LOUISIANA BLUE

palovarotene (Sohonos™)

Policy # 00867
Original Effective Date: 03/11/2024
Current Effective Date: 03/10/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider palovarotene (Sohonos™)‡ for the treatment of fibrodysplasia ossificans progressiva (FOP) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for palovarotene (Sohonos) will be considered when the following criteria are met:

- Initial
  - Patient has a diagnosis of fibrodysplasia ossificans progressiva (FOP); AND
  - Documentation is provided that the patient has the *ACVR1 R206H* genetic mutation; AND
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Patient meets ONE of the following criteria:
    - Patient is female and age 8 years or older; OR
    - Patient is male and age 10 years or older; AND
  - If the patient is a female of reproductive potential, provider attests that the patient is NOT currently pregnant and is willing to use effective contraception
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Continuation
  - Patient has received an initial authorization for Sohonos; AND
  - There is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to reduction in volume of heterotopic ossification, reduction in number of flare-ups) compared to the predicted natural history trajectory of disease.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of palovarotene (Sohonos) when any of the following criteria are not met to be **not medically necessary.****

- For initial requests: Documentation is provided that the patient has the *ACVR1 R206H* genetic mutation
- For continuation requests: Patient has clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to reduction in volume of heterotopic ossification, reduction in number of flare-ups) compared to the predicted natural history trajectory of disease.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of palovarotene (Sohonos) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Sohonos is an oral retinoid indicated for the reduction in volume of new heterotopic ossification in adults and children aged 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva (FOP). Sohonos is the first FDA-approved therapy for FOP. The recommended dosing for Sohonos includes a chronic daily dosage which can then be modified/increased in the event of FOP flare-up symptoms (flare-up dose). For adults and pediatric patients 14 years and older, the daily dose is 5 mg daily. Daily dosing is stopped when flare-up dosing begins. Flare-up dosing is done over a total of 12 weeks: 20 mg daily for 4 weeks, followed by 10 mg daily for 8 weeks, even if symptoms resolve earlier, then return to daily dosing of 5 mg. For pediatric patients aged 8 to 13 years for females and aged 10 to 13 years for males, the daily dose is weight-based ranging from 2.5 mg to 5 mg daily. Flare-up dosing is also weight based. Refer to the package insert for the pediatric dosing flare-up regimen.

Sohonos can cause premature epiphyseal closure which can prevent children from growing to their full height or cause uneven growth. The prescribing information for Sohonos recommends conducting baseline and ongoing assessments in growing children and only using the drug in females 8 years of age and older and males 10 years of age and older, who will have reached approximately 80% of their adult height at that point. Sohonos is also contraindicated in pregnancy. Sohonos was found to be teratogenic in animal reproduction studies, resulting in fetal malformations. Prescribers should verify that females of reproductive potential are not pregnant prior to treatment initiation.

Effective contraception should also be used. Sohonos should be discontinued immediately if pregnancy occurs.

Fibrodysplasia Ossificans Progressiva
Fibrodysplasia ossificans progressiva is an ultra-rare genetic disorder of the connective tissue characterized by abnormal bone growth in areas outside of the skeleton, such as the ligaments, tendons, and muscles. The condition progresses with episodes of painful inflammatory swelling in soft tissues (flare-ups). Most flare-ups lead to rapid heterotopic ossification, transforming soft connective tissues into mature heterotopic bone. Eventually, heterotopic bone permanently replaces muscles and connective tissue, encasing the patient almost like an armor, resulting in disability, immobility, and reduced quality/length of life. The prevalence of fibrodysplasia ossificans progressiva in the United States is estimated to be 0.88 cases per million individuals (around 280 US patients). Most patients (97%), have the same, heterozygous mutation in the glycine-serine activation domain of the Activin A receptor type I gene (*ACVR1 R206H*).

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Sohonos is approved for the reduction in the volume of new heterotopic ossification in adults and children aged 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Sohonos was evaluated in one Phase III, single-arm, placebo-controlled, multicenter, pivotal study in patients ≥ 4 years of age with fibrodysplasia ossificans progressiva (MOVE). Only patients with the *ACVR1 R206H* pathogenic variant were included in the efficacy analysis. All patients in the pivotal study received Sohonos daily dosing with temporary dose increases for flare-ups (according to the FDA-approved dosing based on age/weight). The primary efficacy endpoint was the annualized change in the new heterotopic ossification volume from baseline to Month 18 as assessed by low-dose, whole body CT (WBCT) imaging (excluding head). Data from MOVE were compared with data from patients in a fibrodysplasia ossificans progressiva Natural History Study (NHS) [n = 101] who were untreated beyond standard of care.

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At Month 18, using a weighted linear mixed-effects (wLME) post-hoc analysis of non-square-root transformed data, the least squares mean annualized new heterotopic ossification volume was 9.4 cm^3/year with Sohonos vs. 20.3 cm^3/year among untreated patients in the NHS (treatment difference -10.9 cm^3/year [95% confidence interval {CI}: -21.2, -0.6]; 54% reduction; P = 0.0392).

In total, 39 patients transferred from NHS to MOVE and contributed data to both studies. When these patients were analyzed separately (i.e., served as their own controls), a 54.2% reduction in annualized new heterotopic ossification volume was observed with the patients' MOVE data vs. their NHS data when post-hoc statistical analyses were conducted.

References

1. Sohonos [package insert]. Ipsen Biopharmaceuticals, Inc. Cambridge, Massachusetts. August 2023.
2. Sohonos Drug Evaluation. Express Scripts. Updated August 2023.

Policy History

Original Effective Date: 03/11/2024
Current Effective Date: 03/10/2025
02/01/2024 Medical Policy Committee review
02/14/2024 Medical Policy Implementation Committee approval. New policy.
02/06/2025 Medical Policy Committee review
02/12/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 02/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.
‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.