PRIOR AUTHORIZATION POLICY

POLICY: Methylergonovine Prior Authorization Policy
- Methergine® (methylergonovine maleate tablets – Lupin, generic)

REVIEW DATE: 07/03/2024

OVERVIEW

Methylergonovine, a semi-synthetic ergot alkaloid, is indicated for management of **uterine atony, hemorrhage, and subinvolution of the uterus following delivery of the placenta;** and for control of **uterine hemorrhage** in the second stage of labor following delivery of the anterior shoulder.[1]

Other Uses with Supportive Evidence

Methylergonovine can cause constriction of the smooth muscles in the blood vessels and this effect can be helpful in treating vascular headaches, such as migraines or cluster headaches.[2] However, methylergonovine should only be used for limited periods of time in most patients and only under careful supervision of a physician. The dose of methylergonovine used for migraines is 0.2 to 0.4 mg three times a day; a maximum dose of 1.6 mg/day has been reported (eight 0.2 mg tablets per day).

Guidelines/Recommendations

An updated assessment of the **preventive and acute treatment of migraine** by the **American Headache Society** (AHS) [2018; update 2021] reaffirms previous migraine guidelines.[3,4] Methylergonovine is not addressed in the update. ***Prevention.*** Patients with migraine should be considered for preventive treatment in the following situations: when attacks significantly interfere with patients' daily routines despite acute treatment; frequent attacks (≥ 4 monthly headache days); contraindication to, failure, overuse, or adverse events with acute treatments; or patient preference. Before developing a preventive treatment plan, the appropriate use (e.g., drug type, route and timing of administration, frequency) of acute treatments should be initiated and coupled with education and lifestyle modifications. All patients with migraine should be offered a trial of acute treatment. Based on the level of evidence for efficacy and the American Academy of Neurology scheme for classification of evidence, the following oral treatments have established efficacy and should be offered for migraine prevention: antiepileptic drugs (divalproex sodium, valproate sodium, topiramate [not for women of childbearing potential without a reliable method of birth control]); beta-blockers (metoprolol, propranolol, timolol); calcitonin gene-related peptide (CGRP) receptor antagonists indicated for migraine prevention (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti); and frovatriptan (for short-term preventive treatment of menstrual migraine). The following treatments are probably effective and should be considered for migraine prevention: antidepressants (amitriptyline, venlafaxine); beta-blockers (atenolol, nadolol); and angiotensin receptor blockers (candesartan). ***Treatment.*** Triptans (e.g., almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan) are considered the gold standard for acute treatment of moderate to severe migraine headaches or mild to moderate migraine headaches that respond poorly to over-the-counter analgesics. Nonsteroidal anti-inflammatory drugs (NSAIDs) as a class are mentioned as an option for acute treatment of mild to moderate migraine attacks; celecoxib is not specifically addressed. The potential for cardiovascular and gastrointestinal adverse events with NSAID use is noted. Other treatment options in the mild to moderate setting include nonopioid analgesics, acetaminophen, or caffeinated analgesic combinations. For moderate to severe attacks or attacks which respond poorly to NSAIDs or caffeinated combinations, the update lists the triptans, dihydroergotamine, the oral CGRP receptor antagonists (Nurtec® ODT [rimegepant orally disintegrating tablets,] and Ubrelvy® [ubrogepant tablets]), and Reyvow™ (lasmiditan tablet) as effective treatments. The recommendation remains that clinicians must consider medication efficacy and potential medication-related adverse events when prescribing acute medications for migraine.

