

Package leaflet: Information for the user

ISOTRETINOIN 5MG AND 20MG CAPSULES

WARNING

CAN SERIOUSLY HARM AN UNBORN BABY

Women must use effective contraception

Do not use if you are pregnant or you 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 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 Isotretinoin is and what it is used for
2. What you need to know before you take Isotretinoin Capsules
3. How to take Isotretinoin Capsules
4. Possible side effects
5. How to store Isotretinoin Capsules
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1. WHAT ISOTRETINOIN IS AND WHAT IT IS USED FOR

Isotretinoin belongs to a group of medicines known as retinoids that are normally used to treat skin problems.

Isotretinoin Capsules are used to treat severe acne (such as *nodular* or *conglobate* acne, or acne that is at risk of causing permanent scarring) in adults and adolescents from 12 years of age only after puberty. Isotretinoin Capsules are for patients whose acne has not responded to other treatments.

Their use must be supervised by a dermatologist (a doctor who specialises in the treatment of skin problems).

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ISOTRETINOIN CAPSULES

Do not take Isotretinoin Capsules if:

- you are pregnant, think you may be pregnant or breast-feeding
- there is any chance you could become pregnant, you must follow the precautions under “Pregnancy and prevention programme”, see section on “Warnings and precautions”
- you are allergic to isotretinoin, peanut, soya or any of the ingredients of this medicine (listed in section 6)
- you have liver disease
- you are taking certain antibiotics called tetracyclines
- you have very high levels of vitamin A in your body (Hypervitaminosis A)
- you have very high levels of cholesterol or triglycerides (a fat like substance) in your blood.

Warnings and precautions

Talk to your doctor or pharmacist before taking Isotretinoin Capsules.

Pregnancy prevention programme

Women who are pregnant must not take Isotretinoin Capsules

This medicine can seriously harm an unborn baby (the medicine is said to be ‘teratogenic’) – it can cause serious abnormalities of the unborn baby’s brain, face, ear, eye, heart and certain glands (thymus gland and parathyroid gland). It also makes a miscarriage more likely. This may happen even if Isotretinoin capsules is taken only for a short time during pregnancy.

- You must not take Isotretinoin Capsules if you are pregnant or if you think you may be pregnant.
- You must not take Isotretinoin Capsules if you are breast-feeding. The medicine is likely to pass into your milk and may harm your baby.
- You must not take it 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 Isotretinoin Capsules 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 Isotretinoin Capsules.

Women must use effective contraception before, during and after taking Isotretinoin Capsules

- 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 Isotretinoin Capsules, during treatment and for a month afterwards.
- You must use contraception even if you do not have periods or are not currently sexually active (unless your doctor decides this is not necessary).

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

- 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 Isotretinoin Capsules (unless your doctor decides this is not necessary in your case).
- You must agree to extra pregnancy tests if your doctor asks you.
- 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 Isotretinoin Capsules, **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 Isotretinoin Capsules, you should contact your doctor. Your doctor may send you to a specialist for advice.

Your doctor has written information on pregnancy and contraception for the users of Isotretinoin Capsules which he or she should show you. If you haven't seen this material already, ask your doctor.

Prescriptions for women who could get pregnant are limited to 30 days treatment. A new prescription is needed for more treatment. Each prescription is only valid for 7 days.

Advice for men

The levels of oral retinoid in the semen of men taking Isotretinoin Capsules are too low to harm their partners' unborn baby. However, you must never share your medication with anyone.

Mental health problems

You may not notice some changes in your mood and behaviour and so it is very important that you tell your friends and family that you are taking this medicine. They may notice these changes and help you quickly identify any problems that you need to talk to your doctor about.

