SOHONOS® (palovarotene)

Educational Program Materials for Prescribers and Pharmacists

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.**

Please see Indication and additional Important Safety Information on pages 2-3, and accompanying full Prescribing Information, including BOXED WARNING.

SOHONOS EDUCATIONAL PROGRAM MATERIALS FOR PRESCRIBERS AND PHARMACISTS

SOHONOS EDUCATIONAL PROGRAM MATERIALS FOR PATIENTS AND CAREGIVERS

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.
- **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

Please see additional Important Safety Information on pages 2-3, and accompanying full Prescribing Information, including BOXED WARNING.

IMPORTANT SAFETY INFORMATION (CONT.)

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.

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 full Prescribing Information, including BOXED WARNING.

Please see additional Important Safety Information on pages 2-3, and accompanying full Prescribing Information, including BOXED WARNING.

SOHONOS® (palovarotene)

Understanding the SOHONOS (palovarotene) Educational Program: A Guide for Prescribers and Pharmacists

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.**

Please see additional Important Safety Information on pages 2-3, and accompanying full Prescribing Information, including BOXED WARNING.

Sections that are noted in the below document refer to specific sections of the Prescribing Information

SOHONOS ® (palovarotene) capsules

What is SOHONOS (palovarotene)?

SOHONOS is a retinoid 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).

What are the Serious Risks of SOHONOS?

Embryo-Fetal Toxicity

SOHONOS can cause fetal harm and is contraindicated during pregnancy. SOHONOS is a member of the retinoid class of drugs which is associated with birth defects in humans. In animal reproduction studies, palovarotene administered orally to pregnant rats during organogenesis was teratogenic and caused fetal malformations typical of retinoids including cleft palate, misshapen skull bones, and shortening of the long bones at clinically relevant exposures.

For females of reproductive potential, verify that the patient is not pregnant prior to initiating treatment, periodically during the course of therapy and one month after treatment discontinuation. Advise females of reproductive potential to use an effective method of contraception at least one month prior to treatment, during treatment with SOHONOS and for 1 month after the last dose *[see Use in Specific Populations (8.1, 8.3) and Clinical Pharmacology (12.3)].* If a pregnancy occurs during SOHONOS treatment, discontinue treatment immediately and refer the patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Patients should be informed not to donate blood during SOHONOS therapy and for 1 week following discontinuation because the blood might be given to a pregnant patient whose fetus must not be exposed to palovarotene.

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 *[see Adverse Reactions (6.1) and Use in Specific Populations (8.4)]*.

Monitoring of linear growth is recommended in growing pediatric patients *[see Use in Specific Populations (8.4)].* Prior to starting treatment with SOHONOS, all growing pediatric patients should undergo baseline assessment of skeletal maturity via hand/wrist and knee x-rays, standard growth curves and pubertal staging. Continued monitoring is recommended every 6 to 12 months 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.

Mucocutaneous Adverse Reactions

Mucocutaneous adverse reactions including dry skin, lip dry, pruritus, rash, alopecia, erythema, skin exfoliation [skin peeling], and dry eye occurred in most (98%) 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 *[see Adverse Reactions (6.1)].* Some of these mucocutaneous 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 patients may require dose reduction or drug discontinuation *[see Dosage and Administration (2.4)].*

Please see additional Important Safety Information on pages 2-3, and accompanying full Prescribing Information, including BOXED WARNING.

Photosensitivity

Photosensitivity reactions, such as exaggerated sunburn 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. Excessive exposure to sun or artificial ultraviolet light should be avoided, and protection from sunlight should be used when exposure cannot be avoided (use of sunscreens, protective clothing, and use of sunglasses).

Metabolic Bone Disorders

Bone mineral density and fracture
Retinoids are associated with bone toxicity, including reductions in bone mass and spontaneous reports of osteoporosis and fracture. In FOP clinical trials, SOHONOS resulted in decreased vertebral bone mineral content and bone density, and an increased risk of radiologically observed vertebral (T4 to L4) fractures in treated adult and pediatric patients compared to untreated patients. Periodic radiological assessment of the spine is recommended. *[see Adverse Reactions (6.1)]*.

Hyperostosis
Retinoids have been associated with hyperostotic changes (bone spurs) and calcification of tendons or ligaments and may occur with SOHONOS. These effects generally occur with long-term use, especially at high doses.

Psychiatric Disorders

New or worsening psychiatric events were reported with SOHONOS use. These include 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 *[see Adverse Reactions (6.1)]*. 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

Night blindness has been associated with systemic retinoids, including SOHONOS. This may be dose-dependent, making driving a vehicle at night potentially hazardous during treatment. Night blindness is generally reversible after cessation of treatment but can also persist in some cases. Advise patients to be cautious when driving or operating any vehicle at night and to seek medical attention in the event of vision impairment.

Please see additional Important Safety Information on pages 2-3, and accompanying full Prescribing Information, including BOXED WARNING.

What is the SOHONOS Educational Program?
The SOHONOS Educational Program is a program to educate prescribers, pharmacists, patients, and their caregivers about the serious risks related to SOHONOS.

Healthcare providers are required to review the SOHONOS Educational Program materials before SOHONOS is dispensed to their patients. The following educational materials will be available through the US Specialty Pharmacy, by calling the Ipsen Call Center at +1-855-463-5127 and online on the healthcare provider SOHONOS product website at www.SOHONOS.com.

