BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

JAVYGTOR™ (sapropterin dihydrochloride) oral
KUVAN® (sapropterin dihydrochloride) oral
PALYNZIQ™ (pegvaliase-pqpz) subcutaneous
Sapropterin Dihydrochloride oral
SEPHIENCE™ (sepiapterin) oral
ZELVYSIA™ (sapropterin dihydrochloride) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for JAVYGTOR (sapropterin dihydrochloride), KUVAN (sapropterin dihydrochloride), Sapropterin Dihydrochloride generic, SEPHIENCE (sepiapterin), and ZELVYSIA (sepiapterin dihydrochloride)

ORIGINAL EFFECTIVE DATE: 03/19/2015 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 11/19/2026

PHARMACY COVERAGE GUIDELINE

JAVYGTOR™ (sapropterin dihydrochloride) oral
KUVAN® (sapropterin dihydrochloride) oral
PALYNZIQ™ (pegvaliase-pqpz) subcutaneous
Sapropterin Dihydrochloride oral
SEPHIENCE™ (sepiapterin) oral
ZELVYSIA™ (sapropterin dihydrochloride) oral
Generic Equivalent (if available)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in metabolic or genetic diseases, or in consultation with one

Indication:
- Hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4) responsive phenylketonuria (PKU) to be used in conjunction with a phenylalanine restricted diet

Age Requirement
- 1 month of age or older

Baseline Clinical Evaluation
- Hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4) responsive phenylketonuria (PKU) is documented
- On a phenylalanine (PHE) restricted diet that is adjusted based on blood phenylalanine levels
- Blood phenylalanine (PHE) level is above the recommended level for age or condition, and the baseline phenylalanine level is submitted with the request

Alternative Therapies
- Failure (trial for at least three months duration), contraindication according to the United States Food and Drug Administration (FDA) labeled safety information, intolerance, or is not a candidate for **generic sapropterin dihydrochloride**

Brand Specific Criteria
- **For Sephience (sepiapterin):** Failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- **For Sephience (sepiapterin)**: Does not have concomitant use with **ANY** of the following:
  - Dihydrofolate reductase (DHFR) inhibitors. (e.g., trimethoprim, methotrexate, trimetrexate, pemetrexed, pralatrexate)
  - Sepiapterin reductase (SR) inhibitors. (e.g., sulfasalazine, sulfamethoxazole)
  - Drugs that affect nitric oxide mediated vasorelaxation. (e.g., phosphodiesterase type 5 (PDE 5) inhibitors such as sildenafil, vardenafil, tadalafil)

- No concomitant drug use of Javygtor, Kuvan, sapropterin dihydrochloride generic, Sephience, or Zelvysia with Palynziq

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes supporting: Diagnosis of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4) responsive phenylketonuria (PKU). Current phenylalanine (PHE) restricted diet management
  - Lab results: Baseline blood phenylalanine (PHE) level above recommended target for age or condition
  - Supporting clinical documentation that shows: Rationale for use of brand or specific product over generic sapropterin dihydrochloride or generic equivalent, if applicable

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualifications

- Continues to be seen by a physician specializing in metabolic or genetic diseases, or in consultation with one

Clinical Response

- Baseline blood phenylalanine (PHE) level shows at least a 20 percent decrease while on sapropterin dihydrochloride or sepiapterin (baseline and most recent phenylalanine levels to be submitted with the renewal request)

Adherence

- Adherence with sapropterin dihydrochloride or sepiapterin therapy is documented
- Adherence with the phenylalanine (PHE) restricted diet is documented

Brand Specific Criteria

- **For Kuvan, Javygtor, Zelvysia**: Failure, contraindication according to the United States Food and Drug Administration (FDA) labeled safety information, intolerance, or is not a candidate for **generic sapropterin dihydrochloride**. **Note**: Any failure, contraindication, or intolerance to the generic drug should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

PHARMACY COVERAGE GUIDELINE

JAVYGTOR™ (sapropterin dihydrochloride) oral
KUVAN® (sapropterin dihydrochloride) oral
PALYNZIQ™ (pegvaliase-pqpz) subcutaneous
Sapropterin Dihydrochloride oral
SEPHIENCE™ (sepiapterin) oral
ZELVYSIA™ (sapropterin dihydrochloride) oral
Generic Equivalent (if available)