Advice for all patients:

- Talk to your doctor if you have or have ever had any kind of mental health problems, before taking Isotretinoin Capsules. This includes depression, aggressive tendencies or mood changes. It also includes thoughts about hurting yourself or ending your life. This is because your mood may be affected while taking Isotretinoin Capsules.
- **Severe skin reactions** (e.g. erythema multiforme (EM), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the use of Isotretinoin Capsules. The rash may progress to widespread blistering or peeling of the skin. You should also look for ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes)
- **Rarely, Isotretinoin Capsules may cause severe allergic reactions** some of which can affect skin in the form of eczema, hives and bruises or red patches on arms and legs. If you develop an allergic reaction, stop taking Isotretinoin Capsules, seek urgent advice from a doctor and tell him or her that you are taking this medicine
- **Isotretinoin Capsules may cause dry eyes, intolerance to contact lenses and visual difficulties including decreased night vision.** Tell your doctor if you have any of these symptoms. Your doctor may ask you to use lubricating eye ointment or tear replacement therapy. If you use contact lenses and you have developed intolerance to contact lenses, you may be advised to wear glasses during the treatment. Your doctor may refer you to a specialist for advice if you develop visual difficulties and you may be asked to stop taking Isotretinoin Capsules
- **Cut down on intensive exercise and physical activity.** Isotretinoin can cause muscle and joint pain particularly in children and teenagers undertaking vigorous physical activity
- **Isotretinoin Capsules has been associated with inflammatory bowel disease.** Your doctor will take you off Isotretinoin Capsules if you have severe bloody diarrhoea without any history of gastrointestinal disorders
- **Benign intracranial hypertension has been reported with Isotretinoin Capsules** and in some cases where Isotretinoin Capsules were used together with tetracyclines (a type of antibiotic). Stop taking Isotretinoin Capsules and seek urgent advice from your doctor if you develop symptoms like headache, nausea, vomiting and visual disturbances. Your doctor may refer you to a specialist to check for swelling of optic disk in the eye (papilloedema)
- **Isotretinoin Capsules may increase liver enzyme levels.** Your doctor will do blood tests before, during and after taking Isotretinoin Capsules to check these levels. If they stay high, your doctor may lower your dose or take you off Isotretinoin Capsules
- **Isotretinoin Capsules commonly increase blood fats**, such as cholesterol or triglycerides. Your doctor will test these levels before, during and after treatment with Isotretinoin Capsules. Tell your doctor if you already have high blood fats, diabetes (high blood sugars), are overweight, or an alcoholic. You may need blood tests more often. If your blood fats stay high, your doctor may lower your dose, or take you off Isotretinoin Capsules
- **Tell your doctor if you have any kidney problems.** Your doctor may start you on a lower dose of Isotretinoin Capsules and then increase it to the maximum tolerated dose
- **Isotretinoin Capsules may increase blood sugar levels.** In rare cases, people become diabetic. Your doctor may monitor blood sugar levels during treatment, particularly if you already have diabetes, are overweight, or are an alcoholic
- **Your skin and lips are likely to get dry.** Use a moisturiser and lip balm during treatment

- **Avoid chemical dermabrasion and laser treatment of the skin and wax depilation** during and for at least 6 months after treatment as they could cause scarring or irritation of the skin
- **Avoid too much sun and do not use a sunlamp or sunbed** as your skin may be more sensitive. Before going out in the sun apply a sun block to exposed skin, particularly in strong sunlight

Additional precautions

You should never give this medicinal product to another person. Please take any unused Isotretinoin 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 Isotretinoin Capsules because an unborn baby could be harmed if a pregnant patient receives your blood.

Children and adolescents

The use of Isotretinoin Capsules in children under the age of 12 is not recommended. This is because it is not known if it is safe or effective in this age group. Use in adolescents over 12 years of age only after puberty.

Other medicines and Isotretinoin Capsules

Tell your doctor or pharmacist if you are taking, have recently taken or might use any other medicines including herbal and non-prescription products.

- Do not use any other acne treatments unless your doctor has told you to
- Do not take tetracycline antibiotics when on isotretinoin treatment
- Do not take any vitamin A supplements.

Isotretinoin Capsules with alcohol

It is best that you do not drink alcoholic drinks or that you at least reduce the amount you usually drink while on treatment.

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 for advice before taking this medicine.

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

Pregnancy:

Isotretinoin Capsules **must not** be used during pregnancy. If you are able to get pregnant, you should use effective contraception one month before, during and up to one month after isotretinoin treatment.

If you do get pregnant while taking Isotretinoin Capsules, or in the month after treatment has stopped, stop taking the medicine straight away, and contact your doctor. He or she may refer you to a specialist for advice.

