

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is to be supplied by physician's prescription only

CHOLBAM 50 mg
CHOLBAM 250 mg
Hard capsules

Active ingredient:

Cholic acid 50, 250 mg

For the list of inactive ingredients – see section "Additional information".

Read the entire leaflet carefully before you start using this medicine. This leaflet contains essential information about this medicine. If you have any further questions, refer to the physician or the pharmacist. This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar.

Cholbam contains cholic acid.

Your liver makes cholic acid in your body naturally when it makes bile, which is a fluid that helps with digesting and absorbing fats and vitamins from your food. Cholic acid also helps the normal process of children's growth and development.

Cholbam is intended for use in cases where there is an inborn problem producing cholic acid. **Cholbam** replaces the cholic acid which the body does not make; this helps produce bile acid in your body and prevents accumulation of harmful substances in your liver.

In infants, cholic acid treatment helps normal development of the liver and the blood-bile cycle.

Cholbam can be used from the age of one month. Patients who have been diagnosed with a condition that requires **Cholbam** treatment will need this treatment for the rest of their lives.

What is this medicine used for?

Cholbam is intended to treat infants from one month old, children and adolescents up to 18 years old, and adults who have an inborn problem producing bile acids, because one of the following enzymes is missing:

- Sterol 27-hydroxylase (presented as cerebrotendinous xanthomatosis, CTX)
- 2- (or α -) methylacetyl-CoA racemase (AMACR)
- Cholesterol 7 α -hydroxylase (CYP7A1)
- 3 β -hydroxy-5-C27-steroid oxidoreductase (3 β -hydroxy-5-C27-steroid dehydrogenase/isomerase or 3 β -HSD or HSD3 β 7)

Therapeutic group: Bile acids.

Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient Cholic acid or to any of the other ingredients that this medicine contains (see section "Additional information").
- You are taking phenobarbital (a medicine for treating epilepsy) (see section "Drug interactions").

Special warnings regarding the use of this medicine

- At different times during the course of this treatment your physician will order blood and urine tests to see how this medicine is affecting your body and to find the dose that is best for you. In cases of accelerated growth, illness, or pregnancy, you will need more frequent tests.
- If you have a condition called familial hypertriglyceridemia (high levels of fat in the blood) your physician may raise your dose of **Cholbam**.
- If you need to stop the treatment your physician will give you instructions.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medications and nutritional supplements, inform your physician or pharmacist. In particular, inform the physician or the pharmacist if you are taking:

- Phenobarbital - Do not take this medicine during treatment with **Cholbam**. Phenobarbital may stop **Cholbam** effectiveness (please refer to the Section "Do not use this medicine if").
- Cyclosporine - may affect levels of cholic acid in your body. If your physician decides that it is essential for you to continue taking cyclosporine while you are taking **Cholbam**, the physician will order blood and urine tests to monitor bile acid levels and will adjust your **Cholbam** dose as needed.
- Medicines for lowering cholesterol levels in your blood such as: cholestyramine, colestipol or medicines to treat heartburn that contain aluminum (such as medicines to relieve the digestion). These medicines may affect cholic acid absorption. Take **Cholbam** at least five hours before or after you have taken these medicines.
- Medicines which increase production of cholesterol in the liver may reduce **Cholbam**'s effectiveness, for example: estrogen, oral contraceptives, medicines for lowering fat levels in your body (clofibrate).

Children

There is no information about the safety and efficacy of **Cholbam** in infants under the age of one month.

Adults

There is no information about the safety and efficacy of **Cholbam** in adults over 65 years old.

Taking Cholbam and food

Cholbam is best taken with food because this helps the medicine effectiveness and reduces the incidence of diarrhea as a side effect.

Pregnancy and breastfeeding

If you are pregnant, think you may be pregnant or planning to get pregnant, you should consult the physician before using **Cholbam**. Cholic acid treatment during pregnancy can be considered if your physician decides that the benefits outweigh the potential risk.

You may breastfeed during **Cholbam** treatment because the amount of the active ingredient which passes into the breast milk is too low to harm your baby.

Driving and using machines

Treatment with **Cholbam** is not expected to affect your ability to drive or operate machines.

How should you use the medicine?

Always use according to the physician's instructions. You should check with the physician or with the pharmacist if you are not sure.

The dosage and manner of treatment will be determined only by the physician.

