PRIOR AUTHORIZATION POLICY

POLICY: Inpefa Prior Authorization Policy
- Inpefa™ (sotagliflozin tablets – Lexicon)

REVIEW DATE: 07/10/2024

OVERVIEW

Inpefa, a sodium glucose co-transporter-2 (SGLT-2) inhibitor, is indicated **to reduce the risk of cardiovascular (CV) death, hospitalization for heart failure (HHF), and urgent heart failure visit in adults** with[1]:

- Heart failure; OR
- Type 2 diabetes mellitus, chronic kidney disease (CKD), and other CV risk factors.

Unlike other SGLT-2 inhibitors, Inpefa is not indicated for glycemic control.

Guidelines

The pivotal data with Inpefa are mentioned in many available guidelines. SGLT-2 inhibitors are recommended as first-line treatment for heart failure in the American Heart Association/American College of Cardiology (ACC)/Heart Failure Society of America joint guideline for the management of heart failure (2022).[2] The pivotal trial with Inpefa in patients with heart failure is noted to extend the benefits of SGLT-2 inhibitors to patients with diabetes and acutely decompensated heart failure.[5]

A 2023 ACC expert consensus statement notes the benefit of SGLT-2 inhibitors as part of guideline-directed medical therapy in patients with heart failure with preserved ejection fraction (HFpEF).[8] According to the ACC expert consensus statement, SGLT-2 inhibitors (dapagliflozin, Jardiance™ [empagliflozin tablets]) should be initiated in all individuals with HFpEF who are stable during hospitalization and have no contraindications. The pivotal heart failure trial with Inpefa is mentioned, and it is noted that Inpefa treatment resulted in a significantly lower total number of deaths from CV causes, HHF, and urgent visits for heart failure than placebo, regardless of left ventricular ejection fraction.

A 2023 focused update of the 2021 European Society of Cardiology guidelines for the diagnosis and treatment of acute and chronic heart failure recommends an SGLT-2 inhibitor (dapagliflozin, Jardiance) in patients with symptomatic heart failure with moderately-reduced ejection fraction (HFmrEF) or HFpEF to reduce the risk of HHF or CV death (Class I, Level A).[10] In patients hospitalized for acute heart failure, an intensive strategy of initiation and rapid up-titration of evidence-based treatment (including, but not limited to dapagliflozin or Jardiance) before discharge and during frequent and careful follow-up visits in the first 6 weeks following HHF is recommended to reduce the risk of HHF or death (Class I, Level B). In patients with type 2 diabetes and CKD, SGLT-2 inhibitors (dapagliflozin or Jardiance) are recommended to reduce the risk of HHF or CV death (Class I, Level A).

The 2024 ACC expert consensus decision pathway for heart failure with reduced ejection fraction (HFrEF) recommends SGLT inhibitors (dapagliflozin, Inpefa, and Jardiance) as a core therapy in the "four pillars" of medical care for HFrEF.[11]

The Kidney Diseases: Improving Global Outcomes (KDIGO) clinical practice guideline for diabetes management in CKD (2022) and the American Diabetes Association (ADA)/KDIGO diabetes management in CKD consensus report (2022) recommend an SGLT-2 with proven kidney or CV benefit for patients with type 2 diabetes, CKD, and estimated glomerular filtration rate (eGFR) $\geq$ 20 mL/min/1.73 m^2.[4,6] SGLT-

2 inhibitors are recommended independent of hemoglobin A_{1c} (HbA_{1c}) or the need for additional glucose lowering. This recommendation is based on strong evidence that SGLT-2 inhibitors reduce CKD progression, heart failure, and atherosclerotic CV disease (ASCVD) risk in patients with type 2 diabetes and CKD. Results from pivotal trials with Inpefa are briefly mentioned.

