**AXERT® (almotriptan malate) oral tablet (brand and generic)**

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:**

Axert (almotriptan) is indicated for the acute treatment of migraine attacks in adults with a history of migraine with or without aura and for the acute treatment of migraine headache pain in adolescents age 12-17 years of age with a history of migraine with or without aura, who have migraine attacks usually lasting 4 hours or more. In adolescents, age 12-17 years, efficacy of Axert (almotriptan) on migraine-associated symptoms such as nausea, photophobia, and phonophobia was not established. Axert (almotriptan) is not intended for prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine and it is not indicated for the treatment of cluster headache.

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 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).

Almotriptan is a selective agonist for serotonin (also known as 5-hydroxytryptamine, 5-HT) receptors 1B and 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.

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.

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 Axert (brand) and almotriptan malate (generic) 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. Incomplete forms will be returned.
AXERT® (almotriptan malate) oral tablet (brand and generic) (cont.)

- FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Axert (brand) and almotriptan malate (generic) is considered medically necessary when ALL of the following criteria are met:
  1. Medical record documentation of a confirmed diagnosis of ONE of the following:
     - Individual with a history of migraine with or without aura
       - Individual is 18 years of age or older
     - Individual with a history of migraine with or without aura, and who have migraine attacks usually lasting 4 hours or more
       - Individual is 12 to 17 years of age
  2. Individual is unable to use ALL of the following generics (all formulations):
     - Naratriptan
     - Rizatriptan
     - Sumatriptan
     - Zolmitriptan

- Absence of ALL of the following contraindications:
  - Ischemic heart disease
  - Angina pectoris
  - History of myocardial infarction
  - Documented silent ischemia
  - Coronary artery vasospasm
  - Prinzmetal's variant angina
  - Other significant underlying cardiovascular disease
  - Cerebrovascular syndromes
  - Stroke or transient ischemic attack (TIA)
  - Peripheral vascular disease
  - Ischemic bowel disease
  - Uncontrolled hypertension
  - Use within 24 hours of an ergotamine-containing, or ergot-type medication (Dihydroergotamine, Ergotamine, Methysergide)
  - Use within 24 hours of another triptan
  - Hemiplegic or basilar migraine
  - Known hypersensitivity to Axert

- Axert (brand) and almotriptan malate (generic) 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
  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.
AXERT® (almotriptan malate) oral tablet (brand and generic) (cont.)

This includes but is not limited to the following:
- Prophylactic therapy of migraine
- Treatment of cluster headache

Resources:

FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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<tbody>
<tr>
<td>Axert is a 5HT1B/1D receptor agonist (triptan) indicated for:</td>
<td>Adults and adolescents age 12 to 17 years: 6.25 mg or 12.5 mg single dose; may repeat after 2 hours if headache returns; benefit of second dose in patients who have failed to respond to first dose has not been established; maximum daily dose 25 mg</td>
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<tr>
<td>• Acute treatment of migraine attacks in adults with a history of migraine with or without aura</td>
<td>• Patients with hepatic or severe renal impairment: 6.25 mg starting dose; maximum daily dose 12.5 mg</td>
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<tr>
<td>• Acute treatment of migraine headache pain in adolescents age 12 to 17 years with a history of migraine with or without aura, and who have migraine attacks usually lasting 4 hours or more</td>
<td></td>
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</tbody>
</table>

Important limitations:
- Use only after a clear diagnosis of migraine has been established
- In adolescents age 12 to 17 years, efficacy of Axert on migraine-associated symptoms was not established
- Not intended for the prophylactic therapy of migraine
- Not indicated for the treatment of cluster headache