Drug Coverage Policy

Effective Date 5/15/2026
Coverage Policy Number.....IP0204
Policy Title.....Dichlorphenamide

Dichlorphenamide

- Keveyis® (dichlorphenamide tablets – Xeris, generic [including Ormalvi®])

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Dichlorphenamide, a carbonic anhydrase inhibitor, is indicated for the treatment of **primary hyperkalemic periodic paralysis** (HyperPP), **primary hypokalemic periodic paralysis**

(HypoPP), and related variants.[1] These conditions are heterogeneous and response to dichlorphenamide may vary; therefore, prescribers should evaluate the patient's response to dichlorphenamide after 2 months to decide whether it should be continued.

Disease Overview
The primary periodic paralyses are rare muscle disorders caused by autosomal dominant genetic mutations in ion channels.[2,3] The altered channels cannot properly regulate the flow of ions into muscle cells, which reduces the ability of skeletal muscles to contract, leading to severe muscle weakness or paralysis.[4] Genetic testing is recommended as the first diagnostic step; a heterozygous pathogenic mutation can be identified in 60% to 70% of periodic paralysis cases.[5] When a genetic mutation cannot be identified, periodic paralyses can be distinguished based on clinical presentation. Other causes of hypokalemia or hyperkalemia should be excluded.[5]

Although data are limited to case reports and single-blind trials, acetazolamide, another carbonic anhydrase inhibitor, has been used historically for almost 50 years for both hypoPP and hyperPP.[6,7] Oral potassium salts can be taken as maintenance/prophylactic therapy for patients with HypoPP; however, this does not completely prevent attacks. Acetazolamide treatment is beneficial in approximately 50% of patients with HypoPP and it has no effect in 30% of affected patients. Some patients with certain genetic variants may experience worsening symptoms with acetazolamide; however, may respond to dichlorphenamide.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of dichlorphenamide. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with dichlorphenamide, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires dichlorphenamide to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Dichlorphenamide is considered medically necessary when ONE of the following are met:

FDA-Approved Indications

1. **Hypokalemic Periodic Paralysis (HypoPP) and Related Variants.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A.** Initial Therapy. Approve for 2 months if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):
     - **i.** Patient has a confirmed diagnosis of primary hypokalemic periodic paralysis by meeting at least ONE of the following (a, b, or c):
       - **a.** Patient has had a serum potassium concentration of less than 3.5 mEq/L during a paralytic attack; OR
       - **b.** Patient has a family history of the condition; OR
       - **c.** Patient has a genetically confirmed skeletal muscle calcium or sodium channel mutation; AND
     - **ii.** The prescriber has excluded other reasons for acquired hypokalemia; AND
       Note: Examples of other reasons for acquired hypokalemia include renal, adrenal, or thyroid dysfunction; renal tubular acidosis; and diuretic or laxative abuse.
     - **iii.** Patient has had improvements in paralysis attack symptoms with potassium intake; AND

iv. Patient has tried oral acetazolamide therapy; AND
v. The medication is prescribed by or in consultation with a neurologist or a physician who specializes in the care of patients with primary periodic paralysis (e.g., muscle disease specialist, physiatrist); AND
vi. Preferred product criteria is met for the product(s) as listed in the below table; OR

B. Patient is Currently Receiving Dichlorphenamide. Approve for 1 year if the patient has responded to dichlorphenamide (e.g., decrease in the frequency or severity of paralytic attacks) as determined by the prescriber.

2. Hyperkalemic Periodic Paralysis (HyperPP) and Related Variants. Approve for the duration noted if the patient meets ONE of the following (A or B):

A. Initial Therapy. Approve for 2 months if the patient meets ALL of the following (i, ii, iii, iv and v):
i. Patient has a confirmed diagnosis of primary hyperkalemic periodic paralysis by meeting at least ONE of the following criteria (a, b, c, or d):
a. Patient has had an increase from baseline in serum potassium concentration of greater than or equal to 1.5 mEq/L during a paralytic attack; OR
b. Patient has had a serum potassium concentration during a paralytic attack of greater than 5.0 mEq/L; OR
c. Patient has a family history of the condition; OR
d. Patient has a genetically confirmed skeletal muscle sodium channel mutation; AND
ii. The prescriber has excluded other reasons for acquired hyperkalemia; AND
Note: Examples of other reasons for acquired hyperkalemia include drug abuse, renal dysfunction, and adrenal dysfunction.
iii. Patient has tried oral acetazolamide therapy; AND
iv. The medication is prescribed by or in consultation with a neurologist or a physician who specializes in the care of patients with primary periodic paralysis (e.g., muscle disease specialist, physiatrist); AND
v. Preferred product criteria is met for the product(s) as listed in the below table; OR

B. Patient is Currently Receiving Dichlorphenamide. Approve for 1 year if the patient has responded to dichlorphenamide (e.g., decrease in the frequency or severity of paralytic attacks) as determined by the prescriber.

