SGLT2 Inhibitor Use in Heart Failure

Our easy-to-read fact sheets provide clinicians with reliable information to share with patients and their caregivers.

Heart failure is a condition in which the heart has a structural or functional impairment. Heart failure can be acute, wherein the beginning signs and symptoms occur rapidly; or chronic, wherein the onset of signs and symptoms are gradual.¹ In patients with heart failure, the heart is not efficiently circulating blood throughout the body, which can cause fluid to back-flow, leading to edema, where fluid leaks out from the blood vessels and into nearby tissues. There are many risk factors for heart failure, including coronary heart disease, hypertension, atherosclerotic cardiovascular disease, diabetes, a family history of heart disease, obesity, chronic pulmonary diseases, inflammation or chronic infection, and treatment with cardiotoxic agents.²

There are different types of heart failure, categorized by the percentage of blood that leaves the left ventricle. The left ventricle is responsible for pumping oxygen-rich blood to the rest of the body.³ Normal ejection fraction—measured as a percentage and meant to reflect how much blood the left ventricle pumps out with each contraction—is greater than 55%.⁴ The following are the 3 different types of heart failure:

- **Heart Failure With Reduced Ejection Fraction (HFrEF):** Also known as systolic heart failure or dilated cardiomyopathy. The ejection fraction for patients with HFrEF is less than 40%. This condition is especially prevalent in patients with coronary artery disease.⁵
- **Heart Failure With Mid-Range Ejection Fraction (HFmrEF):** Also known as borderline heart failure, where the ejection fraction is between 40% to 49%. HFmrEF shares symptoms and some risk factors with HFpEF, like hypertension and female sex at birth. Uncontrolled hypertension is the main cause of hospitalization. HFmrEF is a more recent addition to heart failure clinical practice guidelines.⁶
- **Heart Failure With Preserved Ejection Fraction (HFpEF):** The ejection fraction for patients with HFpEF is at least 50%. Patients with HFpEF are usually older adults and/or women with obesity, hypertension, and/or atrial fibrillation.²⁵

Heart Failure Treatment
Before treatment, the provider will order laboratory tests including complete blood count, urinalysis, and blood glucose measurements. Some heart failure is caused by a specific heart condition that will need to be addressed and treated first.7

Treatment for symptomatic HFrEF include the following:7

- **Angiotensin receptor-neprilysin inhibitor (ANRI):** In patients with class II and III HFrEF, sacubitril-valsartan (Entresto®) is recommended
- **Beta blocker:** carvedilol (Coreg®), sustained-release metoprolol succinate (Toprol-XL®), or bisoprolol
- **Mineralocorticoid receptor antagonist:** In patients with class II through IV HFrEF, eplerenone (Inspra®) or spironolactone (Aldactone®)
- **Sodium glucose cotransporter 2 inhibitors (SGLT2 inhibitor):** In patients with symptomatic chronic HFrEF, dapagliflozin (Farxiga®), empagliflozin (Jardiance®), and sotagliflozin (Inpefa®)
- **Isosorbide and hydralazine:** Recommended for Black patients with class II through IV HFrEF.
- **Diuretic:** loop diuretics or thiazide diuretics can be used as needed for fluid build-up

Treatment recommendations for symptomatic HRmrEF include diuretics as needed for fluid build-up; SGLT2 inhibitor therapy, specifically empagliflozin; an angiotensin-converting enzyme inhibitor (sacubitril-valsartan), or an angiotensin (II) receptor blocker; and a mineralocorticoid receptor antagonist.7

Treatment recommendations for HFrEF include diuretics as needed for fluid build-up; SGLT2 inhibitors, specifically empagliflozin; sacubitril-valsartan; an angiotensin (II) receptor blocker; and a mineralocorticoid receptor antagonist. Other medications may be added if specific conditions develop.7

**Mechanism of Action of SGLT2 inhibitors**

Sodium-glucose-cotransporter 2 inhibitors (SGLT2i), like dapagliflozin, canagliflozin (Invokana®), sotagliflozin, and empagliflozin, are oral medications that increase glucose excretion in the urine. These medications work by inhibiting the SGLT2 enzymes in the kidneys that cause glucose reabsorption. They were recently approved for use in patients with heart failure. Adverse events include urinary tract infections and increased urination.8

**Use of SGLT-2 Inhibitors in Patients With Heart Failure**
These medications were originally studied to evaluate their cardiovascular safety in patients with type 2 diabetes and cardiovascular risk factors or atherosclerotic cardiovascular disease. Studies showed an unexpected improvement in patients with diabetes as well as a decrease in major cardiovascular events and hospitalizations within 2 to 3 months in the patients with atherosclerotic cardiovascular disease.\(^8\)

SGLT2 inhibitors were added to heart failure guidelines in 2022. Dapagliflozin and empagliflozin have shown benefits in patients with HFrEF, HFpEF, and HFmrEF with or without diabetes.\(^7\) SGLT2 inhibitors were found to prevent heart failure hospitalization by up to 30%. They also improved blood pressure and reduced adverse renal outcomes. The exact mechanism of how these medications improve the heart remains unclear.\(^8\)

SGLT2 inhibitors including canagliflozin (Invokana®), dapagliflozin, empagliflozin, and sotagliflozin are recommended as first-line treatment for hyperglycemia in patients with type 2 diabetes with heart failure or at high risk for heart failure. In these patients, they are associated with a reduction in major adverse cardiovascular events, like hospitalizations for heart failure and cardiovascular death and all-cause mortality.\(^7\) They have also been shown to reduce the incidence of heart failure in patients with diabetes with varied cardiovascular risk factors.\(^5\)

**Frequently Asked Questions**

**Will the use of SGLT2 inhibitors improve my heart failure?**

SGLT2 inhibitors improve survival, mortality, and hospitalizations in patients with HFrEF, HFmrEF, and HFpEF. They have been associated with preventing the development of symptomatic heart failure.\(^7\)

**Will SGLT2 inhibitors affect my blood sugar?**

While uncommon, there is a risk of developing hypoglycemia, which is increased if you are also taking sulfonylureas, meglitinides, or insulin.\(^9\) If there are signs of hypoglycemia, like shakiness or dizziness, the patient should sit or lie down, and eat or drink 15 to 20 grams of carbohydrates quickly. For adults, this can be 3 to 4 glucose tablets, 4 ounces of juice or nondiet soda, 1 tablespoon of sugar, or 6 to 8 hard candies. If the patient feels like they may faint, they should call 911.\(^10\)
What are the side effects of SGLT2 inhibitors?

The most common side effects associated with SGLT2 inhibitors include urinary tract infection and female genital mycotic infections. If you have a history of Fournier gangrene, recurrent fungal genital/urinary tract infection, are pregnant or breastfeeding, or heavily drink, discuss with your provider before taking this medication.⁹

Can I take SGLT2 inhibitors with my other medications for heart failure?

SGLT2 Inhibitors are safe and recommended to use with other medications for heart failure. However, if you are taking other medications for other conditions, such as diabetes, speak with your provider to make sure the medication does not interact with other medications.⁷⁹