sohonos™
(palovarotene) capsules
1 mg | 1.5 mg | 2.5 mg | 5 mg | 10 mg

ADDRESSING MUCOCUTANEOUS EFFECTS[1]

Mucocutaneous effects have been observed in patients receiving treatment with SOHONOS™. This guide provides information for you to help your patients.

INDICATION

SOHONOS™ is indicated for the reduction in volume of new heterotopic ossification in adults and pediatric patients aged 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva (FOP).

IMPORTANT SAFETY INFORMATION

WARNING: EMBRYO-FETAL TOXICITY and PREMATURE EPIPHYSEAL CLOSURE IN GROWING PEDIATRIC PATIENTS

- **SOHONOS is contraindicated in pregnancy. SOHONOS may cause fetal harm. Because of the risk of teratogenicity and to minimize fetal exposure, SOHONOS is to be administered only if conditions for pregnancy prevention are met.**
- **Premature epiphyseal closure occurs in growing pediatric patients treated with SOHONOS, close monitoring is recommended.**

Contraindications

SOHONOS is contraindicated in patients during pregnancy, or with a history of allergy or hypersensitivity to retinoids, or to any component of SOHONOS. Anaphylaxis and other allergic reactions have occurred with other retinoids.

Warnings and Precautions

- **Embryo-Fetal Toxicity:** SOHONOS can cause fetal harm and is contraindicated during pregnancy. SOHONOS is a retinoid which is associated with birth defects in humans. Advise females of reproductive potential to use an effective method of contraception at least 1 month prior to treatment, during SOHONOS treatment and for 1 month after the last dose. If a pregnancy occurs during treatment, discontinue treatment immediately and refer the patient to an obstetrician/gynecologist experienced in reproductive toxicity. Inform patients not to donate blood during SOHONOS treatment and for 1 week following discontinuation.
- **Premature Epiphyseal Closure in Growing Pediatric Patients:** SOHONOS can cause irreversible premature epiphyseal closure and potential adverse effects on growth. In clinical studies, premature epiphyseal closure occurred with SOHONOS treatment in growing pediatric patients with FOP. Monitoring of linear growth is recommended in growing pediatric patients. Prior to starting treatment with SOHONOS, all growing pediatric patients should undergo baseline assessment of skeletal maturity and continued monitoring until patients reach skeletal maturity or final adult height. If a patient exhibits signs of premature epiphyseal closure or adverse effects on growth based on clinical or radiologic evaluations, further evaluation may be required, including an assessment of the benefits and risks of continued treatment, or temporary or permanent discontinuation of SOHONOS until the patient achieves epiphyseal closure and skeletal maturity.

Please see additional Important Safety Information and the full Prescribing Information including BOXED WARNING for Embryo-Fetal Toxicity and Premature Epiphyseal Closure in Growing Pediatric Patients.

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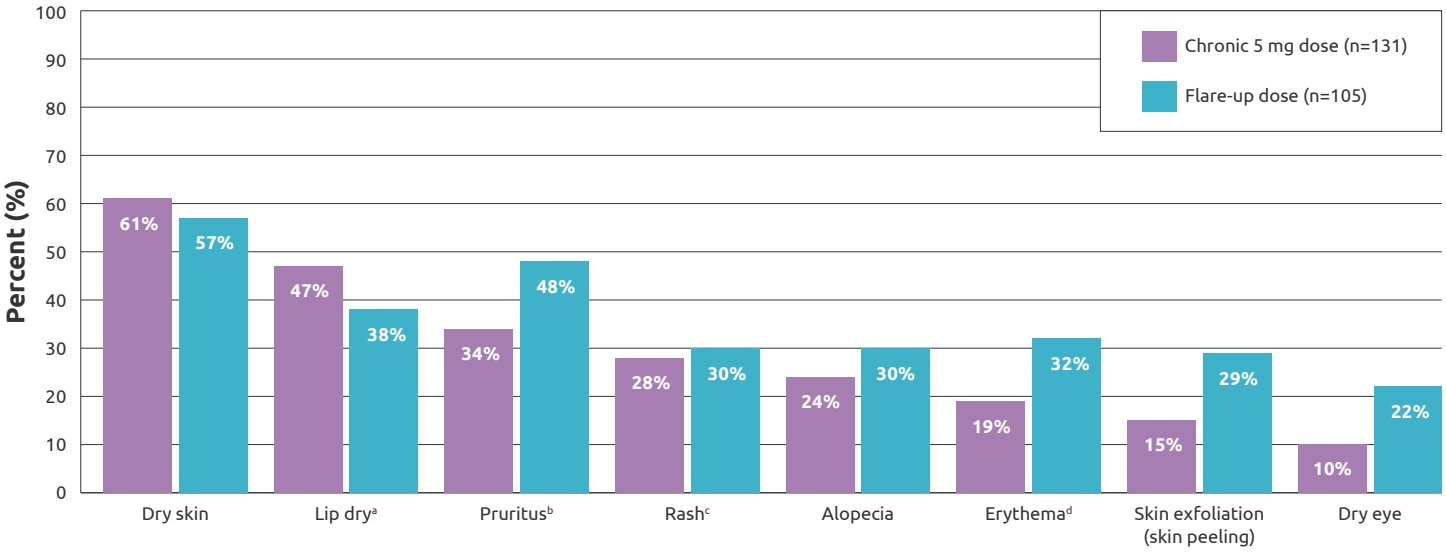
Patients receiving SOHONOS may experience mucocutaneous reactions[1]

