PRIOR AUTHORIZATION POLICY

POLICY: Phenylketonuria – Palynziq Prior Authorization Policy
- Palynziq® (pegvaliase-pqpz subcutaneous injection – BioMarin)

REVIEW DATE: 07/14/2021

OVERVIEW

Palynziq is indicated to reduce blood phenylalanine concentrations in adult patients with **phenylketonuria (PKU)** who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L (µmol/L) on existing management.[1] Treatment with Palynziq should be managed by a healthcare provider experienced in the management of PKU. Baseline blood phenylalanine concentrations should be obtained before initiating treatment.

Dose Titration

The recommended initial induction dosage for Palynziq is 2.5 mg subcutaneously (SC) for 4 weeks.[1] This dose is then titrated over a period of at least 5 weeks to a maintenance dose of 20 mg SC once daily (QD). The maintenance dose should be individualized to achieve blood phenylalanine control (blood phenylalanine concentration ≤ 600 micromol/L). Maintain the Palynziq 20 mg QD dose for at least 24 weeks. Consider increasing the Palynziq dose to 40 mg QD in a patient who has been on 20 mg QD for at least 24 weeks without achieving blood phenylalanine control. Consider increasing the Palynziq dose to a maximum of 60 mg QD in a patient who has been on 40 mg QD for at least 16 weeks without achieving blood phenylalanine control. Discontinue Palynziq in a patient who has not achieved an adequate response after continuous treatment with the maximum dose of 60 mg QD. A dose titration schedule is outlined in Table 1. Therapeutic response may not be achieved until the patient is titrated to an effective maintenance dose.

Table 1. Palynziq Dose Titration.

Treatment	Palynziq Dose	Duration*
Induction	2.5 mg once weekly	4 weeks
Titration	2.5 mg twice weekly to 10 mg QD, escalated in weekly intervals over 5 weeks	5 weeks
Maintenance	20 mg QD	24 weeks
	40 mg QD	16 weeks
Maximum	60 mg QD	16 weeks
Total	--	**65 weeks**

* Additional time may be required prior to each dosage escalation based on patient tolerability.

Because of the risk of anaphylaxis Palynziq is available only through a restricted Risk Evaluation and Mitigation Strategy (REMS) program. It was unclear from the Palynziq clinical trials if all patients had tried and were non-responders to sapropterin.

Guidelines

Recommendations regarding use of Palynziq are not made in guidelines from the American College of Medical Genetics and Genomics (ACMG) [2014] or European guidelines (2017).[2,3] However, a consensus statement regarding use of Palynziq in adults with PKU was published in 2019.[4] Palynziq should be considered for all adults with PKU who have the ability to give informed consent and adhere to treatment. It is noted that some patients may show a response early on, whereas other may take 1 year or more from initiation of treatment before a reduction in blood phenylalanine concentration is observed. The definition

of a "clinically meaningful" efficacy benefit should be determined by the treating clinician based on individual patient goals. Primarily, the efficacy benefit should be determined by a significant reduction in blood phenylalanine concentration from baseline.

Although ACMG and European guidelines do not offer recommendations specific to Palynziq, they do provide general principles for PKU management. ACMG guidelines suggest a target blood phenylalanine level of 120 to 360 micromol/L for all patients.[2] However, European guidelines state that patients ≥ 12 years of age with blood phenylalanine concentration < 600 micromol/L do not require treatment, and the target range for patients ≥ 12 years of age receiving treatment is 120 to 600 micromol/L.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Palynziq. Because of the specialized skills required for evaluation and diagnosis of patients treated with Palynziq as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Palynziq to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 1 year in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Palynziq is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Phenylketonuria.** Approve for the duration noted if the patient meets one of the following (A or B):
   - **A)** Initial Therapy. Approve for 1 year if the patient meets the following criteria (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on at least one existing treatment modality; AND
       Note: Examples of treatment modalities include restriction of dietary phenylalanine and protein intake and prior treatment with sapropterin (Kuvan, generic).
     - **iii.** The medication is prescribed by or in consultation with a metabolic disease specialist (or specialist who focuses in the treatment of metabolic diseases).
   - **B)** Patient is Currently Receiving Palynziq. Approve for 1 year if the patient meets the following criteria (i, ii, and iii):
     Note: A patient who has received < 1 year of therapy or who is restarting therapy with Palynziq should be considered under Initial Therapy criteria.
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets one of the following (a or b):
       - **a)** Patient meets both of the following (1 and 2):
         - **(1)** Patient is continuing to titrate Palynziq to an effective maintenance dose, per the prescriber; AND
         - **(2)** If the patient is receiving a dose of Palynziq 60 mg once daily, the treatment duration at this dose has not exceeded 16 weeks; OR
       - **b)** Patient meets both of the following (1 and 2):
         - **(1)** Patient meets one of the following (a or b):
           - **(a)** Patient's blood phenylalanine concentration is ≤ 600 micromol/L; OR

(b) Patient has achieved a ≥ 20% reduction in blood phenylalanine concentration from pre-treatment baseline (i.e., blood phenylalanine concentration before starting Palynziq therapy); AND

(2) Patient is not receiving concomitant therapy with sapropterin (Kuvan, generic).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Palynziq is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Palynziq™ injection [prescribing information]. Novato, CA: BioMarin; November 2020.
2. Vockley J, Andersson HC, Antshel KM, et al; American College of Medical Genetics and Genomics Therapeutics Committee. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. *Genet Med*. 2014 Feb;16(2):188-200.
3. van Wegberg AMJ, MacDonald A, Ahring A, et al. The complete European guidelines on phenylketonuria: diagnosis and treatment. *Orphanet J Rare Dis*. 2017;12:162.
4. Longo N, Dimmock D, Levy H, et al. Evidence- and consensus-based recommendations for the use of pegvaliase in adults with phenylketonuria. *Genet Med*. 2019 Aug;21(8):1851-1867.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Phenylketonuria – Initial Therapy:** The phrase "in adults" was removed from the approval condition; instead, a criterion was added to verify that the patient is ≥ 18 years of age. Examples of prior treatment modalities were moved to a note. **Phenylketonuria – Patients Continuing Therapy:** The phrase "in adults" was removed from the approval condition and moved into criteria as ≥ 18 years of age. Additionally, "[Maintenance therapy]" was removed from the approval condition; this is not needed. A note was added that patients who have received less than 1 year of Palynziq or who are restarting Palynziq should refer to Initial Therapy criteria. A criterion was added that concomitant use of Kuvan is not permitted (previously this was addressed under Conditions Not Recommended for Approval). **Concomitant Therapy with Palynziq and Kuvan:** Removed from policy. This is now addressed in criteria under the approval condition of "Phenylketonuia – Patients Continuing Therapy".	06/17/2020
Annual Revision	**Phenylketonuria:** For a patient currently receiving Palynziq, a criterion was added such that a patient may use concomitant Kuvan and is not required to meet response criteria, if the following conditions are met: patient is continuing to titrate Palynziq to an effective maintenance dose, per the prescriber; AND if the patient is receiving the maximum dose of 60 mg once daily, the treatment duration at this dose has not exceeded 16 weeks.	07/14/2021

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Washington, D.C. 20201
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