

## Package leaflet: Information for the user

### A-cnotren, 10 mg soft capsules Isotretinoin

**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.

#### What is in this leaflet:

1. What A-cnotren is and what it is used for
2. What you need to know before you take A-cnotren
3. How to take A-cnotren
4. Possible side effects
5. How to store A-cnotren
6. Contents of the pack and other information

#### 1. What A-cnotren is and what it is used for

A-cnotren is used to treat severe forms of acne, (such as nodular or conglobate acne or acne at risk of permanent scarring) which has not got better after other anti-acne treatments including oral antibiotics.

A-cnotren contains the active ingredient isotretinoin belonging to the retinoid class of medicines.

The doctor might have prescribed other treatment. Please follow doctors orders.

The isotretinoin treatment must be supervised by doctors specialised in the treatment of severe acne and fully understands the risk of congenital malformations in children. Isotretinoin is not used to treat acne occurring before puberty, or in children younger than 12 years of age.

#### 2. What you need to know before you take A-cnotren

##### Do not take A-cnotren:

- if you are pregnant or think you may be pregnant
- if you are breastfeeding
- if you have liver disease
- if you have very high levels of lipids (cholesterol, triglycerides) in your blood
- if you have very high levels of vitamin A in your body (hypervitaminosis A)

- if you are allergic to isotretinoin or any of the other ingredients of this medicine (listed in section 6). A-cnotren contains refined soya oil, partially hydrogenated soya oil and hydrogenated soya oil. If you are allergic to peanut or soya, do not use this medicinal product.

- if you are taking tetracyclines (a type of antibiotic medicine; used to treat for example acne)
- if you are taking topical keralytic or exfoliative anti-acne agents, as local irritation may increase.

#### IMPORTANT

**A-cnotren is teratogenic. That means it is likely to damage an unborn baby. There is also an increased risk of miscarriage.**

You must not take Isotretinoin if you are pregnant or may become pregnant at any time during treatment and for one month after treatment has stopped.

#### Warnings and precautions

Talk to your doctor or pharmacist before taking A-cnotren  
**Female patients of childbearing potential can only receive A-cnotren treatment if:**

- You have severe acne, which has not got better after other anti-acne treatments, including oral antibiotics.
- Your doctor has explained the teratogenic risk of isotretinoin, and you understand why you must not get pregnant and how to prevent pregnancy.
- You have discussed using effective contraception (birth control) with your doctor. Your doctor will give you information on pregnancy prevention including a brochure

- A-cnotren therapy may affect your night vision. You may develop dry eyes or sight problems during therapy, which normally returns to normal once treatment is stopped. If you experience any problems with your sight, please inform your doctor immediately and have your sight monitored. Always be cautious when driving or operating machinery at night because these sight changes can happen quite suddenly. If you wear contact lenses and experience dry eyes you may need to wear glasses for the duration of the treatment.

- Your skin may become more sensitive to sunlight during the therapy. Avoid too much sun and do not use a sun-lamp or sun-bed. Before going out in the sun apply a sun-protection product with a high protection factor of at least SPF 15.

- Cosmetic procedures such as dermabrasion or laser treatments (removing horny skin or scars) and wax epilation should be avoided during and for at least 6 months after treatment as this could cause scarring or irritation of the skin. Your skin may become more fragile during the treatment with A-cnotren.

- Use a skin moisturizing ointment or cream and a lip balm during treatment as you may experience skin and/or lip dryness during the therapy.

- Because muscle and joint pain have been observed during the treatment, care should be taken to reduce intensive physical activity during therapy.

- If you have severe kidney problems, the treatment shall be started at a lower dose

- If you suffer from other diseases and are using other medication including herbal medication.

- Do not take vitamin A supplements during A-cnotren therapy. Taking both together may increase the risk of getting side effects.

- Do not donate blood either during or for one month after the treatment. If someone who is pregnant receives your donated blood, her baby may be born with serious birth defects.

#### Other medicines and A-cnotren

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. Do not take vitamin A supplements or tetracyclines (a type of antibiotic; used to treat for example acne) during the therapy.

