Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

Clinical Policy: Palovarotene

Reference Number: CP.PHAR.548
Effective Date: FDA Approval Date
Last Review Date: 08.22
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) [Pending]

Palovarotene is indicated for prevention of heterotopic ossification (HO) associated with flare up symptoms in patients with fibrodysplasia ossificans progressive (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 palovarotene is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Fibrodysplasia Ossificans Progressive (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 ≥ 4 years at therapy initiation;*
4. Presence of R206H ACVR1 mutation;*
5. Documentation of baseline HO volume assessed by low-dose whole body computed tomography (WBCT) scan, excluding the head*
6. If this is the first request for use as flare-up treatment, failure of both of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced (a and b):*
   a. Corticosteroids used for flare-ups;
   b. At least 2 nonsteroidal anti-inflammatory drugs (NSAIDs) between flare-ups;
7. Dose does not exceed the following:*
   a. Chronic treatment: 5 mg per day;
   b. Flare-up treatment: 20 mg per day for 28 days followed by 10 mg per daily 8 weeks;

Approval duration:
Chronic treatment – 6 months

Flare-up treatment – 3 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a or b): *
   a. Reduction in flare-ups;
   b. Improvement in HO volume as assessed by low-dose WBCT scan;
3. If this is the first request for use as flare-up treatment, failure of both of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced:*
   a. Corticosteroids used for flare-ups;
   b. At least 2 nonsteroidal anti-inflammatory drugs (NSAIDs) between flare-ups;
4. If request is for a dose increase, new dose does not exceed the following:*
   a. Chronic treatment: 5 mg per day;
   b. Flare-up treatment: 20 mg per day for 28 days followed by 10 mg per day for 8 weeks.

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

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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 progressive
HO: heterotopic ossification
WBCT: whole body computed tomography

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings [Pending]
- Contraindication(s): pending
- Boxed warning(s): pending

Appendix D: General Information
- Flare-up symptoms include, but are not limited to, pain, swelling, redness, decreased range of motion, stiffness, and warmth.

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
FOP*	Chronic treatment: 5 mg PO once daily Flare-up treatment: 20 mg PO once daily for 28 days followed by 10 mg once daily for 8 weeks	20 mg/day*

VI. Product Availability [Pending]
Pending

VII. References
1. 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 12, 2022.
2. Fibrodysplasia ossificans progressive. Genetic and Rare Disease (GARD) Information Center; 2021. Available at: https://rarediseases.info.nih.gov/diseases/6445/fibrodysplasia-ossificans-progressiva. Accessed May 12, 2022.
3. Pignolo RJ et al. Clinical staging of Fibrodysplasia Ossificans Progressiva (FOP). Bone 109 (2018) 111-114. https://doi.org/10.1016/j.bone.2017.09.014.
4. Current Treatment Guidelines on Fibrodysplasia ossificans progressive. International Clinical Council; 2021. Available at: http://www.iccfop.org/dvlp/wp-content/uploads/2021/04/GUIDELINES-Apr-2021.pdf. Accessed May 12, 2022.

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

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.