Effective Date **4/1/2025**
Coverage Policy Number **IP0204**

Dichlorphenamide

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Related Coverage Resources

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 and have discretion in making individual coverage determinations. 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

This policy supports medical necessity review for the following products:

- dichlorphenamide tablets
- Keveyis® (dichlorphenamide tablets)
- Ormalvi™(dichlorphenamide tablets)

Medical Necessity Criteria

Dichlorphenamide (Keveyis, Ormalvi) is considered medically necessary when the following is met:

1. **Primary Hypokalemic Periodic Paralysis (HypoPP), Primary Hyperkalemic Periodic Paralysis (HyperPP), and Related Variants** (for example, Andersen-Tawil syndrome, paramyotonia congenita). Individual meets **BOTH** of the following:
    A. **ONE** of the following:
        i. Documented failure, contraindication, or intolerance to acetazolamide capsules or tablets

ii. Is currently receiving dichlorphenamide

B. Preferred product criteria is met for the product(s) as listed in the below table

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 would result, per the prescriber, in a significant allergy or serious adverse reaction. [may require prior authorization]
Ormalvi (dichlorphenamide)	The patient has tried **dichlorphenamide (generic for Keveyis)** AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] which would result, per the prescriber, in a significant allergy or serious adverse reaction.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Dichlorphenamide (Keveyis, Ormalvi) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 3 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

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]

Regarding treatment, oral potassium salts can be taken as maintenance/prophylactic therapy for patients with HypoPP; however, this does not completely prevent attacks.[6] Although data are limited to case reports and single-blind trials, acetazolamide, another carbonic anhydrase inhibitor, has been used historically for primary periodic paralysis. Acetazolamide treatment is beneficial in approximately 50% of patients with HypoPP and it has no effect in 30% of affected patients. It can also exacerbate symptoms in 20% of patients. Dichlorphenamide has been reported to be 30 times more potent than acetazolamide in vitro.[7] Prior to initiating dichlorphenamide it is important to verify if the patient has had exacerbation with acetazolamide, since dichlorphenamide is considered to be more potent and may potentially lead to more exacerbations.[8]

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 December 26, 2024.
4. Genetics Home Reference. Hypokalemic periodic paralysis. Reviewed March 1, 2020. Available at: http://ghr.nlm.nih.gov/condition/hypokalemic-periodic-paralysis. Accessed on December 26, 2024.
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 December 26, 2024.
7. Sansone VA, Burge J, McDermott MP, et al. Randomized, placebo-controlled trials of dichlorphenamide in periodic paralysis. *Neurology*. 2016;86:1408-1416.
8. Levitt JO. Practical aspects in the management of hypokalemic periodic paralysis. Commentary. *J Transl Med*. 2008;6:18.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	No criteria changes	4/1/2025

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