Sodium-Glucose Co-transporter-2 (SGLT2) Inhibitor Step Therapy

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Quantity Limit
Brenzavvy (bexagliflozin)	May be subject to quantity limit
Invokamet (canagliflozin/metformin)	
Invokamet XR (canagliflozin/metformin)	
Invokana (canagliflozin)	
Jardiance (empagliflozin)	
Farxiga (dapagliflozin)	
Segluromet (ertugliflozin/metformin)	
Steglatro (ertugliflozin)	
Synjardy (empagliflozin/metformin)	
Synjardy XR (empagliflozin/metformin extended-release)	
Xigduo XR (dapagliflozin/metformin extended-release)	

APPROVAL CRITERIA

Requests for Farxiga (dapagliflozin), Jardiance (empagliflozin), Synjardy (empagliflozin/metformin), Synjardy XR (empagliflozin/metformin extended-release) or Xigduo XR (dapagliflozin/metformin extended-release) may be approved when the following criteria are met:

I. Individual has had a trial and inadequate response or intolerance to metformin (AACE 2023). Medication samples/coupons/discount cards are excluded from consideration as a trial; **OR**

II. Individual has a contraindication to metformin therapy;

OR

III. Farxiga (dapagliflozin) or Jardiance (empagliflozin) may be approved if individual has type 2 diabetes and a history of atherosclerotic cardiovascular disease (ASCVD) including one or more of the following:
   A. Acute coronary syndrome;
   B. Coronary artery disease (CAD);
   C. History of myocardial infarction (MI);
   D. Stable or unstable angina;

E. Stroke;
F. Transient ischemic attack (TIA);
G. Peripheral arterial disease (PAD);

OR

IV. Farxiga (dapagliflozin) may be approved for an individual with New York Heart Association (NYHA) class II, III or IV heart failure symptoms when the following criteria are met:
A. Individual has an ejection fraction of 40% or less; **AND**
B. Individual will be taking Farxiga (dapagliflozin) in combination with a beta blocker (bisoprolol, carvedilol, metoprolol succinate) **AND** an angiotensin-converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB) or Entresto (sacubitril/valsartan) unless contraindicated or not tolerated (McMurray 2019, Packer 2020);

OR

C. Individual has an ejection fraction of greater than 40%;

IV. Farxiga (dapagliflozin) may be approved for an individual with chronic kidney disease at risk for progression when the following criterion is met (Herrington 2023, Heerspink 2020; KDIGO 2022):
A. Individual will be taking Farxiga (dapagliflozin) in combination with an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) unless contraindicated or not tolerated;

OR

V. Jardiance (empagliflozin) may be approved for an individual with New York Heart Association (NYHA) class II, III or IV heart failure symptoms when the following criteria are met:
A. Individual has an ejection fraction of 40% or less; **AND**
B. Individual will be taking Jardiance (empagliflozin) in combination with a beta blocker (bisoprolol, carvedilol, metoprolol succinate) AND an angiotensin-converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB) or Entresto (sacubitril/valsartan) unless contraindicated or not tolerated (McMurray 2019, Packer 2020);

OR

C. Individual has an ejection fraction of greater than 40%.

OR

IV. Jardiance (empagliflozin) may be approved for an individual with chronic kidney disease at risk for progression when the following criterion is met (Herrington 2023; Heerspink 2020; KDIGO 2022):
A. Individual will be taking Jardiance (empagliflozin) in combination with an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) unless contraindicated or not tolerated.