#### A-cnotren with food and drink

A-cnotren should be taken with food. Swallow the capsules whole.

#### 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 or pharmacist for advice before taking this medicine.

#### Pregnancy

A-cnotren must not be taken during pregnancy. Taking isotretinoin during pregnancy cause a high risk of very severe congenital malformations and an increased risk of abortion. Abnormalities seen in pregnant women during therapy are damage to CNS, facial abnormalities, cleft palate, abnormal ears, abnormal eyes, cardiovascular abnormalities, and abnormalities of the thymus gland and parathyroid gland.

#### Breast-feeding

You should not take A-cnotren if you are breastfeeding, because isotretinoin is likely to pass into the milk and may harm the baby.

#### Driving and using machines

Your night vision may get worse during your treatment. This can happen suddenly. In rare cases this has continued after the treatment has stopped. You should therefore be cautious when driving or operating machines. Drowsiness and dizziness have been reported very rarely. If this happens to you, you should not drive, operate

on contraception explaining the different methods.

- You agree to use at least one and preferably two effective methods of contraception for one month before treatment, during treatment and for one month after treatment. Before you start treatment your doctor will ask you to take a pregnancy test, which must be negative.
- You use contraception even if you do not have periods or are not currently sexually active, unless your doctor decides this is not necessary.
- You understand and accept the need for monthly follow up visits and maybe further pregnancy tests as decided by your doctor. You may then have a pregnancy test 5 weeks after stopping your therapy. You must not become pregnant at any time during treatment or for one month after treatment ends.

If you become pregnant while on therapy or during the month after treatment has stopped, immediately stop taking the medicine and contact your doctor. He or she may refer you to a specialist for evaluation and advice. Prescriptions are limited to 30 days treatment for women of childbearing potential. Continuation of treatment requires a new prescription, and each prescription is only valid for seven days.

### Male patients

There are no restrictions on prescriptions for male patients. Isotretinoin and its metabolites are present at very low levels in your semen. These levels are too low to harm the unborn baby of your female partner. Male patients should be reminded that they must not share their medication with anyone, particularly not females.

### Take special care with A-cnotren:

- Isotretinoin may increase the levels of fats such as triglycerides or cholesterol in your blood. Your doctor will do some blood tests in order to monitor these levels before, during and at the end of your treatment. Please tell your doctor if you already have high levels of these substances in your blood or if you have diabetes, are overweight or are an alcoholic as you may need to get blood tests done more frequently.

- Isotretinoin may increase your liver enzyme levels. Your doctor will do some blood tests before, during and at the end of your treatment to check your liver values. In cases where liver enzyme values remain high your doctor may reduce your dose or stop your A-cnotren therapy.

- Isotretinoin may increase your blood sugar levels and in rare cases diabetes mellitus has been diagnosed. Your doctor may monitor your blood sugar levels during your treatment particularly if you have diabetes, are overweight or are an alcoholic.

- Rare cases of depression, worsening depression, anxiety, mood changes, psychotic symptoms and very rarely suicidal thoughts, suicide attempts and suicide have been reported. If you have any kind of mental problems, or if you think you have signs of depression while taking Isotretinoin such as feeling very sad for no reason, crying spells, difficulty concentrating or you become withdrawn from your friends or family, please inform your doctor. Your doctor may refer you for appropriate treatment if necessary. Discontinuation of your A-cnotren therapy may not be enough to relieve symptoms and you may require further psychiatric or psychological help.

- Using of ointments or local treatment against acne should be avoided if not prescribed through your doctor.

- If you experience an allergic reaction (skin redness, itching, sneezing, vomiting, convulsions, difficulty in breathing, low blood pressure) please stop your therapy.

- If you experience a persistent headache, nausea, vomiting and blurred vision, please stop your therapy immediately and contact your doctor as soon as possible.

- If you experience severe haemorrhagic diarrhoea (e.g. blood in your stool), please stop therapy immediately and contact your doctor as soon as possible.

machinery or take part in any other activities where the symptoms could put either you or others at risk.

### Isotretinoin capsules contain soya oil.

If you are allergic to peanuts or soya do not use this medicinal product.

