

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

209091Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use QTERN safely and effectively. See full prescribing information for QTERN.

QTERN® (dapagliflozin and saxagliptin) tablets, for oral use
Initial U.S. Approval: 2017

INDICATIONS AND USAGE

QTERN is a sodium-glucose cotransporter 2 (SGLT-2) inhibitor and a dipeptidyl peptidase-4 (DPP-4) inhibitor combination product indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) who have inadequate control with dapagliflozin or who are already treated with dapagliflozin and saxagliptin. (1, 14)

Limitations of Use:

- Is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis. (1)
- Should only be used in patients who tolerate 10 mg dapagliflozin. (1)

DOSAGE AND ADMINISTRATION

The recommended dose of QTERN is a 10 mg dapagliflozin/5 mg saxagliptin tablet taken orally once daily in the morning with or without food. (2.1)

- Assess renal function before initiation of therapy and periodically thereafter. Do not initiate QTERN if eGFR is below 60 mL/min/1.73 m². (2.2)
- Discontinue QTERN if eGFR falls persistently below 60 mL/min/1.73 m². (2.2)
- Do not coadminister QTERN with strong cytochrome P450 3A4/5 inhibitors. (2.3, 7.1)
- Tablet should be swallowed whole and not be split or cut.

DOSAGE FORMS AND STRENGTHS

Tablet: 10 mg dapagliflozin/5 mg saxagliptin (3)

CONTRAINDICATIONS

QTERN is contraindicated in patients with:

- History of a serious hypersensitivity reaction to dapagliflozin or to saxagliptin, such as anaphylaxis, angioedema, or exfoliative skin conditions. (4, 5.8, 6.2)
- Moderate to severe renal impairment (eGFR <45 mL/min/1.73 m²), end-stage renal disease (ESRD), or patients on dialysis. (4)

WARNINGS AND PRECAUTIONS

Pancreatitis If pancreatitis is suspected, promptly discontinue QTERN. (5.1, 6.2)

Heart Failure Consider the risks and benefits of QTERN in patients who have known risk factors for heart failure. Monitor patients for signs and symptoms. (5.2)

Hypotension Before initiating QTERN, assess volume status and correct hypovolemia in the elderly, in patients with renal impairment or low systolic blood pressure, and in patients on loop diuretics. Monitor for signs and symptoms during therapy. (5.3, 6.1)

Ketoacidosis Assess patients who present with signs and symptoms of metabolic acidosis for ketoacidosis regardless of blood glucose level. If suspected, discontinue QTERN, evaluate and treat promptly. Before initiating QTERN, consider risk factors for ketoacidosis. Patients on

QTERN may require monitoring and temporary discontinuation of therapy in clinical situations known to predispose to ketoacidosis. (5.4, 6.2)

Acute Kidney Injury and Impairment in Renal Function Consider temporarily discontinuing in settings of reduced oral intake or fluid losses. If acute kidney injury occurs, discontinue and promptly treat. Monitor renal function during therapy. (5.5, 6.2)

Urosepsis and Pyelonephritis Evaluate for signs and symptoms of urinary tract infections and treat promptly, if indicated. (5.6, 6.2)

Hypoglycemia Consider lowering the dose of insulin secretagogue or insulin to reduce the risk of hypoglycemia when initiating QTERN. (5.7, 6.1)

Hypersensitivity Reactions (e.g., urticaria, facial edema) There have been postmarketing reports of serious hypersensitivity reactions treated with saxagliptin, such as anaphylaxis, angioedema, and exfoliative skin conditions. Promptly discontinue QTERN, assess for other potential causes, institute appropriate monitoring and treatment, and initiate alternative treatment for diabetes. (5.8, 6.2)

Genital Mycotic Infections Monitor and treat if indicated. (5.9, 6.1)

Increased LDL-C Monitor and treat per standard of care. (5.10, 6.1)

Bladder Cancer An imbalance in bladder cancers was observed in clinical studies with dapagliflozin. QTERN should not be used in patients with active bladder cancer and should be used with caution in patients with a prior history of bladder cancer. (5.11)

Arthralgia Severe and disabling arthralgia has been reported in patients taking DPP-4 inhibitors. Consider as a possible cause for severe joint pain and discontinue drug if appropriate. (5.12, 6.1, 6.2)

Bullous Pemphigoid: There have been postmarketing reports of bullous pemphigoid requiring hospitalization in patients taking DPP-4 inhibitors. Tell patients to report development of blisters or erosions. If bullous pemphigoid is suspected, discontinue QTERN. (5.13)

