pegvaliase (Palynziq™); sapropterin dihydrochloride (Kuvan®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO148

Description

Pegvaliase (Palynziq) is a PEGylated phenylalanine-metabolizing enzyme that works to reduce blood phenylalanine concentrations by converting phenylalanine to ammonia and transcinnamic acid.

Sapropterin dihydrochloride (Kuvan) is a synthetic form of the cofactor BH4 (tetrahydrobiopterin) for the enzyme phenylalanine hydroxylase (PAH). PAH hydroxylates phenylalanine to form tyrosine. BH4 activates residual PAH enzyme, improving normal phenylalanine metabolism and decreasing phenylalanine levels.

Length of Authorization

- Initial:
  - Pegvaliase (Palynziq): Six months
  - Sapropterin dihydrochloride (Kuvan): Two months
- Renewal:
  - Pegvaliase (Palynziq): 12 months
  - Sapropterin dihydrochloride (Kuvan): 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
pegvaliase (Palynziq)	2.5 mg/0.5 mL	Phenylketonuria (PKU)	60 syringes/30 days
	10 mg/0.5 mL		
	20 mg/1 mL		
sapropterin dihydrochloride (Kuvan)	100 mg tablets		20 mg/kg/day
	100 mg powder for oral solution		
	500 mg powder for oral solution		

Initial Evaluation

I. Pegvaliase (Palynziq) and sapropterin dihydrochloride (Kuvan) may be considered medically necessary when the following criteria below are met:
   A. Medication is prescribed by, or in consultation with, a metabolic diseases specialist or a provider who specializes in the treatment of phenylketonuria and other metabolic disorders; **AND**
   B. Documentation of current blood phenylalanine concentration is submitted; **AND**
   C. Documentation of current compliance with a phenylalanine restricted diet is submitted; **AND**
   D. Member is going to continue to restrict phenylalanine from their diet; **AND**

E. A diagnosis of **phenylketonuria (PKU)** when the following are met:
   1. *[Only for pegvaliase (Palynziq)];*
      i. Member is 18 years of age or older; **AND**
      ii. Member has uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management [e.g., phenylalanine restricted diet, Kuvan (sapropterin)]; **AND**
      iii. Not used in combination with sapropterin dihydrochloride (Kuvan); **OR**
   2. *[Only for sapropterin dihydrochloride (Kuvan)];*
      i. Member has tetrahydrobiopterin- (BH4-) responsive PKU; **AND**
      ii. Member has uncontrolled blood phenylalanine concentrations greater than 360 micromol/L on existing management [e.g., phenylalanine restricted diet]; **AND**
      iii. Not used in combination with pegvaliase (Palynziq).

II. Pegvaliase (Palynziq) and sapropterin dihydrochloride (Kuvan) is considered investigational when used for all other conditions, including but not limited to:
   A. Liver Cirrhosis and Portal Hypertension
   B. Autism spectrum disorder
   C. Gastroparesis
   D. Schizophrenia

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Medication is prescribed by, or in consultation with, a metabolic diseases specialist or a provider who specializes in the treatment of phenylketonuria and other metabolic disorders; **AND**
IV. Documentation of current compliance with a phenylalanine restricted diet is submitted; **AND**
V. Member is going to continue to restrict phenylalanine from their diet; **AND**
VI. Documentation of current blood phenylalanine concentration is submitted; **AND**
VII. Attestation of member compliance to therapy with pegvaliase (Palynziq) or dihydrochloride (Kuvan); **AND**
VIII. Member had a response to pegvaliase (Palynziq) therapy; defined as:
   A. At least a 20% reduction in blood phenylalanine levels from baseline; **OR**
   B. Blood phenylalanine concentration less than or equal to 600 micromol/L; **OR**
IX. Member had a response to sapropterin dihydrochloride (Kuvan) therapy; defined as:
   A. At least a 30% reduction in in blood phenylalanine levels from baseline

Supporting Evidence

I. Phenylketonuria (PKU) is an inherited disorder that increases the levels of a substance called phenylalanine in the blood. If PKU is not treated, phenylalanine can build up to harmful levels in the body causing intellectual disability and other serious health problems. Seizures, delayed development, behavioral problems, and psychiatric disorders are also common. Considering all the aspects of this disease state and that it is crucial to identify if a member is responding to therapy, the medication needs to be prescribed by, or in consultation with, a metabolic diseases specialist or a provider who specializes in the treatment of phenylketonuria and other metabolic disorders.

II. For sapropterin dihydrochloride (Kuvan) the response to therapy is determined by change in blood phenylalanine following treatment. If blood phenylalanine does not decrease from baseline at 10 mg/kg per day, the dose may be increased to 20 mg/kg per day. Patients whose blood phenylalanine does not decrease after 1 month of treatment at 20 mg/kg per day are non-responders and treatment should be discontinued.

