

FOR FEMALES ≥ 8 AND MALES ≥ 10 YEARS OLD WITH FIBRODYSPLASIA OSSIFICANS PROGRESSIVA (FOP)

WHAT COULD REDUCING THE AMOUNT OF NEW HETEROTOPIC OSSIFICATION (HO) MEAN FOR YOU?

A GUIDE FOR PEOPLE CONSIDERING SOHONOS

This illustration was co-created with people living with FOP.



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.

Please see additional Important Safety Information throughout and on pages 15-16, and the accompanying Medication Guide with IMPORTANT WARNING on Birth Defects and Bone Growth Changes.

WHAT IS FOP?

Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare genetic disorder

FOP causes new bone to form in muscles, tendons, and ligaments, severely restricting movement.

FIBRODYSPLASIA

Abnormal tissue growth

OSSIFICANS

Bone formation

PROGRESSIVA

Progressive condition



Image from Kitoh H. *Biomedicines*. 2020;8(9):325. Used with permission under Creative Commons CC BY 4.0 license. Left foot is simulated by reflecting the original image. <https://creativecommons.org/licenses/by/4.0/deed.en>

- **FACT: Almost everyone with FOP has big toes that are shortened and bent inward.**

What causes FOP?

Everyone has the **ACVR1 gene**.

- The **ACVR1** gene is responsible for making the **ACVR1** protein
- The **ACVR1** protein interacts with other proteins (called bone morphogenetic proteins) that control some of the signals responsible for building cartilage and bone

In people with FOP, a genetic mutation occurs in the ACVR1 gene.

- In most people with FOP, the genetic mutation happens for no known reason, although it can be inherited in rare cases
- The mutated **ACVR1** gene makes an abnormal protein, which is overactive. This leads to the growth of **extra bone outside the skeleton, called heterotopic ossification (HO)**



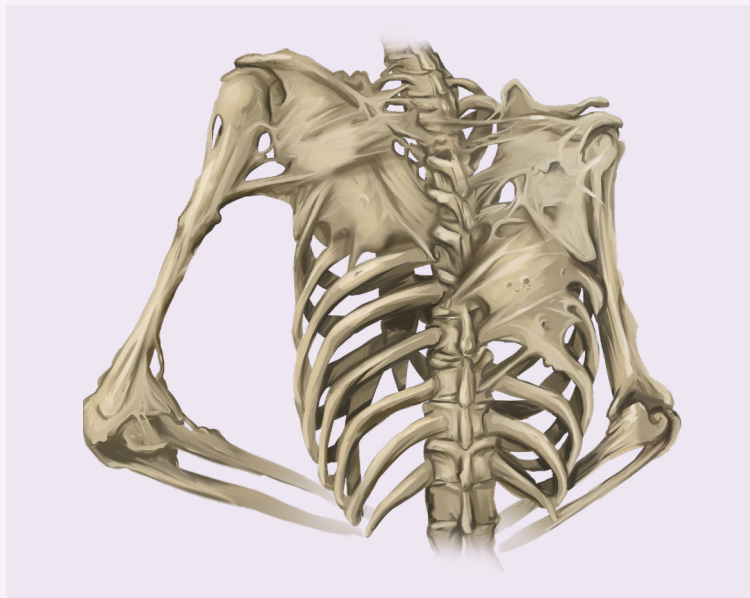
FOP is so rare, only about 900 people in the world are currently diagnosed.

UNDERSTANDING HETEROTOPIC OSSIFICATION (HO)

HO is the process of new bone forming outside the skeleton

- In people with FOP, HO can happen because of an injury, illness, or for no known reason
- The HO that is formed does not go away
- Over time, HO can build up, causing the joints to lock up, making it hard to move

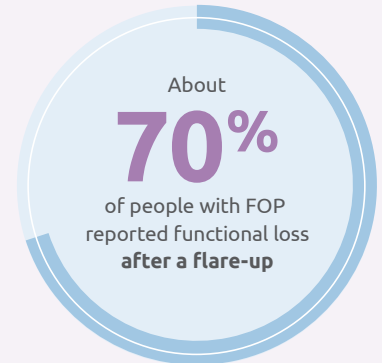
In people with FOP, bone forms outside the skeleton, restricting movement.




Artistic depiction, not an actual person with FOP. Disease progression and HO formation vary for all individuals with FOP.

HO may form with or without a flare-up

In a global survey of 500 people with FOP:



[Learn more about flare-ups on the next page](#) 

The impact of HO on the skeleton

Extra bone has formed over the shoulder joints, shoulder blades, and the left elbow. A person with this much HO would have limited mobility in their upper body.



