Package leaflet: Information for the patient

PROURSAN® 500 mg film-coated tablets

ursodeoxycholic acid

PRO.MED.CS Praha a. s.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Proursan® is and what it is used for

Ursodeoxycholic acid, the active substance in Proursan®, is a naturally-occurring bile acid. Small amounts are found in human bile.
Proursan® is used:
- to dissolve gallstones caused by excess cholesterol in the gall bladder where the gallstones are not visible on a plain x-ray (gallstones that are visible will not dissolve) and not more than 15 mm in diameter. The gall bladder should still be working despite the gallstone(s).
- to treat the symptoms of primary biliary cholangitis (PBC – a chronic biliary tract disorder, which may progress to liver cirrhosis) in patients without decompensated liver cirrhosis (a diffuse, chronic liver disease, in which poor liver function due to disease can no longer be corrected),
- to treat liver disease associated with a condition called cystic fibrosis in children aged 6 to 18 years.

2. What you need to know before you take Proursan®

Do not take Proursan® if
- you are allergic to bile acids (like ursodeoxycholic acid) or any of the other ingredients of this medicine (listed in section 6),
- you have acute inflammation of the gall bladder and biliary tract,
- you have a blockage of the common bile duct or cystic duct (obstruction of the biliary tract),
- you have frequent cramp-like pains in the upper abdomen (biliary colic),
- your doctor has said you have calcified gallstones,
- you have a problem with gall bladder contraction,
- you are a child with biliary atresia and have poor bile flow, even after surgery.

Please ask your doctor about any of the conditions mentioned above. You should also ask if you have previously had any of these conditions.

Warnings and precautions
Talk to your doctor or pharmacist before taking Proursan®.
Your doctor will test your liver function regularly every 4 weeks for the first 3 months of treatment. After this time, it should be monitored at 3 months intervals. When used to dissolve gallstones, your doctor should arrange for a scan of your gall bladder after the first 6–10 months of treatment.
If you are taking Proursan® for the dissolution of gallstones, please inform your doctor in case you are taking any medicines that contain oestrogenic hormones, as these medicines stimulate the formation of gallstones.
When used in the treatment of PBC, in rare cases the symptoms may worsen at the beginning of treatment. If this happens, please speak to your doctor about reducing your initial dose.
Please inform your doctor immediately if you have diarrhoea, as this may require a dose reduction or discontinuation of treatment.

Children
Proursan® is not suitable for children under 6 years due to the pharmaceutical form and strength of the presentation.

Other medicines and Proursan®
Please tell your doctor if you are also taking or using medicines with the following active substances. The effect of these medicines may be altered (interactions):

A **reduction in the effects** of Proursan® is possible when taking it with the following medicines:
- cholestyramine, colestipol (used to lower blood lipid levels) or antacids containing aluminium hydroxide or smectite (aluminium oxide) (used to bind stomach acid): If you must take medication that contains any of these substances, it must be taken at least two hours before or after Proursan®.

A **reduction in the effects** of the following medicines is possible when taking Proursan®:
- ciprofloxacin and dapsone (antibiotics), nitrendipine (used to treat high blood pressure) and other medicines that are metabolized in a similar way. It may be necessary for your doctor to alter the dose of these medicines.

An **increase in the effects** of the following medicines is possible when taking Proursan®:
- ciclosporin (to reduce the activity of the immune system). If you are being treated with ciclosporin, your doctor should check the amount of ciclosporin in your blood. If necessary, your doctor will adjust the dose.
- rosuvastatin (for high cholesterol and related conditions).

If you are taking Proursan® for the dissolution of gallstones, please inform your doctor, in case you are taking any medicines that contain oestrogenic hormones or blood cholesterol lowering agents such as clofibrate. These medicines stimulate the formation of gallstones, which is a counter-effect to the treatment with Proursan®.
Tell your doctor or pharmacist if you are taking or using, have recently taken or used or might take or use any other medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
Pregnancy
There are no or limited amounts of data from the use of ursodeoxycholic acid in pregnant women. Studies in animals have shown reproductive toxicity. Proursan® must not be used during pregnancy unless clearly necessary.
Women of child-bearing potential
Even if you are not pregnant, you should still consult your doctor.
Women of childbearing potential should be treated only if they use reliable contraception: non-hormonal or low-oestrogen oral contraceptive measures are recommended. However, in patients taking Proursan® for dissolution of gallstones, effective non-hormonal contraception should be used, since hormonal oral contraceptives may increase biliary lithiasis.
The possibility of a pregnancy must be excluded before beginning treatment.
Breastfeeding
According to few documented cases of breastfeeding women milk levels of ursodeoxycholic acid are very low and probably no adverse reactions are to be expected in breastfed infants.

Driving and using machines
No effects on the ability to drive and use machines have been observed.

Proursan® contains sodium starch glycolate A
This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially 'sodium-free'.