Educating Patients about the Risk of Birth Defects Associated with SOHONOS
SOHONOS must not be used by female patients who are or may become pregnant. There is a high risk that severe birth defects will result if pregnancy occurs while taking SOHONOS in any amount, even for short periods of time.

Prescribers should:

1. **Determine the reproductive status of female patients**
   - Females of reproductive potential include females who have entered puberty and all females who have a uterus and have not passed through menopause (12 months of spontaneous amenorrhea or postsurgical from bilateral oophorectomy.)

2. **Order pregnancy tests for females of childbearing potential**
   - For females of reproductive potential, obtain a negative serum pregnancy test within one week prior to SOHONOS therapy. Verify that patient is not pregnant periodically, as needed, over the course of treatment with SOHONOS and one month after treatment discontinuation unless they are not at risk of pregnancy.

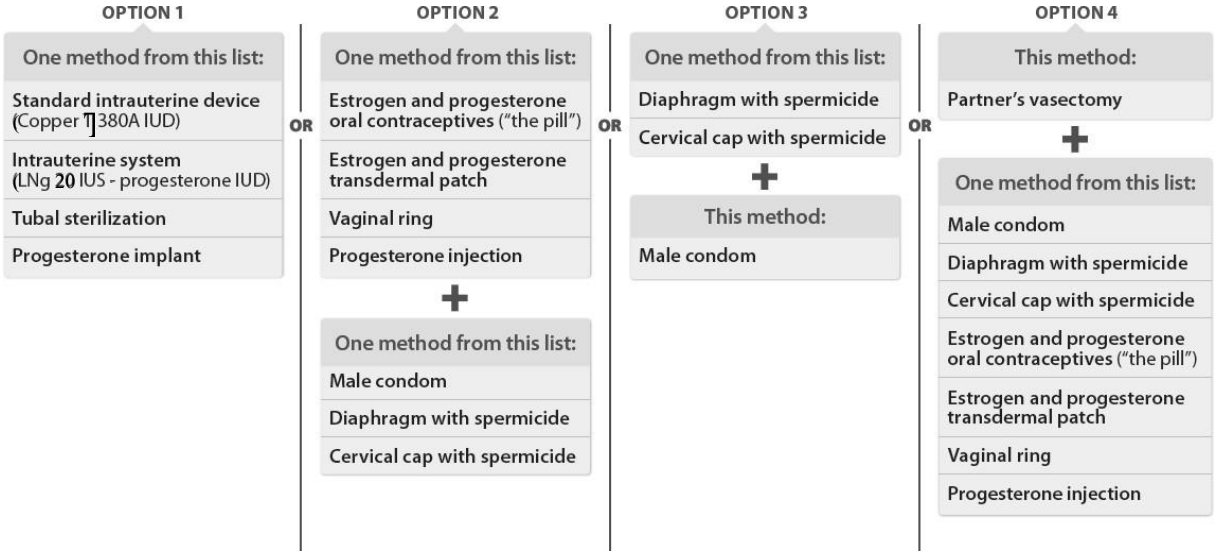
3. **Counsel female patients about the risks of SOHONOS**
   - Review the *Understanding the SOHONOS Educational Program: Guide for Female Patients. The Importance of Avoiding Pregnancy for Female Patients Taking SOHONOS* before initiating SOHONOS treatment
   - Advise females of reproductive potential to use an effective method of contraception at least one month prior to treatment, during treatment with SOHONOS and for 1 month after the last dose *[see Use in Specific Populations (8.1, 8.3) and Clinical Pharmacology (12.3)]*. If a pregnancy occurs during SOHONOS treatment, discontinue treatment immediately and refer the patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling.
   - Patients should be informed not to donate blood during SOHONOS therapy and for 1 week following discontinuation because the blood might be given to a pregnant patient whose fetus must not be exposed to palovarotene.

4. **Review forms of reliable contraception with the patient**
   - Abstinence from heterosexual sex during treatment and for 1 month after treatment,
     -OR-
   - *one highly effective method* of contraception (i.e., IUD) or *two effective methods* (i.e., combined hormonal contraception in combination with another method of contraception such as a barrier method) for at least 1 month before initiating treatment with SOHONOS and continuing these methods of birth control during treatment and for 1 month after treatment if having heterosexual sex.

     Abstinence from heterosexual sex is only acceptable as “true abstinence.” True abstinence occurs when it is in line with the patient’s preferred and usual lifestyle. Periodic abstinence from heterosexual sex (such as calendar, ovulation, symptothermal, post-ovulation methods), the rhythm method, and withdrawal are not acceptable methods of contraception.

Please see additional Important Safety Information on pages 2-3, and accompanying full Prescribing Information, including BOXED WARNING.

Birth Control Options



Option 1: Highly Effective Methods | **Options 2, 3 or 4: Two Effective Methods**

The following are unacceptable forms of birth control:
- Progestin-only "mini-pill"
- Female condom
- Natural family planning (periodic abstinence, such as calendar, ovulation, symptothermal, post- ovulation methods; rhythm method; or breastfeeding) or withdrawal

Educating Caregivers about the Risk of Premature Epiphyseal Closure in Growing Children with Fibrodysplasia Ossificans Progressiva (FOP)

The safety and effectiveness of SOHONOS for the treatment of FOP have been established in pediatric patients aged 8 years and older for females and 10 years and older for males. Use of SOHONOS for this indication is supported by evidence from clinical studies in adults and pediatric subjects *[see Clinical Studies (14)]*.

