

CHOLBAM[®] (cholic acid) in Smith-Lemli-Opitz Syndrome (SLOS)*

A Patient-Caregiver Resource Guide

*No evaluable patients with SLOS were represented in pivotal clinical trials.



CHOLBAM is a prescription medication. It is a bile acid used for the treatment of bile acid synthesis disorders (malfunction in the production of bile acid in the liver) due to a lack of a single enzyme responsible for bile acid production.

The safety and effectiveness of CHOLBAM on symptoms outside of the liver have not been studied.

Please see Important Safety Information on pages 16-17 and accompanying full Prescribing Information.



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Please see Important Safety Information on pages 16-17 and accompanying full Prescribing Information.

Introduction

Your loved one has been diagnosed with [Smith-Lemli-Opitz Syndrome \(SLOS\)](#) and is currently being treated with CHOLBAM® (cholic acid) or is considering taking CHOLBAM.

This resource guide is intended to help get you started on the path to learning about SLOS and CHOLBAM, and to help you be the best advocate you can be for your loved one. In the following pages, you will find useful information about SLOS and CHOLBAM, and a list of organizations to keep you connected to the SLOS community. This information may also help you think of questions to ask your doctor during scheduled visits.

For your convenience, words in the color [blue](#) are defined on page 15 of this resource guide in the [Glossary/Key terms](#) section.



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What is Smith-Lemli-Opitz Syndrome (SLOS)?

Smith-Lemli-Opitz Syndrome is a rare genetic condition caused by a mutation in the *DHCR7* gene involved in [cholesterol](#) production, which disrupts the body's ability to make cholesterol. Cholesterol is essential for proper growth and development.

What happens if the body cannot make cholesterol?

- Low levels of cholesterol may lead to poor nutrition and poor growth.
- Because cholesterol is also necessary for production of bile acids in the liver, it is likely that low cholesterol levels in SLOS impair bile acids from being made.
- In addition to low cholesterol absorption that can delay growth and development, some patients may experience elevated or abnormal liver function levels, such as AST and ALT, which are important measurements of liver health.



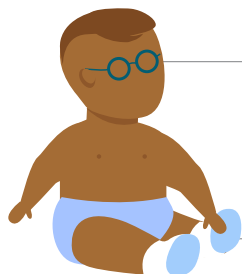
The addition of CHOLBAM® (cholic acid), a bile acid replacement therapy, may be able to help address these key issues.

What are the possible side effects of CHOLBAM?

Serious Side Effects: You will need to undergo laboratory testing periodically while on treatment to assess liver function. CHOLBAM may worsen liver function. Tell your doctor right away if you experience symptoms associated with worsening of liver function (e.g., skin or the whites of eyes turn yellow, urine turns dark or brown [tea colored], pain on the right side of stomach, bleeding or bruising occurs more easily than normal, or increased lethargy). Your doctor will decide if you need to discontinue treatment with CHOLBAM.

How many people have SLOS?

Although rare, SLOS is a common [autosomal recessive](#) disorder.



In the **UNITED STATES**, SLOS
is **ESTIMATED TO OCCUR** in
1 in 20,000 BIRTHS

What is the prognosis for my loved one?

Currently, there is no cure for [Smith-Lemli-Opitz Syndrome](#), but its symptoms may be able to be managed. Some medical problems are generally related to eating, growth, and development. In addition, the effects of low [cholesterol](#) production and use in the body may cause other serious medical problems, such as heart or kidney defects.

Ask your physician how specific issues can be managed, because it is important to manage as many of the symptoms as possible.

What are bile acids, and why are they important?

[Bile acids](#) are made from [cholesterol](#), so a patient with SLOS with very low cholesterol levels cannot make a sufficient amount of bile acids. Therefore, these patients may have a bile acid deficiency.

Bile acids are essential for the absorption of fats and fat-soluble vitamins and nutrients in the intestines.



Without sufficient bile acids, patients cannot properly absorb cholesterol and other nutrients.

Also, bile acids help digest dietary cholesterol in the intestine. Low bile acid levels likely prevent dietary cholesterol from being absorbed properly and contribute to the cholesterol deficiency seen in SLOS.

Two key bile acids necessary for proper digestion, absorption, and toxin removal are:

- [Cholic acid](#)
- [Chenodeoxycholic acid](#)

Abnormal bile flow or production can result in:

- Poor absorption of vital nutrients, which may lead to poor nutrition and growth
- Accumulation of toxic materials in the body

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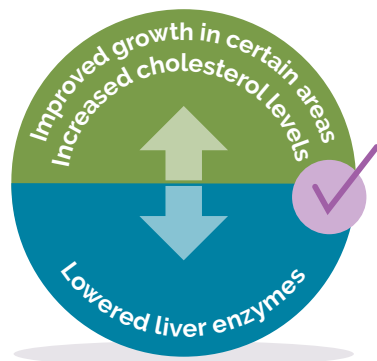
How might CHOLBAM® (cholic acid) help my loved one?

