Original Effective Date: 09/01/2018
Current Effective Date: 09/25/2024
Last P&T Approval/Version: 07/31/2024
Next Review Due By: 07/2025
Policy Number: C14599-A

Keveyis (dichlorphenamide)

PRODUCTS AFFECTED

dichlorphenamide, Keveyis (dichlorphenamide), Ormalvi (dichlorphenamide)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This 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 Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Primary hyperkalemic periodic paralysis, Primary hypokalemic periodic paralysis, and related variants

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PRIMARY HYPER- OR HYPO-KALEMIC PERIODIC PARALYSIS AND VARIANTS:
1. Documented diagnosis of primary hyperkalemic periodic paralysis or primary hypokalemic periodic paralysis

AND

2. Documentation of baseline symptoms for measure of efficacy for reauthorization (e.g., number of attacks per week or month, severity of attacks, short form 36 assessment, etc.)
   AND
3. Documentation of inadequate response (no change in attack rate per week from baseline) after 3 months of adherent therapy, serious side effects, or FDA labeled contraindication, to oral acetazolamide therapy at recommended dosage of 250 to 375mg/day PO in divided doses
   AND
4. a. FOR HYPERKALEMIC PP: Documentation of inadequate response, serious side effects, or contraindication to a thiazide diuretic
   OR
   b. FOR HYPOKALEMIC PP: Documentation of inadequate response, serious side effects, or contraindication to a potassium sparing diuretic
   AND
5. FOR HYPERKALEMIC PERIODIC PARALYSIS: Prescriber attests that member has been counseled on implementing and maintaining dietary and lifestyle changes to help prevent episodes such as eating meals rich in carbohydrates, AND avoiding potassium-rich medications and foods, fasting, strenuous work, and exposure to cold
   AND
6. FOR HYPOKALEMIC PERIODIC PARALYSIS: Prescriber attests that member has been counseled to avoid triggers; follow a low-sodium, low-carbohydrate, high- potassium diet; and take oral potassium supplementation
   AND
7. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to dichlorphenamide include: Concomitant use with high dose aspirin (i.e., greater than 100 mg per day), Severe pulmonary disease or obstruction [e.g., severe chronic obstructive pulmonary disease (COPD)], Hepatic insufficiency, and hypersensitivity to dichlorphenamide or other sulfonamides]

CONTINUATION OF THERAPY:

A. PRIMARY HYPER- OR HYPO-KALEMIC PERIODIC PARALYSIS AND VARIANTS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Documented positive response from baseline in periodic paralysis symptom(s), including a decrease in the frequency or severity of paralytic attacks
   NOTE: Per FDA label, evaluate response and need for continued therapy after 2 months of treatment. If positive response hasn't occurred discontinuation should occur.
   AND
3. Prescriber attests to or clinical reviewer has found that the member does not have any of the following: Concomitant use with high dose aspirin (i.e., greater than 100 mg per day), Severe pulmonary disease or obstruction [e.g., severe chronic obstructive pulmonary disease (COPD)], or Hepatic insufficiency
   AND
4. Prescriber attests that the member has continued to maintain dietary and lifestyle changes to help prevent episodes
   AND
5. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity (e.g., skin rash, persistent metabolic acidosis, patient experiencing falls)

DURATION OF APPROVAL:

Initial authorization: 3 months (Evaluation of response to dichlorphenamide is recommended after 2 months

of treatment), Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified neurologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests.]

AGE RESTRICTIONS:
18 years of age or older

QUANTITY:
Maximum dosage: 200 mg/day, 4 tablets per day

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Carbonic Anhydrase Inhibitors

FDA-APPROVED USES:
Indicated for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants

G72.3 Periodic Paralysis or G71.19 Other specified myotonic disorders

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Primary periodic paralysis Primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants are a group of rare hereditary disorders that affect an estimated 5,000 people in the United States. For most patients, these are not life-threatening conditions, but can be debilitating. (Venance SL, et al).

Primary periodic paralyses often present as episodes of muscle weakness or paralysis, with the majority of patients experiencing inter attack weakness. (Venance SL, et al).

Hypokalemic periodic paralysis, the most common form of primary periodic paralysis, generally begins during the first and second decades of life. Possible triggers for this type of attack include prolonged rest after vigorous exercise, carbohydrate loads on the previous day, and stress. Attacks can last hours to days but are not associated with electromyogram myotonia. Symptoms improve with potassium therapy.