The safety and effectiveness of SOHONOS for the treatment of FOP have not been established in pediatric patients less than 8 years of age in females and less than 10 years of age for males. SOHONOS is not recommended for use in patients younger than 8 years of age for females and 10 years of age for males because of the potential for premature epiphyseal closure. Clinical studies have shown that growing patients with open epiphyses are at risk of developing premature epiphyseal closure when treated with SOHONOS *[see Warnings and Precautions (5.2), Adverse Reactions (6.1) and Clinical Studies (14.1)]*.

Monitoring Recommendation

Prior to starting treatment with SOHONOS, all growing children should undergo baseline clinical and radiological assessments including but not limited to an assessment of skeletal maturity via hand/wrist and knee x-rays, standard growth curves and pubertal staging. Continued monitoring is recommended every 6-12 months until patients reach skeletal maturity (e.g., epiphyseal closure) or final adult height *[see Warnings and Precautions (5.2)]*

Learn more about the SOHONOS Educational Program at www.SOHONOS.com or call +1-855-463-5127 for more information about the SOHONOS Educational Program.

Please see additional Important Safety Information on pages 2-3, and accompanying full Prescribing Information, including BOXED WARNING.

SOHONOS® (palovarotene)

Educational Program Materials for Patients and Their Caregivers

WHAT IS SOHONOS?

SOHONOS is a prescription medicine used to reduce the amount of new heterotopic ossification in adults and children 8 years of age and older for females and 10 years of age and older for males with fibrodysplasia ossificans progressiva (FOP). SOHONOS is not recommended for females younger than 8 years of age or males younger than 10 years of age.

WHAT ARE THE SERIOUS RISKS OF SOHONOS?

- **SOHONOS can cause birth defects (deformed babies) if taken during pregnancy. Females who are pregnant or who plan to become pregnant must not take SOHONOS.**

Females who can become pregnant:
- Your healthcare provider will ask you to take a pregnancy test 1 week before starting treatment with SOHONOS, periodically during treatment, and 1 month after you stop treatment with SOHONOS.
- You must use effective birth control (contraception) starting at least 1 month before starting treatment with SOHONOS, during treatment and for 1 month after the last dose. Talk to your healthcare provider about birth control methods that may be right for you.
- If you become pregnant or think you may be pregnant during treatment with SOHONOS, stop taking SOHONOS and call your healthcare provider right away.

Because SOHONOS can cause birth defects, SOHONOS is only for people who can understand and agree to carry out all instructions for pregnancy prevention.

- **SOHONOS can cause bone growth changes.** Children may stop growing while taking SOHONOS. Bone growth changes such as permanent early closure of the growth plate in growing children have happened with SOHONOS. Your healthcare provider will closely monitor your child's bone growth and height during treatment with SOHONOS.

Please see full Prescribing Information, including Medication Guide with IMPORTANT WARNING on Birth Defects and Bone Growth Changes.

WHAT IS SOHONOS?
SOHONOS is a prescription medicine used to reduce the amount of new heterotopic ossification in adults and children 8 years of age and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva (FOP). SOHONOS is not recommended for females younger than 8 years of age or males younger than 10 years of age.

IMPORTANT SAFETY INFORMATION
What is the most important information I should know about SOHONOS?
SOHONOS can cause birth defects (deformed babies) if taken during pregnancy. Females who are pregnant or who plan to become pregnant must not take SOHONOS.

- Your healthcare provider will ask you to take a pregnancy test 1 week before starting treatment with SOHONOS, periodically during treatment, and 1 month after you stop treatment.
- You must use effective birth control (contraception) starting at least 1 month before starting treatment with SOHONOS, during treatment, and for 1 month after the last dose. Talk to your healthcare provider about birth control methods that may be right for you.
- If you become pregnant or think you may be pregnant during treatment with SOHONOS, stop taking SOHONOS and call your healthcare provider right away.

Because SOHONOS can cause birth defects, SOHONOS is only for people who can understand and agree to carry out all instructions for pregnancy prevention.

SOHONOS can cause bone growth changes. Children may stop growing while taking SOHONOS. Bone growth changes such as permanent early closure of the growth plate in growing children have happened with SOHONOS. Your healthcare provider will closely monitor your child's bone growth and height during treatment with SOHONOS.

Who should not take SOHONOS?
Do not take SOHONOS if you are pregnant, or allergic to medicines known as retinoids or any of the ingredients in SOHONOS.

What should I tell my healthcare provider before taking SOHONOS?
Before taking SOHONOS, tell your healthcare provider about all your medical conditions, including:

- have bone loss (osteoporosis), weak bones or any other bone problems
- have or had mental health problems
- have or have had kidney problems
- have or have had liver problems
- are breastfeeding or plan to breastfeed. It is not known if SOHONOS passes into your breastmilk. Breastfeeding is not recommended during treatment with SOHONOS and for at least 1 month after the last dose of SOHONOS. Talk to your healthcare provider about the best way to feed your baby if you take SOHONOS.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. SOHONOS and certain other medicines can interact with each other, sometimes causing serious side effects. Keep a list of your medicines to show to your healthcare provider and pharmacist when you get a new medicine.

