Original Effective Date: 11/29/2023
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Last P&T Approval/Version: 01/29/2025
Next Review Due By: 01/2026
Policy Number: C26204-A

Inpefa (sotagliflozin)

PRODUCTS AFFECTED

Inpefa (sotagliflozin)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Heart failure, Cardiovascular risk reduction

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. ALL INDICATIONS:
1. (a) Documentation member has a diagnosis of heart failure
   OR
   (b) (i) Documentation member has a diagnosis of Type 2 diabetes AND
   (ii) Documentation member is at high risk for cardiovascular events [(a) established

cardiovascular disease OR (b) age ≥55 years in men/≥60 years in women AND ONE of the following: dyslipidemia, hypertension, or current tobacco use] AND

(iii) Documentation member has chronic kidney disease (eGFR of 25-75 mL/min/1.73m^2 or CKD stage 2, 3, or 4)

AND

2. (a) Documentation in treatment plan that member is concurrently receiving guideline-directed medical therapy for heart failure (Heidenreich 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)
   OR
   (b) Documentation in treatment plan that member is concurrently receiving guideline-directed medical therapy for type 2 diabetes (metformin, etc.) and chronic kidney disease (ACEi or ARB)
   AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Inpefa (sotagliflozin) include: a history of serious hypersensitivity reaction]
   AND
4. Prescriber attests or clinical reviewer has found member has no previous use of dialysis
   AND
5. Prescriber attests that the patient is hemodynamically stable and if necessary has had volume depletion corrected

CONTINUATION OF THERAPY:

A. ALL INDICATIONS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms, stabilization of eGFR, or decline of eGFR <50% from pre-treatment
   AND
4. Documentation member has not progressed to end stage renal disease (ESRD) requiring dialysis
   AND
5. Documentation of concurrent use of guideline-directed medical therapy for heart failure OR diabetes and chronic kidney disease

DURATION OF APPROVAL:

Initial Authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

No requirement

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Maximum 400mg once daily

Maximum Quantity Limits – 30 tabs/30 days

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Cardiovascular Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitor

FDA-APPROVED USES:
Indicated to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with:

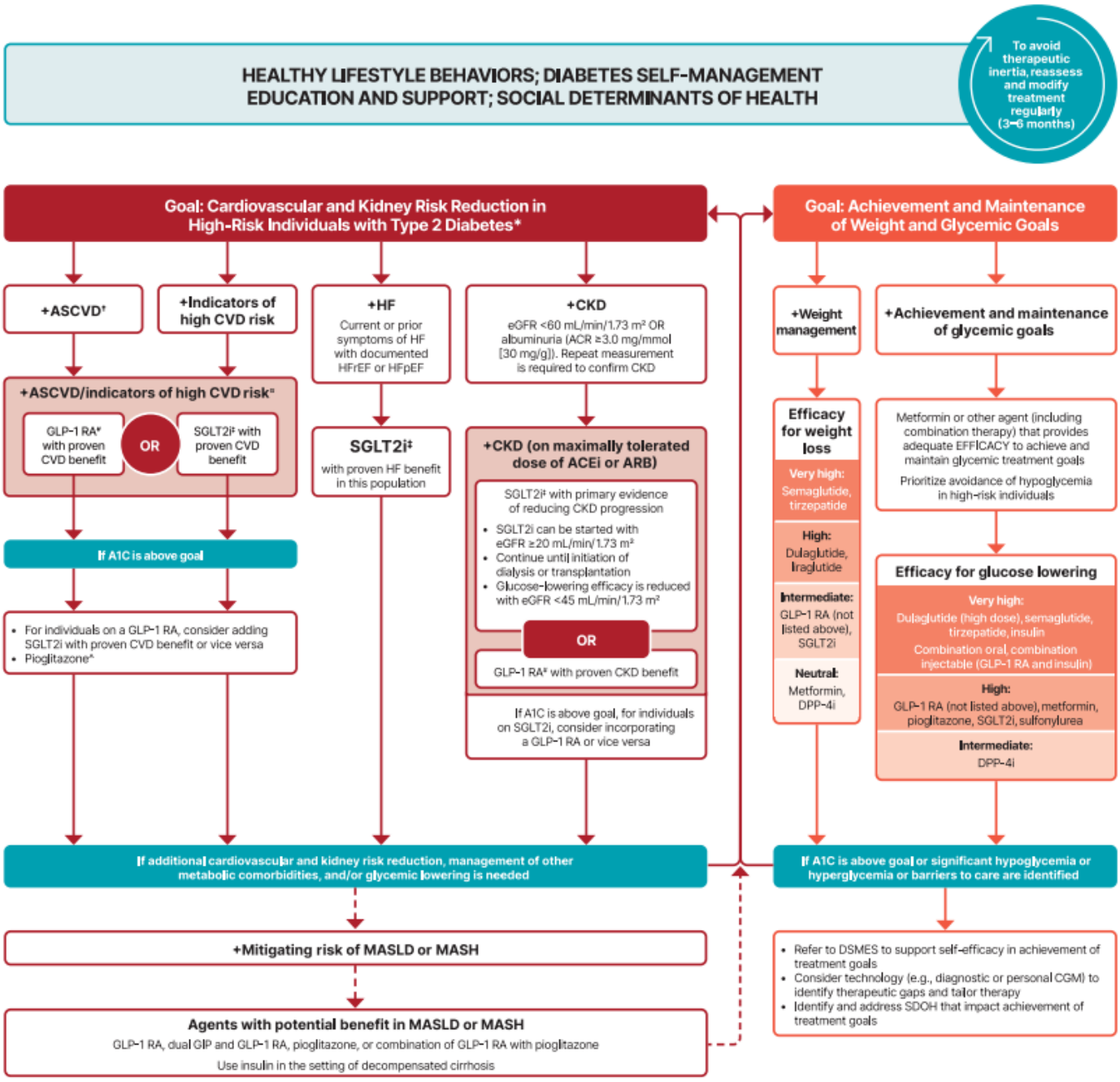
- Heart failure
- Type 2 diabetes mellitus, chronic kidney disease, and other cardiovascular risk factors

