MEDICAL MUTUAL®

Drug Policy

Policy:	**201818**	**Initial Effective Date: 07/21/2018**
Code(s):	**HCPCS J3590, C9399**	**Annual Review Date: 06/19/2025**
SUBJECT:	**Palynziq® (pegvaliase-pqpz)**	**Last Revised Date: 06/19/2025**

Subject to: ☒Site of Care
☐Medication Sourcing

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

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. 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. Palynziq is titrated up over a period of 9 weeks to the maintenance dose of 20 mg administered subcutaneously (SC) once daily (QD). Therapeutic response may not be achieved until the patient is titrated to an effective maintenance dosage. Palynziq 20 mg SC QD should be maintanined for at least 24 weeks. he dose can be increased to a maximum dose of Palynziq 40 mg SC QD in patients who have been maintained continuously on the 20 mg QD dose for at least 24 weeks and who have not achieved either a 20% reduction in blood phenylalanine concentration from pre-treatment baseline levels or a blood phenylalanine concentration ≤ 600 µmol/L. Palynziq should be discontinued in patients who have not achieved a response after 16 weeks of continuous treatment with the maximum dosage of 40 mg QD. In patients who experience blood phenylalanine concentrations < 30 µmol/L during the titration and maintenance phase, the dosage of Palynziq may be reduced and/or dietary protein and phenylalanine intake may be modified to maintain phenylalanine levels within a clinically acceptable range and above 30 µmol/L. 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 Kuvan.

POLICY STATEMENT

This policy involves the use of Palynziq. Prior authorization is recommended for pharmacy benefit coverage of Palynziq. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended

authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

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 be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

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

1. **Phenylketonuria (PKU)**
   Criteria. *Patient must meet the following criteria*
   - **A.** Patient is 18 years of age or older; AND
   - **B.** Patient have uncontrolled blood phenylalanine concentration > 600 micromol/L; AND
   - **C.** Patient has trialed and failed, or has a contraindication to sapropterin (Kuvan, generic); AND
   - **D.** Palynziq is prescribed by or in consultation with a metabolic diseases specialist or a provider who specializes in the treatment of PKU and other metabolic diseases; AND
   - **E.** An epinephrine auto-injector has been prescribed to the patient; AND
     Palynziq will not be used concurrently with Kuvan; AND
   - **F.** Site of care medical necessity is met.*

2. **Continuation of Therapy with Palynziq**
   Criteria. Approve if the patient has had a response to Palynziq therapy evidenced by a 20% reduction in blood phenylalanine levels from baseline or blood Phenylalanine concentration of 600 micromol/L or less and site of care medical necessity is met.*

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

Dosing

The recommended 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. 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.

REFERENCES

1. Palynziq injection [prescribing information]. Novato, CA: BioMarin Pharmaceuticals; May 2018.
2. Pegvaliase-pqpz. In: [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 5 June 2018. Accessed on 23 January 2019.
3. Vockley J, Andersson HC, Antshel KM, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. Available at: https://www.acmg.net/docs/Phenylalanine_Hydrosylase_Deficiency_Practice_Guideline_AOP_Jan_2013.pdf. Accessed on 23 January 2019.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

Prior approval is required for HCPCS CodesJ3590

†When *biologics* (J3590) is determined to be Palynziq

Edits and Denials:

Prior approval: Prior approval is required for Palynziq **(HCPCS Codes J3590)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

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Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

TOPPS: Claims received with **HCPCS Codes J3590** will pend with **Remark Code M3M or M4M** and will be adjudicated in accordance with the Corporate Medical Policy.

Liability: A participating provider will be required to write off charges denied as not medically necessary.

HCPCS Code(s):	
J3590	Unclassified biologics