Talking With Patients About Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors

AMERICAN COLLEGE of CARDIOLOGY

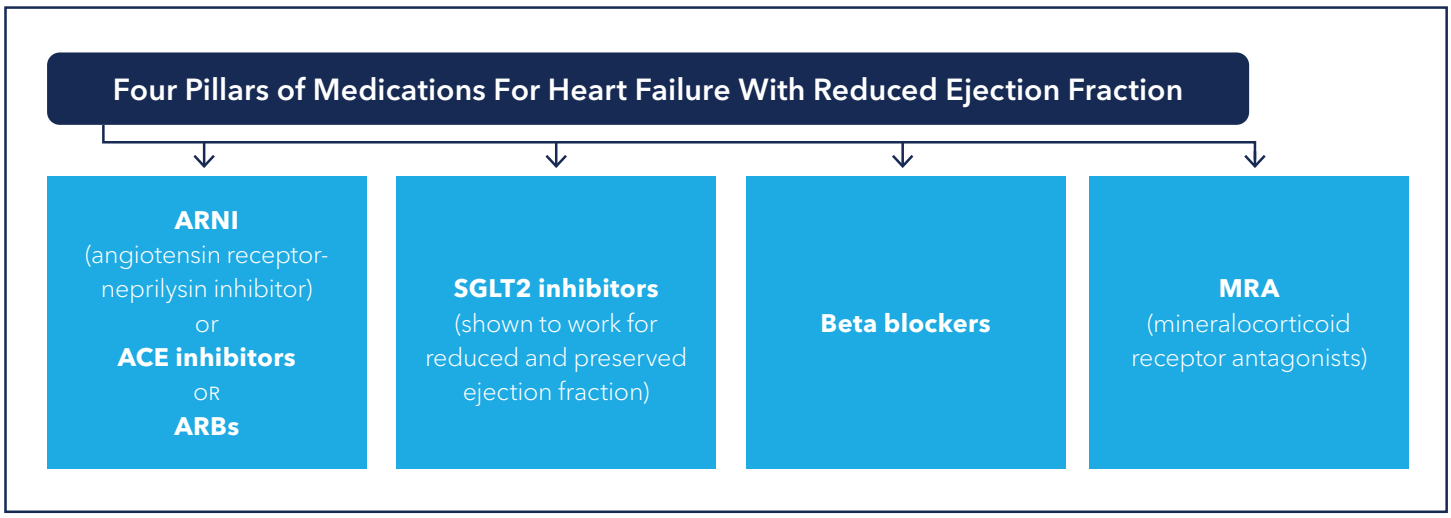
Optimizing SGLT2 inhibitor use to prevent adverse cardiovascular events and improve outcomes in patients with heart failure, diabetes and chronic kidney disease

Sodium-glucose cotransporter-2 (SGLT2) inhibitors have had a somewhat serendipitous story when it comes to their cardiovascular benefits, and these benefits continue to emerge. Against a backdrop of concerns over the cardiovascular risks of newer diabetes medications, the U.S. Food and Drug Administration in 2008 required the collection of safety data. Ironically, a number of large cardiovascular outcomes trials would soon reveal a positive signal, suggesting they had significant cardiovascular benefits. While SGLT2 inhibitors offer a modest reduction in hemoglobin A1C for the management of diabetes, they were shown to significantly lower the risk of major cardiovascular events for these patients. Cardiovascular disease remains the leading cause of mortality in people with type 2 diabetes, accounting for as many as 2 out of 3 deaths.

SGLT2 Inhibitors Approved for Cardiovascular and/or Renal Benefits Beyond Glycemic Control

- Canagliflozin (Invokana)
- Dapagliflozin (Farxiga)
- Empagliflozin (Jardiance)
- Sotagliflozin (Inpefa, a dual SGLT1/2 inhibitor)

Several landmark cardiovascular outcome trials have demonstrated significant cardiovascular benefits and renal protective effects of SGLT2 inhibitors, irrespective of the presence or absence of diabetes and independent of glucose-lowering effects. Studies have found that SGLT2 inhibitors greatly improve cardiovascular outcomes, reducing major cardiovascular events, heart failure hospitalizations and cardiovascular-related death. Moreover, SGLT2 inhibitors have disease-modifying effects for chronic kidney disease (CKD), which affects half of those with heart failure.



As a result, **SGLT2 inhibitors are now included as one of the four pillars of guideline-directed medical therapy for patients with heart failure and are effective across the spectrum of left ventricular ejection fraction**. In studies, SGLT2 inhibitors have also been associated with a reduced risk of arrhythmias and some degree of blood pressure lowering, although more research is needed. Moreover, SGLT2 inhibitors are associated with modest weight loss and improvements in proinflammatory markers.

Despite the clear cardiovascular benefits of SGLT2 inhibitors for patients with heart failure and atherosclerotic cardiovascular disease (ASCVD), **prescriptions of SGLT2 inhibitor therapies remain low**. One study in an August 2023 issue of *JACC Heart Failure* that included data from 130 Veterans Affairs facilities found only 15% of patients with established ASCVD, heart failure and type 2 diabetes in whom an SGLT2 inhibitor would be indicated received one. Other studies have found similarly low prescribing patterns. The explanation for inadequate prescription patterns is multifactorial; for example, siloed health care resulting in ineffective communication across medical specialties, exaggerated worries about side effects, and concerns about cost, though this is less of an issue with generics becoming available. As of August 2024, generic dapagliflozin (Farxiga) is now available in the U.S. with other generic SGLT2 inhibitors under review.