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Appendix 1:
Reference: Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes – 2025. Diabetes Care 2025; 48 (Suppl. 1): S181-S206

Use of Glucose-Lowering Medications in the Management of Type 2 Diabetes



* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be made irrespective of background use of metformin or A1C.

† ASCVD: Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, and arterial revascularization procedure) and variably included conditions such as transient ischemic attack, unstable angina, amputation, and symptomatic or asymptomatic coronary artery disease. Indicators of high risk: While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria).

≈ A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high-risk CVD. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details.

For GLP-1 RAs, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and kidney end points in individuals with T2D with established or high risk of CVD. One kidney outcome trial demonstrated benefit in reducing persistent eGFR reduction and CV death for a GLP-1 RA in individuals with CKD and T2D.

‡ For SGLT2is, CV and kidney outcomes trials demonstrate their efficacy in reducing the risks of composite MACE, CV death, all-cause mortality, MI, HHF, and kidney outcomes in individuals with T2D and established or high risk of CVD.

^ Low-dose pioglitazone may be better tolerated and similarly effective as higher doses.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Per American Diabetes Association (ADA) 2022 guidelines, patients with type 2 diabetes who have established atherosclerotic cardiovascular disease or indicators of high risk, established kidney disease, or heart failure, a sodium– glucose cotransporter 2 inhibitor with demonstrated cardiovascular disease benefit is recommended as part of the glucose-lowering regimen independent of A1C and in consideration of patient-specific factors.

Common signs and symptoms of HF include breathlessness, elevated jugular venous pressure, reduced exercise tolerance, laterally displaced apical impulse, fatigue, hepatojugular reflex orthopnea, paroxysmal nocturnal dyspnea, third heart sound (gallop rhythm), and ankle swelling. Risk factors for HF include a sedentary lifestyle, smoking, obesity, excessive alcohol consumption, hypertension, dyslipidemia, diabetes mellitus, and coronary artery disease. Diagnosis of HF consists of evaluating signs and symptoms of HF, EF, and objective evidence of abnormalities in cardiac structure and function that indicate left ventricular diastolic dysfunction and/or elevated left ventricular filling pressure.

The 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America (AHA/ACC/HFSA) guidelines recommend the use of SGLT2 inhibitors in the management of heart failure. SGLT2 inhibitors are recommended for heart failure with reduced ejection fraction, heart failure with mildly reduced ejection fraction, and heart failure with preserved ejection fraction, unless contraindicated. Several randomized controlled trials conducted on patients with type 2 diabetes and either established cardiovascular disease or a high risk for CVD have demonstrated that SGLT2 inhibitors can prevent hospitalizations due to heart failure when compared to a placebo. The studies revealed an overall reduction of 31% in HF hospitalizations, regardless of whether participants had preexisting HF or not. Interestingly, only 10% to 14% of the participants had HF at the beginning of these trials. These beneficial effects seem to be independent of the glucose-lowering effects of SGLT2i. As a result, researchers initiated several trials to investigate the efficacy of SGLT2i on HF outcomes in patients, regardless of whether they had type 2 diabetes or not.

