PRIOR AUTHORIZATION POLICY

POLICY: Dichlorphenamide Prior Authorization Policy
- Keveyis® (dichlorphenamide tablets – Xeris, generic)

REVIEW DATE: 01/08/2025

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.

CIGNA NATIONAL FORMULARY COVERAGE:

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]

POLICY STATEMENT

Prior Authorization is recommended for prescription 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.

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is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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. According to the prescriber, acetazolamide therapy did not worsen the paralytic attack frequency or severity in the patient; AND
vi. 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); 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. According to the prescriber, acetazolamide therapy did not worsen the paralytic attack frequency or severity in the patient; 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); 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.

CONDITIONS NOT COVERED

- **Keveyis® (dichlorphenamide tablets - Xeris, generic)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following; criteria will be updated as new published data are available

REFERENCES

1. Keveyis® tablets [prescribing information]. Chicago, IL: Xeris; August 2024.
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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.
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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.
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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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	01/03/2024
Annual Revision	No criteria changes.	01/08/2025