Oscar Clinical Guideline: Sohonos (palovarotene) (PG183, Ver. 2)

Sohonos (palovarotene)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Sohonos (palovarotene) is an oral retinoid approved by the FDA for the reduction in volume of new heterotopic ossification (HO) in patients aged 8 years and older with fibrodysplasia ossificans progressiva (FOP). FOP is an ultra-rare, severely disabling genetic disorder characterized by progressive extraskeletal bone formation in muscles, tendons and other soft tissues.

Sohonos is the first FDA-approved therapy for FOP. However, the current clinical evidence is insufficient to conclude that Sohonos provides clinically meaningful benefits that outweigh its risks. The efficacy data have significant limitations due to reliance on post-hoc analyses, lack of a concurrent control group, and unanswered questions about the clinical meaningfulness of the primary endpoint. Additional randomized controlled trials are needed to establish substantial evidence of efficacy and support Sohonos as medically necessary for FOP. Until more conclusive data are available, the Plan considers Sohonos to be unproven for FOP.

Definitions

"**Fibrodysplasia ossificans progressiva (FOP)**" is an ultra-rare autosomal dominant genetic disorder characterized by progressive heterotopic ossification of the skeletal muscle and connective tissue.

"**Heterotopic ossification (HO)**" refers to ectopic bone formations in extraskeletal tissue, typically within skeletal muscle and connective tissue. HO leads to progressive loss of mobility in patients with FOP.

"**Retinoid**" refers to a compound structurally related to vitamin A. Retinoids bind to and activate nuclear retinoic acid receptors involved in cellular differentiation and proliferation.

"**Activin A receptor, type 1 (ACVR1)**" is a gene which when mutated is the underlying genetic cause of FOP.

"**Post-hoc analysis**" refers to statistical analysis conducted after the conclusion of a study that was not pre-specified in the original study protocol or statistical analysis plan. Post-hoc analyses are generally considered exploratory in nature.

"**Concurrent control**" refers to a control group recruited and evaluated concurrently alongside the treatment group within the same study. Use of a concurrent control helps minimize confounding and improves comparability between groups.

Policy Statement on Sohonos (palovarotene) Efficacy Information

Based on review of the available clinical data, there is insufficient evidence to indicate that Sohonos (palovarotene) provides clinically meaningful benefits that outweigh the potential risks for patients with fibrodysplasia ossificans progressiva (FOP). The plan considers Sohonos (palovarotene) to be unproven and not medically necessary for FOP at this time, as evidence of efficacy has not been established.

The current efficacy data for Sohonos in FOP have significant limitations:

- The phase 3 MOVE trial (NCT03312634) failed to meet its prespecified primary endpoint. The efficacy analysis relied entirely on post-hoc analyses, which are generally considered hypothesis-generating and not appropriate for definitive conclusions.
- The MOVE trial lacked a concurrent control group. Efficacy comparisons were made to an external natural history study (NCT02322255), introducing potential bias. There are concerns about comparability of the populations and unmeasured confounding factors.

- The clinical meaningfulness of the primary endpoint (change in HO volume) is unclear. Data are lacking to show that small changes in HO volume translate to tangible clinical improvements for patients.
- Consistency between the phase 2 (NCT02190747, PVO-1A-201) and phase 3 trials is lacking regarding the primary endpoint. The phase 2 data do not provide robust confirmatory evidence.
- No significant benefits were seen in key secondary endpoints assessing clinically meaningful outcomes like physical function, range of motion, or quality of life.

Due to the limited and inconsistent efficacy data, unanswered questions remain regarding whether Sohonos (palovarotene) provides any clinically meaningful therapeutic effect for FOP. Additional randomized controlled trials with longer follow-up are needed to establish substantial evidence of efficacy.

Medical Necessity Criteria for Sohonos (palovarotene)

Due to insufficient efficacy data, potential safety risks, and the absence of robust clinical efficacy data, the Plan has determined that it does not have established medical necessity criteria for coverage of Sohonos at this time.

Given the current evidence and concerns, Sohonos (palovarotene) does not meet the Plan's criteria for proven efficacy and medical necessity for FOP. The Plan remains committed to providing coverage for treatments that demonstrate solid evidence of both safety and effectiveness. We will continue to monitor the evolving clinical data for Sohonos and will reassess our position as more conclusive information becomes available. Until then, we encourage our members to explore other proven treatment options with their healthcare providers.

Experimental or Investigational / Not Medically Necessary

Sohonos (palovarotene) for any indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

References

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Clinical Guideline Revision / History Information

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