- **For Sephience (sepiapterin)**: Failure after adequate trial, contraindication according to the United States Food and Drug Administration (FDA) labeled safety information, intolerance, or is not a candidate for a **generic equivalent** (if available). **Note**: Any failure, contraindication, or intolerance to the generic drug should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety

- **For Sephience (sepiapterin)**: Does not have concomitant use with **ANY** of the following:
  - Dihydrofolate reductase (DHFR) inhibitors (e.g., trimethoprim, methotrexate, trimetrexate, pemetrexed, pralatrexate)
  - Sepiapterin reductase (SR) inhibitors (e.g., sulfasalazine, sulfamethoxazole)
  - Drugs affecting nitric oxide mediated vasorelaxation (e.g., phosphodiesterase type 5 (PDE 5) inhibitors such as sildenafil, vardenafil, tadalafil)
- No concomitant drug use of Javygtor, Kuvan, sapropterin dihydrochloride generic, Sephience, or Zelvysia with Palynziq

Additional Requirements

- Phenylalanine (PHE) restricted diet was not changed in any way during the initial trial of sapropterin dihydrochloride or sepiapterin, so that responsiveness to therapy could be accurately determined
- Response to therapy is determined by change in blood PHE, treatment should be discontinued in those who do not show a biochemical response (blood PHE does not decrease) after 1 month of treatment

Documentation Requirements

- Chart notes that document:
  - Ongoing management by a metabolic or genetic disease specialist or in consultation with one
  - Stable phenylalanine (PHE) restricted diet during the initial response assessment period
- Lab results: Baseline and most recent blood phenylalanine (PHE) levels showing at least a 20 percent decrease on therapy
- Supporting clinical documentation that demonstrates: Ongoing clinical benefit and continued need for therapy

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Medical Necessity Requirements for PALYNZIQ (pegvaliase pqpz)

PHARMACY COVERAGE GUIDELINE

JAVYGTOR™ (sapropterin dihydrochloride) oral
KUVAN® (sapropterin dihydrochloride) oral
PALYNZIQ™ (pegvaliase-pqpz) subcutaneous
Sapropterin Dihydrochloride oral
SEPHIENCE™ (sepiapterin) oral
ZELVYSIA™ (sapropterin dihydrochloride) oral
Generic Equivalent (if available)

Criteria for Initial Therapy:

Prescriber Qualifications

- Prescribed by a physician specializing in metabolic or genetic diseases, or is in consultation with one

Indication

- Phenylketonuria (PKU), to be used to reduce blood phenylalanine (PHE) concentrations in those whose PHE levels remain above 600 micromol/L despite existing management

Age Requirement

- 18 years of age or older

Baseline Clinical Evaluation

- Baseline blood phenylalanine (PHE) level is greater than 600 micromol per liter (which is 10 milligrams per deciliter) on existing phenylketonuria (PKU) management
- On a phenylalanine (PHE) restricted diet

Alternative Therapies

- Failure, contraindication according to the United States Food and Drug Administration (FDA) labeled safety information, intolerance, or is not a candidate for **sapropterin dihydrochloride products**. **Note**: Failure, contraindication or intolerance to the generic should be reported to the FDA (see Definitions section):
  - Kuvan (sapropterin dihydrochloride)
  - Javygtor (sapropterin dihydrochloride)
  - Generic sapropterin dihydrochloride
  - Zelvysia (sepiapterin dihydrochloride)

Brand Specific Criteria

- **For Palynziq (pegvaliase pqpz):** Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Has a current prescription for auto injectable epinephrine
- Will be or has been instructed to carry epinephrine at all times while on Palynziq therapy
- No concomitant drug use of Palynziq (pegvaliase pqpz) with **ANY** of the following:

- Sapropterin dihydrochloride (Kuvan, Javygtor, Zelvysia, or generic sapropterin dihydrochloride)
- Sephience (sepiapterin)

Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes documenting:
    1. Diagnosis of phenylketonuria (PKU)
    2. Prior management approach for PKU, including diet and any use of sapropterin dihydrochloride
    3. Current phenylalanine (PHE) restricted diet.
  - Lab results: Baseline blood phenylalanine (PHE) level greater than 600 micromol per liter (10 milligrams per deciliter) on existing PKU management
  - Supporting clinical documentation that shows:
    1. Rationale for initiation of Palynziq (pegvaliase pqpz)
    2. Documentation of failure, contraindication, intolerance, or lack of candidacy for sapropterin dihydrochloride products and for any available generic equivalent

Initial Therapy Criteria Approval Duration

- 9 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualifications

- Continues to be seen by a physician specializing in metabolic or genetic diseases, or in consultation with one

Clinical Response

- **On maintenance dose** of Palynziq (pegvaliase pqpz) and **ONE** of the following:
  - There is at least a 20 percent decrease in blood phenylalanine (PHE) level from baseline (baseline and most recent phenylalanine levels to be submitted with the renewal request)
  - Blood phenylalanine (PHE) concentration is less than or equal to 600 micromol per liter (10 milligrams per deciliter)
- **Not yet at maximum titration** or has not yet achieved an adequate clinical response during the titration phase, and **ONE** of the following:
  - Has not been titrated to the maximum allowed dose of 60 milligrams once daily

- Has received less than 16 weeks of continuous treatment at the maximum allowed dose of 60 milligrams once daily

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- **For Palynziq (pegvaliase pqpz):** Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Has a current prescription for auto injectable epinephrine and continues to carry it as directed
- Remains on a phenylalanine (PHE) restricted diet
- No concomitant drug use of Palynziq (pegvaliase pqpz) with **ANY** of the following:
  - Sapropterin dihydrochloride (Kuvan, Javygtor, Zelvysia, or generic sapropterin dihydrochloride)
  - Sephience (sepiapterin)

Additional Requirements

- Palynziq is to be discontinued in those who have not achieved an adequate response after 16 weeks of continuous treatment with the maximum dosage of 60 mg once daily

Documentation Requirements

- Chart notes documenting:
  - Ongoing follow up with a metabolic or genetic disease specialist or in consultation with one
  - Titration history and current maintenance dosing schedule of Palynziq
- Lab results: Baseline and follow up blood phenylalanine (PHE) levels that show either a 20 percent or greater decrease from baseline, or current phenylalanine level less than or equal to 600 micromol per liter (10 milligrams per deciliter), or documentation explaining that maximum titration has not yet been completed as described above
- Supporting clinical documentation showing: Evidence of clinical benefit, ongoing need for therapy, and adherence to Palynziq and to the phenylalanine (PHE) restricted diet

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

PHARMACY COVERAGE GUIDELINE

JAVYGTOR™ (sapropterin dihydrochloride) oral
KUVAN® (sapropterin dihydrochloride) oral
PALYNZIQ™ (pegvaliase-pqpz) subcutaneous
Sapropterin Dihydrochloride oral
SEPHIENCE™ (sepiapterin) oral
ZELVYSIA™ (sapropterin dihydrochloride) oral
Generic Equivalent (if available)

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications
2. Off-Label Use of Cancer Medications

Description:

Sapropterin dihydrochloride (brand Kuvan, brand Javygtor, or generic) is an orally administered phenylalanine hydroxylase (PAH) activator approved to reduce blood phenylalanine (PHE) levels in patients one month of age or older with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive phenylketonuria (PKU). Left untreated the condition can lead to profound neurocognitive and developmental defects. Neurologic damage can include severe mental retardation, microcephaly, delayed speech, seizures, and behavioral abnormalities. Conversely, prolonged low levels of blood PHE have been associated with catabolism and protein breakdown. Sapropterin is to be used with a PHE-restricted diet.

Sephience (sepiapterin) is a PAH activator indicated for the treatment of HPA in adult and pediatric patients one month of age or older with sepiapterin-responsive PKU. Sephience (sepiapterin) is a precursor of the enzymatic co-factor BH4 which activates PAH. Sepiapterin is rapidly converted to BH4. Sephience (sepiapterin) is to be used in conjunction with a PHE-restricted diet.

Palynziq (pegvaliase-pqpz) injection, for subcutaneous use is indicated to reduce blood PHE concentrations in adult patients with PKU who have uncontrolled blood PHE concentrations greater than 600 micromol/L on existing management. Palynziq should be discontinued in patients who have not achieved an adequate response after 16 weeks of continuous treatment with the maximum dosage of 60 mg once daily.