Once HO forms, it is irreversible.

HOW TO IDENTIFY A FLARE-UP

Flare-ups are unpredictable episodes of soft-tissue swelling

Starting in early childhood, most people with FOP develop sudden swellings on their head, neck, or back, called “flare-ups.”

- Flare-ups can turn soft tissues—such as muscles, tendons, and ligaments—into bone that does not go away



Image from Tiwari et al. *Cureus*. 2018;10(7):e2955. Used with permission under Creative Commons CC BY 3.0 license. <https://creativecommons.org/licenses/by/3.0/>

These are some of the symptoms of a flare-up



Swelling



Pain



Reduced movement



Stiffness



Warmth (in the affected area)

- **Heterotopic ossification (HO) often forms after a flare-up.**

Flare-ups are different for everyone. Keep track of your flare-up symptoms and share them with your care team.



If you think you are having a flare-up, talk to your healthcare provider as soon as possible.

TRYING TO PREVENT FLARE-UPS IS IMPORTANT

In people with FOP, minor injuries or illness can cause flare-ups that can lead to the formation of disabling heterotopic ossification (HO)

SOME EVENTS THAT CAN CAUSE FLARE-UPS INCLUDE:

Biopsies (the removal of cells or tissue to be looked at under a microscope)

Surgeries

Intramuscular injections (an injection into a muscle), vaccines

Viral illness


Contact sports

Overstretching the jaw at the dentist

Injuries such as bumps, bruises, or falls

Overstretching of muscles or muscle fatigue

Passive range of motion exercises
(where the physical therapist moves the person's body for them)

 **Flare-ups can also appear suddenly, without any known cause.**



Talk to your healthcare provider right away if you experience any of these flare-up triggering events.

Please see additional Important Safety Information throughout and on pages 15-16, and the accompanying Medication Guide with IMPORTANT WARNING.

WHAT IS SOHONOS?

SOHONOS is a prescription medication used to reduce the amount of new heterotopic ossification (HO) in adults and children with FOP (8 years of age and older for females and 10 years of age and older for males)

SOHONOS is part of a class of medicines called retinoids. Retinoids are molecules that are similar to vitamin A, which plays an important role in bone growth, vision, and the immune system.

- SOHONOS reduces the volume of new HO. SOHONOS does not treat flare-up symptoms, such as pain and swelling.



This illustration was co-created with people living with FOP.

IMPORTANT SAFETY INFORMATION (continued)

What is the most important information I should know about SOHONOS? (continued)

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.

HOW WAS SOHONOS STUDIED?

SOHONOS was studied in a clinical trial called MOVE, the largest clinical trial in FOP to date.

TWO STUDIES WERE IMPORTANT FOR ASSESSING HOW WELL SOHONOS WORKS

MOVE: A PHASE 3 CLINICAL TRIAL

A **Phase 3 clinical trial** tests how well a drug works and how safe a drug is. Phase 3 trials typically involve many people with a particular condition.

NATURAL HISTORY STUDY (NHS)

The untreated people were part of a **natural history study**. An NHS gathers information on how a disease changes over time in a group of people. It is not designed to test how well a particular medicine works to treat a disease.

WHO PARTICIPATED?

97 people with FOP who were at least 4 years old and had not had a flare-up for at least 1 month before the start of the trial.

101 people with FOP who did not take SOHONOS.

WHAT WAS THE MAIN OBJECTIVE?

To evaluate how well SOHONOS was able to reduce the formation of new heterotopic ossification (HO) annually for certain people with FOP as assessed by low-dose, whole body CT (WBCT) imaging (excluding head).

To evaluate how FOP progresses and how much HO a person with FOP typically has, considering their current age.

MOVE was designed to evaluate how well SOHONOS works and how safe it is for people with FOP. In the trial, people with FOP were treated with SOHONOS and their doctor and care team assessed how much new HO was forming in their bodies. People taking SOHONOS were also evaluated for potential side effects.

Please see additional Important Safety Information throughout and on pages 15-16, and the accompanying Medication Guide with IMPORTANT WARNING.

HOW WAS SOHONOS STUDIED? (continued)

What dose did people receive during the MOVE trial?

People with FOP received 5 mg of SOHONOS daily. Their daily dose was increased if they experienced a flare-up (at least one symptom [eg, pain, swelling, redness] consistent with a previous flare-up) or a substantial high-risk traumatic event likely to lead to a flare-up.*

Flare-up dosing was 20 mg once daily for 4 weeks followed by 10 mg once daily for 8 weeks.

