Keveyis (dichlorphenamide)

Policy Number: 5.01.642  Last Review: 09/2017
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Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for Keveyis when it is determined to be medically necessary because the following criteria have been met.

When Policy Topic is covered
Initial approval duration 3 months

Keveyis is considered medically necessary for the treatment of 1) primary hyperkalemic periodic paralysis and related variants and 2) primary hypokalemic periodic paralysis and related variants when all of the following criteria are met:
1. Baseline and periodic monitoring of serum potassium and bicarbonate levels required
2. Diagnosis confirmed by ONE of the following:
   a. Genetic testing
      • In hyperkalemic periodic paralysis, SCN4A is primarily associated
         o If no pathogenic variant is identified, sequencing of KCNJ2 and CACNA1S may be considered
      • In hypokalemic periodic paralysis, 3 genes have been associated; all encode subunits of ion channels that are primarily expressed in skeletal muscle cells
         o CACNA1S (60% of patients)
         o SCN4A (20% of patients)
         o KCNJ18 (3.5% of patients)
   b. Provocative testing
   c. Electromyography
   d. Muscle biopsy
3. Documentation that lifestyle modifications, dietary restrictions and exercise have been maximally challenged (see Management strategies below).
4. Inadequate treatment response, intolerance, or contraindication to acetazolamide

AND NONE of the following:
1. Signs of hepatic impairment
2. Severe pulmonary disease
3. Use of high-dose aspirin

Renewal approval duration 12 months

1. Documentation that the patient has had a reduction in the number of paralytic attacks.

AND NONE of the following:
1. Signs of hepatic impairment
2. Severe pulmonary disease
3. Use of high-dose aspirin
Management strategies for Primary Periodic Paralysis

Considerations in Hyperkalemic Periodic Paralysis

Treatment of attacks - Attacks may be minimized with:
- Mild exercise and/or oral ingestion of carbohydrates, inhalation of salbutamol, or intravenous calcium gluconate

Managing attacks (medical and non-medical approaches) - Attacks may be managed by:
- Prescribing medications such as KEVEYIS
- Eating meals rich in carbohydrates
- Avoiding potassium-rich medications and foods, fasting, strenuous work, and exposure to cold

Prevention of secondary complications - Depolarizing anesthetic agents should be avoided during surgery
- These include potassium, suxamethonium, and anticholinesterases
- These may aggravate myotonia and can interfere with intubation and mechanical ventilation

Considerations in Hypokalemic Periodic Paralysis

Treatment of attacks - Attack intensity and duration may be managed by:
- Taking oral potassium salts, as needed for mild-to-moderate attacks
- Intensive management for severe attacks (intravenous potassium infusion, serial measurement of serum potassium concentration, evaluation of possible respiratory involvement, and continuous ECG monitoring)

Managing attacks (medical and non-medical approaches) - Attacks may be managed by:
- Prescribing medications such as KEVEYIS
- Counseling patients to avoid triggers, follow a low sodium, high carbohydrate/potassium diet, and take oral potassium supplementation

Prevention of secondary complications - Complications can be avoided by:
- Creating a safe home environment to prevent falls and accidents
- Taking steps to prevent anesthetic complications (ie, malignant hyperthermia)

When Policy Topic is not covered
Keveyis is considered investigational when the criteria above are not met and for all other indications.

Considerations
Keveyis requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service
Background
Keveyis is an oral carbonic anhydrase inhibitor indicated for the treatment of periodic paralysis. Periodic paralyses are a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis. Types of periodic paralyses are differentiated by criteria including underlying genetic mutations and changes in blood-potassium during attack. Hypokalemic and hyperkalemic are two common types of periodic paralyses (1).

Findings That Suggest Hyperkalemic Periodic Paralysis
- A history of flaccid weakness (limbs, eyes, throat, breathing muscles, trunk)
- Disease manifestations before 20 years of age
- A family history; however, absence does not preclude diagnosis
- Onset or worsening of an attack resulting from oral potassium
- Absence of cardiac arrhythmia between attacks
• EMG with reduced motor units or silence during attacks
• CMAP with a greater than normal increase during exercise followed by a progressive decline in amplitude
• Hyperkalemia with serum potassium >5 mmol/L or an increase of at least 1.5 mmol/L during attacks; normal between attacks
• Elevated serum creatine kinase (CK) concentration
• Identification of a heterozygous pathogenic variant in SNC4A

Findings That Suggest Hypokalemic Periodic Paralysis
• A history of episodes of flaccid paralysis with spontaneous recovery
• A family history consistent with autosomal dominant inheritance
• Low serum concentration of potassium (<3.0 mmol/L) during attacks, but not between
• CMAP with progressive and marked decrease in amplitude
• Precipitating factors such as rest after strenuous exertion or prolonged immobility
• Approximately 60% of patients have pathogenic variants in CACNA1S, ~20% in SCN4A, and ~3.5% in KCNJ18

Regulatory Status
FDA-approved indications: Keveyis is an oral carbonic anhydrase inhibitor indicated for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants (2).

Keveyis includes a contraindication for hepatic insufficiency. Keveyis may aggravate hepatic encephalopathy. Keveyis also includes a contraindication for severe pulmonary disease. Keveyis can cause hyperchloremic non-anion gap metabolic acidosis. Patients with severe pulmonary disease may be unable to compensate for the metabolic acidosis caused by Keveyis. Concomitant use of Keveyis with other drugs that cause metabolic acidosis may increase the severity of metabolic acidosis. Baseline and periodic measurement of serum bicarbonate during Keveyis treatment are recommended. If metabolic acidosis develops or persists, consider reducing the dose or discontinuing Keveyis (2).

The use of Keveyis is contraindicated with concomitant use of high-dose aspirin. Anorexia, tachypnea, lethargy, and coma have been reported with co-administration of high-dose aspirin and Keveyis. Keveyis should be used with caution in patients receiving low-dose aspirin (2).

Keveyis increases potassium excretion and can cause hypokalemia. Baseline and periodic measurement of serum potassium are recommended. If hypokalemia develops or persists, consider reducing the dose or discontinuing Keveyis (2).

The safety and efficacy of Keveyis in pediatric patients 18 years or less have not been established (2).

Rationale
Keveyis is an oral carbonic anhydrase inhibitor indicated for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants. Keveyis has an unknown mechanism of therapeutic effect on patients with periodic paralysis. Keveyis can cause metabolic acidosis and use is contraindicated in patients with severe pulmonary disease. Keveyis may aggravate hepatic encephalopathy and use is contraindicated in patients with hepatic impairment. Co-administration of Keveyis with high-dose aspirin is contraindicated due to the risk of coma. Monitoring of potassium and bicarbonate levels is required at baseline and periodically throughout treatment with Keveyis. The safety and efficacy of Keveyis in pediatric patients 18 years or less have not been established (1-2).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Keveyis while maintaining optimal therapeutic outcomes.
References


Billing Coding/Physician Documentation Information

| NA | Keveyis is a specialty pharmacy benefit |

Additional Policy Key Words

5.01.642

Policy Implementation/Update Information

| 09/2017 | New policy titled Keveyis (dichlorphenamide) |

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