If used during pregnancy, Isotretinoin Capsules are likely to damage your unborn baby (in medical language it is *teratogenic*). It also increases the risk of miscarriage. Isotretinoin Capsules can cause serious abnormalities of brain, face, ear, eye, heart and some glands (called the thymus gland and parathyroid gland) of the unborn baby.

Breast-feeding:

You **must not** take Isotretinoin Capsules if you are breast-feeding. The medicine is likely to pass into your breast milk and may harm your baby.

Driving and using machinery

Your night vision may be affected by this medicine and you may develop dry eyes or sight problems. These changes can happen quite suddenly, so always be cautious when driving or operating machinery at night. Other visual disturbances, drowsiness or dizziness have been reported very rarely. If you experience any of these, you should not drive or operate machinery.

Isotretinoin Capsules contain sorbitol, maltitol and soya

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Isotretinoin Capsules contain soya oil. If you are allergic to peanut or soya, do not use this medicinal product.

3. HOW TO TAKE ISOTRETINOIN CAPSULES

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

Adolescents, adults and the elderly:

The recommended starting dose is 0.5mg/kg daily, e.g. if you weigh 60kg your starting dose will be 30mg/day. Normally, you should not take more than 1mg of isotretinoin per kilogram of bodyweight per day.

- The capsules can be taken either once a day or in two divided doses during the day.
- Take them with a meal or with a glass of milk.
- Swallow the capsules whole, do not suck or chew them.

Your doctor will tell you how many capsules to take, which may change after a few weeks of treatment. This will depend on how you respond to your medicine. For most patients the dose will be between 0.5 and 1.0 mg/kg/day. If you think that Isotretinoin Capsules are too strong or too weak, talk to your doctor or pharmacist.

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.

A normal course of treatment lasts between 16-24 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.

For a few patients, the acne may get worse during the first 7-10 days of treatment. Your acne should improve with continued treatment and may continue to improve for a few months after completion of the treatment course. **Do not** carry on taking this medicine unless your doctor tells you to.

Use in children:

Isotretinoin must NOT be used to treat children less than 12 years of age or before the onset of puberty.

If you take more Isotretinoin Capsules than you should

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

If you forget to take Isotretinoin Capsules

If you miss a dose take it as soon as possible. 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 to make up for a forgotten dose.

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

4. POSSIBLE SIDE EFFECTS

Some of the side effects associated with the use of isotretinoin are related to the dose. The side effects are generally reversible after changing the dose or stopping treatment, however some may continue after treatment has stopped.

Stop taking the capsules and contact your doctor IMMEDIATELY if any of the following occur:

- serious skin rashes (erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis), which are potentially life-threatening and require immediate medical attention. These 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. Additional symptoms such as infection of the eye (conjunctivitis) or ulcers of the mouth, throat or nose may occur. Severe forms of rash may progress to widespread peeling of the skin which can be life threatening. These serious skin rashes are often preceded by headache, fever, body aches (flu-like symptoms)
- symptoms of a severe allergic (hypersensitivity) reaction such as wheezing or difficulty in breathing, swelling of face, tongue or throat, itching, rash
- muscle weakness which can be potentially life-threatening, may be associated with trouble moving arms or legs, painful, swollen, bruised areas of the body, dark-coloured urine, reduced or no urine output, confusion or dehydration. These are signs of rhabdomyolysis, a breakdown of muscle tissue which can lead to kidney failure. This may occur if you are doing intensive physical activity while you're on Isotretinoin Capsules
- persistent headache, nausea, vomiting and blurred vision. You may have a rare condition called intracranial hypertension
- dry eyes, sight problems, colour vision disturbances or reduced night vision. These changes can happen quite suddenly, but rarely persist after treatment. Always be cautious when driving or operating machinery at night. Your doctor may want to monitor your vision
- yellow skin or eyes, and feeling tired. These can be signs of hepatitis
- difficulty urinating (passing water), swollen and puffy eyelids, feeling excessively tired. These may be signs of kidney inflammation
- sudden tight chest, shortness of breath and wheezing, particularly if you have asthma

- severe abdominal (tummy) pain, with or without severe bloody diarrhoea, feeling sick (nausea) and being sick (vomiting). These can be signs of serious gut conditions.