- The 12-week treatment was restarted if they had another flare-up or substantial high-risk traumatic event
- The increased dose could be extended in 4-week increments if their flare-up symptoms did not go away

*Chronic and flare-up dosing was adjusted according to body weight in skeletally immature children (children who had not reached at least 90% skeletal maturity defined as a bone age of ≥ 12 years for girls and ≥ 14 years for boys).

The results of MOVE were compared to the results of another study called the Natural History Study (NHS), where doctors assessed how much new HO was forming in untreated people living with FOP.

To be included in the final analysis, participants needed to have a baseline assessment of their HO volume at the start of the trial and at least 1 assessment after the trial began.

 **Talk to your doctor if you have any questions about how SOHONOS was evaluated.**

IMPORTANT SAFETY INFORMATION (continued)

What should I tell my healthcare provider before taking SOHONOS?

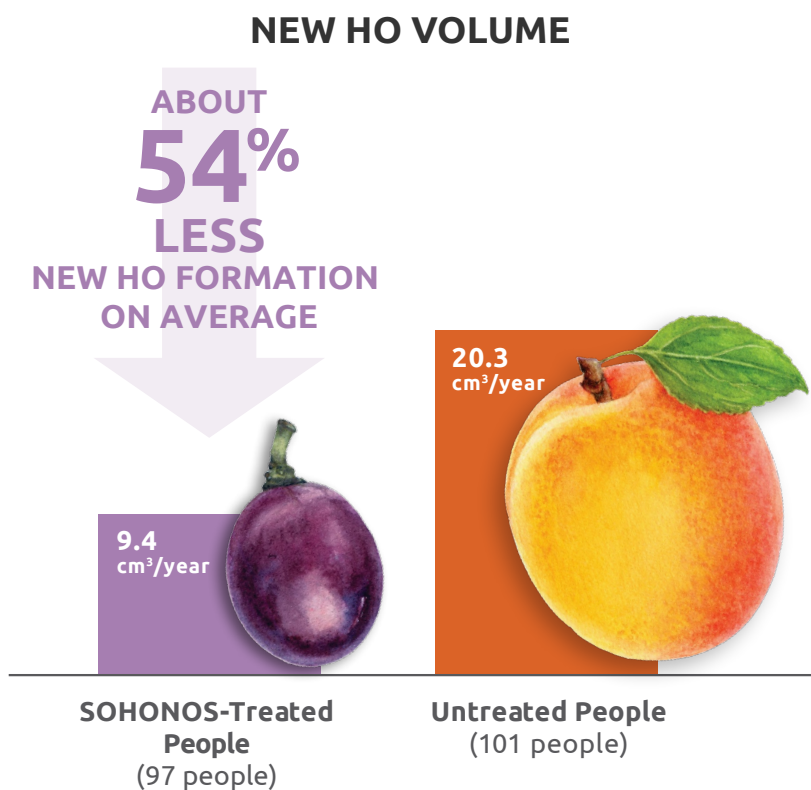
Before taking SOHONOS, tell your healthcare provider about all your medical conditions, including:

- 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.

RESULTS FROM THE MOVE CLINICAL TRIAL

SOHONOS was found to reduce the amount of new heterotopic ossification (HO)

In the MOVE clinical trial over the course of one year, people treated with SOHONOS on average formed less new HO compared to the separate NHS study of people with FOP who were untreated. The difference in volume is comparable to that of a grape and an apricot.



A statistical analysis of the people treated with SOHONOS in MOVE compared to untreated people in another study found the treatment effect was about 10.9 cm³/year with 95% confidence interval (-21.2 cm³/year, -0.6 cm³/year).

IMPORTANT SAFETY INFORMATION (continued)

What should I tell my healthcare provider before taking SOHONOS? (continued)

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.

Please see additional Important Safety Information throughout and on pages 15-16, and the accompanying Medication Guide with IMPORTANT WARNING.

HOW IS SOHONOS TAKEN?

SOHONOS capsules may be swallowed whole or opened and should be taken with food at the same time each day



The recommended dosing for SOHONOS includes a chronic daily dose and modified dosing specific to flare-ups.

