



## PRIOR AUTHORIZATION POLICY

- POLICY:** Keveyis Prior Authorization Policy
- Keveyis® (dichlorphenamide tablets – Strongbridge Biopharma)

**REVIEW DATE:** 12/22/2021

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### OVERVIEW

Keveyis, a carbonic anhydrase inhibitor, is indicated for the treatment of **primary hyperkalemic periodic paralysis (HyperPP)**, **primary hypokalemic periodic paralysis (HypoPP)**, and related variants.<sup>1</sup> These conditions are heterogeneous and response to Keveyis may vary; therefore, prescribers should evaluate the patient's response to Keveyis 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.<sup>2,3</sup> 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.<sup>4</sup> Genetic testing is recommended as the first diagnostic step; a heterozygous pathogenic mutation can be identified in 60% to 70% of periodic paralysis cases.<sup>5</sup> 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.<sup>5</sup>

Regarding treatment, oral potassium salts can be taken as maintenance/prophylactic therapy for patients with HypoPP; however, this does not completely prevent attacks.<sup>6</sup> 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. Keveyis has been reported to be 30 times more potent than acetazolamide in vitro.<sup>7</sup> Prior to initiating Keveyis it is important to verify if the patient has had exacerbation with acetazolamide, since Keveyis is considered to be more potent and may potentially lead to more exacerbations.<sup>8</sup>

### POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Keveyis. 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 Keveyis, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Keveyis to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation:** None.

### RECOMMENDED AUTHORIZATION CRITERIA

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

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## FDA-Approved Indications

1. **Hypokalemic Periodic Paralysis (HypoPP) and Related Variants.** Approve for the duration noted if the patient meets one of the following criteria (A or B):
    - A) **Initial Therapy.** Approve for 2 months if the patient meets the following criteria (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).
    - B) **Patient is Currently Receiving Keveyis.** Approve for 1 year if the patient has responded to Keveyis (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 criteria (A or B):
    - A) **Initial Therapy.** Approve for 2 months if the patient meets the following criteria (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).
    - B) **Patient is Currently Receiving Keveyis.** Approve for 1 year if the patient has responded to Keveyis (e.g., decrease in the frequency or severity of paralytic attacks) as determined by the prescriber.
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### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Keveyis 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. Keveyis® tablets [prescribing information]. Treviso, PA: Strongbridge Biopharma; November 2019.
  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 20, 2021.
  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 20, 2021.
  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 20, 2021.
  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.
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