

Package leaflet: Information for the user

Rotren 10 mg and 20 mg soft capsules

Isotretinoin

WARNING

CAN SERIOUSLY HARM AN UNBORN BABY

Women must use effective contraception

Do not use if you are pregnant or think you may be pregnant

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep the leaflet. You may need to read it again.
- If you have more 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 Rotren is and what it is used for
2. What you need to know before you take Rotren
3. How to take Rotren
4. Possible side effects
5. How to store Rotren
6. Contents of the pack and other information

1. What Rotren is and what it is used for

Rotren is used to treat severe types of acne (such as *nodular* or *conglobate* acne, or acne that is at risk of causing permanent scarring) which have not shown improvement after using other anti-acne treatments, including oral antibiotics.

Rotren contains *isotretinoin* – a substance related to vitamin A, and one of a group of medicines called *retinoids* (for treatment of acne).

Your doctor may have prescribed a prescription for another treatment. Please follow his instructions.

Treatment with isotretinoin should be performed under the supervision of doctors specializing in the treatment of severe acne and with full understanding of the risk of inherent malformations in children. Isotretinoin is not used to treat acne that occurs before adolescence or in children under the age of 12 years.

2. What you need to know before you take Rotren

Do not take Rotren:

- If you are pregnant or breast-feeding
- If there is any chance you could become pregnant, you must follow the precautions under “Pregnancy prevention programme”, see section on “Warnings and precautions”.
- If you are allergic to *isotretinoin*, peanut or soya or any other ingredients of this medicine (listed in section 6).
- If you have liver disease
- If you have very high levels of blood fats (e.g. high cholesterol or triglycerides)
- If you have very high levels of vitamin A in your body (*hypervitaminosis A*)
- If you are receiving treatment with tetracyclines (*a type of antibiotic*) at the same time (see “Other medicines and Rotren”)

If any of these apply to you, go back to your doctor before taking any Rotren.

Warnings and precautions

Talk to your doctor or pharmacist before taking Rotren:

Women who are pregnant should not take Rotren

This medicine can seriously harm an unborn baby (the drug is said to be “teratogenic”) - it can cause severe brain, facial, ear, eye, heart, and certain glands (thymus and parathyroid gland) of the unborn baby. It also makes a miscarriage more likely. This can happen even if Rotren is taken only for a short time during pregnancy.

- You must not take Rotren if you are pregnant or if you think you might be pregnant.
- You must not take Rotren if you are breastfeeding. The medicine is likely to pass into your milk and may harm your baby.
- You must not take Rotren if you could get pregnant during treatment.
- You must not get pregnant for one month after stopping this treatment because some medicine may still be left in your body.

Women who could get pregnant are prescribed Rotren under strict rules. This is because of the risk of serious harm to the unborn baby

These are the rules:

- Your doctor must explain the risk of harm to the unborn baby - you must understand why you must not get pregnant and what you need to do to prevent getting pregnant.
- You must have talked about contraception (birth control) with your doctor. The doctor will give you information on how not to get pregnant. The doctor may send you to a specialist for contraception advice.
- Before you start treatment, your doctor will ask you to take a pregnancy test. The test must show that you are not pregnant when starting treatment with Rotren.

Women must use effective contraception before, during and after taking Rotren

- You must agree to use at least one very reliable method of contraception (for example an intra uterine device or contraceptive implant) or, two effective methods that work in different ways (for example a hormonal contraceptive pill and a condom). Discuss with your doctor which methods would be suitable for you.
- You must use contraception for a month before taking Rotren, during treatment and for a month afterwards.
- You must use contraception even if you do not have periods or you are not sexually active (unless your doctor decides this is not necessary).

Women must agree to pregnancy testing before, during and after taking Rotren

- You must agree to regular follow-up visits, ideally every month.
- You must agree to have regular pregnancy tests, ideally every month during treatment and, because some medicine may still be left in your body, 1 month after stopping Rotren (unless your doctor decides this is not necessary in your case).
- You must not get pregnant during treatment or for a month afterwards because some medicine may still be left in your body.
- Your doctor will discuss all these points with you, using a checklist and will ask you (or a parent/guardian) to sign it. This form confirms that you have been told about the risks and that you will follow the rules above.

If you get pregnant while taking Rotren, **stop taking the medicine straight away**, and contact your doctor. Your doctor may send you to a specialist for advice.

Also, if you become pregnant within one month after you stop taking Rotren, you should contact your doctor. Your doctor may send you to a specialist for advice.

Additional precautions

You should never give this medicinal product to another person. Please take any unused capsules to your pharmacist at the end of treatment.

You should not donate blood during treatment with this medicine and for 1 month after stopping Rotren because an unborn baby could be harmed if a pregnant patient receives your blood.