Mucocutaneous effects were observed with SOHONOS use

Mucocutaneous adverse reactions occurring in ≥10% of patients with FOP treated with SOHONOS (females ≥8 and males ≥10) in clinical trials



Mucocutaneous adverse reactions reported ≥10% frequency

[a]Includes lip dry, chapped lips, cheilitis. [b]Includes pruritus, pruritus generalized, and rash pruritic. [c]Includes rash, rash generalized, rash maculo-papular. [d]Includes erythema, generalized erythema, flushing, rash erythematous.

Risk of infections: Mucocutaneous effects such as dry and peeling skin may increase the risk of certain infections due to the thinning of the skin barrier. Patients should be monitored for paronychia and bed sores (decubitus ulcer).

Photosensitivity: Photosensitivity reactions, such as exaggerated sunburn reactions (e.g., burning, erythema, blistering) have been associated with the use of retinoids and may occur. Patients should therefore avoid excessive exposure to sun or artificial ultraviolet light.

In clinical trials, these effects were generally more common with dose increases due to flare-ups.

Some of these mucocutaneous adverse reactions led to dose reductions which occurred more frequently during flare-up dosing suggesting a dose-response relationship.

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Be prepared to proactively manage mucocutaneous effects[1,2]

The following prophylactic measures are recommended to minimize risk and/or treat these symptoms:

FOR PHOTOSENSITIVITY

- Avoid prolonged exposure to sunlight/UV light
- Apply sting-free sunscreen
- Wear protective head coverings (hats/scarves), sunglasses, and long-sleeved shirts and pants whenever outdoors

FOR LIP DRY/DRY NOSE

- Apply lip balm liberally
- Apply petrolatum/petroleum jelly as needed to lips/corners of mouth and nostrils to help protect from irritation
- Use nasal saline drops as needed to prevent or reduce nasal dryness

FOR DRY EYE

- Discontinue using contact lenses
- Use artificial tears
- Wear sunglasses to help with minor irritation of the delicate skin around the eye

FOR DRY SKIN

- Avoid very hot showers, baths, and hot tubs
- Avoid using skin cleansers/treatments that are harsh and drying*
- Keep skin covered and protected from cold air
- Apply emollients to the body and face liberally during treatment, at least 4 times per day
- Apply petrolatum/petroleum jelly as needed, at least 4 times per day
- Wash gently using gentle skin cleaners
- Use over-the-counter antihistamine tablets or capsules to help with itching, particularly at night

*For example, strong soaps, exfoliants/toners, benzoyl peroxide, salicylic acid/glycolic acid, derm-abrasion, waxing, chemical hair removers, chemical peels, and laser treatments.

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Managing mucocutaneous effects (continued)

FOR DRY MOUTH

- Chew xylitol-containing gum
- Swish and swallow small amounts of water frequently
- Use over-the-counter saliva substitutes such as lozenges, gels, or sprays
- Talk to your dentist about specific toothpastes that are also available to help with general dental health and dry mouth

FOR HAIR/SCALP

- Try to maintain as simple a hair care regimen as possible†
- Use of a shampoo/conditioner that is for sensitive skin, hypoallergenic may be helpful
- If hair is not oily, reduced frequency of washing may be helpful to prevent drying of scalp
- Use hat/scarf to protect scalp from sun exposure
- Intermittent mineral oil/olive oil treatments may also help alleviate dry scalp
- Avoid chemical treatments to the hair, including dyeing/highlights, and perm treatments

†Avoid using heat or chemicals and minimize traction from tight hair styles.

