ANIMAL TOXICOLOGY

Corneal Opacities

Dogs receiving oral sumatriptan developed corneal opacities and defects in the corneal epithelium. Corneal opacities were seen at the lowest dosage tested, 2 mg/kg/day, and were present after 1 month of treatment. Defects in the corneal epithelium were noted in a 60-week study. Earlier examinations for these toxicities were not conducted and no-effect doses were not established; the lowest dose tested is approximately 0.8 times the recommended human oral daily dose of 85 mg sumatriptan on a mg/m^2 basis. There was evidence of alterations in corneal appearance on the first day of intranasal dosing to dogs at all doses tested.

PATIENT INFORMATION

MEDICATION GUIDE
TREXIMET™ [trex' i-met] Tablets
(sumatriptan and naproxen sodium)

What is the most important information I should know about TREXIMET?

TREXIMET, which contains sumatriptan and naproxen sodium [a nonsteroidal anti-inflammatory drug (NSAID)], may increase the chance of a heart attack or stroke that can lead to death. This chance increases:

- with longer use of NSAID medicines
- in people who have heart disease.

NSAID-containing medicines, such as TREXIMET, should never be used right before or after a heart surgery called a coronary artery bypass graft (CABG).

NSAID-containing medicines, such as TREXIMET, can cause ulcers and bleeding in the stomach and intestines at any time during treatment. Ulcers and bleeding:

- can happen without warning symptoms
- may cause death.

The chance of a person getting an ulcer or bleeding increases with:

- the use of medicines called steroid hormones (corticosteroids) and blood thinners (anticoagulants)
- longer use
- more frequent use
- smoking
- drinking alcohol
- older age
- having poor health.

TREXIMET is not recommended for people with risk factors for heart disease unless a heart exam is done and shows no problems.

The risk factors for heart disease include:

- high blood pressure
- high cholesterol levels
- smoking
- obesity
- diabetes
- family history of heart disease
- female who has gone through menopause
- male over age 40.

"Serotonin syndrome" is a serious and life-threatening problem that may occur with TREXIMET, especially if used with antidepressant medicines called selective serotonin reuptake inhibitors (SSRIs) or selective norepinephrine reuptake inhibitors (SNRIs).

Commonly used SSRIs are:

- CELEXA® (citalopram HBr)
- LEXAPRO® (escitalopram oxalate)
- PAXIL® (paroxetine)
- PROZAC®/SARAFEM® (fluoxetine)
- SYMBYAX® (olanzapine/fluoxetine)
- ZOLOFT® (sertraline)
- LUVOX® (fluvoxamine).

Commonly used SNRIs are:

- CYMBALTA® (duloxetine)
- EFFEXOR® (venlafaxine).

Call your healthcare provider if you have symptoms of serotonin syndrome, which include:

- mental changes (hallucinations, agitation, coma)
- fast heartbeat
- changes in blood pressure
- high body temperature or sweating
- tight muscles
- trouble walking
- nausea, vomiting, diarrhea.

TREXIMET should only be used:

- exactly as prescribed
- at the lowest dose possible for your treatment
- for the shortest time needed.

TREXIMET already contains an NSAID (naproxen). Do not use TREXIMET with other medicines to lessen pain or fever without talking to your healthcare provider first, because they may contain an NSAID also.

What is TREXIMET?

TREXIMET is a prescription medicine used to treat migraine attacks in adults. It does not prevent or lessen the number of migraines you have, and it is not for other types of headaches. TREXIMET contains 2 medicines: sumatriptan and naproxen sodium (an NSAID). This Medication Guide provides important information you need to know before taking TREXIMET. It does not take the place of talking with your healthcare provider about your medical condition or your treatment.

How should I take TREXIMET?

- Take 1 TREXIMET tablet to treat your migraine headache. Do not take more than 2 TREXIMET tablets in 24 hours. Doses should be separated by at least 2 hours.
- TREXIMET can be taken with or without food.
- Do not split, crush, or chew TREXIMET tablets.
- If you take too much TREXIMET, call the Poison Control Center at 1-800-222-1222.

Who should not take TREXIMET?
Do not take TREXIMET right before or after heart bypass surgery.
Do not take TREXIMET if you have or have had:
- uncontrolled high blood pressure
- hemiplegic or basilar migraine. (Ask your doctor if you are not sure what type of migraine you have.)
- liver problems
- an asthma attack, hives, or other allergic reaction with aspirin or any other NSAID medicine
- a heart attack or a history or symptoms of heart disease (such as chest pain or angina)
- a stroke, mini-stroke (transient ischemic attack or TIA), or other stroke-like syndrome
- problems with blood circulation to parts of your body, such as less blood flow to your intestines (ischemic bowel disease)
- allergic reactions to sumatriptan, naproxen, or other ingredients in TREXIMET.