Pregnancy and breast-feeding

IMPORTANT

Isotretinoin is teratogenic. This means that it is likely to harm the unborn infant. There is also an increased risk of miscarriage.

You should not take Isotretinoin if you are pregnant or if you are likely to become pregnant during treatment and for one month after it is stopped.

Particular attention should be paid to the use of Isotretinoin

Women with gestational capacity can be treated with Isotretinoin only if:

- You suffer from severe acne, which has not shown improvement after using other treatments against acne, including oral antibiotics.
- Your doctor has explained the risk of teratogenicity associated with isotretinoin and you understand why you should avoid pregnancy and how to avoid pregnancy.
- Have discussed with your doctor the use of effective contraception (birth control) methods. Your doctor will give you information on pregnancy avoidance, including a contraceptive leaflet explaining the various methods.
- You agree to use at least one and preferably two effective forms of contraception for one month before treatment, throughout treatment and one month after the end of treatment. Before starting treatment, your doctor will ask you to have a pregnancy test, which should give you a negative result.
- You are using contraception even if you do not have a period or even if you do not currently have sexual intercourse unless your doctor decides that this is not necessary.
- You understand and accept the need to monitor on a monthly basis, as well as possible further gestation tests, at your doctor's discretion. Then, you may be subjected to a pregnancy test 5 weeks after the end of the treatment. You should not become pregnant during treatment and for one month after the end of treatment.

If you become pregnant during treatment or within one month after the end of treatment, stop taking the medicine immediately and tell your doctor. It may refer you to a doctor for evaluation and advice.

For reproductive women, prescriptions are limited to 30 days of treatment. Continuing treatment requires a new recipe, and each prescription only applies for seven days.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

For more information on contraception, pregnancy and breast-feeding, see section 2 “Pregnancy prevention programme”.

Advice for men

The levels of oral retinoid in the semen of men taking Rotren are too low to harm the unborn baby of their associates. However, you should never share your medicine with anyone.

Additional precautions

You should never give this medicine to another person. Please take all unused <capsules> to your pharmacist at the end of treatment.

You should not have blood donation during treatment with this medicine and for 1 month after discontinuing Rotren therapy because an embryo may be harmed if a pregnant patient receives your blood.

There are no restrictions on prescribing for male patients. The available data suggest that the level of maternal exposure from the semen of patients receiving isotretinoin is not of sufficient magnitude to correlate with the teratogenic effects of isotretinoin. Men should be reminded that patients should not share their medication with anyone else, particularly women.

- If you have ever had mental health problems such as depression, aggressive tendencies or mood swings. This is because taking Rotren can affect your mood.

Mental issues

You may not notice any changes in your mood and behavior and that's why it is very important to tell your friends and family that this medicine can affect your mood and behavior. They may notice these changes and help you identify any problems you should discuss with your doctor.

Particular attention should be paid to the use of Isotretinoin:

- Isotretinoin may increase blood lipid levels, such as triglycerides or cholesterol. Your doctor will ask you to perform some blood tests to monitor your blood levels before, during and at the end of treatment. Please tell your doctor if you already have high levels of these substances in the blood or if you have diabetes, you are overweight or alcoholic as it may require more regular blood tests.

- Isotretinoin may increase levels of liver enzymes. Your doctor will ask you to have a blood test before, during and at the end of the treatment to check your liver values. If hepatic enzyme levels are still high, the doctor may reduce your dose or discontinue treatment with the drug.

- Isotretinoin may increase your blood sugar levels while diabetes is rarely diagnosed Your doctor may monitor your blood sugar levels during treatment, especially if you suffer from diabetes, you are overweight or alcoholic.

- Rare cases of depression, aggravated depression, anxiety, mood swings, psychotic symptoms and very rare suicidal thoughts, attempted suicide and suicide have been reported. If you have any kind of mental problems or if you notice signs of depression while taking Isotretinoin, such as if you feel unhappy with no reason, you have terrible tantrums, difficulty concentrating, or want to move away from your friends or family, please tell your doctor. Your doctor may refer you, if necessary, for appropriate treatment. Stopping treatment with Isotretinoin may not be enough to improve the symptoms and you may need further psychiatric or psychological evaluation.
- The use of ointments or topical acne treatment should be avoided unless instructed by the doctor.
- If you experience allergic reactions (skin redness, itching, sneezing, vomiting, convulsions, difficulty in breathing, low blood pressure), please stop the treatment.
- If you have persistent headache, nausea, vomiting and blurred vision, please stop treatment immediately and contact your doctor as soon as possible.
- If you develop bleeding diarrhea (eg, blood in stools), please stop treatment immediately and contact your doctor as soon as possible.
- Treatment with Isotretinoin may affect your ability to see at night. During treatment, eye dryness or vision problems may occur, which usually return to normal after discontinuation of treatment. If any problem with your vision is observed, please tell your doctor immediately to get an ophthalmologist. Always be careful when driving or operating machines during the night because these changes in vision may appear quite suddenly. If you wear contact lenses and show dryness in your eyes, you may need to wear glasses during the treatment.

