

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

Cardiovascular Thrombotic Events

- Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use [see *Warnings and Precautions (5.1)*].
- TREXIMET® is contraindicated in the setting of coronary artery bypass graft (CABG) surgery [see *Contraindications (4) Warnings and Precautions (5.1)*].

Gastrointestinal Bleeding, Ulceration, and Perforation

- NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events [see *Warnings and Precautions (5.2)*].

INDICATION

TREXIMET® (sumatriptan and naproxen sodium) is a combination of sumatriptan, a serotonin (5-HT) 1b/1d receptor agonist (triptan), and naproxen sodium, a non-steroidal anti-inflammatory drug, indicated for the acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older.

LIMITATIONS OF USE

- Use only if a clear diagnosis of migraine headache has been established.
- Not indicated for the prophylactic therapy of migraine attacks.
- Not indicated for the treatment of cluster headache.

CONTRAINDICATIONS

- History of coronary artery disease or coronary vasospasm.
- In the setting of CABG surgery.
- Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders.
- History of stroke, transient ischemic attack, or hemiplegic or basilar migraine.
- Peripheral vascular disease.
- Ischemic bowel disease.
- Uncontrolled hypertension.
- Recent (within 24 hours) use of another 5-HT₁ agonist (e.g., another triptan) or of ergotamine-containing medication.
- Concurrent or recent (past 2 weeks) use of monoamine oxidase-A inhibitor.
- History of asthma, urticaria, other allergic type reactions, rhinitis, or nasal polyps syndrome after taking aspirin or other NSAID/analgesic drugs.
- Known hypersensitivity to sumatriptan, naproxen, or any other component of TREXIMET® (angioedema and anaphylaxis seen).

- Third trimester of pregnancy.
- Severe hepatic impairment.

WARNINGS AND PRECAUTIONS

- Cardiovascular Thrombotic Events: Perform cardiac evaluation in patients with cardiovascular risk factors.
- Arrhythmias: Discontinue TREXIMET® if occurs.
- Chest/throat/neck/jaw pain, tightness, pressure, or heaviness: Generally not associated with myocardial ischemia; evaluate for coronary artery disease in patients at high risk.
- Cerebrovascular Events: Discontinue TREXIMET® if occurs.
- Other Vasospasm Reactions: Discontinue TREXIMET® if non-coronary vasospastic reaction occurs.
- Hepatotoxicity: Inform patients of warning signs and symptoms of hepatotoxicity. Discontinue if abnormal liver tests persist or worsen or if clinical signs and symptoms of liver disease develop.
- Hypertension: Patients taking some antihypertensive medications may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure.
- Heart Failure and Edema: Avoid use of TREXIMET® in patients with severe heart failure unless benefits are expected to outweigh risk of worsening heart failure.
- Medication overuse headache: Detoxification may be necessary.
- Serotonin syndrome: Discontinue TREXIMET® if occurs.
- Renal Toxicity and Hyperkalemia: Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia. Avoid use of TREXIMET® in patients with advanced renal disease.
- Anaphylactic reactions: TREXIMET® should not be given to patients with the aspirin triad. Seek emergency help if an anaphylactic reaction occurs.
- Serious skin reactions: Discontinue TREXIMET® at first sign of rash or other signs of hypersensitivity.
- Hematologic Toxicity: Monitor hemoglobin or hematocrit in patients with any signs or symptoms of anemia.
- Exacerbation of Asthma Related to Aspirin Sensitivity: TREXIMET® is contraindicated in patients with aspirin-sensitive asthma. Monitor patients with preexisting asthma (without aspirin sensitivity).

ADVERSE REACTIONS

The most common adverse reactions (incidence $\geq 2\%$) were:

- Adults: Dizziness, somnolence, nausea, chest discomfort/chest pain, neck/throat/jaw pain/tightness/pressure, paresthesia, dyspepsia, dry mouth.
- Pediatrics: Hot flush (i.e., hot flash[es]) and muscle tightness.

DRUG INTERACTIONS

- Drugs that Interfere with Hemostasis (e.g. warfarin, aspirin, SSRIs/SNRIs): Monitor patients for bleeding who are concomitantly taking TREXIMET® with drugs that interfere with hemostasis. Concomitant use of TREXIMET® and analgesic doses of aspirin is not generally recommended.
- ACE Inhibitors and ARBs: Concomitant use with TREXIMET® in elderly, volume depleted, or those with renal impairment may result in deterioration of renal function. In such high risk patients, monitor for signs of worsening renal function.
- Diuretics: NSAIDs can reduce natriuretic effect of loop and thiazide diuretics. Monitor patients to assure diuretic efficacy including antihypertensive effects.

- Digoxin: Concomitant use with TREXIMET® can increase serum concentration and prolong half-life of digoxin. Monitor serum digoxin levels.
- Lithium: Increases lithium plasma levels.
- Methotrexate: Increases methotrexate plasma levels.

You are encouraged to report negative side effects of taking TREXIMET® to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

To report adverse events, a product complaint, or for additional information about TREXIMET®, call Pernix Therapeutics at 1-877-745-3667.

Please see Full Prescribing Information, including Boxed WARNINGS, before prescribing TREXIMET®.

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