

Clinical Policy: Pegvaliase-pqpz (Palynziq)

Reference Number: CP.PHAR.140

Effective Date: 07.31.18

Last Review Date: 11.19

Line of Business: Commercial, HIM, Medicaid

[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. Palynziq is not prescribed concurrently with Kuvan;
6. Dose does not exceed 20 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Phenylketonuria (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member meets one of the following (a, b, or c):
 - a. Blood Phe level has decreased by $\geq 20\%$ from pre-treatment baseline;
 - b. Blood Phe level is $\leq 600 \mu\text{mol/L}$;
 - c. Member has been using 20 mg per day for at least 6 months, but a dose titration to 40 mg per day is being requested after failure to meet therapeutic targets (a or b above) [only the 40 mg per day dose will be approved];
3. If request is for a dose increase, new dose does not exceed 40 mg per day.

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 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

Not applicable

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 H₁ blockers, H₂ blockers, and/or antipyretics can also be considered.

- Per the Palynziq PI, discontinuation of Palynziq is recommended if a patient has not achieved a response ($\geq 20\%$ reduction in blood Phe concentration from pre-treatment baseline or a blood Phe concentration $\leq 600 \mu\text{mol/L}$) after 16 weeks of continuous treatment with the maximum dosage of 40 mg QD.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PKU	<p>Initiate dosing with 2.5 mg SC once weekly for 4 weeks. Administer the initial dose under the supervision of a healthcare provider.</p> <p>Titrate the Palynziq dosage in a step-wise manner, based on tolerability, over ≥ 5 weeks, to achieve a dosage of 20 mg SC QD.</p> <p>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 either a 20% reduction in blood Phe concentration from pre-treatment baseline or a blood Phe concentration $\leq 600 \mu\text{mol/L}$.</p> <p>Discontinue Palynziq in patients who have not achieved a response ($\geq 20\%$ reduction in blood Phe concentration from pre-treatment baseline or a blood Phe concentration $\leq 600 \mu\text{mol/L}$) after 16 weeks of continuous treatment with the maximum dosage of 40 mg QD.</p>	40 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.; May 2018. Available at: <http://www.palynziq.com>. Accessed August 19, 2019.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.31.18	11.18
No significant changes; added HIM line of business per SDC.	02.01.19	
4Q 2019 annual review: no significant changes; references reviewed and updated	08.19.19	11.19

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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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