What should I avoid while taking SOHONOS?

- Do not get pregnant while taking SOHONOS.
- Avoid excessive exposure to sunlight and ultraviolet lights (tanning machines). SOHONOS may make your skin more sensitive to the exposure and you may burn more easily. Apply sunscreen and wear protective clothing and sunglasses when in sunlight.
- Avoid driving at night until you know if SOHONOS has affected your vision. SOHONOS may decrease your ability to see in the dark.
- Do not donate blood while taking SOHONOS and for 1 week after stopping SOHONOS.

Please see Important Safety Information on pages 2-3 and accompanying full Prescribing Information, including Medication Guide with IMPORTANT WARNING.

IMPORTANT SAFETY INFORMATION (CONT.)
What are the possible side effects of SOHONOS?
SOHONOS can cause serious side effects, including:

- **Skin-related events** such as dry skin, lip and eye, hair loss, itching, redness, rash, and skin peeling. You may be at increased risk of developing skin and soft tissue infections while taking SOHONOS. If you develop these symptoms, your healthcare provider may tell you to use moisturizer, sunscreen, or artificial tears.
- **Bone mineral density problems** (bone thinning) which can increase the risk of fractures in adults and children. Your healthcare provider should check you for this during treatment with SOHONOS.
- **New or worsening mental health problems** that may include depression, anxiety, mood changes, and suicidal thoughts and behaviors. If you have a history of mental health problems, you may be at a higher risk of developing these side effects. Call your healthcare provider if you develop new or worsening mental health symptoms during treatment with SOHONOS. Your healthcare provider should monitor you for signs of depression and refer you for appropriate treatment, if necessary.
- **Vision problems (night blindness)** which may cause difficulty seeing at night or in low lit areas. Your healthcare provider should send you to see an eye specialist if you experience vision problems.

The most common side effects of SOHONOS include:

- dry skin
- dry lips
- hair loss
- itching
- redness
- rash
- skin peeling
- drug eruption
- skin irritation
- swelling and small cracks in corner of the mouth
- nausea
- muscle and joint pain
- dry eyes
- headache
- fatigue

These are not all the possible side effects of SOHONOS. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1800-FDA-1088.

Please see full Prescribing Information, including Medication Guide with IMPORTANT WARNING on Birth Defects and Bone Growth Changes.

Please see Important Safety Information on pages 2-3 and accompanying full Prescribing Information, including Medication Guide with IMPORTANT WARNING.

SOHONOS® (palovarotene)

Understanding the SOHONOS (palovarotene) Educational Program: A Guide for Patients and Their Caregivers

The health information contained within this guide is provided for general educational purposes only. Your healthcare professional is the best source of information regarding your health. Please consult your healthcare professional if you have any questions about your health or treatment.

Please see full Prescribing Information, including Medication Guide with IMPORTANT WARNING on Birth Defects and Bone Growth Changes.

WHAT IS THE SOHONOS EDUCATIONAL PROGRAM?
The SOHONOS Educational Program is a program to educate prescribers, pharmacists, patients and their caregivers about the important risks related to SOHONOS.

WHAT IS SOHONOS?
SOHONOS is a prescription medicine used to reduce the amount of new heterotopic ossification in adults and children 8 years of age and older for females and 10 years of age and older for males with fibrodysplasia ossificans progressiva (FOP). SOHONOS is not recommended for females younger than 8 years of age or males younger than 10 years of age.

WHAT ARE THE SERIOUS RISKS OF SOHONOS?
- **SOHONOS can cause birth defects (deformed babies) if taken during pregnancy. Females who are pregnant or who plan to become pregnant must not take SOHONOS.**

  Females who can become pregnant:
  - Your healthcare provider will ask you to take a pregnancy test 1 week before starting treatment with SOHONOS, periodically during treatment, and 1 month after you stop treatment with SOHONOS.
  - You must use effective birth control (contraception) starting at least 1 month before starting treatment with SOHONOS, during treatment and for 1 month after the last dose. Talk to your healthcare provider about birth control methods that may be right for you.
  - If you become pregnant or think you may be pregnant during treatment with SOHONOS, stop taking SOHONOS and call your healthcare provider right away.

Because SOHONOS can cause birth defects, SOHONOS is only for people who can understand and agree to carry out all instructions for pregnancy prevention.

- **SOHONOS can cause bone growth changes.** Children may stop growing while taking SOHONOS. Bone growth changes such as permanent early closure of the growth plate in growing children have happened with SOHONOS. Your healthcare provider will closely monitor your child's bone growth and height during treatment with SOHONOS.

WHAT SHOULD I AVOID WHILE TAKING SOHONOS?
- Do not get pregnant while taking SOHONOS. See "**WHAT ARE THE SERIOUS RISKS OF SOHONOS**"
- Avoid excessive exposure to sunlight and ultraviolet lights (e.g., tanning machines). SOHONOS may make your skin more sensitive to sunlight and ultraviolet light and you may burn more easily. You should use sunscreen and wear sunglasses and protective clothing that covers your skin to help protect against sunburn if you must be in the sunlight during treatment with SOHONOS.
- Avoid driving at night until you know if SOHONOS has affected your vision. SOHONOS may decrease your ability to see in the dark.
- Do not donate blood while taking SOHONOS and for 1 week after stopping SOHONOS.

