Package leaflet: Information for the user

Ursogrix 250 mg hard capsules
Ursodeoxycholic acid

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 Ursogrix is and what it is used for

This medicine contains ursodeoxycholic acid – a natural bile acid. However, small amount only is found in human bile.

Ursogrix is used:
- For the dissolution of gallstones that are composed of cholesterol in patients:
  - having one or more radiolucent (radio-negative) gallstones, preferably with a diameter of no more than 2 cm, in a properly functioning gallbladder;
  - for whom surgery is not an option;
  - in whom cholesterol supersaturation has been demonstrated by chemical testing on bile.
  - Before and after gallstone shockwave dissolution (lithotripsy).
- For the treatment of a condition where the bile ducts in the liver become damaged leading to a build-up of bile. This may cause scarring of the liver. The liver should not be so damaged that it is not functioning properly. This condition is called primary biliary cholangitis (PBC, also known as primary biliary cirrhosis).
- For the treatment of liver disease associated with cystic fibrosis (mucoviscidosis) in children and adolescents aged 6-18 years.

2. What you need to know before you take Ursogrix

Do not take Ursogrix
- if you are allergic to ursodeoxycholic acid or bile acids, or any of the other ingredients of this medicine (listed in section 6);
- if you have an acute inflammation of the gall bladder or biliary tract;
- if your bile ducts are closed (common duct or cystic duct occlusion);
- if you suffer from frequent cramp-like pains in the upper abdomen (biliary colic);
- if your doctor has told you that you have a gallstone calcification;
- if your gall bladder ability to contract is impaired;
- if you are a child with a closure of bile ducts (biliary atresia) and have poor bile flow, even after a 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 or if you are unsure whether you have any of them.

Warnings and precautions
Talk to your doctor or pharmacist before taking Ursogrix. This medicine should be used under medical supervision.

In the first 3 months of treatment your doctor should monitor your liver function regularly every 4 weeks. Thereafter, the controls should be carried out every 3 months.

If you are taking this medicine to dissolve gallstones, your doctor should perform scans of your gall bladder after 6-10 months of treatment.

If you are a woman and are taking this medicine to dissolve gallstones, you should use the effective non-hormonal contraceptive measures because hormonal contraceptives (the "pill") may promote the formation of gallstones.

If you take this medicine for the treatment of PBC, in rare cases the symptoms (e.g. itching) may worsen at the beginning of treatment. In this case you should talk to your doctor about reducing your initial dose.

Inform your doctor if you suffer from diarrhoea as this may require a reduction of the dose or discontinuation of the treatment with Ursogrix.

Children
There are no age restrictions for the use of Ursogrix 250 mg hard capsules except for cystic fibrosis (ages 6 to 18 years).

Other medicines and Ursogrix
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
The effect of this medicine can be changed (interactions):
A **reduction in the effects** of the Ursogrix is possible when taking it with the following medicines:
- colestyramine, colestipol (medicines used to lower blood lipid levels) or antacids containing aluminium hydroxide or smectite (aluminium oxide) (preparations binding gastric acids). If you are taking a medicine containing one of these active ingredients, the intake should be with time delay at least 2 hours before or after taking Ursogrix.

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

A **change of the effects** of the following medicines is possible by taking Ursogrix:
- ciclosporin (medicine that reduces the activity of the immune system). If you are being treated with ciclosporine your doctor should check the ciclosporin concentration in your blood. Your doctor will adjust the dose, if necessary;
- rosuvastatin (medicine used to treat high blood lipids).

If you are taking Ursogrix to dissolve gallstones please inform your doctor if you are simultaneously taking medicines containing oestrogen (e.g. the "pill") or certain medicines lowering cholesterol, e.g. clofibrate. These medicines may promote the formation of gallstones and thus counteract the dissolution of gallstones by Ursogrix.

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. You should not take Ursogrix during pregnancy unless your doctor considers it absolutely necessary.
Based on animal studies, use of ursodeoxycholic acid during pregnancy may affect development of the unborn child.