Contact your doctor IMMEDIATELY if you get any of the following symptoms.

Mental problems

Rare effects (may affect up to 1 in every 1,000 people)

- depression or related disorders. Signs of this include sad or empty mood, mood changes, anxiety, crying spells, irritability, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down or trouble concentrating
- 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 the above mentioned mental problems. Your doctor may tell you to stop taking Isotretinoin Capsules. That may not be enough to stop the effects: you may need more help, and your doctor can arrange this.

Other side effects:

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

- inflammation, dryness and cracking of the skin and lips. These can be relieved by the regular use of a good moisturising cream and lip balm from the start of treatment
- skin rash, mild itching and slight peeling of the skin, or red, fragile skin
- inflammation of the eyelids
- dry, irritated eyes or conjunctivitis. This may be a problem if you wear contact lenses. Ask your pharmacist for suitable eye drops to help
- changed levels of fats in the blood (including HDL or triglycerides)
- raised liver enzymes seen in blood tests
- anaemia
- blood clotting may be affected, which means that you may bruise or bleed more easily.

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

- headaches
- increased blood cholesterol
- changes in blood glucose levels especially in diabetics
- blood or protein in the urine
- more liable to get infections if the white blood cells are affected

- the inside of the nose may become dry and "crusted", which may lead to mild nosebleeds. Applying a thin layer of petroleum jelly gently to the inside of the nose will help
- sore or inflamed throat and nose.

Rare side effects (may affect up to 1 in every 1,000 people):

- changes to your hair (either a loss or, more rarely, an increase). This is usually only temporary and persistent hair thinning is rare. Your hair should return to normal after the treatment ends.

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

- generally feeling unwell
- excess sweating or itching
- arthritis; bone disorders (delayed growth, extra growth and changes in bone density); growing bones may stop growing
- calcium deposits in soft tissue, sore tendons, high levels of muscle breakdown products in your blood if you exercise vigorously
- excessive thirst; frequent need to urinate; blood tests show an increase in your blood sugar. These can all be signs of diabetes
- dizziness, drowsiness, fits (convulsions)
- worsening of acne, which usually subsides within 7-10 days of treatment
- thickened scarring after surgery
- inflammation of the pancreas, causing severe pain in the abdomen and back
- dry throat, hoarseness
- increased skin pigmentation
- increased sensitivity to sunlight
- bacterial infections
- slight loss of hearing
- changes in the nails
- local bacterial infections such as infection of the tissue around the base of the nail
- increased levels of a substance in your blood known as uric acid. If you suffer from gout, this could trigger an attack. Very high levels of uric acid may affect your kidney function
- inflammation of blood vessels (sometimes with bruising and red patches)
- disease of the lymph nodes
- increased risk of infection, as leukocytes, which are cells in your blood involved in fighting infections, may decrease in number.

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

- dark or cola-coloured urine
- problems getting or maintaining an erection
- lower libido
- Breast swelling with or without tenderness in males

Most of the unwanted effects of Isotretinoin will disappear when you stop treatment.

If you are concerned about these or any other side effect talk to your doctor.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly

via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard. By reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE ISOTRETINOIN CAPSULES

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

Do not store above 25°C. Store in the original container to protect from light. Do not use this medicine after the expiry date printed on the pack. 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 to protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Isotretinoin Capsules contain:

Each capsule contains 5 or 20mg of the active ingredient isotretinoin.

The capsules also contain refined soya-bean oil, yellow beeswax, hydrogenated soya-bean oil and partially hydrogenated vegetable oil. The capsules are made from gelatin, glycerol, titanium dioxide (E171), ferrous oxide red (E172) and ferrous oxide yellow (E172). The printing ink (432BL) contains Brilliant Blue FCF dye, sorbitol, maltitol, phosphatidylcholine and lysophosphatidylcholine.

What Isotretinoin Capsules look like and contents of the pack:

The soft gelatin capsules are red/orange, the 5mg are marked 'P5', the 20mg are marked 'P20'. Each pack contains either 30 or 56 capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Alliance Pharmaceuticals Limited, Bath Road, Chippenham, SN15 2BB, UK.

Manufacturer: Pharmathen SA, Dervenakion 6, Pallini 15351, Attikis, Greece.

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