WHAT ARE POSSIBLE SIDE EFFECTS OF SOHONOS?
- **Skin-related problems:** SOHONOS may cause skin-related problems including dry skin, lips and eyes, hair loss, itching, redness, rash, and skin peeling. You may be at increased risk of developing skin and soft tissue infections while taking SOHONOS. If you develop these symptoms, your healthcare provider may tell you to use a moisturizer, sunscreen, or artificial tears.

- **Bone mineral density problems:** SOHONOS can cause a reduction in bone mineral density (bone thinning) which can increase the risk of fractures in adults and children. Your healthcare provider should check you for this during treatment with SOHONOS

- **New or worsening mental health problems:** SOHONOS may cause new or worsening mental health problems that include depression, anxiety, mood changes, and suicidal thoughts and behaviors. If you have a

history of mental health problems, you may be at a higher risk of developing these side effects. Call your healthcare provider if you develop new or worsening mental health symptoms during treatment with SOHONOS. Your healthcare provider should monitor you for signs of depression and refer you for appropriate treatment, if necessary.

- **Vision problems:** Decreased vision in the dark (night blindness). You may have difficulty seeing at night or in low lit areas. Your healthcare provider should send you to see an eye specialist if you experience vision problems.

The most common side effects of SOHONOS include:

- dry skin
- dry lips
- hair loss
- itching
- redness
- rash
- skin peeling
- drug eruption
- skin irritation
- swelling and small cracks in corner of the mouth
- nausea
- muscle and joint pain
- dry eyes
- headache
- fatigue

Please read the SOHONOS Medication Guide that comes with your medication for more details regarding the risks described above.

WHAT DO I NEED TO KNOW ABOUT SOHONOS?
Before receiving SOHONOS, you must do the following:

1. **Talk with your doctor to ensure the benefits outweigh the risks of taking SOHONOS.**

2. **Read all the patient information about SOHONOS:**
   a. SOHONOS Medication Guide
   b. **Female Patients**: Understanding the SOHONOS Educational Program: A Guide for Females. The Importance of Avoiding Pregnancy for Female Patients Taking SOHONOS.
   c. **Caregivers of Pediatric Patients:** Understanding the SOHONOS Educational Program: A Guide for Caregivers of Growing Pediatric Patients
   d. All SOHONOS Education materials can be obtained at www.SOHONOS.com.

3. **Understand what you need to do when taking SOHONOS. Ask your doctor about anything you do not understand. These requirements include:**
   a. **For females who can get pregnant:** pregnancy tests and use of appropriate birth control
   b. **For growing children**: regular clinical monitoring

You are encouraged to talk with your healthcare provider about any concerns or questions you may have.

HOW WILL I OBTAIN MY SOHONOS?
Your prescription will be sent to a specialty pharmacy that will ship the medication to your home.

If you have questions or concerns about SOHONOS, talk to your doctor. Please visit www.SOHONOS.com or call +1-855-463-5127 for more information about the SOHONOS Educational Program.

Please see full Prescribing Information, including Medication Guide with IMPORTANT WARNING on Birth Defects and Bone Growth Changes.

Please see Important Safety Information on pages 2-3 and accompanying full Prescribing Information, including Medication Guide with IMPORTANT WARNING.

SOHONOS® (palovarotene)

Understanding the SOHONOS (palovarotene) Education Program: A Guide for Females

This brochure focuses on the risks that affect females who can become pregnant and how these risks must be managed when taking SOHONOS.

The health information contained within this guide is provided for general educational purposes only. Your healthcare professional is the best source of information regarding your health. Please consult your healthcare professional if you have any questions about your health or treatment.

Please see full Prescribing Information, including Medication Guide with IMPORTANT WARNING on Birth Defects and Bone Growth Changes.

WHAT IS THE SOHONOS EDUCATIONAL PROGRAM?

The SOHONOS Educational Program is a program to educate prescribers, pharmacists, patients and their caregivers about the important risks related to SOHONOS.

WHAT IS SOHONOS?

SOHONOS is a prescription medicine used to reduce the amount of new heterotopic ossification in adults and children 8 years of age and older for females and 10 years of age and older for males with fibrodysplasia ossificans progressiva (FOP). SOHONOS is not recommended for females younger than 8 years of age or males younger than 10 years of age.

WHAT ARE THE SERIOUS RISKS OF SOHONOS?

- **SOHONOS can cause birth defects (deformed babies) if taken during pregnancy. Females who are pregnant or who plan to become pregnant must not take SOHONOS.**

  Females who can become pregnant:
  - Your healthcare provider will ask you to take a pregnancy test 1 week before starting treatment with SOHONOS, periodically during treatment, and 1 month after you stop treatment with SOHONOS.
  - You must use effective birth control (contraception) starting at least 1 month before starting treatment with SOHONOS, during treatment and for 1 month after the last dose. Talk to your healthcare provider about birth control methods that may be right for you.
  - If you become pregnant or think you may be pregnant during treatment with SOHONOS, stop taking SOHONOS and call your healthcare provider right away.