This content is for informational purposes only, and should not be taken as medical advice or a substitute for your professional clinical experience. Please counsel patients as you deem appropriate.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Warnings and Precautions (continued)

- **Mucocutaneous Adverse Reactions:** Dry skin, lip dry, pruritus, rash, alopecia, erythema, skin exfoliation (skin peeling), and dry eye occurred in 98% of patients treated with SOHONOS. SOHONOS may contribute to an increased risk of skin and soft tissue infections, particularly paronychia and decubitus ulcer, due to a decreased skin barrier from adverse reactions such as dry and peeling skin. Some of these adverse reactions led to dose reductions which occurred more frequently during flare-up dosing suggesting a dose response relationship. Prophylactic measures to minimize risk and/or treat the mucocutaneous adverse reactions are recommended (e.g., skin emollients, sunscreen, lip moisturizers, or artificial tears). Some may require dose reduction or discontinuation. Photosensitivity reactions (e.g., burning, erythema, blistering) involving areas exposed to the sun have been associated with the use of retinoids and may occur with SOHONOS. Precautionary measures for phototoxicity are recommended (use of sunscreens, protective clothing, and use of sunglasses).
- **Metabolic Bone Disorders:** Retinoids are associated with bone toxicity, including reductions in bone mass and spontaneous reports of osteoporosis and fracture. In FOP clinical studies, SOHONOS resulted in decreased vertebral bone mineral content and bone density, and an increased risk of radiologically observed vertebral fractures in treated patients compared to untreated patients. Periodic radiological assessment of the spine is recommended. Retinoids have been associated with hyperostotic changes (bone spurs) and calcification of tendons or ligaments may occur with SOHONOS.
- **Psychiatric Disorders:** New or worsening psychiatric events were reported with SOHONOS including depression, anxiety, mood alterations, and suicidal thoughts and behaviors. There is a relatively high background prevalence of psychiatric disorders in untreated patients with FOP. Monitor for development of new or worsening psychiatric symptoms during treatment with SOHONOS. Individuals with a history of psychiatric illness may be more susceptible to these adverse effects. Patients and/or caregivers should contact their healthcare provider if new or worsening psychiatric symptoms develop during treatment with SOHONOS.
- **Night Blindness:** This may be dose-dependent, making driving a vehicle at night potentially hazardous during treatment. Advise patients to be cautious when driving or operating any vehicle at night and seek medical attention in the event of vision impairment.

Adverse Reactions

The most common adverse reactions (≥ 10%) are dry skin, lip dry, arthralgia, pruritus, pain in extremity, rash, alopecia, erythema, headache, back pain, skin exfoliation (skin peeling), nausea, musculoskeletal pain, myalgia, dry eye, hypersensitivity, peripheral edema, and fatigue.

It's time to learn more

SOHONOS™ (palovarotene) is the first and only treatment for the reduction in volume of new heterotopic ossification (HO) in fibrodysplasia ossificans progressiva (FOP). Learn more at SOHONOS.com

IMPORTANT SAFETY INFORMATION (CONTINUED)

Drug Interactions

- CYP3A4 inhibitors may increase SOHONOS exposure. Avoid concomitant use of strong or moderate CYP3A4 inhibitors, as well as grapefruit, pomelo or juices containing these fruits.
- CYP3A4 inducers may decrease SOHONOS exposure. Avoid concomitant use of strong or moderate CYP3A4 inducers.
- The use of both vitamin A and SOHONOS at the same time may lead to additive effects. Concomitant administration of vitamin A in doses higher than the recommended daily allowance and/or other oral retinoids must be avoided due to risk of hypervitaminosis A.
- Systemic retinoid use has been associated with cases of benign intracranial hypertension (pseudotumor cerebri), some of which involved the concomitant use of tetracyclines. Avoid coadministration of SOHONOS with tetracycline derivatives.

Use in Specific Populations

- **Pregnancy:** SOHONOS is contraindicated during pregnancy. Obtain a negative serum pregnancy test within 1 week prior to SOHONOS therapy and periodically, as needed, over the course of treatment with SOHONOS and 1 month after treatment discontinuation unless patient is not at risk of pregnancy. If pregnancy occurs during treatment with SOHONOS, stop treatment immediately and refer the patient to an obstetrician/gynecologist or other specialist experienced in reproductive toxicity for evaluation and advice.
- **Lactation:** Advise females that breastfeeding is not recommended during treatment with SOHONOS, and for at least 1 month after the last dose.
- **Females and Males of Reproductive Potential:** Advise females of reproductive potential to use effective contraception at least 1 month prior to and during treatment, and for 1 month after the last dose unless continuous abstinence is chosen.
- **Pediatric Use:** All growing pediatric patients should undergo baseline assessment of growth and skeletal maturity before starting treatment and continued clinical and radiographic monitoring every 6-12 months until patients reach skeletal maturity or final adult height.
- **Renal or Hepatic Impairment:** Use of SOHONOS in patients with severe renal impairment, or with moderate or severe hepatic impairment is not recommended.

Please see additional Important Safety Information and the full Prescribing Information, including BOXED WARNING for Embryo-Fetal Toxicity and Premature Epiphyseal Closure in Growing Pediatric Patients.

References: 1. SOHONOS Full Prescribing Information. Cambridge, MA: Ipsen Biopharmaceuticals, Inc; August 2023. **2.** Data on file. Ipsen Biopharmaceuticals.

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