Two such trials, the DAPA-HF (Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure) trial and the EMPEROR-Reduced (Empagliflozin Outcome Trial in Patients with Chronic Heart Failure with Reduced Ejection Fraction) trial, focused on assessing the impact of SGLT2 inhibitors (dapagliflozin and empagliflozin, respectively) compared to a placebo on outcomes. The follow-up period in these trials ranged from 16 to 18 months. The patients included in these trials had symptomatic chronic heart failure with reduced ejection fraction (HFrEF), characterized by a left ventricular ejection fraction (LVEF) of ≤40%, NYHA class II to IV symptoms, and elevated natriuretic peptides. Additionally, they were already receiving guideline-directed medical therapy (GDMT). The trials had certain exclusion criteria, such as an estimated glomerular filtration rate of less than 20 mL/min/1.73 m² in the EMPEROR-Reduced trial, or less than 30 mL/min/1.73 m² in the DAPA-HF trial. Other exclusions were type 1 diabetes or lower systolic blood pressure below 95 to 100 mm Hg. In summary, the trials demonstrated that SGLT2 inhibitors showed promising results in reducing HF hospitalizations and improving outcomes in patients with symptomatic chronic HFrEF, regardless of the presence of type 2 diabetes. In both the DAPA-HF and EMPEROR- Reduced trials, the use of SGLT2 inhibitors resulted in a reduction of approximately 25% in the combined outcome of cardiovascular death or hospitalization due to heart failure, as compared to a placebo. Notably, the benefit was even more significant (30%) when it came to reducing HF hospitalizations. Dapagliflozin, one of the SGLT2i drugs, showed a significant 18% decrease in the risk of cardiovascular death, as well as a 17% reduction in all-cause mortality. Although a meta-analysis of the DAPA-HF and EMPEROR- Reduced trials did not reveal a significant benefit in cardiovascular mortality with empagliflozin, SGLT2i therapy was still associated with a decrease in both all-cause mortality and cardiovascular death. It's important to note that these benefits were observed regardless of the participants' baseline diabetes status. Moreover, in both trials, SGLT2i treatment led to fewer serious renal outcomes and a slower rate of decline in estimated glomerular filtration rate (eGFR). This suggests potential renal protective effects of

SGLT2i.

In the SOLOIST-WHF trial, which involved patients with diabetes and HF hospitalization, the use of sotagliflozin (a dual inhibitor of sodium-glucose co-transporters 1 and 2) led to a 33% reduction in the combined endpoint of cardiovascular death, HF hospitalization, or urgent HF visits. While SGLT2i drugs were generally well-tolerated in the trials, they did show an increased risk of genital infections. However, it's important to exercise caution in clinical practice, particularly regarding the potential risk of euglycemic ketoacidosis, genital and soft tissue infections, and the need for adjusting diuretics to prevent volume depletion, if necessary, when using SGLT2 inhibitors. The SOLOIST trial was a phase 3 multicenter, randomized, double-blind, placebo-controlled study that evaluated the safety and efficacy of Inpefa in patients' post-hospitalization for worsening heart failure. The SCORED trial was also a phase 3 multicenter, randomized, double-blind, placebo-controlled study that evaluated the efficacy of Inpefa in adult patients with type 2 diabetes, chronic kidney disease, and risk factors for cardiovascular disease. The SOLOIST trial studied hemodynamically stable patients with type 2 diabetes who were hospitalized due to the presence of heart failure signs and symptoms and were given IV diuretic therapy. The SCORED trial studied patients with type 2 diabetes, chronic kidney disease, and additional cardiovascular disease risk factors. The trials had specific inclusion and exclusion criteria regarding the patients' conditions and medical history. The SOLOIST study included patients with type 2 diabetes between the ages of 18 and 85 who were hospitalized due to the presence of heart failure signs and symptoms and were given IV diuretic therapy. It excluded patients with end stage heart failure, recent acute coronary syndrome stroke, percutaneous coronary intervention, coronary artery bypass graft, or eGFR < 30. The SCORED study included patients 18 years of age and over with type 2 diabetes with HbA1c ≥7%, chronic kidney disease, and additional cardiovascular disease risk. It excluded patients that planned to start an SGLT2 inhibitor during the trial. In both the SOLOIST and SCORED trials, participants were randomized to receive either Inpefa or placebo. They both had a starting dose of 200mg once daily, with the option to increase to 400mg based on side effects. The primary endpoint of both the SOLOIST and SCORED trials was the total number of events comprised of deaths from cardiovascular causes, hospitalizations from heart failure, and urgent visits for heart failure in patients treated with Inpefa vs. Placebo. The trials also had secondary endpoints, such as occurrences of specific events, changes in health-related quality of life, and renal function. In the SOLOIST trial, the total number of events comprised of deaths from cardiovascular causes, hospitalizations from heart failure, and urgent visits for heart failure in patients treated was 51.3 for the Inpefa group and 76.4 for the placebo group. The p value was 0.001. In the SCORED trial, the total number of events comprised of deaths from cardiovascular causes, hospitalizations from heart failure, and urgent visits for heart failure in patients treated was 5.6 for the Inpefa group and 7.5 for the placebo group. The p value was less than 0.001.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Inpefa (sotagliflozin) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Inpefa (sotagliflozin) include: a history of serious hypersensitivity to Inpefa.

OTHER SPECIAL CONSIDERATIONS:

Inpefa (sotagliflozin) has warnings for diabetic ketoacidosis in patients with Type 1 Diabetes Mellitus and other ketoacidosis, volume depletion, urosepsis and pyelonephritis, hypoglycemia with concomitant use with insulin and insulin secretagogues, and necrotizing fasciitis of the perineum (Fournier's Gangrene).

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-*

standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Inpefa TABS 200MG
Inpefa TABS 400MG

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Appendix References	Q1 2025
REVISION- Notable revisions: Appendix Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q1 2024
New criteria established	Q4 2023