



Phenylketonuria Prior Authorization Program Summary

POLICY REVIEW CYCLE

Effective Date
12-15-2025

Date of Origin

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Palynziq	pegvaliase-pqpz subcutaneous soln pref syringe	10 MG/0.5ML ; 2.5 MG/0.5ML ; 20 MG/ML	M ; N ; O ; Y	N		
Kuvan	sapropterin dihydrochloride powder packet ; sapropterin dihydrochloride tab	100 MG ; 500 MG	M ; N ; O ; Y	O ; Y		
Sephience	sepiapterin powder packet	1000 MG ; 250 MG	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Kuvan	sapropterin dihydrochloride powder packet ; sapropterin dihydrochloride tab	100 MG ; 500 MG	Balanced ; Balanced Biosimilar ; Basic ; Basic Annual ; Enhanced ; Enhanced Annual ; HIM Annual 2024 ; HIM Quarterly 2024 ; HIM Quarterly 2025 ; HIM Quarterly 2026 ; IL HIM Annual 2025 ; IL HIM Annual 2026 ; IL HMO Performance Quarterly ; IL non-HMO Performance Full ; Jade ; MT Performance Full ; NM HIM Annual 2024 ; NM HIM Annual 2025 ; NM HIM Annual 2026 ; NM Performance Full ; OK Performance Full ; Performance ; Performance Annual ; Performance Biosimilar ; Performance Select ; Performance Select Biosimilar ; TX HIM Annual 2025 ; TX HIM Annual 2026 ; Topaz ; Whole Foods
Palynziq	pegvaliase-pqpz subcutaneous soln pref syringe	10 MG/0.5ML ; 2.5 MG/0.5ML ; 20 MG/ML	Balanced ; Balanced Biosimilar ; Basic ; Basic Annual ; Enhanced ; Enhanced Annual ; HIM Annual 2024 ; HIM Quarterly 2024 ; HIM Quarterly 2025 ; HIM Quarterly 2026 ; IL HIM Annual 2025 ; IL HIM Annual 2026 ; IL HMO Performance Quarterly ; IL non-HMO Performance Full ; Jade ; MT Performance Full ; NM HIM Annual 2024

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			; NM HIM Annual 2025 ; NM HIM Annual 2026 ; NM Performance Full ; OK Performance Full ; Performance ; Performance Annual ; Performance Biosimilar ; Performance Select ; Performance Select Biosimilar ; TX HIM Annual 2025 ; TX HIM Annual 2026 ; Topaz ; Whole Foods
Sephience	sepiapterin powder packet	1000 MG ; 250 MG	Balanced ; Balanced Biosimilar ; Basic ; Basic Annual ; Enhanced ; Enhanced Annual ; HIM Annual 2024 ; HIM Quarterly 2024 ; HIM Quarterly 2025 ; HIM Quarterly 2026 ; IL HIM Annual 2025 ; IL HIM Annual 2026 ; IL HMO Performance Quarterly ; IL non-HMO Performance Full ; Jade ; MT Performance Full ; NM HIM Annual 2024 ; NM HIM Annual 2025 ; NM HIM Annual 2026 ; NM Performance Full ; OK Performance Full ; Performance ; Performance Annual ; Performance Biosimilar ; Performance Select ; Performance Select Biosimilar ; TX HIM Annual 2025 ; TX HIM Annual 2026 ; Topaz ; Whole Foods

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	<p>Initial Evaluation</p> <p>Target Agent(s) will be approved when ALL of the following are met:</p> <ol style="list-style-type: none"> 1. The patient has a diagnosis of phenylketonuria (PKU) AND 2. If the patient has an FDA labeled indication, then ONE of the following: <ol style="list-style-type: none"> A. The patient's age is within FDA labeling for the requested indication for the requested agent OR B. There is support for using the requested agent for the patient's age for the requested indication AND 3. ONE of the following: <ol style="list-style-type: none"> A. BOTH of the following: <ol style="list-style-type: none"> 1. Phenylalanine levels cannot be maintained within the recommended maintenance range with dietary intervention (phenylalanine-restriction) despite strict compliance AND 2. The Phe-restricted diet will continue while being treated with the requested agent OR B. If the requested agent is Palynziq, the patient's current phenylalanine level is less than 360 micromol/L AND 4. ONE of the following: <ol style="list-style-type: none"> A. If the requested agent is Kuvan, sapropterin, or Sephience, the patient has a baseline (prior to therapy for the requested indication) blood Phe level greater than 360 micromol/L OR B. If the requested agent is Palynziq, the patient has a baseline (prior to therapy for the requested indication) blood Phe level greater than 600 micromol/L AND