- Avoid consuming foods or drinks that have grapefruit in them while taking SOHONOS, as they may increase the medication levels in your blood
- This medicine is not recommended for girls under 8 years of age and boys under 10 years of age due to the risk of stopping normal bone growth

If swallowing the capsule is challenging:

- The capsules may be opened and the contents sprinkled onto a teaspoon of soft food and taken immediately.
- If not taken immediately, it can be taken after a maximum of 1 hour after the sprinkling provided it was maintained at room temperature and not exposed to direct sunlight.

If the dose has been missed by more than 6 hours:

- Skip the missed dose and continue with the next scheduled dose. Do not take two doses at the same time or in the same day.

If a patient takes more than the prescribed dose:

- Call your healthcare provider or poison control center right away.

For females taking SOHONOS who can become pregnant:

- Your doctor will require a negative pregnancy test within one week prior to initiating and periodically during SOHONOS therapy
- If you become pregnant or think you may be pregnant during treatment with SOHONOS, stop taking SOHONOS and call your doctor right away



Take SOHONOS exactly as your healthcare provider prescribes it.

IMPORTANT SAFETY INFORMATION (continued)

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.

HOW IS A SOHONOS DOSE DETERMINED?

SOHONOS dosing is different for every person, and changes could be made by your doctor throughout treatment

For females 8-13 and males 10-13 years old dosing is weight-based. It is important that your healthcare provider has an accurate weight and that they check your weight often as you grow.

If you experience a flare-up your doctor will temporarily increase your dose. Talk to your doctor if you experience symptoms of a flare-up or experience a flare-up triggering event (such as the flu or a fall).

RECOMMENDED DOSAGE FOR PEOPLE 14 YEARS AND OLDER	
Daily (chronic) dose	Flare-up dose
5 mg once daily	<p>20 mg once daily, for 4 weeks</p> <p>FOLLOWED BY</p> <p>10 mg once daily, for 8 weeks (even if symptoms resolve earlier)</p>

RECOMMENDED SOHONOS WEIGHT-BASED DOSAGE FOR CHILDREN AGED 8 TO 13 YEARS FOR FEMALES AND 10 TO 13 YEARS FOR MALES*			
Weight	Daily Dosage	Week 1 to 4 Flare-up Dosage	Week 5 to 12 Flare-up Dosage
10 kg to 19.9 kg (22 lbs to 43.9 lbs)	2.5 mg	10 mg	5 mg
20 kg to 39.9 kg (44 lbs to 87.9 lbs)	3 mg	12.5 mg	6 mg
40 kg to 59.9 kg (88 lbs to 132.1 lbs)	4 mg	15 mg	7.5 mg
≥ 60 kg (≥ 132.2 lbs)	5 mg	20 mg	10 mg

*Once daily.

This table is provided for educational purposes only. Always consult with your doctor before making any changes to your dose.

Please see additional Important Safety Information throughout and on pages 15-16, and the accompanying Medication Guide with IMPORTANT WARNING.

HOW IS A SOHONOS DOSE DETERMINED? (continued)

Your SOHONOS dose is increased during a flare-up

Flare-up treatment should begin at the onset of the first symptom of an FOP flare-up or substantial high-risk traumatic event likely to lead to a flare-up. Talk to your doctor if you think a flare-up is starting or if you experience an event likely to lead to a flare-up.*

- Your chronic dose should stop at the time of initiation of flare-up treatment; re-initiation of the chronic (daily) dosing should occur after completion of the flare-up treatment
- If flare-up symptoms do not resolve at the end of the 12-week period, the week 5 to 12 once-daily-dose modification may be extended in 4-week intervals until the flare-up symptoms resolve
- If you experience marked worsening of the original flare-up or another flare-up at a new location at any point during flare-up treatment, the 12-week treatment should be restarted

*High-risk traumatic events include surgery, intramuscular immunization, mandibular blocks for dental procedures, muscle fatigue, blunt muscle trauma from bumps, bruises, or falls, or influenza-like viral illnesses. Symptoms of an FOP flare-up typically include, but are not limited to, localized pain, soft-tissue swelling/inflammation, redness, warmth, decreased joint range of motion, and stiffness.

Side effects may require your doctor to reduce your daily or flare-up dose

If side effects continue, your doctor may continue to lower your dose or discontinue SOHONOS.

If you are taking certain medications called moderate CYP3A inhibitors, your doctor will reduce your dose as outlined in the full Prescribing Information. Talk to your doctor about all the medications you take, in addition to SOHONOS.

 **Please see the full Prescribing Information and Medication Guide for complete dosing information. Talk to your doctor if you have any questions about how SOHONOS is given.**

IMPORTANT SAFETY INFORMATION (continued)

What should I avoid while taking SOHONOS? (continued)

- 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.

