PRIOR AUTHORIZATION POLICY

POLICY: Sohonos Prior Authorization Policy
- Sohonos® (palovarotene capsules – Ipsen)

REVIEW DATE: 10/09/2024

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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Sohonos. All approvals are provided for the duration noted below. In the clinical criteria, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: males are defined as individuals with the biological traits of a male, regardless of the individual's gender identity or gender expression; females are defined as individuals with the biological traits of a female, regardless of the individual's gender identity or gender expression. Because of the specialized skills required for evaluation and diagnosis of patients treated with Sohonos as well as the monitoring required for adverse events and long-term efficacy, approval requires Sohonos to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Sohonos is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Fibrodysplasia ossificans progressiva.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient meets ONE of the following (i or ii):
     - **i.** Patient is female* and ≥ 8 years of age; OR
     - **ii.** Patient is male* and ≥ 10 years of age; AND
   - **B)** Patient has had a genetic test confirming a mutation in Activin A Type 1 Receptor $(ACVR1)^{R206H}$ consistent with a diagnosis of fibrodysplasia ossificans progressiva; AND
   - **C)** Patient has heterotopic ossification as confirmed by radiologic testing; AND
     Note: Examples of radiologic testing are x-ray, computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET) scan.
   - **D)** The medication is prescribed by or in consultation with an endocrinologist or physician who specializes in bone disease.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Sohonos is not recommended in the following situations:

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.[7]

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.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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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 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.