

Phenylketonuria

Goal(s):

- Promote safe and cost effective therapy for the treatment of phenylketonuria.

Length of Authorization:

- Initial: 1 to 9 months;
- Renewal: 16 weeks to 1 year

Requires PA:

- Sapropterin and pegvaliase (pharmacy and physician administered claims)

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. Is the diagnosis funded by OHP?	Yes: Go to #2	No: Pass to RPh. Deny; not funded by OHP
2. Is the request for renewal of therapy previously approved by the FFS system?	Yes: Go to Renewal Criteria	No: Go to #3
3. Is the drug prescribed by or in consultation with a specialist in metabolic disorders?	Yes: Go to #4	No: Pass to RPh. Deny; medical appropriateness
4. Is the request for sapropterin?	Yes: Go to #5	No: Go to #8
5. Is the diagnosis tetrahydrobiopterin-(BH4-) responsive phenylketonuria?	Yes: Go to #6	No: Pass to RPh. Deny; medical appropriateness
6. Is the patient currently compliant with a Phe-restricted diet and unable to achieve target blood phenylalanine level?	Yes: Go to #7	No: Pass to RPh. Deny and recommend Phe-restricted diet.
7. Is the patient's baseline blood phenylalanine level provided in the request and above the target range (see Clinical Notes)?	Yes: Approve for 2 months if initial dose is 5-10 mg/kg/day (to allow for titration to 20 mg/kg/day). Approve for 1 month if initial dose is 20 mg/kg/day (adults and children).	No: Request information from provider.
8. Is the request for pegvaliase?	Yes: Go to #9	No: Pass to RPh. Deny; medical appropriateness

Approval Criteria

9. Is the patient 18 years of age or older with a diagnosis of phenylketonuria?	Yes: Go to #10	No: Pass to RPh. Deny; medical appropriateness
10. Is the patient's blood phenylalanine concentration documented in the request and greater than 600 µmol/L on existing management (such as dietary phenylalanine restriction or sapropterin)?	Yes: Go to #11	No: Pass to RPh. Deny; medical appropriateness If not documented, request information from provider.
11. Is the medication prescribed concurrently with epinephrine based on claims history or chart notes?	Yes: Approve for 9 months based on FDA-approved induction, titration, and maintenance dosing*	No: Pass to RPh. Deny; medical appropriateness

Renewal Criteria

1. Is the request for sapropterin?	Yes: Go to #2	No: Go to #4
2. Did the patient meet the target phenylalanine level set by the specialist (see Clinical Notes)?	Yes: Go to #3	No: Pass to RPh. Deny for lack of treatment response.
3. Is the patient remaining compliant with the Phe-restricted diet?	Yes: Approve for 12 months	No: Pass to RPh. Deny and recommend Phe-restricted diet.
4. Is the request for pegvaliase?	Yes: Go to #5	No: Pass to RPh. Deny; medical appropriateness
5. Has there been a reduction from baseline phenylalanine concentration of 20% or greater?	Yes: Approve for 12 months	No: Go to #6
6. Has there been a reduction in blood phenylalanine concentration to less than or equal to 600 µmol/L?	Yes: Approve for 12 months	No: Go to #7

Renewal Criteria

7. Is the request for a first renewal of pegvaliase therapy and the patient had been on pegvaliase 20 mg daily for at least 24 weeks?

Yes: Approve for 16 weeks for trial of maximum dose of 40 mg once daily. Continued approval at this dose requires documentation of improvement (>20% reduction from baseline or less than 600 µmol/L in phenylalanine concentration).

No: Pass to RPh. Deny for lack of treatment response.

Clinical Notes:

Target blood phenylalanine levels in the range of 120-360 µmol/L for patients in all age ranges.¹ In addition to the recommended Phe concentrations, a 30% or more reduction in blood Phe is often considered a clinically significant change from baseline and should occur after the initial trial.² If not, the patient is a non-responder and will not benefit from sapropterin therapy. Sapropterin doses above 20 mg/kg/day have not been studied in clinical trials.

***Pegvaliase FDA-Recommended Dosage and Administration:**

Treatment	Pegvaliase Dosage	Duration*
Induction	2.5 mg once weekly	4 weeks
Titration	2.5 mg twice weekly	1 week
	10 mg once weekly	1 week
	10 mg twice weekly	1 week
	10 mg four times per week	1 week
	10 mg once daily	1 week
Maintenance	20 mg once daily	24 weeks
Maximum**	40 mg once daily	16 weeks***

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

**Individualize treatment to the lowest effective and tolerated dosage. Consider increasing to a maximum of 40 mg once daily in patients who have not achieved a response ($\geq 20\%$ reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration ≤ 600 µmol/L) with 20 mg once daily continuous treatment for at least 24 weeks.

***Discontinue pegvaliase treatment in patients who have not achieved a response ($\geq 20\%$ reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration ≤ 600 µmol/L) after 16 weeks of continuous treatment with the maximum dosage of 40 mg once daily.

References:

- Vockley J, Andersson HC, Antshel KM, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. *Genet Med*. 2014;16(2):188-200. doi:10.1038/gim.2013.157
- Blau N., Belanger-Quintana A., Demirkol M. Optimizing the use of sapropterin (BH₄) in the management of phenylketonuria. *Molecular Genetics and Metabolism* 2009;96:158-163.

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