Pregnancy, breastfeeding and fertility

Do not use Rotren if you are pregnant or are thinking about becoming pregnant. Your doctor may give you more information.

Pregnancy

Isotretinoin should not be taken during pregnancy.

Taking isotretinoin during pregnancy can cause a high risk of very serious congenital malformations and an increased risk of miscarriage. Abnormalities observed in pregnant women during treatment include CNS damage, facial abnormalities, hyperopia, abnormal ears, abnormal eyes, cardiovascular abnormalities and abnormalities of the thyroid gland and parathyroid gland.

Lactation

You should not take Isotretinoin if you are breast-feeding because isotretinoin may pass into your milk and harm your baby.

Other medicines and Rotren

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. During treatment, do not take vitamin A supplements or tetracyclines (a type of antibiotic used in the treatment of exemplary acne).

The use of ointments or topical acne treatment (topical keratolytic or anti-acne medications) should be avoided unless instructed by the doctor.

Rotren with food, drink and drinks

Isotretinoin should be taken with food. Swallow the capsules whole.

Driving and using machines

You may not see as well at night during your treatment. This can happen suddenly. In rare cases this has continued after the treatment has stopped. Drowsiness and dizziness have been reported very rarely. If this happens to you, you should not drive or operate machinery.

Rotren contains Soya-bean oil. If you are allergic to peanut or soya, do not take this medicinal product.

3. How to take Rotren

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

The usual starting dose is 0.5 mg per kilogram body weight per day (0.5 mg/kg/day).

During treatment, your doctor may adjust your dose. This depends on how you are getting on with your medicine. For most patients the dose will be between 0.5 and 1.0 mg/kg/day. If you think that Rotren is too strong or too weak, talk to your doctor or pharmacist.

If you can not tolerate the recommended dose, your doctor may continue to treat you with a lower dose: in this case, your treatment will last longer and the risk of relapse will be higher. Always follow the doctor's instructions. There are differences in the way each person reacts.

Capsules should be taken with food once or twice daily. Swallow the whole.

Occasionally acne may worsen during the first few weeks of treatment. It is expected to improve with continued treatment

A course of treatment usually lasts for 16 to 24 weeks. Most patients only need one course. Your acne may continue to improve for up to 8 weeks after treatment. You won't usually start another course until then.

Some people find their acne gets worse during the first weeks of treatment. It usually improves as treatment goes on.

Only the doctor can prescribe, modify or discontinue treatment. Please return any unused capsule to your pharmacist at the end of the treatment. Keep unused capsules only if your doctor tells you to. Remember that this medicine is for you. The prescription may only be made by a doctor. Never give your medicine to others. It can cause harm to them, even when their symptoms are the same as yours.

Children

Isotretinoin is not used to treat acne that occurs before adolescence or in children under the age of 12 years

If you have severe kidney problems, you will usually start on a lower dose (such as 10 mg/day) which will be increased up to the highest dose your body can tolerate. If your body can't tolerate the recommended dose, you may be prescribed a lower dose: that can mean you are treated for longer and your acne might be more likely to come back.

If you take more Rotren capsules than you should

If you take too many capsules or someone else accidentally takes your medicine, contact your doctor, pharmacist or nearest hospital immediately.

Isotretinoin is vitamin A acid derivative. Symptoms of Isotretinoin poisoning are similar to those caused by vitamin A poisoning, for example, headache, nausea, vomiting, dizziness, irritability and pruritus.

If you forget to take a dose

If you miss a dose take it as soon as you can. However, if it is nearly time for your next dose, skip the missed dose and carry on as before. Do not take a double dose.

Phenomena observed when Isotretinoin treatment is stopped:

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The effects often wear off, or stop when treatment is stopped. Others can be serious and you must immediately contact your doctor.

Serious undesirable effects, which are rare ($> 1 / 10,000$ and $< 1 / 1,000$) or very rare ($< 1 / 10,000$)

Mental problems

Rare effects (*may affect up to 1 in every 1000 people*)

- Depression or related disorders. Signs of this include sad or altered mood, anxiety, feelings of emotional discomfort,
- Existing depression getting worse.
- Becoming violent or aggressive.

Very rare effects (*may affect up to 1 in every 10,000 people*)

- Some people have had thoughts about hurting themselves or ending their own lives (suicidal thoughts), have tried to end their own lives (attempted suicide), or have ended their lives (suicide). These people may not appear to be depressed.
- Unusual behaviour.
- Signs of psychosis: a loss of contact with reality, such as hearing voices or seeing things that are not there.