Do not take TREXIMET if you take or have taken an antidepressant medicine called a monoamine oxidase (MAO) inhibitor within the last 2 weeks. Common MAO inhibitors are isocarboxazid (MARPLAN®), phenelzine (NARDIL®), tranylcypromine (PARNATE®), and selegiline (ELDEPRYL®, EMSAM®). Ask your healthcare provider if you are not sure if your medicine is an MAO inhibitor.
Do not take TREXIMET if you have taken other migraine medicines in the last 24 hours such as:
- ergotamine-containing medicine or
- another triptan medicine.

Before starting TREXIMET, tell your healthcare provider about:
- all of your medical conditions including kidney or liver problems
- all allergies to any medicines
- chest pain, shortness of breath, irregular heartbeats
- medicines you may take for migraines, depression, or other health problems such as MAO inhibitors, SSRIs, or SNRIs
- all the prescription and non-prescription medicines you take, including vitamins and herbal supplements. Some medicines can interact with TREXIMET and cause serious side effects.

Keep a list of your medicines to show to your healthcare provider.
Before starting TREXIMET, tell your healthcare provider if you:
- are pregnant, think you might be pregnant, or are trying to become pregnant. **TREXIMET should not be used by pregnant women late in their pregnancy.**
- are breastfeeding
- have a headache that is different from your usual migraine
- have or have had epilepsy or seizures.

What are the possible side effects of TREXIMET?

Serious side effects include:
- heart attack
- heartbeat problems
- stroke
- high blood pressure

Other side effects include:
- pain, tightness, or pressure in the chest, neck, and throat
- stomach pain
- constipation
- diarrhea

- heart failure from body swelling (fluid retention)
- kidney problems including kidney failure
- bleeding and ulcers in the stomach and intestine
- low red blood cells (anemia)
- life-threatening skin reactions
- life-threatening allergic reactions
- liver problems including liver failure
- asthma attacks in people who have asthma
- loss of blood circulation to areas of your body
- serotonin syndrome (See list of symptoms in “What is the most important information I should know about TREXIMET?”)
- gas
- heartburn
- nausea
- vomiting
- dizziness
- drowsiness
- tiredness
- weakness
- tingling and numbness
- unusual body sensations
- redness of face (flushed)

Get emergency help right away if you have any of the following symptoms:
- shortness of breath or trouble breathing
- chest pain
- swelling of the face or throat
- weakness in one part or on one side of your body
- slurred speech.

Stop TREXIMET and call your healthcare provider right away if you have any of the following symptoms:
- nausea that seems out of proportion to your migraine
- stomach pain
- sudden/severe pain in your belly
- vomit blood
- blood in your bowel movement or it is black and sticky like tar
- itching
- skin rash or blisters with fever
- yellow skin or eyes
- swelling of the arms and legs, hands, feet, face, lips, or tongue
- unusual weight gain
- more tired or weaker than usual

- flu-like symptoms

- serotonin syndrome. See list of symptoms in “What is the most important information I should know about TREXIMET?”

Tell your healthcare provider if you have any side effects that bother you or do not go away. These are not all of the side effects of TREXIMET. For more information ask your healthcare provider.
Call your healthcare provider for medical advice about side effects. You may report side effects at FDA at 1-800-FDA-1088.

How should I store TREXIMET?

- Store TREXIMET at room temperature, 59° to 86°F (15° to 30°C).

- Keep TREXIMET and all medicines out of the reach of children.

General information about TREXIMET

- Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use TREXIMET for a condition for which it was not prescribed.

- Do not give TREXIMET to other people, even if they have the same problem you have. It may harm them.

- This Medication Guide contains the most important information about TREXIMET. If you would like more information, talk with your healthcare provider.

- You can ask your healthcare provider for information written for healthcare professionals.

- For more information call 1-888-825-5249 (toll-free), or visit www.TREXIMET.com.

What are the ingredients in TREXIMET?

Active ingredients: sumatriptan succinate and naproxen sodium
Inactive ingredients: croscarmellose sodium, dextrose monohydrate, dibasic calcium phosphate, FD&C Blue No. 2, lecithin, magnesium stearate, maltodextrin, microcrystalline cellulose, povidone, sodium bicarbonate, sodium carboxymethylcellulose, talc, and titanium dioxide.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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