Keveyis Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
7/1/2023	3/1/2018

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Keveyis® (dichlorphenamide) Tablets	Treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants		

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Primary Periodic Paralyses	Primary periodic paralyses are rare autosomal dominant conditions characterized by episodes of flaccid paralysis secondary to abnormal sarcolemmal excitability. All forms are associated with mutations in the skeletal muscle sodium, calcium, and potassium channels. These conditions are rarely life threatening, but a number of patients develop permanent weakness and muscle degeneration with age.(3) The two most common forms are hypokalemic periodic paralysis and hyperkalemic periodic paralysis.(2) There are related variants that have overlapping features with hyper- and hypokalemic periodic paralysis, including paramyotonia congenita, potassium aggravated myotonia, and congenital myasthenic syndrome. Treatment options include trigger avoidance, potassium supplementation, and carbonic anhydrase inhibitors.(2,3) Treatment and prevention varies by the form of periodic paralysis diagnosed:
	
	• Hypokalemic(2,3)
	  ○ Recommendations for trigger avoidance:
	  ▪ Follow a low-carbohydrate, low-Na diet
	  ▪ Avoid alcohol
	  ▪ Reduce stressors and physiological stress
	  ▪ Avoid hyperosmolar states (dehydration, hyperglycemia)
	  ○ Pharmacological prevention:
	  ▪ Acetazolamide: 125-1000 mg daily for adults, and 5-10 mg/kg/d for children
	  ▪ Potassium supplementation: 30-60 mEq daily
	  ▪ Dichlorphenamide: 50-200 mg daily
	  ▪ Potassium sparing diuretics: triamterene 50-150 mg daily, spironolactone 25-100 mg daily, eplerenone 50-100 mg daily
	  ○ Acute Attack:
	  ▪ Non-pharmacologic: mild exercise at attack onset

	▪ Potassium supplement: oral potassium supplementation of 1 mEq/kg to a max of 200 mEq in 24 hours (avoid slow release formulations) • Hyperkalemic(2,3) ○ Recommendations for trigger avoidance: ▪ Regularly ingest carbohydrate rich foods low in potassium ▪ Avoid fasting ▪ Avoid strenuous exercises after meals ▪ Avoid cold exposure ▪ Avoid potassium sparing agents ○ Pharmacological prevention: ▪ Acetazolamide: 125-1000 mg daily for adults, and 5-10 mg/kg/d for children ▪ Dichlorphenamide: 50-200 mg daily ▪ Hydrochlorothiazide: 25-75 mg daily ○ Acute attacks: ▪ Non-pharmacologic: light exercise and a carbohydrate snack ▪ Beta agonist: albuterol 1-2 puffs
Efficacy(1)	Dichlorphenamide for hypokalemic and hyperkalemic periodic paralysis was studied in two clinical studies. Study 1 was a 9-week, double-blind, placebo-controlled multi-center study examining the average number of self-reported attacks of muscle weakness per week with 44 hypokalemic periodic paralysis patients and 21 hyperkalemic periodic paralysis patients. Hypokalemic patients experienced 2.2 fewer episodes per week vs. placebo (p=0.02). Hyperkalemic patients experienced 3.9 fewer episodes per week vs. placebo (p=0.08). Study 2 was a 35-week, double-blind, placebo-controlled, multi-center, two-period crossover study with 42 hypokalemic periodic paralysis patients and 31 hyperkalemic periodic paralysis patients. In hypokalemic periodic paralysis patients, the primary endpoint was the incidence of acute intolerable worsening necessitating withdrawal. Two hypokalemic periodic paralysis patients on dichlorphenamide and 11 patients on placebo observed intolerable worsening (p=0.02). In hyperkalemic periodic paralysis patients, the primary endpoint was average number of self-reported episodes per week. Patients on dichlorphenamide had 2.3 fewer attacks per week compared to patients on placebo (p=0.006). For both studies, patients naïve to therapy were started at 50 mg twice daily, patients previously on dichlorphenamide were continued on the same dose, and patients previously on acetazolamide were given a dichlorphenamide dose at 20% of the acetazolamide dose. Primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants are a heterogeneous group of conditions, for which the response to dichlorphenamide may vary. Therefore, prescribers should evaluate the patient's response to dichlorphenamide after 2 months of treatment to decide whether dichlorphenamide should be continued.
Safety(1)	Dichlorphenamide has the following contraindications: • Hepatic insufficiency • Severe pulmonary obstruction • Hypersensitivity to dichlorphenamide or other sulfonamides • Concomitant use with high dose aspirin

REFERENCES

Number	Reference
1	Keveyis prescribing information. Taro Pharmaceuticals USA, Inc. November 2019.
2	Venance SL, Cannon SC, Fialho D, et al. CINCH Investigators. The Primary Periodic Paralyses: Diagnosis, Pathogenesis and Treatment. Brain. 2006;129:8–17.

Number	Reference
3	Statland JM, Fontaine B, Hanna MG, et al. Review of the Diagnosis and Treatment of Periodic Paralysis. Muscle Nerve. 2017;57(4):522-530.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
Keveyis	dichlorphenamide tab	50 MG	M ; N ; O ; Y	N ; O ; Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Keveyis	dichlorphenamide tab	50 MG	120	TABS	30	DAYS				

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Keveyis	dichlorphenamide tab	50 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Keveyis	dichlorphenamide tab	50 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when BOTH of the following are met: 1. ONE of the following: A. The patient has a diagnosis of primary hypokalemic periodic paralysis, primary hyperkalemic periodic paralysis, or a related variant of familial periodic paralysis (e.g., congenital myasthenic syndrome, Andersen-Tawil syndrome, paramyotonia congenita, potassium-associated myotonia) AND BOTH of the following: 1. The patient has implemented and maintained dietary and lifestyle changes to help prevent episodes **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response to acetazolamide **OR** B. The patient has an intolerance or hypersensitivity to acetazolamide **OR**

Module	Clinical Criteria for Approval
	C. The patient has an FDA labeled contraindication to acetazolamide **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that acetazolamide cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** B. The patient has another FDA approved indication for the requested agent **AND** 2. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 3 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. If the patient has a diagnosis of primary hypokalemic periodic paralysis, primary hyperkalemic periodic paralysis, or a related variant of familial periodic paralysis, the patient has continued to maintain dietary and lifestyle changes to help prevent episodes **AND** 3. The patient has had clinical benefit with the requested agent **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Evaluation** **Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND**

Module	Clinical Criteria for Approval
	B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: Initial approval - 3 months, Renewal approval - 12 months