The ADA standards of care (2024) recommend an SGLT-2 inhibitor or glucagon-like peptide-1 (GLP-1) agonist with demonstrated CV disease benefit as part of the glucose lowering regimen and comprehensive CV risk reduction strategy, independent of HbA_{1c} in patients with established CV disease or indicators of high CV risk, established kidney disease, or heart failure.[3] The data with Inpefa from its pivotal trials (SCORED and SOLOIST-WHF) are mentioned and it is noted that both trials were terminated early due to a loss of funding. Of note, the standards state that the early termination of SOLOIST-WHF limited the ability to determine the effects of Inpefa in HFpEF specifically. An ADA and European Association for the Study of Diabetes consensus statement on the management of type 2 diabetes (2022) is reflected in the ADA standards of care.[9]

The American Association of Clinical Endocrinology (AACE) comprehensive type 2 diabetes management algorithm (2023) builds on the 2022 AACE diabetes clinical practice guideline.[5,7] SGLT-2 inhibitors with 'proven benefit' are an alternative to GLP-1 agonists to reduce the risk of major adverse CV events or CV death in patients with type 2 diabetes and established CV disease. For patients with type 2 diabetes and established ASCVD or at high risk for ASCVD, the use of an SGLT-2 inhibitor reduces the risk of HHF and in patients with heart failure and/or CKD, SGLT-2 inhibitors should be used as first-line therapy. SGLT-2 inhibitors are recommended in patients with type 2 diabetes and heart failure regardless of glycemic goal or other antihyperglycemic treatments. There are robust data for the benefit of SGLT-2 inhibitors to reduce adverse renal outcomes. Use of an SGLT-2 inhibitor with 'proven benefits' is recommended as initial therapy to reduce the progression of diabetic kidney disease and CV disease risk for patients with type 2 diabetes and diabetic kidney disease with eGFR $\geq$ 25 mL/min/1.73 m^2 or $\geq$ 20 mL/min/1.73 m^2 if heart failure is also present.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Inpefa. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Inpefa is recommended in those who meet the following criteria:

FDA-Approved Indication(s)

1. **Heart Failure, To Reduce the Risk of Cardiovascular Death, Hospitalization for Heart Failure, and Urgent Heart Failure Visit.** Approve for 1 year if the patient is ≥ 18 years of age.

2. **Type 2 Diabetes, To Reduce The Risk of Cardiovascular Death, Hospitalization for Heart Failure, and Urgent Heart Failure Visit.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has chronic kidney disease; AND
   - **C)** Patient has one or more cardiovascular risk factor(s), according to the prescriber.
     Note: Patients with heart failure should be reviewed under criteria for *Heart Failure*.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Inpefa is not recommended in the following situations:

1. **Type 1 Diabetes.** Inpefa is not approved for glycemic control. Note: Patients with heart failure should be reviewed under criteria for *Heart Failure.*

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Inpefa™ tablets [prescribing information]. Lexicon; The Woodlands, TX: May 2023.
2. Heidenreich PA, Bozkurt B, Aguilar D et al. 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America (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. *J Card Fail.* 2022;28:e1-e167.
3. American Diabetes Association – Standards of Care in Diabetes – 2024. *Diabetes Care.* 2024;47(Suppl 1):S1-S321.
4. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group: Rossing P, Muiza Caramori M, Chan JCN, et al. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int.* 2022;102(5S):S1-S127.
5. Blonde L, Umpierrez GE, Reddy SS, et al. American Association of Clinical Endocrinology clinical practice guideline: developing a diabetes mellitus comprehensive care plan – 2022 update. *Endocr Pract*. 2022;18:923-1049.
6. Boer IH, Khunti K, Sadusky T, et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney International.* 2022;102:974-989.
7. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology consensus statement: comprehensive type 2 diabetes management algorithm – 2023 update. *Endocr Pract.* 2023;29:305-340.
8. Kittleson MM, Panjrath GS, Amancherla K, et al. 2023 ACC expert consensus decision pathway on management of heart failure with preserved ejection fraction. *JACC*. 2023;81(18):1835-1878.
9. Davies MJ, Aroda VR, Collins BS, et al. Management of hyperglycemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care.* 2022;45:2753-2786.
10. McDonagh TA, Metra M, Adamo M, et al; and the ESC Scientific Document Group. 2023 focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2023;44(37):3627-3639.
11. American College of Cardiology Solution Set Oversight Committee. 2024 ACC expert consensus decision pathway for treatment of heart failure with reduced ejection fraction. *JACC.* 2024;85(15): 1444-1488