Women of childbearing potential
Even if you are not pregnant, you should still discuss this matter with your doctor. Women of childbearing potential should be only treated with concomitant use of reliable contraceptive measures. Non-hormonal contraceptive measures or oral contraceptive containing low dose of oestrogen (the "pill") are recommended. If you are taking Ursogrix to dissolve gallstones you should use effective non-hormonal contraceptive measures because hormonal contraceptives can promote the formation of gallstones.

Before starting treatment your doctor will check that you are not pregnant.

Breast-feeding
There are only a few documented cases of taking of ursodeoxycholic acid during lactation. The levels of ursodeoxycholic acid in breast milk are very low. Therefore adverse reactions in nursing infants are unlikely.

Fertility/ability to give birth
Animal studies have shown no effect of this medicine on the fertility/ability to give birth.
So far there is no experience showing an influence of this medicine on human fertility/childbearing.

Driving and using machines
No particular precautions are necessary.

3. How to take Ursogrix

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

For dissolution of cholesterol gallstones (alone or in combination with lithotripsy)

Dosage
The recommended dose is 2-4 capsules of Ursogrix (8-10 mg/kg body weight of ursodeoxycholic acid), to be taken with a meal as follows:
- at a daily dose of 2 capsules: both capsules with an evening meal;
- at a daily dose of 3 capsules: 1 capsule in the morning and 2 in the evening;
- at a daily dose of 4 capsules: 2 capsule in the morning and 2 in the evening.

OR

take a daily dose of 2-4 capsules in the evening before bedtime.

Method of administration
Swallow the capsules whole with a drink of water or other liquid. Take the capsules regularly.

Duration of treatment
It generally takes 6-24 months to dissolve the gallstones. The duration of the treatment depends on the size of the existing gallstones at the start of the treatment. 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.
Even if your symptoms have disappeared, you should continue treatment: interruption of treatment results in the extension of the total treatment duration. After the dissolution of gallstones treatment should be continued for 3-4 months.

For the treatment of primary biliary cholangitis (chronic inflammatory disease of the bile ducts)

Dosage
Stage I-III

The daily dose depends on body weight. During the first 3 months of treatment you should take Ursogrix in the morning, afternoon and in the evening. With improvement of the liver function values the daily dose may be taken once a day in the evening.

Body weight (kg)	**Ursogrix 250 mg hard capsules**			
	First 3 months			**Subsequently**
	Morning	Afternoon	Evening	Evening (once daily)
47-62	1	1	1	3
63-78	1	1	2	4
79-93	1	2	2	5
94-109	2	2	2	6
over 110	2	2	3	7

Stage IV
In the beginning of the treatment 2 to 3 capsules per day of Ursogrix should be used with meal:
- at a daily dose of 2 capsules: 1 capsule in the morning and 1 in the evening;
- at a daily dose of 3 capsules: 1 capsule in the morning and 2 in the evening.

If you have good response to this dosage (after blood test and/or in the judgment of your doctor), your doctor will prescribe a higher dose (dosage as for the treatment of stage I-III).

Method of administration
Swallow the capsules whole with a drink of water or other liquid. Take the capsules regularly.

Duration of administration
The administration of Ursogrix in primary biliary cholangitis is not time limited.

Note
If you suffer from primary biliary cholangitis the symptoms of your illness, e.g. the itching, may worsen at the beginning of treatment. This occurs in rare cases only. In this case the therapy can be continued with a reduced daily dose of Ursogrix. Then your doctor will increase the daily dose every week until the required dose is reached again.

Use in children and adolescents (from 6 to 18 years) for the treatment of liver disease associated with cystic fibrosis

Dosage
The recommended daily dose is 20 mg/kg of body weight, divided into 2-3 doses. If necessary, your doctor may increase the dose to 30 mg/kg of body weight daily.

