Premier Health Plan

POLICY AND PROCEDURE

POLICY TITLE: ***Keveyis (dichlorphenamide)***
DEPARTMENT: **Clinical Pharmacy Services- Utilization Management**
ORIGINAL DATE: ***October 2015***

Last P & T Committee Approval Date: *February 2018*

Product Applicability: *mark all applicable products below:*

COMMERCIAL	[ ] HMO [ ] PPO *Products*: [ ] Small [ ] Indiv. [ ] Large *Exchange*: [ ] Shop [ ] Indiv. [x] All
OTHER	[x] Self-funded/ASO

PURPOSE

The purpose of this policy is to define the prior authorization process for Keveyis (dichlorphenamide).

Keveyis (dichlorphenamide) indicated for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.

DEFINITIONS

c.2014C>A: missense point mutation of SCN4A changes the coding DNA at nucleotide number 2014 which causes a change in the protein amino acid sequence from the arginine amino acid at residue 672 to a serine

c.2014C>G: missense point mutation of SCN4A changes the coding DNA at nucleotide number 2014 which causes a change in the protein amino acid sequence from the arginine amino acid at residue 672 to a glycine

Long exercise test (LET): recording evoked compound motor action potentials (CMAP) over 30-45 minutes, every one to two minutes and then every five minutes, after long effort (2-5 minutes, with brief 3 to 4 second rest periods every 15-45 seconds).

Interpretation of LET:
CMAP amplitude decrement = [(maximum CMAP amplitude prior to exercise – minimum CMAP amplitude post exercise)/ maximum CMAP amplitude prior to exercise] x 100%
CMAP area decrement = [(maximum CMAP area prior to exercise – minimum CMAP area post exercise)/ maximum CMAP area prior to exercise] x 100%
Positive LET for periodic paralysis is identified by one of the following:
1. Minimum 40% CMAP amplitude decrement post exercise, OR
2. Minimum 50% CMAP area decrement post exercise

Missense point mutation: a form of point mutation resulting in a codon that codes for a different amino acid, and thus, causes the synthesis of a protein with an altered amino acid sequence during translation.

SCNA4: sodium channel protein type 4 subunit alpha

POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Pharmacy & Therapeutics Committee of the criteria for prior authorization, as described in RX.002 Pharmacy and Therapeutics Committee and RX.003-Prior Authorization Process.

The drug, Keveyis (dichlorphenamide), is subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

Must meet all of the criteria listed under the respective diagnosis:

1. **For all diagnoses:**
   - Must be prescribed by a neurologist
   - Must have a diagnosis of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, or related variants
   - Must not have any of the following:
     - Concomitant use with high dose aspirin
     - Severe pulmonary disease, limiting compensation to metabolic acidosis that may be caused by dichlorphenamide (Keveyis)
     - Hepatic encephalopathy

2. Primary hypokalemic periodic paralysis:

- Must have documentation confirming diagnosis, defined as one of the following scenarios:
    - Two or more attacks of muscle weakness with documented serum K <3.5mEq/L, OR
    - One attack of muscle weakness in the member with documented serum potassium <3.5mEq/L and one attack of weakness in a relative with a history of the condition, OR
    - Three of the following clinical/laboratory features:
        - Onset of symptoms in the first or second decade of life
        - Duration of attack (muscle weakness involving one or more limbs) longer than two hours
        - The presence of triggers (previous carbohydrate rich meal, symptom onset during rest after exercise or during stressful situations) for attacks
        - Improvement in symptoms with potassium intake
        - A family history of the condition or genetically confirmed skeletal calcium or sodium channel mutation
        - Positive long exercise test (see definitions)
- Must have chart documentation excluding other causes of hypokalemia (renal, adrenal, thyroid dysfunction; renal tubular acidosis; diuretic and laxative abuse)
- Must have an adequate trial and failure or an inadequate response of acetazolamide unless has one of the following mutations in SCNA4:
    - c.2014C>G
    - c.2014C>A
- Must be using a potassium supplement
- Must have been counseled on appropriate dietary restrictions (high potassium intake, low sodium intake, and low carbohydrate intake)

3. Hyperkalemic periodic paralysis:

- Must have documentation confirming diagnosis::
    - For diagnosis confirmed by genetic testing, must have both of the following:
        - A family history of the condition or genetically confirmed skeletal sodium channel mutation associated with hyperkalemic periodic paralysis, AND

- A history of at least two attacks of flaccid limb weakness (which may also include weakness of the muscles of the eyes, throat, and trunk) or 1 attack with a family history of attacks of hyperkalemic periodic paralysis

OR

- For diagnosis made based on clinical presentation, must have all of the following:
  - A history of at least two attacks of flaccid limb weakness (which may also include weakness of the muscles of the eyes, throat, and trunk) or 1 attack with a family history of attacks of hyperkalemic periodic paralysis
  - Serum potassium >5mEq/L or an increase of serum potassium concentration of at least 1.5 mEq/L during an attack of weakness and/or onset/worsening of an attack as a result of oral potassium intake
  - Presence of myotonia OR any 3 of the following clinical features:
    - Typical attack duration less than 2 hours
    - Onset before 30 years.
    - Positive long exercise test (>40% decrement in CMAP)
    - Typical external triggers (rest after exercise, potassium load, fasting)

- Must have chart documentation of normal serum potassium concentration and muscle strength between attacks
- Must have chart documentation of ECG recording for the exclusion of a long QT and ventricular arrhythmias
- Must not have either of the following:
  - Secondary hyperkalemic periodic paralysis due to ingestion of potassium or of a potassium sparing diuretic
  - Paramyotonia (i.e. muscle stiffness that is worsening after exercise or cold-induced)
- Must have documentation of exclusion of other hereditary forms of hyperkalemia (i.e., Andersen-Tawil syndrome) and acquired forms of hyperkalemia (drug abuse, renal and adrenal dysfunction)
- Must have an adequate trial of acetazolamide with an inadequate response
- Must have been counseled on appropriate dietary restrictions (frequent meals high in carbohydrate)

Reauthorization Criteria:

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals based upon chart documentation from the prescriber that the member's condition has improved based upon the prescriber's assessment while on therapy.

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	Up to 2 months
Reauthorization	Up to 1 year
Quantity Level Limit	
Keveyis	120 tablets per 30 days

If the established criteria are not met, the request is referred to a Medical Director for review.

REFERENCES

1. Keveyis [prescribing information]. Taro Pharmaceuticals U.S.A., Inc. Hawthorne, NY. August 2015.
2. Vicart S, Sternberg D, Arzel-Hézode M, et al. Hypokalemic Periodic Paralysis. 2002 Apr 30 [Updated 2014 Jul 31]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1338/?report=classic
3. Jurkat-Rott K, Lehmann-Horn F. Hyperkalemic Periodic Paralysis Type 1. 2003 Jul 18 [Updated 2011 May 31]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1496/

RECORD RETENTION

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Annual review	*02/17, 02/18*