1. INDICATIONS AND USES

1.1 Use in Type 2 Diabetes Mellitus

Dapagliflozin is indicated for the treatment of type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control. Clears urine glucose.

2. WARNINGS

2.1 Hypoglycemia

Hypoglycemia is uncommon with dapagliflozin, but it may occur with dose increases, concomitant use of thiazolidinediones, insulin, or insulin secretagogues, when dietary intake of calories is decreased, or during times of stress or illness. hypoglycemic episodes may increase in severity if concomitant metformin use is added.

2.2 Fluid Volume Excess

Volume excess (which may be severe or life-threatening) can occur when dapagliflozin is administered to patients with moderate renal impairment (eGFR less than 30 mL/min/1.73 m^2) and those with diabetic ketoacidosis. Fluid volume excess may result in life-threatening edema, including pulmonary edema, and death.

2.3 Metabolic Acidosis

Acute metabolic acidosis should be assessed for ketoacidosis regardless of blood glucose levels. Consider testing serum bicarbonate and serum inorganic phosphorus in patients with glucose concentrations above 400 mg/dL. Monitor patients for signs and symptoms of lactic acidosis.

2.4 Iodinated Contrast Imaging Procedures

Prior to Initiation of XIGDUO XR

Patients taking dapagliflozin should discontinue treatment 48 hours prior to iodinated contrast imaging procedures. The recommended use of iodinated contrast imaging procedures is limited to patients with normal renal function (eGFR ≥90 mL/min/1.73 m^2).

5.5 Urosepsis and Pyelonephritis

Cases of urosepsis and pyelonephritis have occurred in patients taking dapagliflozin. Prompt evaluation and treatment of pyelonephritis is recommended.

5.6 Severe Necrotizing Fasciitis and Necrotizing Soft Tissue Infections

Serious cutaneous adverse reactions, including necrotizing fasciitis, have been reported in patients taking dapagliflozin. These reactions can present with life-threatening necrotizing infection requiring urgent surgical intervention, have been identified in patients taking dapagliflozin. Prompt evaluation and treatment of necrotizing fasciitis and necrotizing soft tissue infections is recommended.

5.8 Vitamin B12 and Folic Acid

Vitamin B12 and folic acid deficiencies have been reported due to dapagliflozin use. Consider vitamin B12 and folic acid supplementation for patients at risk.

7.2 Interference with 1,5-anhydroglucitol (1,5-AG) Assay

Monitoring glycemic control with urine glucose tests is not recommended in patients taking dapagliflozin.
Lactic Acidosis.

XIGDUO 850 mg o

850 mg lowering HbA1c.

weight compared with metformin alone and was noninferior to metformin XR monotherapy in alone (see Table 11 and Figure 2). Dapagliflozin 10 mg as monotherapy also provided placebo, or metformin XR (up to 2000 mg/day) plus placebo. Metformin XR dose was up-titrated (NCT00859898) in combination with metformin XR formulation.

coadministered dapagliflozin and metformin hydrochloride immediate-release (IR) tablets have There was no evidence of a mutagenic potential of metformin in the following dapagliflozin does not represent a genotoxic risk to humans.

Dapagliflozin had no effects on mating, fertility, or early embryonic development in treated rats. No animal studies have been conducted with XIGDUO XR to evaluate carcinogenesis, §

Table 8:  Effect of Metformin on Coadministered Drug Systemic Exposure

AUC(0-24 hr) reported.

HbA1c (%)

Sitagliptin (100 mg)

Cimetidine (400 mg)

R-warfarin

No dosing adjustments required for the following:

‡

§

Table 14: Results at Week 52 (LOCF*) in an Active-Controlled Study Comparing

Least squares mean adjusted for baseline value.

‡

¶

†

<table>
<thead>
<tr>
<th>Efficacy Parameter</th>
<th>dapagliflozin</th>
<th>metformin XR</th>
<th>placebo</th>
<th>Difference from dapagliflozin</th>
<th>Difference from metformin XR</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c reduction from baseline (%)</td>
<td>2.0</td>
<td>2.7</td>
<td>1.2</td>
<td>(−0.7, 1.3)</td>
<td>(−0.2, 0.2)</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>−2.0</td>
<td>−2.7</td>
<td>−1.2</td>
<td>(−0.7, 1.3)</td>
<td>(−0.2, 0.2)</td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>0.6</td>
<td>1.3</td>
<td>1.0</td>
<td>(−0.4, 0.4)</td>
<td>(−0.1, 0.1)</td>
</tr>
<tr>
<td>Body Weight at Week 52 (mean)</td>
<td>82.6</td>
<td>83.9</td>
<td>84.6</td>
<td>(−1.3, 0.7)</td>
<td>(−0.8, 0.1)</td>
</tr>
</tbody>
</table>

Instruct patients to inform their doctor that they are taking XIGDUO XR prior to any surgical or other procedure that might lead to dehydration or stress, including serious illness, severe infection, or other critical illnesses. Inform patients that necrotizing infections of the perineum (Fournier’s gangrene) have occurred with the components of XIGDUO XR. Advise patients to immediately report any of the following symptoms that may be signs of lactic acidosis:

- Drowsiness or sleepiness
- Feeling like you might pass out
- Feeling weak or tired
- Feeling short of breath or shortness of breath
- Feeling cold or clammy
- Feeling nauseous or vomiting
- Having a fast or irregular heart beat
- Feeling pain in your side, are plain on the reverse side, and are available in the strengths and packages listed in

How Supplied

Inform patients that necrotizing infections of the perineum (Fournier’s gangrene) have occurred with the components of XIGDUO XR. Advise patients to immediately report any of the following symptoms that may be signs of lactic acidosis:

- Drowsiness or sleepiness
- Feeling like you might pass out
- Feeling weak or tired
- Feeling short of breath or shortness of breath
- Feeling cold or clammy
- Feeling nauseous or vomiting
- Having a fast or irregular heart beat
- Feeling pain in your side, are plain on the reverse side, and are available in the strengths and packages listed in

How Supplied

Inform patients that necrotizing infections of the perineum (Fournier’s gangrene) have occurred with the components of XIGDUO XR. Advise patients to immediately report any of the following symptoms that may be signs of lactic acidosis:

- Drowsiness or sleepiness
- Feeling like you might pass out
- Feeling weak or tired
- Feeling short of breath or shortness of breath
- Feeling cold or clammy
- Feeling nauseous or vomiting
- Having a fast or irregular heart beat
- Feeling pain in your side, are plain on the reverse side, and are available in the strengths and packages listed in

How Supplied