The **AHS** issued an update to their position statement (2024) specifically regarding therapies targeting CGRP for the prevention of migraine.[5] The evidence for the efficacy, tolerability, and safety of CGRP-targeting migraine preventive therapies (specifically, the monoclonal antibodies: Aimovig® [erenumab-aooe subcutaneous {SC} injection], Ajovy® [fremanezumab-vfrm SC injection], Emgality® [galcanezumab-gnlm SC injection], and Vyepti® [eptinezumab-jjmr intravenous infusion], and the gepants: Nurtec ODT [rimegepant orally disintegrating tablets] and Qulipta® [atogepant tablets]) is substantial and consistent across different individual CGRP-targeting treatments. Extensive "real-world" clinical experience corroborates clinical trials. This data indicates that the efficacy and tolerability of CGRP-targeting therapies are equal to or greater than those of previous first-line therapies. The CGRP-targeting therapies should be considered as a first-line approach for migraine prevention along with previous first-line treatments without a requirement for prior failure of other classes of migraine preventive treatment. Additionally, Botox® (onabotulinumtoxinA SC injection) is considered a first-line therapy for prevention of chronic migraine.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of methylergonovine, for prescriptions with quantities exceeding 28 tablets per 30 days. Twenty-eight (28) tablets per month will be sufficient to treat uterine atony, hemorrhage, and subinvolution of the uterus following the delivery of the placenta (FDA-approved indication). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients with migraines who are treated with methylergonovine as well as the monitoring required for adverse events and long-term efficacy, approval requires methylergonovine to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: Methylergonovine prescriptions for ≤ 28 tablets (0.2 mg strength) per 30 days are excluded from Prior Authorization (PA). The PA policy will only apply to methylergonovine prescriptions with quantities exceeding 28 tablets per 30 days.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of methylergonovine is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Uterine Atony, Hemorrhage, and Subinvolution of the Uterus.** Do not approve. The initial quantity of 28 tablets is sufficient to treat this condition; quantities > 28 tablets for this indication will not be approved.

Other Uses with Supportive Evidence

2. **Migraine Headaches – Acute Treatment.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Patient is already receiving methylergonovine therapy; OR
     - **ii.** Patient meets ALL of the following (a, b, and c):
       - **a)** Patient has tried and had inadequate efficacy and/or unacceptable side effects to at least one triptan therapy; AND

Note: Examples of triptans are almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan.

b) Patient has tried and had inadequate efficacy and/or unacceptable side effects to at least one other type of abortive therapy; AND
Note: Examples of abortive therapies include analgesics (acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs]), butalbital-containing products (butalbital-acetaminophen, butalbital-acetaminophen-caffeine, butalbital-acetaminophen-caffeine-codeine, butalbital-aspirin-caffeine, butalbital-aspirin-caffeine-codeine), dihydroergotamine (DHE, Migranal, generic), oral calcitonin gene-related peptide (CGRP) receptor antagonists (Nurtec ODT [rimegepant orally disintegrating tablets], Ubrelvy [ubrogepant tablets], Reyvow [lasmiditan tablet]).

c) The medication is prescribed by or in consultation with a neurologist or headache specialist.

3. Migraine Headaches – Prevention. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age: AND

B) Patient has tried at least two standard prophylactic pharmacologic therapies, each from a different pharmacologic class; AND
Note: Examples of prophylactic pharmacologic therapies include angiotensin receptor blocker, angiotensin converting enzyme inhibitor, anticonvulsant, beta-blocker, calcium channel blocker, calcitonin gene-related peptide (CGRP) receptor antagonists indicated for migraine prevention, tricyclic antidepressant, other antidepressant.

C) The medication is prescribed by or in consultation with a neurologist or headache specialist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of methylergonovine is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Methergine® tablets [prescribing information]. Baltimore, MD: Lupin; January 2016.
2. Saper JR, Evans RW. Oral methylergonovine maleate for refractory migraine and cluster headache prevention. *Headache.* 2013;53(2):378-81.
3. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. *Headache*. 2019;59:1-18.
4. Ailani J, Burch RC, Robbins MS, on behalf of the Board of Directors of the American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache*. 2021;00:1–19.
5. Charles AC, Digre KB, Goadsby PJ, et al; American Headache Society. Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update. *Headache*. 2024 Mar 11. Epub ahead of print.