Contact your doctor straight away if you get signs of any of these mental problems. Your doctor may tell you to stop taking Rotren. That may not be enough to stop the effects: you may need more help, and your doctor can arrange this.

Allergic reactions

If you experience chest tightness and difficulty in breathing (especially if you suffer from asthma) or skin rashes and itching, it may mean that you have an allergic reaction to severe anaphylactoid reactions caused by isotretinoin. Stop taking isotretinoin and contact your doctor immediately

Nervous system problems

Very rare hypertension has been observed particularly when isotretinoin is taken together with an antibiotic (tetracyclines). If you experience a persistent headache with nausea, vomiting and blurred vision, this means you experience benign intracranial hypertension. Stop taking isotretinoin as soon as possible and contact your doctor immediately.

Gastrointestinal disorders

If you observed severe abdominal (tummy) pain, with or without severe bloody diarrhoea, feeling sick (nausea) and being sick (vomiting). Stop taking isotretinoin as soon as possible and contact your doctor. There are very rare reports of patients who have experienced severe gastrointestinal disorders, such as pancreatitis, gastrointestinal bleeding, colitis, ileitis and inflammatory bowel disease.

Liver problems

If you observe yellow skin or eyes accompanied by fatigue, stop taking the medicine as soon as possible and contact your doctor. Very rarely, patients experienced severe liver problems (hepatitis).

Kidney problems

In very rare cases, patients have kidney inflammation. Symptoms include feeling of excessive fatigue, difficulty in passing urine, and swelling of the eyelids. If this happens during treatment, stop taking the medicine and contact your doctor.

Skin problems

Serious skin rashes (erythema multiforme), which appear initially as circular patches often with central blisters usually on arms and hands or legs and feet, more severe rashes may include blistering of the chest and back but may occur anywhere in the body.. If this rash occurs, stop taking Rotren and contact your doctor.

Other side effects:

Very common side effects with Rotren: *(may affect more than 1 in 10 people)*

Reduced liver function (increased transaminase activity in blood), anemia, blood disorders (thrombocytopenia, thrombocytosis), inflammation of the eyelid region (blepharitis) and eye (conjunctivitis), dry eyes, eye irritation, swollen lips, swollen skin (dermatitis), dry skin, skin peeling, itching, rash, brittle skin, joint and muscle pain, back pain, increased blood levels of fat-like substances.

Common side effects with Rotren: *(may affect up to 1 in 10 people)*

Blood disorders (neutropenia), headache, nasopharyngitis, nasal dryness, cold, elevated levels of cholesterol, glucose, protein and uric acid in the blood.

Rare side effects with Rotren: *(may affect up to 1 in 1,000 people)*

- Hair loss (*alopecia*). This is usually only temporary. Your hair should return to normal after the treatment ends.

Very rare side effects with Rotren: *(may affect up to 1 in 10,000 people)*

Bacterial infections, lymph node disorders (lymphadenopathy) diabetes mellitus, hyperuricemia, convulsions, sleepiness, blurred vision, corneal opacity, cataracts, color blindness, discomfort from contact lenses, keratitis, reduced night vision, photophobia, vasculitis, , nausea, aggravation and increased acne, facial erythema, hair growth (shingles), nail changes, infection of the tissue around the base of the nails, sensitivity to light, rash, skin inflammation, excessive sweating, arthritis, bone disorders, soft tissue calcification, tendon pain, increased granulation tissue, disease (feeling sick), increased level of muscle degeneration (creatine phosphokinase activity) in the blood. Inflammation of the blood vessels (sometimes with bruising, red patches).

Unknown frequency: *(frequency cannot be estimated from the available data)*

- Dark or cola-coloured urine
- Problems getting or maintaining an erection
- Lower libido

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

Pharmaceuticals Services

Ministry of Health

CY-1475, Nicosia

www.moh.gov.cy/phs

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

5. How to store Rotren

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date (EXP) stated on the pack and blister.

Do not store above 30° C.

Store in the original package and keep blister in the outer carton in order to protect from moisture and light.

Return left over capsules to your pharmacist. Only keep them if your doctor tells you to.

6. Contents of the pack and other information

What Rotren contains:

- **The active substance** in Rotren is isotretinoin. Each soft capsule contains 10mg or 20mg isotretinoin.
- **The other ingredients** are **refined soya-bean oil, hydrogenated soya-bean oil, partially hydrogenated soya-bean oil, yellow beeswax, gelatin, glycerol**, titanium dioxide (E171), red and yellow iron oxide (E172)

What Rotren looks like and contents of the pack:

The 10 mg capsules are oval, coloured red / orange (size 3)

The 20 mg capsules are oval, coloured red / orange (size 6)

The capsules come in blister packs of 10, 20, 30 capsules

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:

Marketing Authorisation Holder

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