based on the updated 2021 CKD Epidemiology Collaboration (CKD-EPI) equation for estimated glomerular filtration rate (eGFR).[12]
- Diabetes is the leading cause of new cases of blindness for adults aged 18-64 years. In 2021, 10.1% of adults with diagnosed diabetes reported severe vision difficulty or blindness.[12]

Mortality

- Diabetes was the 8th leading cause of death in the US in 2021, based on 103,294 death certificates listing diabetes as an underlying cause (a rate of 31.1 per 100,000 people).[12] Including diabetes as a contributing cause of death, the rate increases to 120.3 per 100,000 people (399,401 death certificates).[12]
- In Maryland, the age-adjusted rate of diabetes death and diabetes-related death in adults aged 18 years older was 33.5 and 145.5 per 100,000 people, respectively, in 2022.[13]

Heart Failure (HF)

Prevalence

- Based on National Health and Nutrition Examination Survey (NHANES) 2017-2020, approximately 6.7 million US adults have HF (overall population rate of 1.9-2.6%).

Prevalence progressively increases with each decade of life; individuals over age 65 have a 4-fold higher prevalence of HF (8-9.1%) vs. those under 65 years.[17]

- Within Maryland, the 2016 age adjusted prevalence of heart failure is approximately 1100 per 100,000 persons. Relative to other states, MD prevalence is moderately elevated (prevalence range 700-1300 per 100,000 persons).[17,18]

Incidence

- A variation in incidence rates reported in studies is surmised to be due to differences in data sources, population demographics and composition, HF ascertainment methodology, and periodic differences. The inclusion of HFpEF also influences results as it becomes the dominant phenotype, attributed to increasing prevalence of underlying risk factors for HF (including diabetes and obesity).[17]

Disease Severity

- Heart failure severity is categorized by the AHA/ACC into stages A, B, C and D. The following table defines each stage.[18] Stages A & B represent those individuals without signs or symptoms of heart failure but either are at risk for or with pre-heart failure. Stages C & D represent individuals with symptomatic heart failure. Stage D represents more severe symptoms that interfere with activities of daily living.[19]

[17] Bozkurt B, Ahmad T, Alexander KM, et.al.; Writing Committee Members. Heart Failure Epidemiology and Outcomes Statistics: A Report of the Heart Failure Society of America. J Card Fail. 2023 Oct;29(10):1412-1451. https://doi.org/10.1016/j.cardfail.2023.07.006.
[18] Global Burden of Cardiovascular Diseases Collaboration; Roth GA, Johnson CO, et.al. The Burden of Cardiovascular Diseases Among US States, 1990-2016. JAMA Cardiol. 2018 May 1;3(5):375-389. https://doi.org/10.1001/jamacardio.2018.0385.
[19] Heidenreich PA, Bozkurt B, et.al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145:e895–e1032. https://doi.org/10.1161/CIR.0000000000001063.

Table 2. Stages of HF[19]

Stages	Definition and Criteria
Stage A: At Risk for HF	At risk for HF but without symptoms, structural heart disease, or cardiac biomarkers of stretch or injury (eg, patients with hypertension, atherosclerotic CVD, diabetes, metabolic syndrome and obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or positive family history of cardiomyopathy).
Stage B: Pre-HF	No symptoms or signs of HF and evidence of 1 of the following:
	*Structural heart disease** Reduced left or right ventricular systolic function Reduced ejection fraction, reduced strain Ventricular hypertrophy Chamber enlargement Wall motion abnormalities Valvular heart disease
	*Evidence for increased filling pressures** By invasive hemodynamic measurements By noninvasive imaging suggesting elevated filling pressures (eg, Doppler echocardiography)
	Patients with risk factors and *Increased levels of BNPs** *or* *Persistently elevated cardiac troponin* in the absence of competing diagnoses resulting in such biomarker elevations such as acute coronary syndrome, CKD, pulmonary embolus, or myopericarditis
Stage C: Symptomatic HF	Structural heart disease with current or previous symptoms of HF.
Stage D: Advanced HF	Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT.