Current treatments for [Smith-Lemli-Opitz Syndrome](#) include supplementing the patient's diet with [cholesterol](#), antioxidants, and [cholic acid](#).

CHOLBAM is a [bile acid replacement therapy](#) for cholic acid,

CHOLBAM may help patients*:

- Increase cholesterol levels†
- Grow on schedule*‡
- Lower liver enzymes



CHOLBAM has been FDA approved and available since 2015.

It is used for the treatment of bile acid synthesis disorders (BASDs), which are caused by defects in the enzyme that makes bile acids. Among the different known BASDs, SLOS is one of the few conditions caused by a defect in only a single enzyme.

The safety and effectiveness of CHOLBAM on symptoms outside of the liver have not been studied.

*No SLOS patients were included in the pivotal clinical trials for CHOLBAM. Patients had other bile acid synthesis disorders due to single enzyme defects.

†CHOLBAM was studied in a pilot study. Long-term studies are needed to determine durability of effect and possible clinical benefits.

‡In a two-month pilot study, 9 of 12 patients showed an increasing trend in weight gain from baseline but did not reach statistical significance.

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As with any medication, there is a possibility of side effects. In clinical studies, the most common side effect in about 2% of patients taking CHOLBAM was diarrhea. All other side effects were less than or equal to 1% of patients.

Patients taking CHOLBAM will need to undergo laboratory testing periodically while on treatment to assess liver function. CHOLBAM may worsen liver function. Call your child's doctor right away if any of the following occur, as these may be signs of worsening liver function:

- Yellowing of the skin or whites of the eyes.
- Dark or brown (tea-colored) urine.
- Pain on the right side of the stomach.
- Bleeding or bruising that occurs more easily than normal.
- Increased tiredness.



What is Mirum Access Plus?

Mirum Access Plus is a comprehensive support program for patients who have been prescribed CHOLBAM® (cholic acid) capsules and their caregivers. Once enrolled in the program, patients and caregivers are assigned a dedicated team of professionals to help them throughout the treatment journey.



If you have any questions about Mirum Access Plus, contact us at: 1-855-MRM-4YOU (1-855-676-4968) Monday through Friday, 8:00 AM through 8:00 PM ET.



Mirum Access Plus includes coordinators, pharmacists, and navigators who can:

- Help you understand your loved one's disease
- Provide you with tips to help manage your loved one's treatment
- Answer your questions about dosing and treatment regimens
- Offer support with questions about or issues you may have with insurance
- Coordinate monthly prescription refills and send reminders so patients never run out of medication
- Arrange for delivery of medication directly to patients
- Communicate with your doctors

Please visit www.Cholbam.com to learn more about the patient support services **Mirum Access Plus** provides

Please see Important Safety Information on pages 16-17 and accompanying full Prescribing Information.

How to take CHOLBAM® (cholic acid)

- CHOLBAM is available in 50 mg and 250 mg capsules.
- The recommended dosage of CHOLBAM is 10 to 15 mg per kg of body weight taken orally once daily, or in 2 divided doses. Do not adjust the dose without first consulting with your loved one's doctor.
- The recommended dosage will change as weight changes. Your loved one's doctor will adjust as needed, particularly during periods of rapid growth or based on certain other conditions or diagnoses.
- Talk to your loved one's doctor about the right dosage and how many capsules should be taken each day.
- Take CHOLBAM with food.
- Take CHOLBAM at least 1 hour before or 4 to 6 hours after taking a bile acid binding resin or an aluminum-based antacid.
- Do not crush or chew the capsules.



For patients who cannot swallow capsules, the capsules can be opened and the contents mixed with either infant formula or expressed breast milk (for younger children), or soft food such as mashed potatoes or apple puree (for older children and adults) in order to mask any unpleasant taste.

- 1 Hold the capsule over the prepared liquid/food, gently twist open, and allow the contents to fall into the liquid/food.
- 2 Mix the entire capsule contents with one or two tablespoons (15 mL to 30 mL) of infant formula, expressed breast milk, or soft food such as mashed potatoes or apple puree.
- 3 Stir for 30 seconds.
- 4 The capsule contents will remain as fine granules in the milk or food and will not dissolve.
- 5 Administer the mixture immediately.

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What questions should I ask during routine check-ups?

Here you can jot down your questions or observations for your loved one's next scheduled healthcare appointment.

- What signs/symptoms should I be watching for in my loved one?
- Which specialists might help my loved one?
- When and how often should my loved one be evaluated by a specialist?
- Is my loved one's growth on schedule?
- Should I modify my loved one's diet?
- What are my loved one's latest test results and what do they mean?
- If my loved one has _____, what therapy might help to manage it? (insert specific symptom)
- How might my loved one's symptoms change over time?
- Where can I get more information or support?

My questions

Please see Important Safety Information on pages 16-17 and accompanying full Prescribing Information.

What other resources are available?

