Empagliflozin (Jardiance) is one of three approved sodium-glucose cotransporter 2 (SGLT2) inhibitors for type 2 diabetes mellitus. It lowers blood glucose by reducing reabsorption of glucose in the kidney, which leads to increased urinary excretion of glucose.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Dose form</th>
<th>Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empagliflozin</td>
<td>10 mg or 25 mg daily</td>
<td>10- or 25-mg tablets</td>
<td>$410</td>
</tr>
</tbody>
</table>

*S—Estimated retail price of one month’s treatment based on information obtained at http://www.goodrx.com (accessed October 20, 2016).

SAFETY

For all SGLT2 inhibitors, there have been rare postmarket case reports (less than 1%) of pyelonephritis, sepsis of urinary origin, and diabetic ketoacidosis without high blood glucose levels. Other rare serious adverse effects include hypovolemia and hypotension (number needed to harm [NNH] = 335). Although infrequent, severe hypoglycemia may occur in patients taking multiple-dose injection insulin. Mild or moderate hypoglycemia occurs most often when combining empagliflozin with any insulin and less often with sulfonylureas. No human studies have included pregnant or breastfeeding mothers. Empagliflozin is U.S. Food and Drug Administration pregnancy risk category C and should be avoided in the late second and third trimesters, during fetal renal development.

EFFECTIVENESS

Empagliflozin may reduce mortality in patients with diabetes who are at high risk of cardiovascular death. One study that added empagliflozin or placebo to existing type 2 diabetes treatment (75% of participants were already taking metformin) in older patients with preexisting cardiovascular disease demonstrated lower all-cause mortality (5.7% vs. 8.3%; number needed to treat [NNT] = 38 over 3.3 years), cardiovascular mortality (3.7% vs. 5.9%; NNT = 45 over 3.3 years), and hospitalization for heart failure (2.7% vs. 4.1%; NNT = 71) in the empagliflozin group vs. the placebo group. However, empagliflozin is not approved by the U.S. Food and Drug Administration to decrease mortality in patients with cardiovascular disease. There are no long-term data on morbidity or mortality benefits in patients without preexisting cardiovascular disease, and this benefit has not been documented with other SGLT2 inhibitors.

TOLERABILITY

Empagliflozin is generally well tolerated, with no greater discontinuation rate than placebo. There is no difference in the risk of urinary tract infection between the treatment and placebo groups. However, women and men are both more prone to genital fungal infections while taking empagliflozin. Over three years of treatment, 10% of women (NNH = 14) and 5% of men (NNH = 29) report a genital mycotic infection. Empagliflozin can cause minor increases in low-density lipoprotein cholesterol levels, a small decrease (less than 5 mm Hg) in systolic blood pressure, and a slight increase in hematocrit levels, which typically do not warrant additional treatment.
2% body weight (about 4.3 to 4.8 lb [1.94 to 2.16 kg]), and the medication will induce further weight loss in patients already treated with linagliptin (Tradjenta).

When used alone, empagliflozin decreases hemoglobin A1C levels by 0.7 to 0.9 percentage points, with only a small increase in effect with the higher dose. When added to other antidiabetic agents, empagliflozin produces an additional average A1C decrease of 0.6 percentage points. Its effectiveness decreases in patients with lower renal function, and it is not effective in patients with a glomerular filtration rate of less than 45 mL per minute.

**PRICE**

The cost of a one-month supply of empagliflozin is approximately $410. This cost is similar to other SGLT2 inhibitors and is significantly more expensive than metformin or glipizide (Glucofrexp), which both cost about $5 per month.

**SIMPLICITY**

Empagliflozin is taken orally once daily as monotherapy or add-on therapy. The recommended starting dosage is 10 mg once per day, which can be increased to 25 mg once per day if A1C goals are not achieved, although, on average, the dosage increase will produce only minor A1C changes.

**Bottom Line**

Empagliflozin can be added to existing type 2 diabetes treatment to lower A1C levels, although there are less expensive options. In older patients with preexisting cardiovascular disease, empagliflozin can decrease all-cause mortality, cardiovascular mortality, and hospitalization for heart failure.

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**REFERENCES**