The American College of Cardiology created this discussion guide to help encourage conversations about the role of SGLT2 inhibitors – in reducing cardiovascular events and declines in kidney function and extending survival – and ensure timely initiation of therapy in appropriate populations to improve outcomes. Integration of this class of medicines also underscores the need for multidisciplinary, coordinated care across a patient's lifespan.

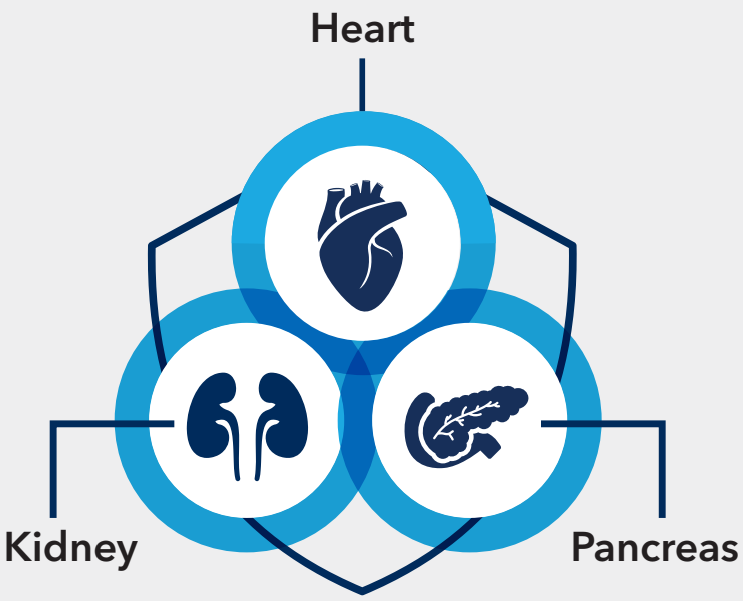
Benefits of SGLT2 Inhibitors

In major clinical outcomes trials, compared with placebo, SGLT2 inhibitors showed significant reductions in:

- Composite endpoints of major adverse cardiovascular events (cardiovascular mortality, nonfatal stroke, myocardial infarction)
- Cardiovascular and all-cause mortality
- Heart failure hospitalizations, a key indicator of disease progression
- Declines in glomerular filtration rate over time and against risk of renal death

Multiple Organ Protection

SGLT2 inhibitors have emerged as an effective way to improve outcomes for heart failure, chronic kidney disease and type 2 diabetes, which are often overlapping diseases.



How SGLT2 Inhibitors Work

Research is ongoing to unravel the mechanisms and multisystem effects of SGLT2 inhibitors. We know SGLT2 inhibitors block the reabsorption of glucose and sodium in the kidneys, increasing the excretion of both. In addition to volume regulation, other possible effects on the heart include reduction of volume overload by improving endothelial function and vascular stiffness, reducing hypertrophy, promoting left ventricular remodeling and myocardial relaxation, lowering inflammation and oxidative stress, among others.

5 Tips for Talking With Patients About SGLT2 Inhibitors

TIP 1 Explain, using clear and simple language, why an SGLT2 inhibitor is being – or should be – added to other medications and lifestyle changes.

These drugs are no longer just diabetes medications, as initially designed (and as many patients may read about). SGLT2 inhibitors have proven benefits for the heart and kidneys too. For patients with heart failure, they lower the chance of acute heart failure episodes, heart attack, stroke and death. As a result, SGLT2 inhibitors are now a standard part of what's called "guideline-directed heart failure management" along with other key heart medicines and lifestyle changes.

In general, these medications help many people:

- Feel better by easing symptoms.
- Stay out of the hospital and reduce the need for urgent heart failure-related health visits.
- Have a better quality of life.
- Avoid or delay dialysis.
- Live longer.

Use the teach-back method to make sure patients understand why an SGLT2 inhibitor is needed. It will also give them language to be able to explain to other health professionals why an SGLT2 inhibitor was added when reviewing their medications.

A Deeper Dive

A quick explainer for patients who want more information about how SGLT2 inhibitors work:

- SGLT2 receptors are found in the kidneys.
- These receptors help the body reabsorb most of the glucose and sodium into the blood.
- SGLT2 inhibitors inhibit or block this activity. This causes the kidneys to remove sodium and glucose, in turn, helping the heart work better.

TIP 2 Talk through and educate patients about potential side effects.

Doing so will help patients be able to 1) self-monitor for possible adverse effects and report them and 2) take steps to lower the chance of related issues. These discussions can also help put into appropriate context the actual risk of experiencing certain – often scary – adverse effects.