Module	Clinical Criteria for Approval
	<p>5. If the request is for a brand agent, then ONE of the following:</p> <ul style="list-style-type: none"> A. The request is for a BCBS IL Fully Insured, ASO Cost/BBF, HIM, or Non-ERISA ASO/Self-insured Municipalities/Counties member OR B. The patient is currently being treated with the requested agent and the patient is currently stable on the requested agent [chart notes are required] OR C. The patient has tried and had an inadequate response to generic sapropterin despite monitored adherence to treatment [chart notes are required] OR D. The patient has an intolerance or hypersensitivity to generic sapropterin that is NOT expected to occur with the requested brand agent [chart notes are required] OR E. The patient has an FDA labeled contraindication to generic sapropterin that is NOT expected to occur with the requested brand agent [chart notes are required] OR F. Generic sapropterin was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event [chart notes are required] OR G. Generic sapropterin is expected to be ineffective based on the known clinical characteristics of the patient and the known characteristics of the prescription drug; OR cause a significant barrier to the patient’s adherence of care; OR worsen a comorbid condition; OR decrease the patient’s ability to achieve or maintain reasonable functional ability in performing daily activities; OR cause an adverse reaction or cause physical or mental harm [chart notes are required] OR H. Generic sapropterin is not in the best interest of the patient based on medical necessity [chart notes are required] OR I. The patient has tried another prescription drug in the same pharmacologic class or with the same mechanism of action as generic sapropterin and that prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event [chart notes are required] OR J. There is support for use of the requested brand agent over generic sapropterin (e.g., presence of two null mutations) AND <p>6. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., metabolic disorders) or the prescriber has consulted with a specialist in the area of the patient’s diagnosis AND</p> <p>7. The patient will NOT be using the requested agent in combination with another phenylketonuria agent (e.g., Kuvan, Palynziq, sapropterin, Sephience) for the requested indication AND</p> <p>8. The patient does NOT have any FDA labeled contraindications to the requested agent AND</p> <p>9. The requested quantity (dose) is within FDA labeled dosing for the requested indication</p> <p>Length of Approval:</p> <p>BCBSOK: 36 months BCBSIL and BCBSMT: approve for 12 months; BCBSNM: Kuvan: approve for 3 months, Palynziq: approve for 9 months, Sephience: approve for 3 months</p> <p><u>For all other plans:</u></p> <p>Kuvan (sapropterin): Approve for 2 months if initial dose is 5 mg/kg/day to less than 20 mg/kg/day, and for 1 month if initial dose is 20 mg/kg/day</p> <p>Palynziq (pegvaliase-pqpz): 9 months</p> <p>Sephience (sepiapterin): Approve for 2 months if initial dose is 7.5 mg/kg/day to less than 60 mg/kg/day, and for 1 month if initial dose is 60 mg/kg/day</p> <p>The requested agent will also be approved when ONE of the following is met:</p>