BNP indicates B-type natriuretic peptide; CKD, chronic kidney disease; CVD, cardiovascular disease; GDMT, guideline-directed medical therapy; and HF, heart failure.
*For thresholds of cardiac structural, functional changes, elevated filling pressures, and biomarker elevations, refer to Appendix 3.

Cost of Illness/Financial Impact

- In 2012, the total cost for HF was estimated to be $30.7 billion (2010 dollars), of which more than two-thirds was attributable to direct medical costs. Projections suggest that by 2030 the total cost of HF will increase by 127% to $69.8 billion, amounting to approximately$244 for every US adult.[20]
- In a systematic review of HF-associated medical costs in the United States from 2014 to 2020, the annual median total cost was estimated at $24,383 per patient, with HF hospitalizations accounting for the majority ($15,879 per patient).[20]

Morbidity

- In 2019, there were 8,054,000 physician office visits in the US with a primary diagnosis of HF. In 2020, there were 1,361, 493 emergency department visits for HF. In 2020, there were 1,111,500 principal diagnosis hospital discharges for HF.[20]

Mortality

- One-third of all cardiovascular deaths are usually attributable to HF, however coding guidelines consider HF as a mediator rather than the underlying cause of death. Accordingly, mortality from HF is underestimated. The reported absolute number of deaths with HF as an underlying cause of death was 85,855, whereas the total number of cardiovascular deaths

[20] Martin SS, Aday AW, Almarzooq ZI, et al.; American Heart Association Council on Epidemiology and Prevention Statistics Committee; Stroke Statistics Subcommittee. 2024 heart disease and stroke statistics: a report of US and global data from the American Heart Association. Circulation. 2024;149:e347–913.

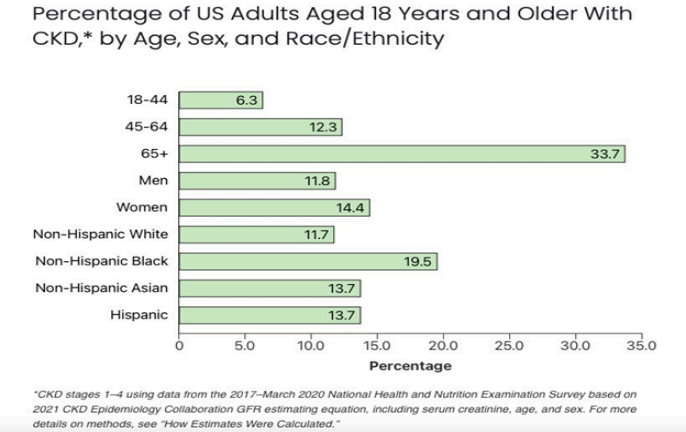
were 928,741 deaths in the US by 2020. By including any mention of HF on a death certificate, HF was a contributing cause in 415,922 deaths in the US in 2020.[17]
- In 2022, heart failure was mentioned on 457,212 death certificates (and responsible for 13.9% of all causes of death).[21]
- HF is associated with a loss of 15 years of median survival for adults aged 65–90 years of age compared with the general US population.[17]
- The 1-year HF mortality rate is approximately 30%, increasing to approximately 40% at 5 years.[22]

Chronic Kidney Disease (CKD)

Prevalence

- Based on data from 2017 through March 2020, 35.5 million US adults (14%) have CKD.[12,14] About 1 in 3 people with diabetes and 1 in 5 people with high blood pressure have kidney disease.[15]

Figure 1. Percentage of US Adults Aged 18 years and Older with CKD*, by Age, Sex and Race/Ethnicity[23]



Incidence

- There are approximately 360 new dialysis starts per day.[23]

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[21] Centers for Disease Control and Prevention. About Heart Failure [Internet]. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2024. Available from: https://www.cdc.gov/heart-disease/about/heart-failure.html.

[22] 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 Feb;28(2):157-167. https://doi.org/10.18553/jmcp.2022.28.2.157.

[23] Centers for Disease Control and Prevention. Chronic Kidney Disease in the United States, 2023 [Internet]. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2023. Available from: https://www.cdc.gov/kidney-disease/php/data-research/index.html.