Because SOHONOS can cause birth defects, SOHONOS is only for people who can understand and agree to carry out all instructions for pregnancy prevention.

- **SOHONOS can cause bone growth changes.** Children may stop growing while taking SOHONOS. Bone growth changes such as permanent early closure of the growth plate in growing children have happened with SOHONOS. Your healthcare provider will closely monitor your child's bone growth and height during treatment with SOHONOS.

WHAT SHOULD I AVOID WHILE TAKING SOHONOS?

- Do not get pregnant while taking SOHONOS. See "**WHAT ARE THE SERIOUS RISKS OF SOHONOS**"
- Avoid excessive exposure to sunlight and ultraviolet lights (e.g., tanning machines). SOHONOS may make your skin more sensitive to sunlight and ultraviolet light and you may burn more easily. You should use sunscreen and wear sunglasses and protective clothing that covers your skin to help protect against sunburn if you must be in the sunlight during treatment with SOHONOS.
- Avoid driving at night until you know if SOHONOS has affected your vision. SOHONOS may decrease your ability to see in the dark.
- Do not donate blood while taking SOHONOS and for 1 week after stopping SOHONOS.

WHAT ARE POSSIBLE SIDE EFFECTS OF SOHONOS?

- **Skin-related problems:** SOHONOS may cause skin-related problems including dry skin, lips and eyes, hair loss, itching, redness, rash, and skin peeling. You may be at increased risk of developing skin and soft tissue infections while taking SOHONOS. If you develop these symptoms, your healthcare provider may tell you to use a moisturizer, sunscreen, or artificial tears.

- **Bone mineral density problems:** SOHONOS can cause a reduction in bone mineral density (bone thinning) which can increase the risk of fractures in adults and children. Your healthcare provider should check you for this during treatment with SOHONOS

- **New or worsening mental health problems:** SOHONOS may cause new or worsening mental health problems that include depression, anxiety, mood changes, and suicidal thoughts and behaviors. If you have a

Please see Important Safety Information on pages 2-3 and accompanying full Prescribing Information, including Medication Guide with IMPORTANT WARNING.

history of mental health problems, you may be at a higher risk of developing these side effects. Call your healthcare provider if you develop new or worsening mental health symptoms during treatment with SOHONOS. Your healthcare provider should monitor you for signs of depression and refer you for appropriate treatment, if necessary.

- **Vision problems:** Decreased vision in the dark (night blindness). You may have difficulty seeing at night or in low lit areas. Your healthcare provider should send you to see an eye specialist if you experience vision problems.

The most common side effects of SOHONOS include:

- dry skin
- dry lips
- hair loss
- itching
- redness
- rash
- skin peeling
- drug eruption
- skin irritation
- swelling and small cracks in corner of the mouth
- nausea
- muscle and joint pain
- dry eyes
- headache
- fatigue

Please read the SOHONOS Medication Guide that comes with your medication for more details regarding the risks described above.

WHAT TO KNOW ABOUT SOHONOS IF YOU ARE FEMALE

SOHONOS must not be used by female patients who are or may become pregnant. There is a high risk that severe birth defects will result if pregnancy occurs while taking SOHONOS in any amount, even for short periods of time.

Your doctor will obtain a blood sample prior to SOHONOS treatment to determine if you are pregnant. Pregnancy testing will be done by your doctor periodically over the course of treatment with SOHONOS and one month after treatment discontinuation unless you are not at risk of becoming pregnant.

You must read and understand the information below. You and your doctor must talk about the steps to take to be treated with SOHONOS safely.

If you are a female who can get pregnant:

- Your doctor will explain the risk of harm to the unborn baby so you must understand why you must not get pregnant and what you need to do to prevent pregnancy.

- Your doctor will request that you do pregnancy tests before initiating treatment, periodically during treatment and one month after stopping your SOHONOS treatment.

- You must remain *abstinent* from heterosexual sex during treatment and for 1 month after treatment.

