Effective Date **12/15/2024**
Coverage Policy Number **IP0596**

Palovarotene

Table of Contents

Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for palovarotene capsules (**Sohonos**™).

Medical Necessity Criteria

Palovarotene (Sohonos) is considered medically necessary when the following are met:

Fibrodysplasia ossificans progressiva. Individual meets **ALL** of the following criteria:

A. **ONE** of the following:
   i. Individual is female and age 8 years or older
   ii. Individual is male and age 10 years or older
B. Genetic test confirming an R206H pathogenic variant in *ACVR1* (*ALK2*) consistent with a diagnosis of fibrodysplasia ossificans progressive
C. Heterotopic ossification as confirmed by radiologic testing (for example, x-ray, computed tomography [CT], magnetic resonance imaging [MRI], or positron emission tomography [PET] scan)

D. Medication is prescribed by, or in consultation with, an endocrinologist or physician who specializes in bone disease

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Continuation of palovarotene (Sohonos) is considered medically necessary for Fibrodysplasia Ossificans Progressiva when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Chronic Obstructive Pulmonary Disease (COPD).** Sohonos is not indicated for the management of COPD.[1] Palovarotene was previously studied for the treatment of COPD, but was found to be ineffective for this condition.[4]

2. **Osteochondroma(s).** Sohonos is not indicated for the treatment and/or prevention of osteochondroma.[1] One Phase II study was initiated to evaluate Sohonos for the prevention of disease progression in pediatric patients with multiple osteochondromas.[6] However, this study was terminated early in order to analyze accumulated data and evaluate the future of Sohonos for this use. Results are not available. More data are needed.

Background

OVERVIEW
Sohonos, a retinoid, is indicated for the reduction in volume of new heterotopic ossification in females ≥ 8 years of age and males ≥ 10 years of age with **fibrodysplasia ossificans progressiva**.[1]

Disease Overview
Fibrodysplasia ossificans progressiva is an ultra-rare, autosomal dominant genetic disorder of connective tissue characterized by progressive heterotopic ossification resulting in disability, immobility, and reduced quality/length of life.[2] Patients experience episodes of painful inflammatory swelling in soft tissues (flare-ups), some of which will spontaneously resolve, but most will transform soft connective tissues into mature heterotopic bone. Eventually, plates, sheets, and ribbons of heterotopic bone permanently replace muscles and connective tissue, encasing the patient almost like an armor, resulting in progressive and permanent immobility. There are no formal diagnostic criteria for fibrodysplasia ossificans progressiva.[2,3] A clinical diagnosis can be made in patients with great toe malformations, tissue swelling, and heterotopic ossification, but genetic confirmation of an Activin A Type 1 Receptor (ACVR1) gene mutation is needed. All patients with fibrodysplasia ossificans progressiva have a mutation in ACVR1, a gene encoding a bone morphogenetic protein type I receptor kinase.[2,4] Approximately 97%

of these patients have the same, heterozygous, single-nucleotide change in the glycine-serine activation domain of the ACVR1 (ACVR1^{R206H}).

Clinical Efficacy
In the pivotal study of Sohonos, patients were required to have fibrodysplasia ossificans progressiva as confirmed by a pathogenic variant in ACVR1^{R206H}.[1,5]

Guidelines
Medical management guidelines from the International Clinical Council on Fibrodysplasia Ossificans Progressiva (2024) recommend that each patient with the disease should have a primary provider who is able to consult with an fibrodysplasia ossificans progressiva expert and help coordinate a local care team.[2] The diagnosis of fibrodysplasia ossificans progressiva is based on clinical findings, but requires genetic confirmation (i.e., ACVR1 gene mutation), which can be detected by DNA sequence analysis.

References

1. Sohonos® capsules [prescribing information]. Cambridge, MA: Ipsen; August 2023.
2. Kaplan FS, Al Mukaddam M, Baujat G, et al, for the Internation council on FOP (ICC) & Consultants. The medical management of fibrodysplasia ossificans progressive: current treatment considerations. Updated July 2024. Available at: https://www.iccfop.org/dvlp/wp-content/uploads/2022/05/guidelines-updated-May-2022.pdf. Accessed on October 3, 2024.
3. Akesson LS, Svarirayan R, Adam MP, et al., editors. Fibrodysplasia ossificans progressiva. Gene Reviews® [Internet]. Seattle, WA: University of Washington, Seattle. Last revised May 23, 2024. Available at: https://www.ncbi.nlm.nih.gov/books/NBK558090/?report=printable. Accessed on October 3, 2024.
4. Pignolo RJ, Baujat G, Brown MA, et al. The natural history of fibrodysplasia ossificans progressive: a prospective, global 36-month study. *Genet Med*. 2022;24(12):2422-2433.
5. Pignolo RJ, Hsiao EC, Mukaddam MA, et al. Reduction of new heterotopic ossification (HO) in the open-label, phase 3, MOVE trial of palovarotene for fibrodysplasia ossificans progressive (FOP). *J Bone Miner Res*. 2023;38(3):381-394.
6. US National Institutes of Health. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2024 Sep 3]. Available from: https://clinicaltrials.gov/. Search term: palovarotene.
7. Food and Drug Administration (FDA). Palovarotene: NDA 215559. FDA briefing document for the Endocrinologic and Metabolic Drugs Advisory Committee. Meeting Date: June 28, 2023. Available at: https://www.fda.gov/media/169787/download. Accessed on October 3, 2024.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	No criteria changes	12/15/2024

The policy effective date is in force until updated or retired.