3. How to take Proursan®

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

To dissolve cholesterol gallstones
Dosage
The recommended dose is about 10 mg ursodeoxycholic acid per kg body weight (BW) daily, as follows:

up to 60 kg	1 tablet
61–80 kg	1 ½ tablets
81–100 kg	2 tablets
over 100 kg	2 ½ tablets

If you weigh less than 47 kg or if you are unable to swallow Proursan® other formulations containing ursodeoxycholic acid might be available to you.
Method of administration
Swallow the tablets whole with a glass of water or other liquid. Take the tablets in the evening at bedtime. Take your medicine regularly.
Duration of treatment
It generally takes 6–24 months to dissolve gallstones. If there is no reduction in the size of the gallstones after 12 months, therapy should be stopped.
Every 6 months, your doctor should check whether the treatment is working. At each of these follow-up examinations, it should be checked whether a build-up of calcium causing hardening of the stones has occurred since the last time. If this happens, your doctor will stop the treatment.

For primary biliary cholangitis (chronic inflammatory disease of the biliary tract)
Dosage
During the first 3 months of treatment, you should take Proursan® in the morning, at midday and in the evening. As liver function values improve, the total daily dose can be taken once daily in the evening.

Body weight BW (kg)	Proursan® 500 mg film-coated tablets			
	First 3 months			Subsequently
	morning	midday	evening	evening (once daily)
47–62	½	½	½	1 ½
63–78	½	½	1	2
79–93	½	1	1	2 ½
94–109	1	1	1	3
over 110	1	1	1 ½	3 ½

If you weigh less than 47 kg or if you are unable to swallow Proursan® another formulation containing ursodeoxycholic acid might be available to you.
Method of administration
Swallow the tablets whole (not chewed) with a glass of water or other liquid. Take your medicine regularly.
Duration of treatment
Proursan® may be continued indefinitely in cases of primary biliary cholangitis.
Note
If you have primary biliary cholangitis, your symptoms may worsen at the start of treatment. One sign of this may be increased itching. This happens only in rare cases. In this event, treatment can be continued with a reduced daily dose of Proursan®. Your doctor will then increase the daily dose every week, until the required dose is once again reached.

For the treatment of children (aged 6 to 18 years) with cystic fibrosis
The recommended dose is about 20 mg/kg/day in 2–3 divided doses, with a further increase to 30 mg/kg/day if necessary.

Body weight (kg)	Proursan® 500 mg film-coated tablets		
	morning	midday	evening
20–29	½	–	½
30–39	½	½	½
40–49	½	½	1
50–59	½	1	1
60–69	1	1	1
70–79	1	1	1 ½
80–89	1	1 ½	1 ½
90–99	1 ½	1 ½	1 ½
100–109	1 ½	1 ½	2
over 110	1 ½	2	2

If you feel that the effect of Proursan® is too strong or too weak, please talk to your doctor or pharmacist.

If you take more Proursan® than you should
Diarrhoea may occur in the event of an overdose. Please inform your doctor immediately if you have persistent diarrhoea. If you do suffer from diarrhoea, make sure you glass enough liquids to replace your fluid and electrolyte balance.

If you forget to take Proursan®
Do not take a double dose to make up for a forgotten dose, but just continue the treatment with the prescribed dose.

If you stop taking Proursan®
Always talk to your doctor before you decide to interrupt treatment with Proursan® or to stop your treatment early.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Common side effects (may affect up to 1 in 10 people):
– soft, loose stools or diarrhoea.

Very rare side effects (may affect up to 1 in 10,000 people):
– during the treatment of primary biliary cholangitis: severe, right-sided upper abdominal pain, severe worsening of liver scarring – this partially eases after treatment is stopped,
– hardening of gallstones,
– nettle rash (urticaria).

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2;
Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: *www.hpra.ie*; e-mail: *medsafety@hpra.ie*.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Proursan®

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the carton and blister after "EXP". The expiry date refers to the last day of that month.
This medicine does not require any special storage conditions.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Proursan® contains
The active substance is ursodeoxycholic acid. Each tablet contains 500 mg of ursodeoxycholic acid.
The other ingredients are:
– tablet core: maize starch, maize starch pregelatinised, sodium starch glycolate A (E468), silica colloidal anhydrous (E551), magnesium stearate (E470b),
– tablet coating: hypromellose 6 (E464), titanium dioxide (E171), macrogol 400.

What Proursan® looks like and contents of the pack
Proursan® are almost white, oblong film-coated tablets with a break line on each side, length 17 mm and width 9 mm. The tablet can be divided into equal doses.
The film-coated tablets are packed in PVC-PVDC/Al blisters in a cardboard box.
Proursan® is available in packs of 10, 20, 30, 40, 50, 60, 80, 90 or 100 tablets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
PRO.MED.CS Praha a. s.
Telčská 377/1
Michle, 140 00 Praha 4
Czech Republic

This medicinal product is authorised in the Member States of the EEA under the following names:

Belgium	Ursosan 500 mg comprimés pelliculés
Estonia	Ursosan
Finland	Ursosan 500 mg
Ireland	Proursan 500 mg
Latvia	Ursosan 500 mg apvalkotās tabletes
Lithuania	Ursonorm 500 mg plėvele dengtos tabletės
Luxembourg	Ursosan 500 mg
Netherlands	Ursonorm 500 mg
Slovenia	Ursosan 500 mg filmsko obložene tablete
United Kingdom	Ursonorm 500 mg film-coated tablets

This leaflet was last approved in