PATIENT PACKAGE INSERT IN ACCORDANCE WITH **THE PHARMACISTS' REGULATIONS - 1986**

This medicine is dispensed with a 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 and allergens in the preparation, see section 6 - "Additional information".

Read this leaflet carefully in its entirety before using the **medicine.** This leaflet contains concise information about the medicine. If you have any further questions, consult your physician or 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.

1. What is this medicine intended for?

Cholbam is intended for the treatment of infants from one month old, children and adolescents up to 18 years old, and adults who have an inborn error in bile acid synthesis due to a deficiency of one of the following enzymes:

- · Sterol 27-hydroxylase
- (presenting as cerebrotendinous xanthomatosis, CTX)
- 2- (or alpha-) methylacyl-CoA racemase (AMACR)
- · Cholesterol 7alpha-hydroxylase (CYP7A1)
- 3β -hydroxy-5-C27-steroid oxidoreductase (3β -hydroxy-5-C27-steroid dehydrogenase/isomerase or 3β -HSD or HSD 3β 7)

Therapeutic group: Bile acids.

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 in the process of children's growth and normal development.

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

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

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.

2. Before using the medicine

Do not use this medicine if:

 You are sensitive (allergic) to the active ingredient Cholic acid or to any of the additional ingredients that the medicine contains (please see section 6 - "Additional information").

Special warnings regarding the use of the medicine

- If you suffer from 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.
- The use of Cholbam may increase the severity of liver damage. Inform your physician immediately of any symptoms indicating impaired function of the liver (e.g., yellowing of the body's skin or of the white of the eye, dark or brown colored urine [tea colored], pain in the right side of the abdomen, increased tendency to bleed or to bruise and increased state of lethargy, a state of inactivity and unresponsiveness).

Children

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

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

Tests and follow-up

At various times during the course of treatment with this medicine, your physician will order blood and urine tests to see how this medicine is affecting your body and to find the dose that is most suitable for you.

During the period of treatment with this medicine, your physician will refer you for periodic laboratory tests to assess your liver function. Levels of the liver enzymes aspartate aminotransferase (AST) and alanine transaminase (ALT), gamma-glutamyl transferase (GGT), alkaline phosphatase, bilirubin and clotting testing (INR) must be monitored 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. In case of rapid growth, illness or pregnancy, more frequent testing will be needed. The lowest effective dose of Cholbam that maintains liver function should be given.

Stop using Cholbam if liver function does not improve within 3 months of beginning treatment, if complete blockage of the biliary tract develops, or if there are clinical or laboratory signs indicating that liver function has worsened or that the flow of bile has stopped (cholestasis).

In such cases liver function should be monitored, and when values return to normal, resumption of treatment at a lower dose should be considered.

Drug interactions

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

- · Medicines that inhibit the passage of bile acids from the liver into the bile (e.g., cyclosporine) - the administration of these medicines concurrently with **Cholbam** should be avoided. Taking these medicines concurrently with **Cholbam** may cause the accumulation of bile salts in the liver. In the event that your physician decides that treatment with these medicines concurrently with Cholbam is essential, blood and urine tests should be performed to monitor liver enzyme and bilirubin levels.
- Medicines for lowering cholesterol levels in your blood, such as: cholestyramine, colestipol, colesevelam or medicines to treat heartburn - which contain aluminum. These medicines may impair the absorption of bile acids and impair the efficacy of Cholbam. These medicines may affect the absorption

of cholic acid. Take Cholbam at least five hours before or after taking these medicines. Taking Cholbam and food It is preferable to take Cholbam with food, as this enhances the

effect of the medicine and reduces the incidence of diarrhea as a side effect.

Pregnancy, breastfeeding and fertility If you are pregnant, think you may be pregnant, or are planning a pregnancy or are breastfeeding, you should consult your physician before using Cholbam. Your physician will decide whether the benefit of the treatment outweighs the possible risk.

Driving and operating machinery

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

3. How should you use the medicine?

Always use this preparation according to your physician's instructions. You should check with your physician or pharmacist if you are unsure about the dosage or treatment regimen with this preparation.

The dosage and treatment regimen will be determined by your physician only.

- The usual dosage is in accordance with body weight 10-15 mg per kilogram of body weight. The required 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 enhance the efficacy of cholic acid and reduce 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 fruit puree in a suitable clean container. You must give this mixture immediately after preparing it.
- Mixing the capsule contents with food is intended to mask the medicine's unpleasant taste. The capsule's contents will remain in granular form in the milk or food.

It is important to give the infant or child the entire contents of the capsule. If the infant or child spits out the prepared mixture or refuses to take a 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 exceed the recommended dose.

If you, or your child, have accidentally taken a higher dose of this medicine, consult your physician.

If you forgot to take or to give to your child the medicine, or if your child forgot to take the medicine, at the required time, do not take a double dose. Take the next dose at the regular time and consult your physician.

Adhere to the treatment regimen as recommended by your physician.

If you, or your child, 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 with your physician or pharmacist.

Do not take medicines in the dark! Check the label and the dose $\underline{each\ time}$ you take a medicine. Wear glasses if you need

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

4. Side effects

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

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

- Heartburn (gastroesophageal reflux)
- Diarrhea
- Malaise
- · Yellow colored skin (jaundice)
- Skin lesions
- Nausea
- Tingling sensation (peripheral neuropathy)
- · Abdominal pain
- Bowel polyps
- Urinary tract inflammation

Side effects whose frequency is not known:

- · Effects in the digestive tract: discomfort and feeling bloated, vomiting, constipation
- · General effects: fever
- Skin effects: rash

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult your physician.

Reporting of side effects:

Side effects can be reported to the Ministry of Health by clicking on the link "Report on Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il/

5. How should the medicine be stored?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a closed place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by your physician.
- Do not use this medicine after the expiry date (exp. date) which appears on the package wrapping. 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 imprinted on the package.

6. Additional information

• In addition to the active ingredient (cholic acid), this medicine also contains:

Capsule content:

Silicified microcrystalline cellulose (Prosolv SMCC 90), Magnesium stearate Capsule shell:

Red iron oxide (Cholbam 50 mg), Titanium dioxide, Gelatin Inscription on the capsule: Shellac, Propylene Glycol, Strong Ammonia Solution, Potassium

Hydroxide, Black Iron Oxide

What the medicine looks like and what the package contains: **Cholbam 50 mg** - a hard orange capsule containing a white powder, inscribed in black text with "ASK001" and 50mg.

Cholbam 250 mg - a hard white capsule containing a white powder, inscribed in black text with "ASK002" and 250mg. The medicine is packaged in a plastic bottle containing 90

- Registration holder and address: Megapharm Ltd., Hatidhar St. 15. Ra'anana, Israel.
- Manufacturer and address: Patheon Pharmaceuticals Inc., Cincinnati, Ohio, USA.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: Cholbam 50 mg:

155-88-34268 155-89-34270 Cholbam 250 mg:

· Revised in November 2022 according to Ministry of Health guidelines