Because of the risk of anaphylaxis, Palynziq is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Palynziq REMS. All patients prescribed Palynziq must have a prescription for auto-injectable epinephrine. Patients should be instructed to carry the auto-injectable epinephrine with them at all times.

The underlying defect in PKU is a deficiency or a decrease in activity of the hepatic enzyme PAH. PAH deficiency is an autosomal-recessive disorder. The gene is located on chromosome 12. More than 500 different mutations in the PAH gene have been described.

Sapropterin dihydrochloride is a biologically active synthetic form of naturally occurring BH4. It reduces blood PHE levels in patients with HPA by improving the normal metabolism of PHE. BH4 is a cofactor for the enzyme

PHARMACY COVERAGE GUIDELINE

JAVYGTOR™ (sapropterin dihydrochloride) oral
KUVAN® (sapropterin dihydrochloride) oral
PALYNZIQ™ (pegvaliase-pqpz) subcutaneous
Sapropterin Dihydrochloride oral
SEPHIENCE™ (sepiapterin) oral
ZELVYSIA™ (sapropterin dihydrochloride) oral
Generic Equivalent (if available)

PAH that hydroxylates PHE through an oxidative reaction to form tyrosine (TYR). PAH activity is absent or deficient among patients with PKU. While these individuals are not deficient in endogenous BH4, some patients with PAH deficiency, who have some residual enzyme activity respond to administration of sapropterin dihydrochloride with an increase in the metabolism of PHE to TYR.

Sepiapterin is metabolized by SR/carbonyl reductase (CR) and DHFR in a 2-step unidirectional process to form pharmacologically active metabolite BH4. BH4 is further metabolized non-enzymatically or enzymatically mediated by aromatic amino acid hydroxylases, such as PAH, tyrosine hydroxylase (TH), tryptophan hydroxylase (TPH), pterin-4a-carbinolamine dehydratase (PCD), dihydropteridine reductase (DHPR), xanthine oxidase (XO), and nitric oxide synthase (NOS) in various tissues.

The mechanism by which residual PAH activity is enhanced is unclear, but BH4 may act as a pharmacologic chaperone leading to improved folding and increased stability of the mutant protein. In clinical trials, approximately 20–75% of the patients with PAH deficiency are BH4-responsive. Patients whose blood PHE does not decrease after 1 month of treatment with sapropterin at 20 mg/kg per day are considered non-responders and treatment with sapropterin dihydrochloride should be discontinued in these patients. Current literature cites a 30% reduction in PHE levels as evidence for responsiveness to sapropterin dihydrochloride.

Sapropterin dihydrochloride and sepiapterin must be used in conjunction with a PHE restricted diet. Active management of dietary PHE intake is the mainstay of therapy and requires restriction of dietary PHE intake necessitating a decrease in the intake of natural protein and replacing it with a protein (amino acid mixture) source devoid of PHE. A provider experienced in metabolic disorders and a nutritionist team-based approach should manage this therapy. Dietary manipulation will be required to maintain appropriate blood PHE levels with frequent dietary modification to respond to growth, life stages, concurrent illness, and comorbidities.

Pegvaliase-pqpz is a PHE-metabolizing enzyme composed of recombinant phenylalanine ammonia lyase (rAvPAL) conjugated to N-hydroxysuccinimide (NHS)-methoxypolyethylene glycol (PEG). Pegvaliase-pqpz converts PHE to ammonia and trans-cinnamic acid. Trans-cinnamic acid and its final product, benzoic acid, are conjugated with glycine and excreted in the urine. Pegvaliase-pqpz substitutes for the deficient PAH enzyme activity in patients with PKU and reduces blood PHE concentrations. The metabolism of phenylalanine ammonia lyase is expected to occur via catabolic pathways and be degraded into small peptides and amino acids.

The American College of Medical Genetics and Genomics 2014 practice guideline suggests blood PHE levels should be maintained in the range of 120–360 µmol/L for all patients, although there is no evidence to suggest normalization of PHE levels is required and lower levels of 60-120 µmol/L should not be viewed as too low. It should be noted that measurement of PHE levels in blood varies and is dependent on the analytical method used, requiring consistency in testing methodology in order to interpret the resultant values.

