Clinical Policy: Palovarotene (Sohonos)

Reference Number: CP.PHAR.548
Effective Date: 08.16.23
Last Review Date: 8.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Palovarotene is a retinoic acid receptor (RAR)-γ agonist.

FDA Approved Indication(s)

Palovarotene (Sohonos™) is indicated for 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 (FOP).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Sohonos is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Fibrodysplasia Ossificans Progressiva (must meet all)**:**

1. Diagnosis of FOP;
2. Prescribed by or in consultation with a pediatric or adult orthopedics, orthopedic surgery, rheumatology, endocrinology, or metabolic disease specialist;
3. Age meets one of the following (a or b):
   a. For females: ≥ 8 years;
   b. For males: ≥ 10 years;
4. Presence of R206H *ACVR1* mutation;
5. Documentation of baseline heterotopic ossification (HO) volume assessed by low-dose whole body computed tomography (WBCT) scan, excluding the head;
6. Failure of both of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated (a and b):
   a. Prednisone used for flare-ups;
   b. Two nonsteroidal anti-inflammatory drugs (NSAIDs) between flare-ups;
7. Request meets both of the following (a and b):
   a. Dose does not exceed either of the following (i and ii):
      i. For chronic treatment, both of the following (1 and 2):
         1) 5 mg per day;
         2) 1 capsule per day;

ii. For flare-up treatment, both of the following (1 and 2):
1) 20 mg per day for 4 weeks followed by 10 mg per day for 8 weeks;
2) 2 capsules per day for 4 weeks followed by 1 capsule per day for 8 weeks;

b. Chronic treatment and flare-up treatment are not used concurrently.

Approval duration:
Chronic treatment – 6 months
Flare-up treatment – 3 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Fibrodysplasia Ossificans Progressiva (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. One of the following (a or b):
   a. Member is responding positively to therapy as evidenced by one of the following (i, ii, or iii):
      i. Reduction in flare-ups from baseline;
      ii. Improvement in annualized new HO volume as assessed by low-dose WBCT scan;
      iii. Increased or stabilized mobility;
   b. Member has not received ≥ 18 months of Sohonos treatment;
3. Request meets both of the following (a and b):
   a. If request is for a dose increase, new dose does not exceed either of the following (i and ii):

i. For chronic treatment, both of the following (1 and 2):
   1) 5 mg per day;
   2) 1 capsule per day;
ii. For flare-up treatment, both of the following (1 and 2):
   1) 20 mg per day for 4 weeks followed by 10 mg per day for 8 weeks;
   2) 2 capsules per day for 4 weeks followed by 1 capsule per day for 8 weeks;

b. Chronic treatment and flare-up treatment are not used concurrently.

Approval duration:
Chronic treatment – 12 months
Flare-up treatment – 3 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
FOP: fibrodysplasia ossificans progressiva
HO: heterotopic ossification
NSAID: nonsteroidal anti-inflammatory drug
RAR: retinoic acid receptor
WBCT: whole body computed tomography

Appendix B: Therapeutic Alternatives

Drug Name*	Dosing Regimen*	Dose Limit/ Maximum Dose
prednisone	2 mg/kg/day PO	100 mg*

Drug Name*	Dosing Regimen*	Dose Limit/ Maximum Dose
NSAIDs		
ibuprofen	Pediatrics: 4-10 mg/kg PO Q6H Adults: 200-800 mg PO Q6H	Refer to dosing regimen
indomethacin	Pediatrics: 2-4 mg/kg/day PO or 150-200 mg/day (whichever is less), divided TID Adults: 50 mg PO TID	Refer to dosing regimen
celecoxib	Pediatrics and adults: 100-200 mg PO BID	600 mg/day*

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Medications and doses recommended per the 2022 The International Clinical Council on FOP Medical Management guidelines*

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): pregnancy; hypersensitivity to retinoids or any component of Sohonos
- Boxed warning(s): embryo-fetal toxicity and premature epiphyseal closure in growing pediatric patients

Appendix D: General Information
- A flare-up is painful soft tissue swelling that may lead to extraskeletal HO
- Flare-up symptoms include, but are not limited to pain, swelling, redness, decreased range of motion, stiffness, and warmth.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
FOP	*Adults and pediatric patients ≥ 14 years*: 5 mg PO QD, with an increase in dose at the time of a flare-up to 20 mg PO QD for 4 weeks, followed by 10 mg PO QD for 8 weeks for a total of 12 weeks (20/10 mg flare-up treatment). Stop daily dosing when flare-up dosing begins. *Pediatric patients < 14 years*: Weight-adjusted for daily and flare-up dosing. Recommended dosage range from 2.5 to 5 mg PO QD. Stop daily dosing when flare-up dosing begins. Refer to table in Prescribing Information for complete pediatric dosing.	Age ≥ 14 years: 20 mg/day Age < 14 years: 10 mg/day

VI. Product Availability

Capsules: 1 mg, 1.5 mg, 2.5 mg, 5 mg, 10 mg

VII. References

1. Sohonos Prescribing Information. Cambridge, MA: Ipsen Biopharmaceuticals; August 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215559s000lbl.pdf. Accessed May 13, 2024.
2. ClinicalTrials.gov. An efficacy and safety study of palovarotene for the treatment of fibrodysplasia ossificans progressiva. Available at: https://clinicaltrials.gov/ct2/show/NCT03312634. Accessed May 29, 2024.
3. Fibrodysplasia ossificans progressiva. Genetic and Rare Disease (GARD) Information Center; 2021. Available at: https://rarediseases.info.nih.gov/diseases/6445/fibrodysplasia-ossificans-progressiva. Accessed May 29, 2024.
4. Pignolo RJ, Kaplan FS. Clinical staging of fibrodysplasia ossificans progressiva (FOP). Bone. 2018 Apr;109:111-114. doi: 10.1016/j.bone.2017.09.014.
5. Kaplan FS, Al Mukaddam M, Baujat G, et al. The medical management of fibrodysplasia ossificans progressiva: current treatment considerations. Proc Intl Clin Council FOP; 2022. Available at: https://assets.nationbuilder.com/ifopa/pages/1043/attachments/original/1665444347/GUIDELINES__updated_May_2022.pdf?1665444347. Accessed May 29, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	07.01.21	08.21
3Q 2022 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	05.12.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.06.22	
3Q 2023 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	04.27.23	08.23
Drug is now FDA-approved: maximum dose and male and female-specific age criteria were updated per FDA-labeled indication, corticosteroids trial for flare-ups was revised to specifically prednisone per FOP guidelines, positive response to therapy criteria updated per pivotal trial results and expert criteria review, added dosing clarification that chronic treatment and flare-up treatment are not used concurrently, and chronic treatment authorization duration extended to 12 months given chronic progressive nature of FOP; references reviewed and updated.	09.26.23	11.23
3Q 2024 annual review: no significant changes; references reviewed and updated.	05.13.24	08.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical

policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.