



# Dapagliflozin/metformin extended-release (Xigduo XR™) Abbreviated New Drug Update

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## OVERVIEW<sup>1</sup>

- Fixed-dose combination tablet of dapagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, and metformin extended-release (ER), a biguanide
- Approved for:
  - ❑ Treatment of type 2 diabetes in adults as an adjunct to diet and exercise to improve glycemic control when treatment with both dapagliflozin and metformin are appropriate
- Not indicated for treatment of type 1 diabetes mellitus or diabetic ketoacidosis
- Strengths: dapagliflozin/metformin ER tablets (5 mg/500 mg, 5 mg/1,000 mg, 10 mg/500 mg, 10 mg/1,000 mg)
- Dosage:
  - ❑ Once daily in the morning with food
  - ❑ Gradual dose escalation in to minimize metformin's gastrointestinal (GI) adverse events
  - ❑ Maximum daily dose- 10 mg dapagliflozin; 2,000 mg metformin
  - ❑ Do not crush, chew, or cut
  - ❑ Renal impairment:
    - ❖ Mild- no dosage adjustments
    - ❖ Moderate-severe- do not use in eGFR <60 mL/min/1.73 m<sup>2</sup> or CrCL <60 mL/min or end-stage renal disease (ESRD)
- Boxed warning: lactic acidosis
- Contraindications: moderate-severe renal impairment, hypersensitivity, metabolic acidosis including diabetic ketoacidosis
- Similar warnings and adverse events as individual components:
  - ❑ Metformin: lactic acidosis (avoid in hepatic impairment, temporarily withhold in intravascular contrast studies with iodinated materials), GI side effects, vitamin B12 deficiency

- ❑ Dapagliflozin: genital mycotic infections, increased LDL-C, bladder cancer (not associated with increased incidence but avoid in active bladder cancer; caution in prior bladder cancer history)
- ❑ Both cause weight loss; hypoglycemia not expected but consider a lower dose if taking with insulin or insulin secretagogue, hypovolemia, possible increased fracture risk
- Cationic drugs (e.g., cimetidine, digoxin, etc.) are eliminated by renal tubular secretion so may reduce metformin elimination; use with caution
- No clinical studies with Xigduo XR *combination* tablets. Bioequivalence was demonstrated in healthy adults between Xigduo XR and the individual components, dapagliflozin and metformin.
- In studies of the *individual* drugs, in patients who did not achieve glycemic control with metformin, adding dapagliflozin lowered HbA1c by 0.5-0.9%, reduced weight by 1.4-2 kg, and lowered systolic blood pressure by up to 5 mm Hg

## CLINICAL CONSIDERATIONS<sup>2</sup>

- There are several classes of medications for adults with type 2 diabetes. Although metformin is first line, patients ultimately require multiple classes for glycemic control.
- Other SGLT2 inhibitors on the market include canagliflozin (Invokana<sup>®</sup>), canagliflozin/metformin (Invokamet<sup>®</sup>), dapagliflozin (Farxiga<sup>™</sup>), and empagliflozin (Jardiance<sup>®</sup>).
- AstraZeneca's dapagliflozin/metformin ER (Xigduo XR) does not offer a clinical advantage over the individual components. It offers a convenient fixed-dose combination tablet.

## SUGGESTED UTILIZATION MANAGEMENT

<b>Anticipated Therapeutic Class Review (TCR) Placement</b>	Hypoglycemics, SGLT2 Inhibitors
<b>Clinical Edit</b>	Prior authorization will be required if it is determined that this product will be non-preferred in the appropriate PDL class
<b>Quantity Limit</b>	Max dose: 10 mg dapagliflozin; 2,000 mg metformin
<b>Duration of Approval</b>	One year
<b>Drug to Disease Hard Edit</b>	None

## REFERENCES

<sup>1</sup> Xigduo XR [package insert]. Wilmington, DE; AstraZeneca; October 2014.

<sup>2</sup> Invokamet and Xigduo XR—Two new combinations for type 2 diabetes. Med Ltr. 2014; 56(1457):123-125. Available at [www.medicalletter.org](http://www.medicalletter.org). Accessed December 8, 2014.