Body weight (kg)	Daily dose (mg/kg of body weight)	**Ursogrix 250 mg hard capsules**		
		Morning	Afternoon	Evening
20-29	17-25	1	--	1
30-39	19-25	1	1	1
40-49	20-25	1	1	2
50-59	21-25	1	2	2
60-69	22-25	2	2	2
70-79	22-25	2	2	3
80-89	22-25	2	3	3
90-99	23-25	3	3	3
100-109	23-25	3	3	4
> 110		3	4	4

Method of administration
Swallow the capsules whole with a drink of water or other liquid. Take the capsules regularly.
If you have difficulty swallowing or have a bodyweight below 47 kg, other formulations with ursodeoxycholic acid are available.

Please talk to your doctor or pharmacist if you feel that the effect of Ursogrix is too strong or too weak.

If you take more Ursogrix than you should
Diarrhoea may occur as a result of overdose. Inform your doctor immediately if you have persistent diarrhoea. If you do suffer from diarrhoea, make sure you drink enough liquids to replace your fluid and salt (electrolyte) balance.

If you forget to take Ursogrix
Do not take more capsules the next time, but just continue the treatment with the prescribed dose.

If you stop taking Ursogrix
Always talk to your doctor before you decide to interrupt treatment with Ursogrix or decide 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 (may affect less than 1 in 10 patients):
- soft, loose stools or diarrhoea.

Very rare (may affect less than 1 in 10 000 patients):
- in the treatment of primary biliary cholangitis: severe right-sided upper abdominal pain,, severe worsening of liver scarring which partially eases after treatment is stopped;
- calcification (hardening of gallstones due to build-up of calcium) of gallstones;
- hives (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 Ursogrix

Do not store above 30 °C.
Store in the original packaging material in order to protect from moisture.

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 after the "EXP". The expiry date refers to the last day of that month.

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 Ursogrix contains
- The active substance is ursodeoxycholic acid.
  Each hard capsule contains 250 mg ursodeoxycholic acid.

- The other excipients are: maize starch, silicon dioxide (E 551), magnesium stearate (E 470B), hard gelatin capsule (body and cap composition): titanium dioxide (E 171), gelatin (E 441).

What Ursogrix looks like and contents of the pack
White hard gelatin capsules size 0, approximately 21.7 mm x 7.64 mm. The content – white or almost white powder.

The capsules are packed in PVC/aluminium blisters.
10 capsules per blister.
5, 6 or 10 blisters (50, 60 or 100 capsules) are packed per cardboard box.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
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This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Ursogrix 250 mg Hartkapseln
Belgium	URSOGRIX 250 mg harde capsules
Bulgaria	Ursogrix 250 mg hard capsules Урсогрикс 250 mg твърди капсули
Czech Republic	URSOGRIX
Croatia	URSOGRIX 250 mg tvrde kapsule
Denmark	Ursogrix
Estonia	URSOGRIX
France	ACIDE URSODESOXYCHOLIQUE GRINDEKS 250 mg, gélule
Germany	Ursogrix 250 mg Hartkapseln

Greece	Ursogrix 250 mg Σκληρά καψάκια
Hungary	Urzodezoxikólsav Grindeks 250 mg kemény kapszula
Ireland	Ursogrix 250 mg hard capsules
Latvia	URSOGRIX 250 mg cietās kapsulas
Lithuania	URSOGRIX 250 mg kietosios kapsulės
the Netherlands	GRINTEROL 250 mg harde capsules
Norway	URSOGRIX 250 mg harde kapsler
Poland	URSOXYN
Portugal	GRINTEROL 250 mg cápsulas duras
Romania	Ursogrix 250 mg capsule
Slovakia	Ursogrix 250 mg tvrdé kapsuly
Spain	Ácido Ursodesoxicólico Grindeks 250 mg cápsulas duras
Sweden	Ursogrix 250 mg hårda kapslar
United Kingdom	Ursodeoxycholic Acid 250 mg Capsules, hard

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