- Incidence rates are not available for new diagnoses of CKD, however it is estimated that 1 in 3 US adults is at risk for CKD. This estimate is based on the prevalence of diabetes, hypertension (high blood pressure) and obesity in the population and living without treatment.[16]

Disease Severity

- CKD severity is based on estimated glomerular filtration rate (eGFR), a calculation to estimate how well an individual's kidneys filter blood, and albumin to creatinine ratio (ACR), a measure of protein in the urine. Lower eGFR values and higher albuminuria levels (ACR) correspond to reduced kidney function. In the following table, eGFR categories G1-G5, are equivalent to Stages 1-5 in subsequent table(s).[24]

Table 3. Percentage by eGFR and ACR, 2017-March, 2020[24]

Percentage | Number of Persons | Publications

(a) Percentage by eGFR and ACR, 2017-March, 2020

eGFR Categories	A1: Normal to mildly increased (ACR <30 mg/g)	A2: Moderately increased (ACR 30-299 mg/g)	A3: Severely increased (ACR ≥300 mg/g)	Total
G1: Normal or high (eGFR ≥90mL/min/1.73m²)	59.8	5.0	0.68	65.5
G2: Mildly decreased (eGFR 60-89 mL/min/1.73m²)	26.2	2.4	0.35	28.9
G3a: Mildly to moderately decreased (eGFR 45-59 mL/min/1.73m²)	3.1	0.79	0.12	4.0
G3b: Moderately to severely decreased (eGFR 30-44 mL/min/1.73m²)	0.61	0.32	0.18	1.1
G4: Severely decreased (eGFR 15-29 mL/min/1.73m²)	0.07	0.08	0.18	0.34
G5: Kidney failure (eGFR <15 mL/min/1.73m²)	0.00	0.02	0.13	0.15
Total	89.8	8.6	1.6	100

Cost of illness/Financial Impact

- Medicare beneficiaries with CKD cost $87.2 billion in 2019.[23]
- Medicare spending for beneficiaries with CKD (not including ESKD) ages 66 or older was nearly $77 billion in 2021, representing 24.1% of Medicare spending in this age group.[25]
- In 2021, annual per-person spending attributable to Medicare Parts A, B, and D was more than double for beneficiaries ages 66 or older with CKD ($28,162) compared with those without CKD ($13,604).[25]

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[24] United States Renal Data System. 2024 USRDS Annual Data Report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2024. Available from: https://usrds-adr.niddk.nih.gov/2024/chronic-kidney-disease/3-morbidity-and-mortality-in-patients-with-ckd.

[25] National Institute of Diabetes and Digestive and Kidney Diseases. Kidney Disease Statistics for the United States [Internet]. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, US Department of Health and Human Services; 2023. Available from: https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease.

Table 4. Per person per year Medicare FFS Spending among older adults with CKD, by CKD stage overall and by patient characteristics, 2022[24]

	All CKD	Stages 1-2	Stage 3	Stages 4-5
Patient counts	2,649,040	280,940	1,565,020	234,060
Patient years at risk	2,461,388	267,024	1,461,236	200,395
All patients	$28,116	$24,640	$27,327	$38,691
Age				
66-69	$27,795	$23,405	$27,676	$44,136
70-74	$26,330	$22,152	$26,102	$40,598
75-79	$27,705	$24,505	$26,821	$36,833
80-84	$28,258	$25,926	$26,825	$38,892
85+	$30,591	$29,299	$29,230	$36,668
Sex				
Female	$27,290	$23,475	$25,954	$37,343
Male	$28,990	$25,862	$28,963	$40,498
Race				
White	$27,636	$24,650	$26,784	$37,726
Black	$32,384	$26,062	$31,561	$45,473
Other	$29,305	$23,418	$29,811	$40,274
Diabetes				
No	$24,093	$20,783	$23,293	$32,287
Yes	$32,591	$29,120	$32,129	$43,725
Heart Failure				
No	$22,689	$20,369	$21,784	$30,548
Yes	$44,973	$42,832	$43,582	$52,022

Data source: Medicare 5% FFS sample. Point prevalent individuals aged ≥66 years on January 1, 2022 with CKD and Medicare Parts A, B, & D coverage in 2021 (ESRD excluded)