  -or-

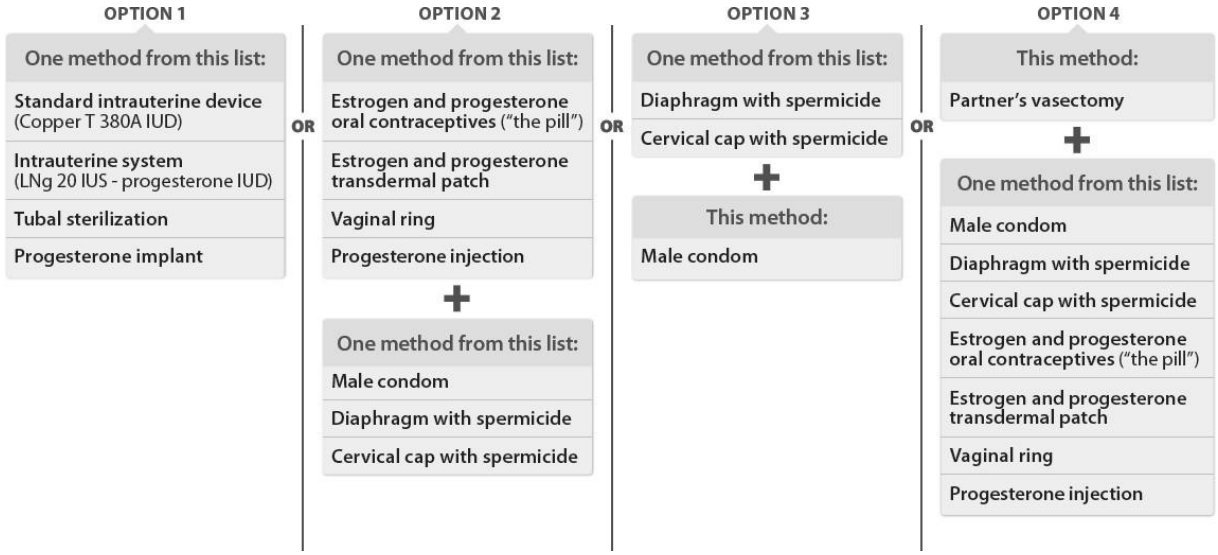
- You must use at least one *highly effective method of birth control* (such as an IUD) or *two effective methods (*such as combined hormonal contraception in combination with another method of contraception such as a barrier method*)* for at least 1 month before you start treatment with SOHONOS and continue using these methods of birth control during treatment and for 1 month after treatment if you are having heterosexual sex.

Please see Important Safety Information on pages 2-3 and accompanying full Prescribing Information, including Medication Guide with IMPORTANT WARNING.

Abstinence from heterosexual sex is only acceptable as “true abstinence.” True abstinence occurs when it is in line with your preferred and usual lifestyle. Periodic abstinence from heterosexual sex (such as calendar, ovulation, symptothermal, post-ovulation methods), the rhythm method, and withdrawal are not acceptable methods of contraception.

Refer to the table below for further details on birth control options.

Your Birth Control Options



Option 1: High Effective Methods | **Options 2, 3 or 4: Two Effective Methods**

The following are **unacceptable** forms of birth control:

- Progestin-only “mini-pill”
- Female condom
- Natural family planning (periodic abstinence, such as calendar, ovulation, symptothermal, post-ovulation methods; rhythm method; or breastfeeding) or withdrawal

If you are female and become pregnant during your treatment or in the month after stopping the treatment, you must notify your doctor immediately.

If you have any questions about acceptable birth control options while treated with SOHONOS, please ask your healthcare provider. You are encouraged to talk with your healthcare provider about any concerns or questions you may have.

HOW WILL I OBTAIN MY SOHONOS?

Your prescription will be sent to a specialty pharmacy that will ship the medication to your home.

If you have questions or concerns about SOHONOS, talk to your doctor. Please visit www.SOHONOS.com or call +1-855-463-5127 for more information about the SOHONOS Educational Program.

Please see full Prescribing Information, including Medication Guide with IMPORTANT WARNING on Birth Defects and Bone Growth Changes.

SOHONOS® (palovarotene)

Understanding the SOHONOS (palovarotene) Educational Program: A Guide for Caregivers of Growing Pediatric Patients

This brochure focuses on the risk that affects growing children and how these risks must be managed when taking SOHONOS.

The health information contained in this guide is provided for general educational purposes only. Your healthcare professional is the best source of information regarding your health. Please consult your healthcare professional if you have any questions about your health or treatment.

Please see full Prescribing Information, including Medication Guide with IMPORTANT WARNING on Birth Defects and Bone Growth Changes.

WHAT IS THE SOHONOS EDUCATIONAL PROGRAM?

The SOHONOS Educational Program is a program to educate prescribers, pharmacists, patients and their caregivers about the important risks related to SOHONOS.

WHAT IS SOHONOS?

SOHONOS is a prescription medicine used to reduce the amount of new heterotopic ossification in adults and children 8 years of age and older for females and 10 years of age and older for males with fibrodysplasia ossificans progressiva (FOP). SOHONOS is not recommended for females younger than 8 years of age or males younger than 10 years of age.

WHAT ARE THE SERIOUS RISKS OF SOHONOS?

- **SOHONOS can cause birth defects (deformed babies) if taken during pregnancy. Females who are pregnant or who plan to become pregnant must not take SOHONOS.**

  Females who can become pregnant:
  - Your healthcare provider will ask you to take a pregnancy test 1 week before starting treatment with SOHONOS, periodically during treatment, and 1 month after you stop treatment with SOHONOS.
  - You must use effective birth control (contraception) starting at least 1 month before starting treatment with SOHONOS, during treatment and for 1 month after the last dose. Talk to your healthcare provider about birth control methods that may be right for you.
  - If you become pregnant or think you may be pregnant during treatment with SOHONOS, stop taking SOHONOS and call your healthcare provider right away.

Because SOHONOS can cause birth defects, SOHONOS is only for people who can understand and agree to carry out all instructions for pregnancy prevention.

- **SOHONOS can cause bone growth changes.** Children may stop growing while taking SOHONOS. Bone growth changes such as permanent early closure of the growth plate in growing children have happened with SOHONOS. Your healthcare provider will closely monitor your child's bone growth and height during treatment with SOHONOS.

WHAT SHOULD I AVOID WHILE TAKING SOHONOS?