Requests for Brenzavvy (bexagliflozin), Invokamet (canagliflozin/metformin), Invokamet XR (canagliflozin/metformin), Invokana (canagliflozin), Segluromet (ertugliflozin/metformin), Steglatro (ertugliflozin), may be approved when the following criteria are met:

I. Individual has a contraindication to metformin therapy;
AND
II. Documentation is provided that individual has had a trial and inadequate response or intolerance to A. and B. Medication samples/coupons/discount cards are excluded from consideration as a trial
   A. Jardiance (empagliflozin) or Synjardy (empagliflozin/metformin) or Synjardy XR (empagliflozin/metformin extended release);
   AND
   B. Farxiga (dapagliflozin) or Xigduo XR (dapagliflozin/metformin extended-release);

A SGLT2 inhibitor may not be approved for any of the following:

I. Individual is on dialysis (KDIGO 2022); **OR**
II. Individual is requesting Jardiance (empagliflozin), Farxiga (dapagliflozin), Invokana (canagliflozin), Steglatro (ertugliflozin) or Brenzavvy (bexagliflozin) with an eGFR less than 20 mL/min/1.73 m2 (unless individual is stabilized on the requested agent and using it treat chronic kidney disease) (KDIGO 2022); **OR**
III. Individual is requesting Invokamet (canagliflozin/metformin), Invokamet XR (canagliflozin/metformin), Segluromet (ertugliflozin/metformin), Synjardy (empagliflozin/metformin), Synjardy XR (empagliflozin/metformin extended release) or Xigduo XR (dapagliflozin/metformin extended-release) with an eGFR less than 45 mL/min/1.73m^2; **OR**
IV. Individual is requesting for the treatment of type 1 diabetes mellitus; **OR**
V. Individual is requesting for weight loss or the treatment of obesity alone.

NOTE:
Invokamet/XR, Segluromet, Synjardy/XR and Xigduo XR have a black box warning for lactic acidosis as they contain metformin. Post-marketing cases of metformin-associated lactic acidosis have resulted in death, hypothermia, hypotension and resistant bradyarrhythmias. Risk factors include renal impairment, concomitant use of certain agents, age > 65 years, radiological studies with contrast, surgery and other procedures, hypoxic states, excessive alcohol intake and hepatic impairment. If lactic acidosis is suspected, discontinue the metformin-containing agent and institute general supportive measures in a hospital setting. Prompt hemodialysis is recommended.

Key References:

1. Anker SD, Butler J, Filippatos G, et al; EMPEROR-Preserved Trial Investigators. Empagliflozin in Heart Failure with a Preserved Ejection Fraction. *N Engl J Med*. 2021 Oct 14;385(16):1451-1461.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 5, 2024.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al; DAPA-CKD Trial Committees and Investigators. Dapagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med*. 2020 Oct 8;383(15):1436-1446.
5. Heidenreich P, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2022 May, 79 (17) e263–e421.
6. Herrington WG, Staplin N, et al. Empagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med*. 2023 Jan 12;388(2):117-127.

7. 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. Available at: https://kdigo.org/wp-content/uploads/2022/10/KDIGO-2022-Clinical-Practice-Guideline-for-Diabetes-Management-in-CKD.pdf. Accessed: July 11, 2024.
8. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
9. McMurray JJV, Solomon SD, Inzucchi SE, et al; DAPA-HF Trial Committees and Investigators. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. *N Engl J Med*. 2019 Nov 21;381(21):1995-2008.
10. Packer M, Anker SD, Butler J, et al; EMPEROR-Reduced Trial Investigators. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. *N Engl J Med*. 2020 Oct 8;383(15):1413-1424.
11. Perkovic V, Jardine MJ, Neal B, et al; CREDENCE Trial Investigators. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. *N Engl J Med*. 2019 Apr 14.
12. Samson SL, Vellanki P, Blonde L, et. al. American Association of Clinical Endocrinologists (AACE) Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update. *Endocrine Practice*. 2023;29:305-340.
13. US Food and Drug Administration. FDA Drug Safety Communication: FDA revises warnings regarding use of the diabetes medicine metformin in certain patients with reduced kidney function. Last updated: November 14, 2017. Available at https://www.fda.gov/Drugs/DrugSafety/ucm493244.htm. Accessed: July 7, 2024.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.