Hyperkalemic periodic paralysis generally begins during the first decade of life. Triggers for this type of attack include prolonged rest after exercise, consumption of potassium-rich foods, stress, and fatigue. Attacks last 1 to 4 hours and are associated with electromyogram myotonia. Both types of periodic paralysis are associated with fixed proximal weakness but not with cardiac arrhythmias and skeletal development anomalies. [(Venance SL, et al) (Vicart S, et al et al.)] Management includes symptomatic treatment and behavioral methods (e.g., avoidance of triggers). Administration of potassium in the hypokalemic subtype may be useful but may precipitate attacks in the hyperkalemic subtype. Acetazolamide and dichlorphenamide, carbonic anhydrase inhibitors, are potentially useful in the treatment of both subtypes. [(Venance SL, et al) (Vicart S, et al et al.)] Generally, acetazolamide has been the most commonly used carbonic anhydrase inhibitor for the treatment of periodic paralysis. (Sansone V, et al.) Keveyis (dichlorphenamide) is a carbonic anhydrase inhibitor; the mechanism by which dichlorphenamide exerts its therapeutic effects in patients with periodic paralysis is unknown. Clinical Studies The efficacy of Keveyis was evaluated in two clinical studies. In the first, a nine- week, double-blind, placebo-controlled multicenter study, patients with hypokalemic periodic paralysis treated with Keveyis (n = 24) had 2.2 fewer self-reported attacks of muscle weakness per week over the final eight weeks of the trial than patients (n = 20) treated with placebo. Patients with hyperkalemic periodic paralysis treated with Keveyis (n = 12) had 3.9 fewer attacks per week than patients (n = 9) treated with placebo. The second study was a 35-week, double-blind, placebo- controlled, multicenter, two-period crossover study that included 31 patients with hyperkalemic periodic paralysis and 42 patients with hypokalemic periodic paralysis. Hyperkalemic periodic paralysis patients treated with Keveyis had 2.3 fewer attacks per week than those on placebo. Acute intolerable worsening necessitating withdrawal was observed in two hypokalemic periodic paralysis patients on Keveyis versus 11 patients on placebo. In clinical studies, the most common side effects of Keveyis were a burning or pricking sensation, difficulty thinking and paying attention, changes in taste, and confusion. Keveyis may cause a drop in the amount of potassium in the body, which can lead to heart problems. The body may produce too much acid or may not be able to remove enough acid from body fluids while taking Keveyis. Keveyis may also increase the risk of falls, especially in elderly patients and patients taking high doses of Keveyis.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of dichlorphenamide are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to dichlorphenamide include: hepatic insufficiency, severe pulmonary obstruction, hypersensitivity to dichlorphenamide or other sulfonamides, concomitant use with high dose aspirin.

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:

Dichlorphenamide TABS 50MG
Keveyis TABS 50MG
Ormalvi TABS 50MG

REFERENCES

1. Keveyis (dichlorphenamide) [prescribing information]. Chicago, IL: Xeris Pharmaceuticals Inc; January 2024.
2. Ormalvi (dichlorphenamide) tablets, for oral use [prescribing information]. Cambridge, CB3 0FA, United Kingdom: Cycle Pharmaceuticals LTD; February 2024.
3. Keveyis (dichlorphenamide). Primary Periodic Paralysis (PPP) Diagnosis and Management. Strongbridge US. Available at: https://www.keveyis.com/hcp/diagnosis-and-management/ Accessed July 2018.
4. Burge J, Horga A, Griggs RC, Hanna MG. Double-blind, placebo-controlled, parallel group, phase III study comparing dichlorphenamide vs placebo for the treatment of periodic paralysis (HYP HOP trial) [abstract]. Neuromuscul Disord. 2011;21(suppl 1):S13.
5. Hyper- and hypokalemic periodic paralysis study (HYP-HOP). ClinicalTrials.gov website. Hyper- and Hypokalemic Periodic Paralysis Study - Full Text View - ClinicalTrials.gov
6. Sansone V, Meola G, Links TP, Panzeri M, Rose MR. Treatment for periodic paralysis. Cochrane Database Syst Rev.2008(1):CD005045.[PubMed18254068]10.1002/14651858.CD005045.pub2
7. Venance SL, Cannon SC, Fialho D, et al; CINCH Investigators. The primary periodic paralyses: diagnosis, pathogenesis and treatment. Brain. 2006;129(pt 1):8- 17.[PubMed16195244]

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Available Dosage Forms References	Q3 2024
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy Available Dosage Forms	Q3 2023
REVISION- Notable revisions: Required Medical Information Prescriber Requirements Contraindications/Exclusions/Discontinuation References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file