Keveyis
Prior Authorization with Quantity Limit
Program Summary

This prior authorization applies to Commercial, GenPlus, NetResults A series, SourceRx and Health Insurance Marketplace formularies only.

OBJECTIVE
The intent of the prior authorization with quantity limit program is to encourage appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines.

For initial therapy, the program will be approved for members who have a diagnosis of primary hypokalemic periodic paralysis, primary hyperkalemic periodic paralysis, or a related variant; who have implemented and maintained dietary and lifestyle changes to help prevent episodes; and who have a documented intolerance, FDA labeled contraindication, or hypersensitivity to acetazolamide, or have previously tried acetazolamide and did not achieve a successful response. The program will also be approved for use in another FDA approved indication.

For continued therapy, the program requires that the member be previously approved for initial therapy through Prime's prior authorization and quantity limit program; the member has continued to maintain dietary and lifestyle changes to help prevent episodes; and that the prescriber has indicated that the patient's periodic paralysis symptoms have improved with the requested therapy.

The program will not be approved for those who have any FDA labeled contraindication to the requested agent. The program will approve for doses within the set limit. Doses above the set limit will be approved if the requested quantity is below the FDA limit and cannot be dose optimized or when the quantity is above the FDA limit and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis. Requests will be reviewed when patient specific documentation is provided.

TARGET AGENT(S)
Keveyis (dichlorphenamide)

PROGRAM PRIOR AUTHORIZATION AND QUANTITY LIMITS

Brand (generic)	GPI	Multisource Code	Quantity Limit
Keveyis (dichlorphenamide)			
50 mg tablet	37100020000305	M, N, O, Y	4 tablets per day

PRIOR AUTHORIZATION AND QUANTITY LIMIT CRITERIA FOR APPROVAL
Initial Evaluation
Keveyis will be approved when ALL 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 **AND** BOTH of the following:
        i. The patient has implemented and maintained dietary and lifestyle changes to help prevent episodes
        AND

ii. ONE of the following:
1. The patient has previously tried acetazolamide and did not achieve a successful response
OR
2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to acetazolamide
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
AND
3. ONE of the following:
   a. The requested quantity (dose) is NOT greater than the program quantity limit
   OR
   b. ALL of the following:
      i. The requested quantity is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
      AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

   OR

   c. ALL of the following:
      i. The requested quantity is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) is greater than the FDA labeled dose
      AND
      iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 3 months

Renewal Evaluation

1. The patient has been previously approved for the requested agent through Prime Therapeutics Prior Authorization Review process
AND
2. The patient has continued to maintain dietary and lifestyle changes to help prevent episodes
AND
3. The prescriber has indicated that the patient's periodic paralysis symptom(s) have improved with the requested agent
AND
4. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
5. ONE of the following:
   a. The requested quantity (dose) is NOT greater than the program quantity limit
   OR
   b. ALL of the following:
      i. The requested quantity is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
      AND

iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

OR

c. ALL of the following:
   i. The requested quantity is greater than the program quantity limit
   AND
   ii. The requested quantity (dose) is greater than the FDA labeled dose
   AND
   iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 12 months

FDA APPROVED INDICATIONS AND DOSAGE[1]

Agent	Indication	Dosage & Administration
Keveyis™ (dichlorphenamide) tablets	Treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants	Initial dose: 50 mg orally twice daily Titrate to individual response Maximum recommended dose is 200 mg daily

CLINICAL RATIONALE

Periodic paralysis is a rare autosomal dominant condition with considerable variation in penetrance characterized by episodes of flaccid paralysis with loss of deep tendon reflexes and failure of muscle to respond to electrical stimulation. The two most common forms are hypokalemic periodic paralysis and hyperkalemic periodic paralysis.[3] Treatment varies by the form of periodic paralysis diagnosed:

- Hypokalemic[3]
    - Episodes are managed by giving 2-10 grams of KCl in an unsweetened oral solution or giving KCl IV.
    - Recommendations for prevention:
        - Follow a low-carbohydrate, low-Na diet
        - Avoid strenuous activity
        - Avoid alcohol after periods of rest
        - Take acetazolamide 250 mg orally twice a day
- Hyperkalemic[1,4]
    - Mild episodes can be aborted at onset by light exercise and a 2g/kg oral carbohydrate load
    - Established episodes can be treated with thiazides, acetazolamide, or inhaled β –agonists
    - Severe episodes can be treated with calcium gluconate or insulin and dextrose IV.
    - Recommendations for prevention:
        - Regularly ingest carbohydrate rich foods low in potassium
        - Avoid fasting
        - Avoid strenuous exercises after meals
        - Avoid cold exposure

Efficacy

Dichlorphenamide for hypokalemic and hyperkalemic periodic paralysis was studied in two clinical studies. Study 1 was a 9 week, double blind, placebo-controlled multicenter study examining the average number of self-reported 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 (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.[1]

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.[1]

Safety

Dichlorphenamide has the following contraindications:[1]

- Hepatic insufficiency
- Severe pulmonary obstruction
- Hypersensitivity to dichlorphenamide or other sulfonamides
- Concomitant use with high dose aspirin

REFERENCES

1. Keveyis prescribing information. Taro Pharmaceuticals USA, Inc. August 2015.
2. Rubin, M. Familial periodic paralysis. *Merck Manual*. Accessed on 10/12/2015 at http://www.merckmanuals.com/professional/pediatrics/inherited-muscular-disorders/familial-periodic-paralysis.
3. Hypokalemic periodic paralysis. Medline Plus. US National Library of Medicine. Accessed 02/02/2018. https://www.nlm.nih.gov/medlineplus/ency/article/000312.htm.
4. Hyperkalemic periodic paralysis. Medline Plus. US National Library of Medicine. Accessed 10/27/2015. https://www.nlm.nih.gov/medlineplus/ency/article/000316.htm.