Figure 2. All-cause hospitalization rates in older adults, Medicare FFS, 2012-2022, by CKD status, adjusted for demographics and comorbidities[24]

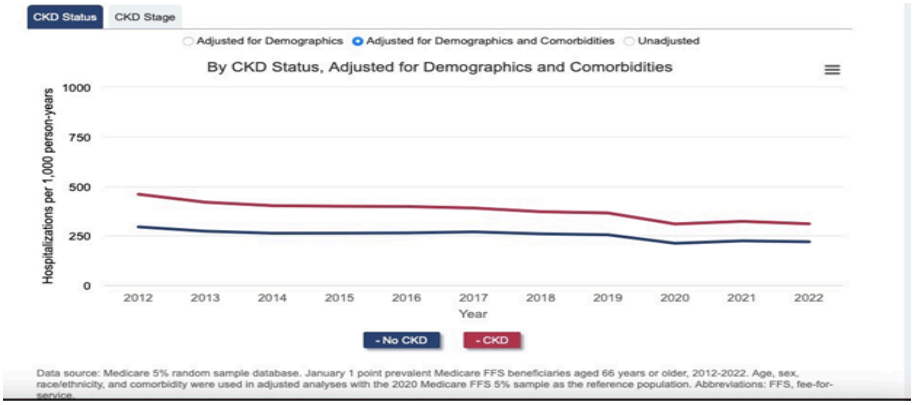
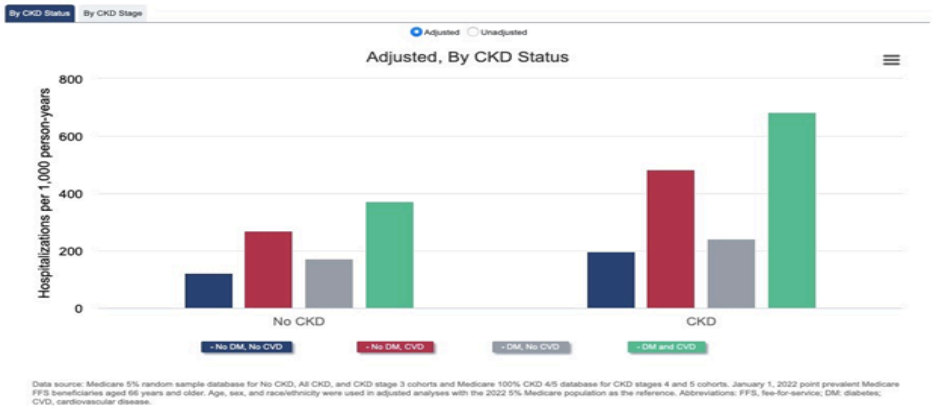


Figure 3. All-cause hospitalization rates in older adults, by presence of diabetes mellitus and cardiovascular disease, Medicare FFS, 2022, Adjusted by CKD Status[24]



Mortality

- In 2021, the demographic-adjusted mortality rate was more than twice as high among Medicare beneficiaries ages 66 years or older with CKD (101.8 per 1,000 person-years) than among those without CKD (46.3 per 1,000 person-years).[25]
- In Maryland, all-cause mortality in older adults in 2022 in persons without CKD vs. all stages of CKD was 39.4 vs 114.5 per 1,000 person year, respectively.[24]

Section 3: Regulatory Approval and Market Context

Element 3.1: COMAR 14.01.04.05.C(1)(g)(ix)—Analysis of the prescription drug product's approval process

The U.S. Food and Drug Administration (FDA) approved Farxiga on January 8, 2014.[26] In 2011, the FDA referred the drug to the advisory committee because it would have been the first-in-class drug. At the July 19, 2011 FDA Endocrinologic and Metabolic Drugs Advisory Committee meeting, the committee voted six to nine (yes/no) on the question "Do the efficacy and safety data provide substantial evidence to support approval of dapagliflozin as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus?"[27]

[26] Drugs@FDA Search

[27] http://web.archive.org/web/20161023221930/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM268726.pdf