III. For pegvaliase (Palynziq) the response to therapy is determined by change in blood phenylalanine following treatment. In patients who have not achieved a response (at least a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration less than or equal to 600 micromol/L) after 16 weeks of continuous treatment with the maximum dosage of 40 mg once daily, pegvaliase (Palynziq) should be discontinued.

IV. It is crucial for treatment and prevention of disease progression to obtain the blood levels of phenylalanine prior to treatment start.

V. According to the American College of Medical Genetics and Genomics (ACMG) Practice Guidelines, dietary therapy, with restriction of dietary phenylalanine intake, remains the mainstay of therapy for PAH deficiency. The goal of the diet is to provide enough natural protein for the patient to be healthy and grow normally with sufficient restriction to keep blood phenylalanine in the treatment range. PKU medication is not a replacement for diet.

VI. Pegvaliase (Palynziq) is indicated to reduce blood phenylalanine concentrations in adult patients with PKU who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management [e.g., phenylalanine restricted diet, Kuvan (sapropterin)].

VII. The safety and efficacy of pegvaliase (Palynziq) in pediatric patients has not been assessed in clinical trials and therefor there is no robust evidence to support the use.

VIII. There is no robust clinical trial data to show an increase benefit and the safety profile of concomitant use of pegvaliase (Palynziq) and sapropterin dihydrochloride (Kuvan).

IX. Sapropterin dihydrochloride (Kuvan) is indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive PKU. Kuvan is to be used in conjunction with a Phe-restricted diet.

Investigational or Not Medically Necessary Uses

I. Pegvaliase (Palynziq);
   A. There is limited or no published clinical trial data to support the use of pegvaliase (Palynziq) in conditions other than PKU.

II. Sapropterin dihydrochloride (Kuvan);
    A. Liver Cirrhosis and Portal Hypertension
        i. A randomized, blinded, and placebo controlled trial was conducted to assess the effects of sapropterin dihydrochloride (Kuvan) on hepatic and systemic hemodynamics in patients with liver cirrhosis and portal hypertension. The trial data showed that sapropterin dihydrochloride (Kuvan), did not reduce portal pressure in patients with cirrhosis.
    B. Autism spectrum disorder (ASD)
        i. A prospective 16-week open-label outpatient treatment trial of sapropterin dihydrochloride (Kuvan) for core and associated ASD symptoms in 2–6-year-old children with confirmed language and/or social delays extended the understanding of the effect of BH_4 treatment on the cognitive and behavioral symptoms of individuals with ASD
        ii. The results of a double-blind placebo-controlled crossover study, designed to examine the tetrahydrobiopterin pathway genes in autism, indicated a possible effect of BH4 treatment in children with autistic disorder, but the study does not have enough power and it wasn't designed to show efficacy and safety of the use of sapropterin dihydrochloride (Kuvan) in the treatment of autism spectrum disorder. There is no robust safety and efficacy data to support the use of sapropterin dihydrochloride (Kuvan) in patients with autism spectrum disorder.
    C. Gastroparesis
        i. One small open label trial consisting of low quality evidence. Further evaluation is needed to support the use of sapropterin dihydrochloride (Kuvan) in this setting.
    D. Schizophrenia
        i. One small open label trial consisting of low quality evidence is available with ongoing trials recruiting as of 2019. Further evaluation is need to support use of sapropterin dihydrochloride (Kuvan) in this setting.

References

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13. ClinicalTrials.gov. Impact of KUVAN® on Gastric Relaxation in Women With Diabetic Gastroparesis. NCT01135186.
14. ClinicalTrials.gov. Kuvan in People With Schizophrenia and Schizoaffective Disorder. NCT01706965.

Policy Implementation/Update:

	sapropterin dihydrochloride (Kuvan)	pegvaliase (Palynziq)
Date Created	January 2009	July 2018
Date Effective	February 2009	August 2018
Last Updated	December 2019	
Last Reviewed	December 2019	

Action and Summary of Changes	**Date**
• Updated criteria to policy format and combined separate polices into one • Ensured sapropterin dihydrochloride (Kuvan) is not used in combination with pegvaliase (Palynziq) • Requirement of member requesting sapropterin dihydrochloride (Kuvan) to have tetrahydrobiopterin- (BH4-) responsive PKU • Added criteria to require documentation of current blood phenylalanine concentration and of current compliance with a phenylalanine restricted diet • Adjusted requirement of phenylalanine levels in use of sapropterin dihydrochloride (Kuvan) to be greater than 360 micromol/L for all ages • Updated renewal duration with Kuvan to 1 year to align with Palynziq	12/2019