Employer Plans:

Product	Criteria
Keveyis (dichlorphenamide)	The patient has tried the bioequivalent generic product **dichlorphenamide** AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.
Ormalvi (dichlorphenamide)	The patient has tried **dichlorphenamide** AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] which, per the prescriber, would result in a significant allergy or serious adverse reaction.

Conditions Not Covered

Dichlorphenamide for any other use is considered not medically necessary. Criteria will be updated as new published data are available

References

1. Keveyis® tablets [prescribing information]. Chicago, IL: Xeris; August 2024.
2. Sansone V, Meola G, Links T, et al. Treatment for periodic paralysis. *Cochrane Database Syst Rev*. 2008, Issue 1. Art. No.: CD005045.
3. Genetics Home Reference. Hyperkalemic periodic paralysis. Reviewed February 2019. Available at: http://ghr.nlm.nih.gov/condition/hyperkalemic-periodic-paralysis. Accessed on January 02, 2026.
4. Genetics Home Reference. Hypokalemic periodic paralysis. Reviewed March 1, 2020. Available at: http://ghr.nlm.nih.gov/condition/hypokalemic-periodic-paralysis. Accessed on January 02, 2026.
5. Statland JM, Fontaine B, Hanna MG, et al. Review of the Diagnosis and Treatment of Periodic Paralysis. *Muscle Nerve*. 2018;57(4):522-530.
6. Vicart S, Sternberg D, Arzel-Hezode M, et al. Hypokalemic periodic paralysis. Initial posting April 30, 2002. Updated July 26, 2018. GeneReviews® - NCBI Bookshelf. Available at: http://www.ncbi.nlm.nih.gov/books/NBK1338/?report=printable. Accessed on January 02, 2026.
7. Statland JM, Fontaine B, Hanna MG, et al. Review of the Diagnosis and Treatment of Periodic Paralysis. *Muscle Nerve.* 2018 Apr;57(4):522-530.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	No criteria changes	4/1/2025
Annual Revision	**Primary Hypokalemic Periodic Paralysis (HypoPP), Primary Hyperkalemic Periodic Paralysis (HyperPP), and Related Variants** were divided into separate indications for coverage: **Hypokalemic Periodic Paralysis (HypoPP) and Related Variants and Hyperkalemic Periodic Paralysis (HyperPP) and Related Variants.** **Hypokalemic Periodic Paralysis (HypoPP) and Related Variants:** **Updated** approval duration **from** 3 months **to** 2 months. **Added** "Patient has a confirmed diagnosis of primary hypokalemic periodic paralysis by meeting at least ONE of the following: Patient has had a serum potassium concentration of less than 3.5 mEq/L during a paralytic attack, Patient has a family history of the condition, or Patient has a genetically confirmed skeletal muscle calcium or sodium channel mutation" **Added** "The prescriber has excluded other reasons for acquired hypokalemia"	5/15/2026

	Added "Note: Examples of other reasons for acquired hypokalemia include renal, adrenal, or thyroid dysfunction; renal tubular acidosis; and diuretic or laxative abuse." **Added** "Patient has had improvements in paralysis attack symptoms with potassium intake" **Updated from** "Documented failure, contraindication, or intolerance to acetazolamide capsules or tablets" **to** "Patient has tried oral acetazolamide therapy" **Added** "The medication is prescribed by or in consultation with a neurologist or a physician who specializes in the care of patients with primary periodic paralysis (e.g., muscle disease specialist, physiatrist)" Patient is Currently Receiving Dichlorphenamide: **Added** "the patient has responded to dichlorphenamide (e.g., decrease in the frequency or severity of paralytic attacks) as determined by the prescriber" **Hyperkalemic Periodic Paralysis (HyperPP) and Related Variants:** **Updated** approval duration **from** 3 months **to** 2 months. **Added** Patient has a confirmed diagnosis of primary hyperkalemic periodic paralysis by meeting at least ONE of the following criteria: Patient has had an increase from baseline in serum potassium concentration of greater than or equal to 1.5 mEq/L during a paralytic attack, Patient has had a serum potassium concentration during a paralytic attack of greater than 5.0 mEq/L, Patient has a family history of the condition or, Patient has a genetically confirmed skeletal muscle sodium channel mutation" **Added** "The prescriber has excluded other reasons for acquired hyperkalemia" **Added** "Note: Examples of other reasons for acquired hyperkalemia include drug abuse, renal dysfunction, and adrenal dysfunction." **Updated from** "Documented failure, contraindication, or intolerance to acetazolamide capsules or tablets" **to** "Patient has tried oral acetazolamide therapy" **Added** "The medication is prescribed by or in consultation with a neurologist or a physician who specializes in the care of patients with primary periodic paralysis (e.g., muscle disease specialist, physiatrist)" Patient is Currently Receiving Dichlorphenamide: **Added** "the patient has responded to dichlorphenamide (e.g., decrease in the frequency	

	or severity of paralytic attacks) as determined by the prescriber” **Employer Plans Preferred Product Table: Removed** [may require prior authorization] from Keveyis criteria.	

The policy effective date is in force until updated or retired.