Package leaflet: Information for the user

ISOTRETINOIN 5MG AND 20MG CAPSULES

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
6. Contents of the pack and other information

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 allergic to isotretinoin, peanut, soya or any of the ingredients of this medicine (listed in section 6)
- are pregnant or think you may be pregnant (see 'Important advice for female patients' in the box below)
- are able to become pregnant but you haven’t followed the necessary pregnancy prevention measures that are listed in the pregnancy prevention plan
- are breast-feeding
- have liver disease
- are taking certain antibiotics called tetracyclines
- have very high levels of vitamin A in your body (Hypervitaminosis A)
- 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.

<table>
<thead>
<tr>
<th>Important Advice for Female Patients.</th>
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<tbody>
<tr>
<td><strong>Isotretinoin will damage an unborn baby</strong> (in medical language it is <em>teratogenic</em>). <strong>It also increases the risk of miscarriage so:</strong></td>
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<tr>
<td>- You must not take Isotretinoin Capsules if you are pregnant or think you may be pregnant.</td>
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<tr>
<td>- You must not take Isotretinoin Capsules if you are breast-feeding. The medicine is likely to pass into your milk and harm your baby</td>
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<tr>
<td>- You must not take it if you could get pregnant during treatment, or during the month after treatment.</td>
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<table>
<thead>
<tr>
<th>Women who could get pregnant are only prescribed Isotretinoin Capsules under strict rules, because of the risk of birth defects (damage to the unborn baby). These are the rules:</th>
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<tbody>
<tr>
<td>- You must only take Isotretinoin Capsules if you have severe acne that has not got better after any other anti-acne treatments, including antibiotics and skin treatment</td>
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<tr>
<td>- Your doctor must have explained the risk of birth defects: you understand why you must not get pregnant and what you need to do to prevent it</td>
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<td>- You must have discussed contraception (birth control) with your doctor. They will give you information on preventing pregnancy. He or she may refer you to a specialist for contraceptive advice</td>
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<td>- You must agree to use one, preferably two, effective methods of contraception (including condoms, or a cap plus spermicide) for one month before taking Isotretinoin Capsules, during treatment and for one month after treatment ends. Before you start treatment your doctor will ask you to take a pregnancy test, which must be negative</td>
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<tr>
<td>- 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)</td>
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<tr>
<td>- You must be capable of complying with the necessary pregnancy prevention measures that are listed in the pregnancy prevention plan</td>
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<td>- You must accept the need for monthly follow up visits and more pregnancy tests as decided by your doctor. You may have a test 5 weeks after stopping Isotretinoin Capsules. You must not become pregnant at any time during treatment or for one month after treatment ends</td>
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<tr>
<td>- Your doctor may ask you (or a guardian) to sign a form that confirms that you have been told about the risks, and that you accept the necessary precautions</td>
</tr>
<tr>
<td>- Contact your dermatologist immediately if you do become pregnant or think you may be pregnant during treatment or in the first month after treatment ends.</td>
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</table>

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 Male patients
Isotretinoin treatment does not appear to damage sperm. Isotretinoin and its metabolites are present at very low levels in your semen. These levels are considered too low to harm the unborn baby of your female partner. You must remember not to share your medication with anyone, particularly not women.

Advice for all patients:
- Tell your doctor if you have or have had any mental illness including depression, psychosis or suicidal behaviour
- 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.

• Do not donate blood during therapy or for at least one month after treatment with Isotretinoin.

• Do not give your medication to anyone else. Return any unused capsules to the pharmacy.

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 and breast-feeding
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.

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.

Isotretinoin 5 & 20mg PIL UK 005
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

Like all medicines, this medicine can cause side effects, although not everybody gets them. These effects often wear off as your treatment continues and your doctor can help you to deal with them.

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. Your doctor may tell you to stop taking this medicine.

- 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 interest in appetite, school or work performance going down or trouble concentrating
- existing depression getting worse
- becoming violent or aggressive
- 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.

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

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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