Clinical Policy: Pegvaliase-pqpz (Palynziq)

Reference Number: CP.PHAR.140
Effective Date: 12.01.18
Last Review Date: 11.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Pegvaliase-pqpz (Palynziq™) is a PEGylated phenylalanine ammonia lyase (PAL) enzyme that converts phenylalanine to ammonia and trans-cinnamic acid. It substitutes for the deficient phenylalanine hydroxylase (PAH) enzyme activity in patients with phenylketonuria (PKU) and reduces blood phenylalanine concentrations.

FDA Approved Indication(s)

Palynziq is indicated to reduce blood phenylalanine concentrations in adult patients with PKU who have uncontrolled blood phenylalanine concentrations > 600 µmol/L on existing management.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Palynziq is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Phenylketonuria (must meet all)**:**

1. Diagnosis of PKU;
2. Prescribed by or in consultation with an endocrinologist, metabolic disease specialist, or genetic disease specialist;
3. Age ≥ 18 years;
4. Recent (within 90 days) phenylalanine (Phe) blood level is > 600 µmols/L;
5. Member is currently on a phenylalanine-restricted diet and will continue this diet during treatment with Palynziq;
6. Failure of sapropterin (Kuvan®) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Palynziq is not prescribed concurrently with sapropterin (Kuvan);
8. Dose does not exceed 20 mg per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Phenylketonuria (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is currently on a phenylalanine-restricted diet and will continue this diet during treatment with Palynziq;
3. Palynziq is not prescribed concurrently with sapropterin (Kuvan);
4. Member meets one of the following (a, b, or c):
   a. Member has achieved blood Phe control (i.e., blood Phe level is ≤ 600 µmol/L);
   b. Request is for 40 mg per day and member has previously used 20 mg per day continuously for at least 6 months without achieving blood Phe control;
   c. Request is for 60 mg per day and member meets both of the following (i and ii):
      i. Member has previously used 40 mg per day continuously for at least 16 weeks without achieving blood Phe control;
      ii. Member has not used 60 mg per day continuously for more than 16 weeks without achieving blood Phe control;
5. If request is for a dose increase, new dose does not exceed 60 mg per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
PAH: phenylalanine hydroxylase
PAL: phenylalanine ammonia lyase
Phe: phenylalanine
PKU: phenylketonuria

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
sapropterin (Kuvan)	Age 1 month to ≤ 6 years (starting dose): 10 mg/kg PO QD Age ≥ 7 years (starting dose): 10 to 20 mg/kg PO QD	20 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): risk of anaphylaxis

Appendix D: General Information

- Palynziq has a black box warning for the potential to cause anaphylaxis and enrollment in a REMS program is required, along with supervision of the initial dose by a healthcare professional and the need to carry auto-injectable epinephrine at all times while using Palynziq. Use of premedication with H_1 blockers, H_2 blockers, and/or antipyretics can also be considered.
- Per the Palynziq PI, discontinuation of Palynziq is recommended if a patient has not achieved an adequate response (blood Phe concentration ≤ 600 µmol/L) after 16 weeks of continuous treatment with the maximum dosage of 60 mg QD.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PKU	Initiate dosing with 2.5 mg SC once weekly for 4 weeks. Administer the initial dose under the supervision of a healthcare provider. Titrate the Palynziq dosage in a step-wise manner, based on tolerability, over ≥ 5 weeks, to achieve a dosage of 20 mg SC QD. Maintain the Palynziq dosage at 20 mg SC QD for ≥ 24 weeks. Consider increasing the Palynziq dosage to 40 mg SC QD in patients who have been maintained continuously on 20 mg QD for ≥ 24 weeks and who have not achieved a blood Phe concentration ≤ 600 µmol/L. Consider increasing the dosage to a maximum of 60 mg SC QD in patients who have been on 40 mg QD continuously for ≥ 16 weeks and who have not achieved a blood Phe concentration ≤ 600 µmol/L. Discontinue Palynziq in patients who have not achieved a response (blood Phe concentration ≤ 600 µmol/L) after 16 weeks of continuous treatment with the maximum dosage of 60 mg QD.	60 mg/day

VI. Product Availability

Injection, single-dose prefilled syringe: 2.5 mg/0.5 mL, 10 mg/0.5 mL, 20 mg/mL

VII. References

1. Palynziq Prescribing Information. Novato, CA: BioMarin Pharmaceutical Inc.; November 2020. Available at: http://www.palynziq.com. Accessed July 15, 2024.
2. Vockley J, Andersson HC, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. Genet Med. Feb 2014;16(2):188-200.

3. Thomas J, Levy H, et al. Pegvaliase for the treatment of phenylketonuria: results of a long-term phase 3 clinical trial program (PRISM). Molecular Genetics and Metabolism. 2018;124:27-38.
4. Harding CO, Amato RS, et al. Pegvaliase for the treatment of phenylketonuria: a pivotal, double-blind randomized discontinuation phase 3 clinical trial. Molecular Genetics and Metabolism. 2018;124:20-26.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3590, C9399	Unclassified drugs or biologics

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: added requirement for current and continued use of Phe-restricted diet; added requirement for a prior trial of Kuvan; RT4: revised continuation criteria to reflect updated dosing recommendations in the package labeling; references reviewed and updated.	11.03.20	11.20
4Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; added C9399 as HCPCS code; references reviewed and updated.	08.17.21	11.21
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.25.22	11.22
4Q 2023 annual review: no significant changes; added differentiation of approval duration depending on line of business, for Commercial allowing only the standard "6 months or member's renewal date, whichever is longer"; references reviewed and updated.	08.10.23	11.23
4Q 2024 annual review: no significant changes; added exclusion against concomitant use with sapropterin (Kuvan) for Continued Therapy to mirror Initial Approval Criteria; references reviewed and updated.	07.15.24	11.24

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical

policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.