SOHONOS CAN CAUSE SERIOUS SIDE EFFECTS



Birth defects

SOHONOS can cause birth defects (deformed babies) if taken during pregnancy. People 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 with SOHONOS.

You must use effective birth control (contraception) and pregnancy must be avoided:

- 1 month before starting SOHONOS
- While taking SOHONOS (including periods between flare-up treatment)
- 1 month after stopping SOHONOS
- Because SOHONOS can cause birth defects, SOHONOS is only for people who can understand and agree to carry out all instructions for pregnancy prevention

Talk to your healthcare provider about birth control methods that may be right for you.



Bone and 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.



The SOHONOS Educational Program was created to teach you about the important risks related to taking SOHONOS. All people taking SOHONOS must complete the program.

 [LEARN MORE AT SOHONOS.COM](https://www.sohonos.com)

Please see additional Important Safety Information throughout and on pages 15-16, and the accompanying Medication Guide with IMPORTANT WARNING.

SKIN AND MUCOUS TISSUES CAN BE AFFECTED BY SOHONOS

SOHONOS can cause mucocutaneous side effects related to the skin and mucous tissues (ie, inside the mouth) that should be managed proactively

SOME PEOPLE WHO TAKE SOHONOS MAY EXPERIENCE:	TO HELP MANAGE THESE SIDE EFFECTS, TRY USING:
Dry/red/irritated/peeling/itchy skin	Creams/lotions
Rash	Sunscreen
Eczema	Lip moisturizers
Possible sun sensitivity	Eye drops
Dry eye	Protective clothing
Hair loss	Sunglasses



If you have any questions about side effects, talk to your healthcare provider.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about SOHONOS?

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- 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.

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Who should not take SOHONOS?

Do not take SOHONOS if you are pregnant, or allergic to medicine called 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.

IMPORTANT SAFETY INFORMATION (continued)

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.

What are the possible side effects of SOHONOS?

SOHONOS can cause serious side effects, including:

- **skin-related problems** 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 | • rash | • nausea |
| • dry lips | • skin peeling | • muscle and joint pain |
| • hair loss | • drug eruption | • dry eyes |
| • itching | • skin irritation | • headache |
| • redness | • swelling and small cracks
in corner of the mouth | • 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 1-800-FDA-1088.

Please see accompanying full Prescribing Information, including Medication Guide with IMPORTANT WARNING.

DEDICATED SUPPORT

IPSENCARES[®]

Coverage, Access, Reimbursement & Education Support

IPSEN CARES patient support program can help you get access to your SOHONOS (palovarotene) prescription with the information and support you need

Your IPSEN CARES Team

Patient Access Managers (PAM)

are knowledgeable about health insurance and can help you understand what is needed to get access to, and afford, SOHONOS.

Your PAM can:

- Provide information and support to help you prepare to talk to your healthcare provider, specialty pharmacy, and insurance company
- Work with you to understand your specific situation and healthcare coverage needs
- Help to identify possible financial support programs for which you may qualify

Patient Education Liaisons (PEL)

are healthcare educators and are experienced in working with individuals living with certain conditions.

Your PEL can:

- Provide educational information to help you, your family, and your caregivers better understand your condition, access needs, and prescribed treatment expectations
- Help you to understand your specific situation and healthcare needs based on the direction and advice provided by your healthcare provider
- Work in connection with your healthcare providers to support you and your caregivers through some of the many challenges of living with your condition

Personalized Support Services



Financial & Insurance Assistance



Dedicated, Individualized Support



Continuity of Care



Educational Materials & Programs

Getting Started with IPSEN CARES

Enrolling in IPSEN CARES is quick and easy. Your healthcare provider must complete the IPSEN CARES Enrollment Form, and you must review and sign the patient authorization section.



TO LEARN MORE ABOUT IPSEN CARES

Phone: 1-866-435-5677

Hours: 8:00 am – 8:00 pm ET Monday – Friday

Website: www.IPSENCARES.com

Email: Support@ipsencares.com

TALK TO YOUR DOCTOR ABOUT SOHONOS

THE *FIRST AND ONLY* MEDICINE TO REDUCE THE AMOUNT OF NEW HO IN FOP

FOR FEMALES ≥ 8 AND MALES ≥ 10 YEARS OLD

This illustration was co-created
with people living with FOP.



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[SOHONOS.COM](https://sohonos.com)

IMPORTANT SAFETY INFORMATION

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, and fatigue.

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