After receiving additional information, FDA approved Farxiga in 2014. At the time of approval, Farxiga became the second SGLT-2 inhibitor approved.[28] Since the original approval, the FDA has approved 22 supplemental applications. Eight of these 22 supplemental applications relate to new efficacy data, including four for new indications and one for a new patient population. Farxiga was originally approved as "a sodium-glucose cotransporter 2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus."[29]

FDA approved Farxiga with the post-market commitment to conduct:

> [a] randomized, double-blind, placebo-controlled trial (the DECLARE trial) evaluating the effect of dapagliflozin on the incidence of major adverse cardiovascular events (MACE) in patients with type 2 diabetes mellitus. The primary objective of the trial should be to demonstrate that the upper bound of the 2-sided 95% confidence interval for the estimated risk ratio comparing the incidence of MACE (non-fatal myocardial infarction, non-fatal stroke, cardiovascular death) observed with dapagliflozin to that observed in the placebo group is less than 1.3. The long-term effects of dapagliflozin on the incidence of liver toxicity, bone fractures, nephrotoxicity/acute kidney injury, breast and bladder cancer, complicated genital infections, complicated urinary tract infections/pyelonoephritis/urosepsis, serious events related to hypovolemia and serious hypersensitivity reactions should also be assessed. The estimated glomerular filtration rate (eGFR) should also be monitored over time to assess for worsening of renal function.[30]

The results of this post-marketing commitment led to the FDA approving, on October 18, 2019, a second indication "to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors."[31]

The sponsors submitted a supplemental application for Type I diabetes. In July 2019 the FDA issued a complete response letter advising that the application was not approved.[32]

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[28] Drugs@FDA Search
[29] https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/202293s000lbl.pdf
[30] https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2014/202293Orig1s000ltr.pdf
[31] https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/202293s018lbl.pdf
[32] https://www.astrazeneca.com/media-centre/press-releases/2019/update-on-us-regulatory-decision-for-farxiga-in-type-1-diabetes-15072019.html#

On May 5, 2020, the FDA approved Farxiga for a new indication "to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure with reduced ejection fraction (NYHA class II-IV)."[33]

On April 30, 2021, the FDA approved Farxiga "to reduce the risk of sustained eGFR decline, end stage kidney disease cardiovascular death and hospitalization for heart failure in adults with chronic kidney disease at risk of progression."[34]

On May 8, 2023, the FDA approved Farxiga "to reduce the risk of cardiovascular death, hospitalization for heart failure and urgent heart failure visit in adults with heart failure."[35]

On June 12, 2024, the FDA expanded Farxiga's diabetes indication to children ages 10 and above.[36] This fulfilled a Pediatric Research Equity Act (PREA) requirement.[37] They have no outstanding PREA requirements.[38]

The FDA granted Farxiga Fast Track Designation in the US for heart failure following acute myocardial infarction.[39] The FDA granted Farxiga Breakthrough Therapy Designation for chronic kidney disease.[40] The FDA granted Farxiga Priority Review for the treatment of patients with chronic kidney disease.[41]

Element 3.2: COMAR 14.01.04.05.C(1)(g)(x)- Analysis of the prescription drug product's shortage status

Farxiga is not in shortage.[42]

[33] https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/202293s020lbl.pdf
[34] https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/202293s024lbl.pdf
[35] https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/202293s026lbl.pdf
[36] https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/202293s031lbl.pdf
[37] https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2024/202293Orig1s031,205649Orig1s022ltr.pdf
[38] https://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm
[39] https://www.astrazeneca.com/media-centre/press-releases/2020/farxiga-granted-fast-track-designation-in-the-us-for-heart-failure-following-acute-myocardial-infarction-leveraging-an-innovative-registry-based-trial-design.html#
[40] https://www.astrazeneca.com/media-centre/press-releases/2020/farxiga-granted-breakthrough-therapy-designation-in-us-for-chronic-kidney-disease.html#
[41] https://www.astrazeneca.com/media-centre/press-releases/2021/farxiga-granted-us-priority-review-for-ckd.html#
[42] FDA Drug Shortage Databases. https://dps.fda.gov/drugshortages