These medications are usually well-tolerated, but it is important, especially when recommending or initiating therapy, to review possible side effects to watch for. Here are some of the main ones:

- **Urinary tract infections (UTI) and/or genital yeast infections** (those of the penis or vagina) are the most common side effects of SGLT2 inhibitors. These infections can occur because there is more glucose in the urine and, as a result, around the genitals, which can be an especially hospitable environment for germs to grow. To help avoid problems, advise patients to:
  - Drink plenty of water to prevent infection
  - Keep the genital area clean and healthy
  - Know and watch for signs and symptoms (for example, itching or irritation in the area, foul-smelling odor/unusual discharge, burning when urinating)
  - Share any personal history of UTIs and genital infections
- **Dehydration** can also be a concern, especially if a patient is taking other diuretics. Review all medications, including any over the counter and dietary supplements, and talk about whether adjustments might be needed. Also discuss how individual patients can best stay hydrated – drinking enough water without drinking too much. Drinking enough fluids is also important because SGLT2 inhibitors can **lower blood pressure.**

- ❑ **Hypoglycemia,** rarely, but sometimes in patients also taking insulin or sulfonylureas. Dosing may need to be adjusted and, in some cases, it may be necessary to withhold the SGLT2 inhibitor for a short period.

- ❑ For patients with diabetes, **diabetic ketoacidosis** is rare, but should be discussed as it is a medical emergency if it happens. Let them know what symptoms to watch for (for example, nausea, vomiting, abdominal pain, weakness) and remind them that blood glucose readings aren't always a good indicator. Also advise patients on how to avoid the ketoacidosis – for example, the need to pause this medication if they are unable to tolerate oral intake or before a procedure.

Make sure there are no contraindications to initiating SGLT2 inhibitor therapy.
For example:

- Previous issues/hypersensitivity to the drug
- Pregnancy or breastfeeding
- Being on dialysis
- eGFR <25 ml/min (dapagliflozin)

TIP 3 Set expectations for what patients might need to consider and think about. For example:

- Other medications or doses of medications – diuretics (water pills) and diabetes medicines, especially sulfonylureas and insulin – may need to be adjusted over time. It's important to routinely review a complete list of medications they take. For patients starting an SGLT2 inhibitor, it's good practice to check their weight before initiating therapy to know if their weight drops.
- SGLT2 inhibitors should be discontinued 3-4 days prior to most planned procedures or surgeries to minimize the risk of serious complications. SGLT2 inhibitors are associated with metabolic acidosis and euglycemic ketoacidosis during the perioperative period. Remind patients that it's important to tell their health care team of any dental or other procedures ahead of time. These medications may also need to be withheld if a patient needs to fast for a period of time or in the event of serious, acute illness (e.g., infections, liver or kidney dysfunction) or dehydration. But in certain cases of acute heart failure, the benefit may outweigh any risk and, therefore, should be decided on a case-by-case basis.
- Drinking enough water (and not too much) is important as some people tend to urinate more, which can lead to dehydration.
- Periodic blood work to monitor kidney function, electrolytes and other health measures, as well as urinalysis to check serial protein levels in the urine as SGLT2 inhibitors can lower proteinuria.

TIP 4 Encourage shared decision-making by asking about individual patient priorities and goals.

Presenting options and information about risks and benefits helps to engage them in the process. Doing so can markedly improve adherence and enhance patient-clinician communication.

TIP 5 Check in with patients about cost and other concerns, including assessing social determinants of health.

Affordability is a major barrier to filling or taking SGLT2 inhibitors for many patients. Patients may be able to apply for a drug savings card or financial assistance programs. As more generic options become available, there may be a delay in insurance coverage; therefore, proactively seeking prior authorization may be advisable.

Some patients may be hesitant to add yet another medication to the many they are already taking. It can be helpful to explain how these medications work in complementary ways. Review medications and try to address pill burden.

In addition to educating patients about the cardio and renal protective role SGLT2 inhibitors play, remind them to:

- ❑ Report any new or worsening symptoms (for example, signs of swelling, more shortness of breath, weakness).
- ❑ Take daily weights.
- ❑ Make healthy lifestyle choices.
- ❑ Share anything that makes managing their heart failure more difficult.

Additional Patient Resources

For more information, scan the QR code or visit ***CardioSmart.org/HeartFailure***.
You will find information and tools to share with your patients about SGLT2 inhibitors.

SGLT2 Inhibitors: What Are SGLT2 Inhibitors?

SGLT2 inhibitors are a type of medication. They are now recommended for many people with heart failure, ongoing coronary artery disease, kidney disease, or diabetes.

SGLT2 Inhibitors For Heart Failure: What You Need To Know

If you have heart failure, your doctor may prescribe an SGLT2 (sodium-glucose cotransporter 2) inhibitor to help you feel better and live longer. Use this handout to learn more about SGLT2 inhibitors to treat heart failure.

SGLT2 Inhibitors: 8 Common Questions

If you're taking an SGLT2 inhibitor to treat your heart failure, here are answers to some common questions that might help you.

Tips for Starting an SGLT2 Inhibitor to Treat Your Heart Failure

If you're starting an SGLT2 inhibitor to treat your heart failure, use this handout. It has helpful tips and includes a worksheet to review what you're taking for your heart.

Heart Failure Medication List