



PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 1/21/16
LAST REVIEW DATE: 1/18/18
LAST CRITERIA REVISION DATE: 1/18/18
ARCHIVE DATE:

KEVEYIS™ (dichlorphenamide) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

KEVEYIS™ (dichlorphenamide) oral tablet (cont.)

Description:

Keveyis (dichlorphenamide) 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 (such as paramyotonia congenita with periodic paralysis and Andersen-Tawil syndrome). The precise mechanism by which it exerts its therapeutic benefit in patients with periodic paralysis is not known.

Primary periodic paralysis

- Primary periodic paralyses are a group of rare neuromuscular disorders in the family of diseases called channelopathies
 - It is thought that they are caused by mutations in skeletal muscle ion channel genes
 - They are characterized by episodes of flaccid weakness affecting one or more limbs, lasting several hours to several days
- There are a number of variants of primary periodic paralysis and secondary causes such as thyrotoxic periodic paralysis of hyperthyroidism have been identified
- Therapy is directed by the type of periodic paralysis and instituting various lifestyle modifications according to type of disease
 - Carbonic anhydrase inhibitors are established therapies and their adverse effect profiles are well characterized
 - There are no trials that compare dichlorphenamide and acetazolamide and as such there is no evidence that one is safer or more effective than the other in preventing paralytic attacks
 - Clinical trials of dichlorphenamide have compared it to placebo
 - Use of acetazolamide has not been evaluated in clinical trials but has shown efficacy in improving muscle strength
 - Other diuretics are also used off-label for periodic paralysis
- Hypokalemic periodic paralysis (hypoKPP) is the most common disorder
 - It has autosomal dominant inheritance and is thought to be caused by a mutation in the voltage-gated calcium channel or voltage-gated sodium channel
 - Acquired cases of hypoKPP have been described in association with hyperthyroidism (thyrotoxic periodic paralysis)
 - Painless muscle weakness may be precipitated by heavy exercise, fasting, or high-carbohydrate meals
 - Acute attacks of hypoKPP are treated with oral potassium chloride 60-120 mEq
 - Non-pharmacological interventions include a low-carbohydrate diet and abstaining from vigorous exercise
 - Potassium supplementation, potassium-sparing diuretics, and carbonic anhydrase inhibitors are used when lifestyle changes are not effective
 - Prevention of hypoKPP is achieved by use of a carbonic anhydrase inhibitor, either acetazolamide 250 mg twice daily or dichlorphenamide 50 mg twice daily
 - Spironolactone 100 mg daily can be used as a supplement to carbonic anhydrase inhibitor or as an alternative to carbonic anhydrase inhibitor if a patient worsens or cannot tolerate the carbonic anhydrase inhibitor

KEVEYIS™ (dichlorphenamide) oral tablet (cont.)

- Triamterene 150 mg daily may also be used
 - Hyperkalemic periodic paralysis (hyperKPP)
 - It has autosomal dominant inheritance and is thought to be caused by point mutations in the voltage-gated sodium channel
 - Transient episodes of paralysis are usually precipitated by cold exposure, rest after exercise, fasting, or ingestion of small amounts of potassium
 - Acute attacks with moderate or severe weakness and hyperkalemia can be treated by interventions that lower potassium levels such as:
 - Thiazides diuretics
 - Inhaled beta-adrenergic agonists
 - Intravenous calcium
 - Dietary modifications include avoiding foods rich in potassium and avoiding carbohydrate loading
 - Strenuous activity should also be avoided
 - Prophylaxis of hyperKPP is achieved with use of carbonic anhydrase inhibitors and/or hydrochlorothiazide
 - Andersen-Tawil is characterized by a triad of periodic paralysis, ventricular dysrhythmias, and dysmorphic features such as short stature, hypertelorism, clinodactyly, micrognathia
 - Prolonged QT interval is also a feature
 - Paralytic attacks are commonly precipitated by rest after exercise
 - A dietary trigger is rarely identified
 - It is clinically and genetically distinct from other periodic paralyses
 - Carbonic anhydrase inhibitors are reported to limit attacks of weakness in some patients
 - Paramyotonia congenita with periodic paralysis is caused by mutations in the sodium channel
 - It is generally characterized by muscle stiffness which is made worse by cold temperatures or physical activity, but patients also have attacks of weakness and/or paralysis
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Definitions:

Periodic paralysis

	Hypokalemic Periodic Paralysis	Hyperkalemic Periodic Paralysis	Andersen-Tawil Syndrome	Paramyotonia congenita
Age at onset	First or second decade	First decade	First or second decade	First decade
Attack frequency	Infrequent (a few times a year)	Frequent (up to several a day)	Monthly	
Attack duration	Hours to days	Minutes to hours	Days	Days to weeks
Precipitants	Exercise Carbohydrate load Stress	Exercise Fasting Stress K-rich food	Rest after exercise	Exercise Cold
Potassium level during attack	Low	Normal or elevated	Low, normal, or elevated	Low, normal, or elevated
Associated features	Later onset myopathy	Myotonia on examination and/or EMG Later onset myopathy	Dysmorphic features Ventricular arrhythmias Long QT interval	Myotonia of face or upper extremities, lower extremities are less affected, may also affect respiratory muscles
Etiology	Autosomal dominant inherited defect in calcium or sodium ion channel on muscle membrane	Autosomal dominant inherited defect of sodium ion	Autosomal dominant inherited defect of inward rectifying potassium channel	Autosomal dominant defect in a sodium channel
Preventive treatment	Carbonic anhydrase inhibitors Potassium-sparing diuretics	Carbonic anhydrase inhibitors Thiazide diuretics Inhaled beta-agonists as needed	Carbonic anhydrase inhibitors	Carbonic anhydrase inhibitors Thiazide diuretics or Loop diuretic

Keveyis (dichlorphenamide)

Medication class:

Carbonic anhydrase inhibitor

FDA-approved indication(s):

- Treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants

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Recommended Dose:

- 50 mg twice daily
- **Maximum dosage**
- 100 mg twice daily

Available Dosage Forms:

- 50 mg scored tablets

Warnings, Precautions, and other Clinical Information:

- Discontinue at first appearance of skin rash or any sign of immune-mediated or idiosyncratic adverse effect
- Reduce dose or discontinue for persistent hypokalemia
- Reduce dose or discontinue for persistent metabolic acidosis
- Reduce dose or discontinue in patients who experience falls
- Keveyis causes hypokalemia through increased excretion of potassium
- Keveyis can cause hyperchloremic non-anion gap metabolic acidosis
- Keveyis increases salicylate levels
- Keveyis is not indicated for the treatment of acute attacks

Criteria:

- **Criteria for initial therapy:** Keveyis (dichlorphenamide) is considered **medically necessary** and will be approved when **ALL** of the following criteria are met:

1. Individual is 18 years of age or older
2. A confirmed diagnosis of **ONE** of the following:
 - Primary hyperkalemic periodic paralysis
 - Primary hypokalemic periodic paralysis
 - Paralysis in either of the related variants:
 - Paramyotonia congenita with periodic paralysis
 - Andersen-Tawil syndrome
3. Individual has failure, contraindication or intolerance to **acetazolamide**
4. Baseline serum potassium and bicarbonate levels have been completed before initiation of treatment
5. There are **NO** contraindications:
 - Contraindications include:
 - Hepatic insufficiency
 - Severe pulmonary disease
 - Hypersensitivity to dichlorphenamide or other sulfonamides
 - Concomitant use with high dose aspirin

Initial approval duration: 12 months

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- **Criteria for continuation of coverage (renewal request):** Keveyis (dichlorphenamide) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
1. Individual's condition responded while on therapy
 - Response is defined as:
 - Reduction in severity of and number of attacks
 2. Individual has been adherent with the medication
 3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
 - Contraindications as listed in the criteria for initial therapy section
 - Significant adverse effect such as:
 - Hypersensitivity
 - Signs and symptoms may include: hives over neck and face, itching, nasal congestion, difficulty breathing, edema of throat, swelling of lips, mouth or tongue, oral ulcers
 4. There are no significant interacting drugs

Renewal duration: 12 months

Resources:

Keveyis. Package Insert. Reference ID 3803244. Revised by manufacturer 8/2015. Accessed 10-08-2015, 12-05-2016

Keveyis. Package Insert. Revised by manufacturer 01/2017. Accessed 12-15-2017

UpToDate: Hypokalemic periodic paralysis. Current through Oct 2017. https://www.uptodate.com.mwu.idm.oclc.org/contents/hypokalemic-periodic-paralysis?source=search_result&search=Primary%20periodic%20paralysis&selectedTitle=1~150

UpToDate: Hyperkalemic periodic paralysis. Current through Oct 2017. https://www.uptodate.com.mwu.idm.oclc.org/contents/hyperkalemic-periodic-paralysis?source=search_result&search=Primary%20periodic%20paralysis&selectedTitle=2~150



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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
 Call 866-325-1794 to check the status of a request.
 All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
 Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.

REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information			
Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information			
Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information		
Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information			
Medication Name:	Strength:	Dosage Form:	
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

Check if requesting **brand** only Check if requesting **generic**

Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review	
<input type="checkbox"/> Standard <input type="checkbox"/> Urgent. Sign here: _____	<input type="checkbox"/> Exigent (requires prescriber to include a written statement)

Clinical Information	
1. What is the diagnosis? Please specify below. ICD-10 Code: _____ Diagnosis Description: _____	
2. <input type="checkbox"/> Yes <input type="checkbox"/> No Was this medication started on a recent hospital discharge or emergency room visit?	
3. <input type="checkbox"/> Yes <input type="checkbox"/> No There is absence of ALL contraindications.	

4. What medication(s) has the individual tried and failed for this diagnosis? Please specify below.
 Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. Are there any supporting labs or test results? Please specify below.

Date	Test	Value

Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature:	Date:
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Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.