TREXIMET® (sumatriptan and naproxen sodium) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member’s specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms “experimental” and “investigational” are considered to be interchangeable.

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Description:

Treximet is a fixed-dose combination of sumatriptan and naproxen indicated for the acute treatment of migraine attacks with or without aura in adults and pediatric patients 12 years of age and older. The combination of sumatriptan and naproxen has been shown to be superior for acute migraine treatment compared to either agent alone.

Sumatriptan is a selective agonist for serotonin receptors 5-HT$_{1B}$ and 5-HT$_{1D}$ located on intracranial blood vessels and sensory nerves of the trigeminal system. Activation of these receptors results in vasoconstriction of cranial vessels, inhibition of pro-inflammatory neuropeptide release by trigeminal nerves, and blockage of pain pathways in the brainstem. The medications in the “triptan” class include almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan. All of the triptans have been found to be effective for the treatment of acute migraine. Patients who do not respond well to one triptan may respond to another.

Naproxen is a nonsteroidal anti-inflammatory drug (NSAID) that reversibly inhibits cyclooxygenase 1 and 2 (COX-1 and -2) enzymes, which results in decreased formation of prostaglandin precursors. NSAIDs have antipyretic
Migraine is a common episodic disorder, the hallmark of which is a disabling headache generally associated with nausea, and/or light and sound sensitivity. Migraine with aura refers to the occurrence of transient visual, sensory, language, or motor disturbance that is generally followed by a migraine headache. The exact mechanisms of migraine are unknown, but currently it is believed to initiate from a primary neuronal dysfunction that leads to a sequence of intracranial and extracranial changes accounting for migraine, including the four phases of premonitory symptoms, aura, headache and post-drome. Specifically, activation of the trigeminovascular system, cortical spreading depression, and neuronal sensitization all seem to play a role.

Selection of medication for treatment is directed mainly by the severity of the attacks, presence of associated nausea and vomiting, treatment setting, and patient-specific factors. Abortive treatments are usually more effective if they are given early in the course of the headache (within in the first hour if possible). The 2015 updated guideline assessment published by the American Headache Society lists the following medications as Level A (established as effective) for acute migraine treatment: all triptan drugs, combination of sumatriptan and naproxen, dihydroergotamine nasal spray, NSAIDs (naproxen, ibuprofen, aspirin, diclofenac), acetaminophen/aspirin/caffeine, and acetaminophen (for acute treatment of non-incapacitating migraine).

**Definitions:**

**Drug related events:**

*Ineffective / failure*

Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

**Adverse Drug Event:** Allergic reaction / Hypersensitivity / Intolerance

Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record. A significant adverse drug event is when an individual's outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals' body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.

*Allergic reaction / hypersensitivity* – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.
TREXIMET® (sumatriptan and naproxen sodium) oral tablet (cont.)

If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline.

*Intolerance* – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record.

*Contraindication*
Use of a drug that is not recommended by the manufacturer or FDA labelling.

Use of any drug in the face of a contraindication is outside of the FDA and manufacturer’s labelled recommendation and is considered investigational or experimental.

*Non-adherence*
Individual does not follow prescribe regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record.

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**Precertification:**

Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

This Pharmacy Coverage Guideline does not apply to FEP or other states’ Blues Plans.

Information about medications that require precertification is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy).

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

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**Criteria:**

See “Resources” section for FDA-approved dosage.

- Precertification for Treximet (sumatriptan and naproxen sodium) requires completion of the specific request form in its entirety. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com). Incomplete forms will be returned.

- FDA-approved dosage of Treximet (sumatriptan and naproxen sodium) is considered *medically necessary* for acute treatment of confirmed migraine with or without aura when **ALL** of the following criteria are met:
TREXIMET® (sumatriptan and naproxen sodium) oral tablet (cont.)

1. Individual is 12 years of age or older

2. Medical record documentation of trial and failure or intolerance to ALL of the following preferred triptans:
   - Rizatriptan
   - Sumatriptan
   - Naratriptan
   - Zolmitriptan

   WITH simultaneous use of ONE of the following at doses listed:
   - Aspirin 500 mg
   - Diclofenac 50 mg
   - Ibuprofen 200 mg
   - Naproxen 500 mg

3. ALL of the following baseline tests have been completed before initiation of treatment:
   - Aspartate transaminase (AST), alanine transaminase (ALT)
   - Comprehensive metabolic panel

4. Absence of ALL of the following contraindications:
   - History of ischemic coronary artery disease or coronary artery vasospasm
   - History of coronary artery bypass graft (CABG) surgery
   - Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders
   - History of stroke, transient ischemic attack (TIA), or hemiplegic or basilar migraine
   - Peripheral vascular disease
   - Ischemic bowel disease
   - Uncontrolled hypertension
   - Recent (within 24 hours) use of another 5-HT1 agonist (triptan) OR an ergotamine-containing or ergot-type medication (such as dihydroergotamine or methysergide)
   - Concurrent use with or within 14 days of a monoamine oxidase (MAO) – type A inhibitor
   - Asthma, rhinitis, with or without nasal polyps, urticaria, or allergic-type reaction to aspirin or other NSAIDs
   - Hypersensitivity to any component of Treximet
   - Third trimester of pregnancy
   - Severe hepatic impairment

5. Absence of ALL of the following exclusions:
   - Creatinine clearance < 30 mL/min
   - Active and/or clinically significant bleeding from any source
   - History of ulcer disease or gastrointestinal bleeding with concomitant use of oral corticosteroids, anticoagulants, or antiplatelets

➢ Treximet (sumatriptan and naproxen sodium) for all other indications not previously listed is considered experimental or investigational based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
TREXIMET® (sumatriptan and naproxen sodium) oral tablet (cont.)

3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

This includes but is not limited to the following:
- Cluster headache
- Migraine prophylaxis
- Perioperative pain in the setting of coronary artery bypass graft (CABG) surgery

Resources:


FDA-approved indication and dosage:

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<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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| TREXIMET 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. | Adults:  
Recommended dosage: 1 tablet of 85/500 mg.  
Maximum dosage in a 24-hour period: 2 tablets of 85/500 mg; separate doses by at least 2 hours. |
| 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. | Pediatric Patients 12 to 17 years of Age:  
Recommended dosage: 1 tablet of 10/60 mg.  
Maximum dosage in a 24-hour period: 1 tablet of 85/500 mg. |
| Mild to Moderate Hepatic Impairment:  
Recommended dosage: 1 tablet of 10/60 mg. |