- Do not get pregnant while taking SOHONOS. See "**WHAT ARE THE SERIOUS RISKS OF SOHONOS**"
- Avoid excessive exposure to sunlight and ultraviolet lights (e.g., tanning machines). SOHONOS may make your skin more sensitive to sunlight and ultraviolet light and you may burn more easily. You should use sunscreen and wear sunglasses and protective clothing that covers your skin to help protect against sunburn if you must be in the sunlight during treatment with SOHONOS.
- Avoid driving at night until you know if SOHONOS has affected your vision. SOHONOS may decrease your ability to see in the dark.
- Do not donate blood while taking SOHONOS and for 1 week after stopping SOHONOS.

WHAT ARE POSSIBLE SIDE EFFECTS OF SOHONOS?

- **Skin-related problems:** SOHONOS may cause skin-related problems including dry skin, lips and eyes, hair loss, itching, redness, rash, and skin peeling. You may be at increased risk of developing skin and soft tissue infections while taking SOHONOS. If you develop these symptoms, your healthcare provider may tell you to use a moisturizer, sunscreen, or artificial tears.

- **Bone mineral density problems:** SOHONOS can cause a reduction in bone mineral density (bone thinning) which can increase the risk of fractures in adults and children. Your healthcare provider should check you for this during treatment with SOHONOS

- **New or worsening mental health problems:** SOHONOS may cause new or worsening mental health problems that include depression, anxiety, mood changes, and suicidal thoughts and behaviors. If you have a

Please see Important Safety Information on pages 2-3 and accompanying full Prescribing Information, including Medication Guide with IMPORTANT WARNING.

history of mental health problems, you may be at a higher risk of developing these side effects. Call your healthcare provider if you develop new or worsening mental health symptoms during treatment with SOHONOS. Your healthcare provider should monitor you for signs of depression and refer you for appropriate treatment, if necessary.

- **Vision problems:** Decreased vision in the dark (night blindness). You may have difficulty seeing at night or in low lit areas. Your healthcare provider should send you to see an eye specialist if you experience vision problems.

The most common side effects of SOHONOS include:

- dry skin
- dry lips
- hair loss
- itching
- redness
- rash
- skin peeling
- drug eruption
- skin irritation
- swelling and small cracks in corner of the mouth
- nausea
- muscle and joint pain
- dry eyes
- headache
- fatigue

Please read the SOHONOS Medication Guide that comes with your medication for more details regarding the risks described above.

ABOUT BONE GROWTH AND GROWTH PLATE CLOSURE

Young children and adolescents who are still growing have open growth plates. Growth plates are the area of growing tissue near the ends of the long bones in children and adolescents where growth occurs until the growth plates close.

The term “growth plate closure” refers to the point at which the growth plates no longer have the ability to increase the length of the bone. This typically occurs gradually over childhood, with full closure occurring near the end of puberty. This is also known as skeletal maturity.

ABOUT SOHONOS AND PREMATURE GROWTH PLATE CLOSURE

SOHONOS can cause the growth plates to close prematurely. For this reason, your child’s healthcare provider will closely monitor your child’s bone growth and height during treatment. Continued monitoring is recommended every 6-12 months until patients reach skeletal maturity or final adult height. Once the patient’s growth plates have all closed, indicating skeletal maturity or the patient has reached the final adult height, no further monitoring is necessary.

Should evidence of adverse effects on growth and/or premature epiphyseal closure be observed, further evaluation and increased monitoring may be required. The decision to temporarily interrupt SOHONOS during the evaluation period or permanently discontinue treatment should be made based on the individual benefit-risk determination. You are encouraged to talk with your healthcare provider about any concerns or questions you may have.

HOW WILL MY CHILD RECEIVE SOHONOS?

Your child’s prescription will be sent to a specialty pharmacy that will ship the medication to your home.

If you have questions or concerns about SOHONOS, talk to your doctor. Please visit www.sohonos.com or call +1-855-463-5127 for more information about the SOHONOS Educational Program.

Please see full Prescribing Information, including Medication Guide with IMPORTANT WARNING on Birth Defects and Bone Growth Changes.

SOHONOS® (palovarotene)

Attestation form for the SOHONOS® Educational Program

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.

Please see additional Important Safety Information on Page 3 and full Prescribing Information including BOXED WARNING and Medication Guide.

12/2025 SOH-US-000232 V3.0

Attestation Form for the SOHONOS® (palovarotene) Educational Program

Please complete and return this document to SOHONOSEducation@ipsen.com.

Prescriber Name: _____

Prescriber NPI: _____

Facility Name: _____

Facility Address: _____

City: _____ **State:** _____ **Zip code:** _____

I attest that I have read and understand the following materials for the SOHONOS Educational Program:

- SOHONOS® (palovarotene) Prescribing Information, including Medication Guide
- SOHONOS® (palovarotene) Educational Program – A Guide for Prescribers and Pharmacists
- SOHONOS® (palovarotene) Educational Program – A Guide for Female
- SOHONOS® (palovarotene) Educational Program – A Guide for Growing Patients and their Caregiver
- SOHONOS® (palovarotene) Educational Program – A Guide for Patients and their Caregivers

Signature: _____ **Date:** _____

IMPORTANT SAFETY INFORMATION (CONT.)

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.
- **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.

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 full Prescribing Information, including BOXED WARNING.