- **The usual dosage** is determined by body weight; 10-15 mg per kilogram body weight. The appropriate dosage will be given once a day, or divided into two doses, one in the morning and one in the evening.
- Swallow the capsule whole with water immediately before or after eating, because food can make cholic acid work more effectively and reduces the likelihood of diarrhea.
- Use in children - for infants and children who are unable to swallow the capsule, gently open the capsule and add the contents to infant formula, expressed breast milk, or mashed fruits, in a suitable clean container. You must give this mixture immediately after preparing it.
- Mixing the capsule content with the specified food is intended to mask the medicine's unpleasant flavor. The capsule's content will stay in granular form in the milk or food.
It is important to give the infant or child the entire content of the capsule. If the infant or child spits out the prepared mixture or refuses to take part of it, try to give it again so that the child gets the full dose.
- Do not crush or chew the capsule.
- Do not take more capsules than your physician has prescribed for you.

Tests and follow-up

Levels of the liver enzymes aspartate transaminase (AST) and alanine transaminase (ALT), gamma-glutamyl transferase (GGT), alkaline phosphatase, levels of bilirubin and clotting test (INR) must be monitored once a month during the first three months of treatment, once in three months for the next nine months, once in six months for the next three years, and once a year after that. You must be given the lowest possible dose needed to maintain efficient liver function.

Stop taking **Cholbam** if your liver function does not improve after three months of treatment, or if you develop complete blockage of the biliary tract, or if there are clinical signs or blood test results that indicate that liver function has worsened or that you have cholestasis. In such cases liver function must be monitored and when values return to normal, reconsider treatment with a lower dose.

If you, or your child, have accidentally taken a higher dose of this medicine, this is unlikely to cause serious side effects, but you must consult your physician.

If you forget to take the medicine at the scheduled time, do not take a double dose.

If there are more than 12 hours until the next dose, take the forgotten dose immediately.

If you stop taking the medicine

Even if there is an improvement in your health, do not stop treatment with this medicine or change the dosage without consulting the physician or the pharmacist.

This medicine is intended for long-term use, if you stop using it, the level of the harmful substances to your liver, in your body may go up again.

Do not take medicines in the dark! Check the label and the dose each time you take the medicine. Wear glasses if you need them.

If you have any further questions regarding the use of this medicine, consult the physician or the pharmacist.

Side effects

As with any medicine, the use of **Cholbam** may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

Common side effects (effects that appear in 1-10 users out of 100):

- Heartburn (reflux esophagitis)
- Diarrhea
- Malaise
- Yellowish skin (jaundice)
- Skin lesions
- Feeling sick (nausea)
- Tingling (peripheral neuropathy)

Side effects of unknown frequency:

- Increase in liver enzyme Levels
- Gallstones
- Light tingling (pruritus)

If any side effect appears, if any of the side effects worsens, or if you suffer from a side effect which is not mentioned in this leaflet, consult with the physician.

Reporting side effects:

Side effects can be reported to the Ministry of Health (MoH) by clicking on the "Report on side effects due to medication therapy" link on the MoH home page (www.health.gov.il) which refers to the online form for side effects reporting, or by entering the link:

<https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>

How to store the medicine?

- Avoid poisoning! This medicine and any other medicine should be kept in a close place out of the reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.
- Do not use the medicine after the expiry date (exp. date) appearing on the outer package. The expiry date refers to the last day of that month.
- Do not store at a temperature higher than 25°C.
- Store in the original package in order to protect from light.
- This medicine can be used for three months after first opening of the bottle, but no later than the expiry date embossed on the package.

Additional information

- In addition to the active ingredient (cholic acid) the medicine also contains:
Capsule content: Silicified microcrystalline cellulose (Prosolv SMCC 90), Magnesium stearate
Capsule shell: Red iron oxide (**Cholbam** 50 mg), Titanium dioxide, Gelatin
Text on the capsules:
Shellac, Propylene Glycol, Strong Ammonia Solution, Potassium Hydroxide, Black Iron Oxide
- What does the medicine look like and what are the contents of the package:
Cholbam 50 mg is a hard orange capsule containing a white powder and imprinted in black with "ASK001" and 50mg.
Cholbam 250 mg is a hard white capsule containing a white powder and imprinted in black with "ASK002" and 250mg.
The medicine is packaged in a plastic bottle containing 90 capsules.
- Registration holder name and address: MegaPharm Ltd., P.O.B. 519, Hod Hasharon 4510501.
- Manufacturer name and address: Patheon Pharmaceuticals Inc., Cincinnati, Ohio, USA for Retrophin Inc., Cambridge Massachusetts, USA.
- This leaflet was checked and approved by the Ministry of Health in May 2016.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Cholbam 50 mg: 155-88-34268
Cholbam 250 mg: 155-89-34270