Module	Clinical Criteria for Approval
	<p>1. The request is for a BCBS MT Fully Insured or MT HIM member AND</p> <ul style="list-style-type: none"> A. The patient is under the age of 18 years old AND B. The patient does NOT have any FDA labeled contraindications to the requested agent AND C. The patient has an indication that is supported in TWO articles from major peer-reviewed professional medical journals [e.g., Journal of American Medical Association (JAMA), New England Journal of Medicine (NEJM), Lancet] as generally safe and effective. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. NOTE: Case studies are not acceptable [journal articles required] AND D. There is support for an age in the patient's given age bracket in TWO articles from major peer-reviewed professional medical journals as generally safe and effective. The age brackets are: 1. infancy (birth up to, but not including, 2 years of age), 2. childhood (2 years of age through 11 years of age), 3. adolescence (12 years of age through 17 years of age). Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. NOTE: Case studies are not acceptable [journal articles required] OR <p>2. The request is for a BCBS NM Fully Insured or NM HIM member and ALL of the following:</p> <ul style="list-style-type: none"> A. The patient does NOT have any FDA labeled contraindications to the requested agent AND B. The requested indication is a rare disease AND C. ONE of the following: <ul style="list-style-type: none"> 1. The patient has another FDA labeled indication for the requested agent and route of administration OR 2. The patient has another indication that is supported in compendia for the requested agent and route of administration OR <p>3. ALL of the following:</p> <ul style="list-style-type: none"> A. The member resides in Ohio AND B. The plan is Fully Insured or HIM Shop (SG) AND C. The patient does NOT have any FDA labeled contraindications to the requested agent AND D. ONE of the following: <ul style="list-style-type: none"> 1. The patient has another FDA labeled indication for the requested agent and route of administration OR 2. The patient has another indication that is supported in compendia for the requested agent and route of administration OR 3. The prescriber has submitted TWO articles from major peer-reviewed professional medical journals [e.g., Journal of American Medical Association (JAMA), New England Journal of Medicine (NEJM), Lancet] supporting the proposed use(s) as generally safe and effective. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. NOTE: Case studies are not acceptable [journal articles required] <p>Non-oncology compendia allowed: DrugDex level 1, 2A or 2B, AHFS-DI (narrative text must be supportive)</p> <p>Oncology compendia allowed: NCCN 1 or 2A, AHFS-DI (narrative text must be supportive), DrugDex level 1, 2A, or 2B, or Clinical Pharmacology (narrative text must be supportive), Lexi-Drugs evidence level A, peer-reviewed medical literature</p> <p>Length of Approval:</p> <p>BCBSOK: 36 months All other plans: 12 months</p> <p>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria</p>

Module	Clinical Criteria for Approval
	<p>Renewal Evaluation</p> <p>Target Agent(s) will be approved when ALL of the following are met:</p> <ol style="list-style-type: none"> 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process (Note: patients not previously approved for the requested agent will require initial evaluation review) AND 2. The patient has had clinical benefit with the requested agent AND 3. ONE of the following: <ol style="list-style-type: none"> A. The patient is currently on a phenylalanine (Phe) restricted diet and will continue while being treated with the requested agent OR B. If the requested agent is Palynziq, the patient's phenylalanine level is less than 360 micromol/L AND 4. If the request is for a brand agent, then ONE of the following: <ol style="list-style-type: none"> A. The request is for a BCBS IL Fully Insured, ASO Cost/BBF, HIM, or Non-ERISA ASO/Self-insured Municipalities/Counties member OR B. The patient is currently being treated with the requested agent and the patient is currently stable on the requested agent [chart notes are required] OR C. The patient has tried and had an inadequate response to generic sapropterin agent [chart notes are required] OR D. The patient has an intolerance or hypersensitivity to generic sapropterin that is NOT expected to occur with the requested brand agent [chart notes are required] OR E. The patient has an FDA labeled contraindication to generic sapropterin that is NOT expected to occur with the requested brand agent [chart notes are required] OR F. Generic sapropterin was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event [chart notes are required] OR G. Generic sapropterin is expected to be ineffective based on the known clinical characteristics of the patient and the known characteristics of the prescription drug; OR cause a significant barrier to the patient's adherence of care; OR worsen a comorbid condition; OR decrease the patient's ability to achieve or maintain reasonable functional ability in performing daily activities; OR cause an adverse reaction or cause physical or mental harm [chart notes are required] OR H. Generic sapropterin is not in the best interest of the patient based on medical necessity [chart notes are required] OR I. The patient has tried another prescription drug in the same pharmacologic class or with the same mechanism of action generic sapropterin and that prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event [chart notes are required] OR J. There is support for use of the requested brand agent over generic sapropterin (e.g., presence of two null mutations) AND 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., metabolic disorders), or the prescriber has consulted with a specialist in the area of the patient's diagnosis AND 6. The patient will NOT be using the requested agent in combination with another phenylketonuria agent (e.g., Kuvan, Palynziq, sapropterin, Saphience) for the requested indication AND 7. The patient does NOT have any FDA labeled contraindications to the requested agent AND 8. The requested quantity (dose) is within FDA labeled dosing for the requested indication <p>Length of Approval:</p> <p>BCBSOK: 36 months All other plans: 12 months</p>

