IMPORTANT REMINDER
This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description
Dichlorphenamide (Keveyis) is an oral carbonic anhydrase inhibitor used for the prevention of paralytic attacks associated with primary hypokalemic periodic paralysis (hypoKPP), hyperkalemic periodic paralysis (hyperKPP), and other related variants (e.g. paramyotonia congenita, Andersen-Tawil syndrome).
Policy/Criteria

I. Most contracts require prior authorization approval of dichlorphenamide prior to coverage. Dichlorphenamide may be considered medically necessary in patients with primary periodic paralysis when criteria A, B and C below are met.

A. A diagnosis of primary periodic paralysis [i.e. primary hypokalemic periodic paralysis (hypoKPP), primary hyperkalemic periodic paralysis (hyperKPP), paramyotonia congenita, Andersen-Tawil syndrome] confirmed by genetic testing or a positive family history.

AND

B. Documentation that lifestyle modifications (i.e. dietary restrictions, exercise restrictions) are maximally managed.

AND

C. Acetazolamide therapy has been ineffective, not tolerated, or contraindicated.

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers dichlorphenamide to be a self-administered medication.

B. When prior authorization is approved, dichlorphenamide may be authorized in quantities of up to 120 tablets per month.

C. Authorization shall be reviewed as follows to confirm that current medical necessity criteria are met and that the medication is effective.

1. **Initial authorization** shall be reviewed at two months, as response to therapy may vary and some patients may experience no improvement or worsening of disease.

2. **Continued authorization or re-authorization** (after the initial two month period) shall be reviewed at least every six months, and clinical documentation indicating that dichlorphenamide is effective (i.e. reduction in the number of paralytic attacks).

III. Dichlorphenamide is considered investigational when used all other conditions.

Position Statement

- The primary periodic paralyses are a group or rare neuromuscular disorders characterized by episodes of flaccid weakness affecting one or more limbs, lasting several hours to several days, caused by mutations in skeletal muscle channel genes.

- There are a number of variants of primary periodic paralyses, and secondary causes (e.g. thyrotoxic periodic paralysis associated with hyperthyroidism) have also been identified.

- The primary periodic paralyses that have been studied in clinical trials evaluating the safety and effectiveness of dichlorphenamide (Keveyis) include primary hypokalemic periodic paralysis (hypoKPP), primary hyperkalemic periodic paralysis (hyperKPP), paramyotonia congenita, and Andersen-Tawil syndrome.
Dichlorphenamide (Keveyis) is an oral carbonic anhydrase inhibitor approved for the treatment of hypoKPP, hyperKPP, and related variants.

Patients with frequent attacks that are not adequately controlled with nonpharmacologic measures alone (e.g. dietary modifications, exercise modifications), may benefit from preventative therapy (e.g. potassium sparing diuretics, potassium supplementation, carbonic anhydrase inhibitors). [1,2]

Carbonic anhydrase inhibitors, including generic acetazolamide, have been the mainstay for chronic treatment of primary periodic paralyses for many years. [1,2]

There is no evidence that one carbonic anhydrase inhibitor [acetazolamide or dichlorphenamide (Keveyis)] is safer or more effective than the other for preventing paralytic attacks, as there are no direct comparative studies.

The use of carbonic anhydrase inhibitors for primary periodic paralyses has been associated with worsening of symptoms in some patients and the response to treatment may vary from patient to patient, regardless of subtype. Prescribers should evaluate the patient’s response to dichlorphenamide (Keveyis) after two months of treatment to decide whether therapy should be continued.

Clinical Efficacy

The primary evidence of efficacy for dichlorphenamide (Keveyis) in the treatment of hypoKPP, hyperKPP, and paramyotonia congenita comes from two (one published and one unpublished) low quality clinical trials evaluating attack rates in subgroups of patients receiving dichlorphenamide (Keveyis) compared to patients receiving placebo. [3,4]

- Baseline attack rates for included patients ranged from 2.5 attacks per week (hypoKPP) to 3.8 attacks per week (hyperKPP and paramyotonia congenita).

- Relative to placebo, dichlorphenamide (Keveyis) demonstrated a decrease in attack rates following eight weeks of treatment. The reduction in number of attacks ranged from one to four fewer attacks per week, and varied by type of periodic paralysis, with greater improvements observed in patients with hyperKPP.

- The overall quality of these studies is low, mainly due to the use of a subjective, self-reported outcome coupled with a high likelihood of loss of blinding (due to adverse events).

Acetazolamide, the other carbonic anhydrase inhibitor, has not been evaluated in clinical trials for the endpoint of attack rate; however, it has demonstrated improvement in muscle strength. There is no evidence to conclude dichlorphenamide (Keveyis) is more effective than acetazolamide, but carbonic anhydrase inhibitors (as a class) are considered the standard of care for preventative treatment.

Safety [4]

- The use of dichlorphenamide (Keveyis) has been associated with worsening of symptoms in some patients. Close monitoring during initiation of treatment is recommended.
- Dichlorphenamide (Keveyis) is contraindicated in patients with hypersensitivity to sulfonamides, when given concomitantly with high-dose aspirin, and in patients with hepatic insufficiency.
- The most commonly reported adverse events (incidence ≥ 10% and greater than placebo) with dichlorphenamide (Keveyis) include paresthesias, cognitive disorder, dysgeusia, and confusional state.

**Dosing**

- The starting dose of dichlorphenamide (Keveyis) is 50 mg twice daily.
- The initial dose may be increased or decreased based on individual patient response, at weekly intervals (or sooner in case of adverse reactions).
- The maximum recommended total daily dose is 200 mg.

<table>
<thead>
<tr>
<th>Cross References</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**References**