For more information, you can visit the following resources:*



smithleliopitz.org

The Smith-Lemli-Opitz Foundation works worldwide to improve the quality of life for people with Smith-Lemli-Opitz Syndrome. The Smith-Lemli-Opitz Foundation raises awareness of the syndrome and funds research to improve treatments with the hope of someday finding a cure.



rarediseases.org

The National Organization for Rare Disorders (NORD) is an organization dedicated to identifying, treating, and curing rare disorders through education, advocacy, research, and service.



GARD Genetic and Rare Diseases Information Center

rarediseases.info.nih.gov

GARD is a program of the National Institutes of Health (NIH) that provides free access to reliable, easy-to-understand information about genetic and rare diseases.



hpo.jax.org

The Human Phenotype Ontology (HPO) project provides an ontology of medically relevant phenotypes, disease-phenotype annotations, and the algorithms that operate on these.

*Disclaimer: Mirum Pharmaceuticals is not affiliated with the listed resources.

Glossary/Key terms

Autosomal: An abnormal gene where one copy must be inherited from each parent for a trait to appear.

Autosomal recessive: Both genes in a pair must be abnormal to cause disease.

Bile: Bile is a fluid that contains water, certain minerals, and other materials including bile acids, lipids, cholesterol, and an orange-yellow pigment (bilirubin). Bile aids in digestion and absorption of dietary fats, vitamins, and other nutrients and it aids in the elimination of excess cholesterol, bilirubin, waste, and toxins from the body.

Bile acids: Bile acids are compounds that aid in digestion and absorption of dietary fats, vitamins, and other nutrients and in the elimination of excess cholesterol, bilirubin, waste, and toxins from the body.

Cholesterol: A waxy substance that is present in animal cells and tissues, and is important in bodily processes.

Cholic acid: One of the primary bile acids made in the liver under healthy conditions.

Liver enzymes: Special proteins that help the body break down and use (metabolize) other substances. Liver enzymes can also provide information on the health of the liver.

Replacement therapy: Treatment that aims to replace, or make up a deficit of, a substance normally present in the body.

Smith-Lemli-Opitz Syndrome (SLOS): SLOS results from an autosomal recessive mutation on a gene involved in cholesterol production, which disrupts the body's ability to make cholesterol.

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WHAT IS CHOLBAM® (cholic acid) capsules?

CHOLBAM is a prescription medicine. It is a bile acid used for

- Treatment of bile acid synthesis disorders (malfunction in the production of bile acid in the liver) due to a lack of a single enzyme responsible for bile acid production.
- Treatment (in addition to other treatments) of peroxisomal disorders (a loss of function in important parts of the cell), including Zellweger spectrum disorders, in patients who show signs or symptoms of liver disease, pale stools due to too much fat, or problems resulting from not absorbing certain vitamins (A, D, E, K).

The safety and effectiveness of CHOLBAM on symptoms outside of the liver have not been studied.

IMPORTANT SAFETY INFORMATION

CHOLBAM may not be right for you. Before taking CHOLBAM, tell your doctor about:

- **All health conditions you may have and any medications you may be taking.**
- **If you are pregnant or plan to become pregnant.**
- **If you are breastfeeding or plan to breastfeed.**

What are the possible side effects of CHOLBAM?

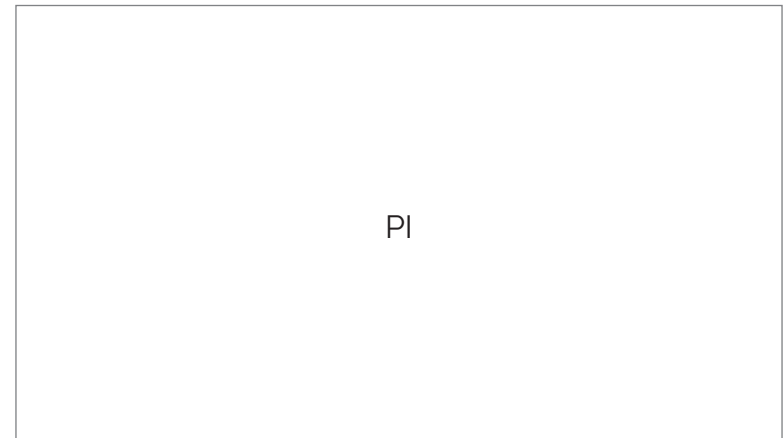
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- **Most Common Side Effects:** Diarrhea, acid reflux that damages the lining of the esophagus, discomfort and fatigue, yellowing of skin or eyes, skin lesion, nausea, abdominal pain, formation of growths in the intestinal tract, urinary tract infection, nerve damage causing change in sensation in extremities.

These are not all the possible side effects of CHOLBAM. Tell your doctor if you have any side effect that bothers you or that does not go away.

You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Mirum Pharmaceuticals at 1-855-MRM-4YOU.

Please see accompanying full Prescribing Information.



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Smith-Lemli-Opitz Syndrome (SLOS) is a rare genetic condition with a range of symptoms and severity.

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- Increase cholesterol†
- Grow on schedule*‡
- Lower liver enzymes

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- Once enrolled in the program, you will be assigned a dedicated team of professionals to provide education and support throughout the treatment journey.

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