Definitions:

PHARMACY COVERAGE GUIDELINE

JAVYGTOR™ (sapropterin dihydrochloride) oral
KUVAN® (sapropterin dihydrochloride) oral
PALYNZIQ™ (pegvaliase-pqpz) subcutaneous
Sapropterin Dihydrochloride oral
SEPHIENCE™ (sepiapterin) oral
ZELVYSIA™ (sapropterin dihydrochloride) oral
Generic Equivalent (if available)

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Palynziq dosing:

Treatment phase	Palynziq 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
	40 mg once daily	16 week
Maximum¶	60 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 40 mg once daily in patients who have not achieved a response with 20 mg once daily continuous treatment for at least 24 weeks. Consider increasing to a maximum of 60 mg once daily in patients who have not achieved a response with 40 mg once daily continuous treatment for at least 16 weeks.
¶ Discontinue Palynziq in patients who have not achieved an adequate response after 16 weeks of continuous treatment at the maximum dosage of 60 mg once daily.

Resources:

Kuvan (sapropterin) tab & oral powder product information, revised by BioMarin Pharmaceutical, Inc. 08-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 24, 2025.

Javygtor (sapropterin) tab & oral powder product information, revised by Dr. Reddys Laboratories, Inc. 10-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 24, 2025.

Sephience (sepiapterin) oral powder product information, revised by Allphamed Pharbil Arzneimittel GmbH. 09-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 24, 2025.

Sapropterin tab product information, revised by Camber Pharmaceuticals, Inc. Inc. 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 24, 2025.

Palynziq (pegvaliase-pqpz) subcutaneous injection product information, revised by BioMarin Pharmaceutical, Inc. 10-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 24, 2025.

Zelvysia (sapropterin dihydrochloride) oral powder product information, revised by Aucta Pharmaceuticals, Inc. 04-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 24, 2025.

Bodamer OA. Overview of phenylketonuria. In: UpToDate, Sutton VR, Kremen J (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through December 2025. Topic last updated August 20, 2025. Accessed January 31, 2026.

Longo N, Dimmock D, Levy H, et al.: Evidence- and consensus-based recommendations for the use of pegvaliase in adults with phenylketonuria. Genetics in Medicine 2019 Aug; 21 (8):1851-1867. Accessed on November 10, 2022. Re-evaluated January 06, 2025.

Vockley J, Andersson HC, Antshel KM, et al.: Phenylalanine hydroxylase deficiency: diagnosis and management guideline. Genetics in Medicine 2014 Feb; 16 (2): 188-200. doi:10.1038/gim.2013.157. Accessed November 01,2018. Re-evaluated January 06, 2025.

Van Wegberg AMJ, MacDonald A, Ahring K, et al.: The complete European guidelines on phenylketonuria: diagnosis and treatment. Orphanet J Rare Diseases 2017;12:162. DOI 10.1186/s13023-017-0685-2. Accessed January 28, 2021. Re-evaluated January 06, 2025.

Regier DS, Greene CL. Phenylalanine hydrolase deficiency. 2000 Jan 10 [Updated 2017 Jan 5]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available at: https://www.ncbi.nlm.nih.gov/books/. Accessed January 25, 2023. Re-evaluated January 06, 2025.

Bratkovic D, Margvelashvili L, Tchan MC, et al.: PTC923 (sepiapterin) lowers elevated blood phenylalanine in subjects with phenylketonuria: a phase 2 randomized, multi-center, three-period crossover, open-label, active controlled, all-comers study. Metab Clin Exper 2022; 128 available at https://doi.org/10.1016/j.metabol.2021.155116. Accessed August 09, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT05099640: A Phase 3 Study of PTC923 in Subjects With Phenylketonuria. Available from: http://clinicaltrials.gov. Last update posted January 10, 2024. Last verified December 2023. Accessed August 09, 2025. Re-evaluated January 30, 2026.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT06302348: A Phase 3b Open-Label Study of Long-Term Neurocognitive Outcomes in Children With Phenylketonuria Treated With Sepiapterin. Available from: http://clinicaltrials.gov. Last update posted July 17, 2025. Last verified July 2025. Accessed August 09, 2025. Re-evaluated January 30, 2026.