Macrovascular Outcomes There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with QTERN. (5.14)

ADVERSE REACTIONS

Adverse reactions reported in ≥5% of subjects treated with 10 mg dapagliflozin and 5 mg saxagliptin were: upper respiratory tract infection, urinary tract infection, and dyslipidemia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca at 1-800-236-9933 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Strong CYP3A4/5 Inhibitors (e.g., *Ketoconazole*) Do not coadminister QTERN with strong cytochrome P450 3A4/5 inhibitors. (2.3, 7.1)

USE IN SPECIFIC POPULATIONS

Pregnancy Advise females of the potential risk to a fetus especially during the second and third trimesters. (8.1)

Lactation QTERN is not recommended when breastfeeding. (8.2)

Geriatrics Higher incidence of adverse reactions related to volume depletion and reduced renal function. (5.3, 5.5, 8.5)

Renal Impairment Higher incidence of adverse reactions related to reduced intravascular volume and renal function. (5.5, 6.1, 8.6)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 02/2017

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

QTERN (dapagliflozin and saxagliptin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) who have inadequate control with dapagliflozin or who are already treated with dapagliflozin and saxagliptin [*see Clinical Studies (14)*].

Limitations of Use

QTERN is not indicated for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

QTERN should only be used in patients who tolerate 10 mg dapagliflozin.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

In patients with volume depletion, correct this condition prior to initiation of QTERN [*see Warnings and Precautions (5.3), and Use in Specific Populations (8.5, 8.6)*].

The recommended dose of QTERN is a 10 mg dapagliflozin/5 mg saxagliptin tablet taken orally once daily in the morning with or without food.

Do not split or cut QTERN tablets.

2.2 Patients with Renal Impairment

Assessment of renal function is recommended prior to initiation of QTERN therapy and periodically thereafter.

Do not initiate QTERN in patients with an estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m².

Discontinue QTERN if eGFR falls persistently below 60 mL/min/1.73 m² [*see Warnings and Precautions (5.5) and Use in Specific Populations (8.6)*].

QTERN is contraindicated in patients with an eGFR less than 45 mL/min/1.73 m² [*see Contraindications (4)*].

2.3 Use with Strong CYP3A4/5 Inhibitors

Do not coadminister QTERN with strong cytochrome P450 3A4/5 inhibitors (e.g., ketoconazole, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin) [*see Drug Interactions (7.1)*].

3 DOSAGE FORMS AND STRENGTHS

QTERN tablets containing 10 mg dapagliflozin and 5 mg saxagliptin are light brown to brown, biconvex, round, film-coated, with “1122” printed on one side, in blue ink.

4 CONTRAINDICATIONS

QTERN is contraindicated in patients with:

- History of a serious hypersensitivity reaction to dapagliflozin or to saxagliptin, including anaphylaxis, angioedema or exfoliative skin conditions [see *Warnings and Precautions (5.8)* and *Adverse Reactions (6.1)*].
- Moderate to severe renal impairment (eGFR less than 45 mL/min/1.73 m²), end-stage renal disease (ESRD), or patients on dialysis [see *Use in Specific Populations (8.6)*].

5 WARNINGS AND PRECAUTIONS

5.1 Pancreatitis

There have been postmarketing reports of acute pancreatitis in patients taking saxagliptin. In a cardiovascular outcomes trial enrolling participants with established atherosclerotic cardiovascular disease (ASCVD) or multiple risk factors for ASCVD (SAVOR trial), cases of definite acute pancreatitis were confirmed in 17 of 8240 (0.2%) patients receiving saxagliptin compared to 9 of 8173 (0.1%) receiving placebo. Pre-existing risk factors for pancreatitis were identified in 88% (15/17) of those patients receiving saxagliptin and in 100% (9/9) of those patients receiving placebo.

After initiation of QTERN, observe patients for signs and symptoms of pancreatitis. If pancreatitis is suspected, promptly discontinue QTERN and initiate appropriate management. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using QTERN.

5.2 Heart Failure

In a cardiovascular outcomes trial enrolling participants with established ASCVD or multiple risk factors for ASCVD (SAVOR trial), more patients randomized to saxagliptin (289/8280, 3.5%) were hospitalized for heart failure compared to patients randomized to placebo (228/8212, 2.8%). In a time-to-first-event analysis the risk of hospitalization for heart failure was higher in the saxagliptin group (estimated Hazard Ratio: 1.27; 95% CI: 1.07, 1.51). Subjects with a prior history of heart failure and subjects with renal impairment had a higher risk for hospitalization for heart failure, irrespective of treatment assignment.

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