Clinical Policy: Pegvaliase-pqpz (Palynziq)
Reference Number: CP.PHAR.140
Effective Date: 12.01.18
Last Review Date: 11.20
Line of Business: Commercial, HIM, Medicaid

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 Kuvan® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      7. Palynziq is not prescribed concurrently with Kuvan;
      8. 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
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 is currently on a phenylalanine-restricted diet and will continue this diet during treatment with Palynziq;
      3. 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;
      4. If request is for a dose increase, new dose does not exceed 60 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
   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.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuvan (sapropterin)</td>
<td>Age 1 month to ≤ 6 years (starting dose): 10 mg/kg PO QD</td>
<td>20 mg/kg/day</td>
</tr>
<tr>
<td></td>
<td>Age ≥ 7 years (starting dose): 10 to 20 mg/kg PO QD</td>
<td></td>
</tr>
</tbody>
</table>

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 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 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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>PKU</td>
<td>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</td>
<td>60 mg/day</td>
</tr>
</tbody>
</table>
### Pegvaliase-pqpz

#### Indication

**Dosing Regimen**

- 16 weeks of continuous treatment with the maximum dosage of 60 mg QD.

### VI. Product Availability

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

### VII. References


### 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

<table>
<thead>
<tr>
<th>Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J3590</td>
<td>Unclassified biologics</td>
</tr>
</tbody>
</table>

### Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Policy created</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>No significant changes; added HIM line of business per SDC.</td>
<td>02.01.19</td>
<td>11.18</td>
</tr>
<tr>
<td>4Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>08.19.19</td>
<td>11.19</td>
</tr>
<tr>
<td>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.</td>
<td>11.03.20</td>
<td>11.20</td>
</tr>
</tbody>
</table>

### 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.