### 3. How to take A-cnotren

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

The recommended dose is:

The usual starting dose is 0.5 mg per kilogram bodyweight per day (0.5 mg/kg/day). During the treatment your doctor may adjust your dose. This will depend 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 have the impression that the effect of A-cnotren is too strong or too weak, talk to your doctor or pharmacist.

If you do not tolerate the recommended dose, your doctor may continue your treatment at a lower dose with the consequence of a longer therapy duration and a higher risk of relapse.

Always follow the doctor's direction. There are differences in how single persons react.

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

Occasionally your acne may get worse during the first weeks of treatment. It should improve with continued treatment.

A course of treatment usually lasts for 16 to 24 weeks. Your acne may continue to improve for up to 8 weeks after the treatment finishes.

Therefore, a further course of treatment should not be started until at least this period has elapsed. Most patients only need a single course of treatment.

The doctor should only prescribe change or stop of the treatment. Please return any unused capsules to your pharmacist at the end of treatment. Only keep it if your doctor tells you to. Remember this medicine is for you. Only a doctor can prescribe it for you. Never give it to others. It may harm them even if their symptoms look similar to yours.

### Use in children

A-cnotren is not used to treat acne occurring before puberty, or in children younger than 12 years of age.

### Decreased kidney function

If you have severe kidney problems, the treatment should be started at a lower dose such as 10mg/day and then increased up to the highest tolerated dose.

### If you take more A-cnotren 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 a vitamin A acid derivate. The poisoning symptoms for Isotretinoin are similar to the ones caused by vitamin A poisoning, for example headache, nausea, vomiting, dizziness, irritability and itching.

### If you forget to take A-cnotren

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 capsule.

### If you stop taking A-cnotren

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

05.10.15  
Mary  
7/10/2015

#### 4. Possible side effects

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

Some of the side effects associated with the use of isotretinoin are dose-related.

These effects often wear off as your treatment continues or after treatment has stopped. Your doctor can help you to deal with them.

See also Section 2 What you need to know before you take A-cnotren

#### Serious adverse effects, which are rare (>1/10 000 and <1/1000) or very rare (<1/ 10 000)

##### Mental problems

On rare occasions, some patients taking isotretinoin or soon after stopping isotretinoin have become depressed or developed other serious mental problems. Symptoms 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. Rarely, patients who already have depression may feel worse. Very rarely, some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people have tried to end their own lives (suicide attempt), and some people have ended their lives (suicide). There have been reports that some of these people did not appear depressed.

Rarely, there have been reports of patients on isotretinoin becoming violent or aggressive.

As mental problems can be caused by many different factors, it is important to tell your doctor if you have ever had any mental illness including depression, suicidal behaviour or psychosis (psychosis means a loss of contact with reality, such as hearing voices or seeing things that are not there). Also tell your doctor if you take medicines for any of these conditions.

If you think you are developing any of these mental conditions or the symptoms of depression you should contact your doctor right away. You may be advised to stop taking isotretinoin. However, stopping your isotretinoin may not be sufficient to relieve your symptoms and you may need further help which your doctor can arrange.

##### Allergic reactions

If you experience a tightness in your chest and difficulty breathing (especially if you suffer from asthma) or skin rashes and itching you may have an allergic reaction or serious anaphylactic reactions caused by isotretinoin. Stop taking isotretinoin and contact your doctor immediately.

##### Neurological disorders

Very rarely benign intracranial hypertension has been reported, particularly when isotretinoin was taken together with some antibiotics (tetracyclines). If you experience a persistent headache with nausea, vomiting and blurred vision, this may mean that you have developed a benign intracranial hypertension. Stop taking isotretinoin as soon as possible and contact your doctor.

##### Gastrointestinal disorders

If you experience severe abdominal pain with or without bloody diarrhoea, nausea and vomiting, stop taking isotretinoin as soon as possible and contact your doctor. There have been very rare reports of patients experiencing serious gastrointestinal disturbances, such as pancreatitis, gastrointestinal haemorrhage, colitis, ileitis and inflammatory bowel disease.

##### Liver problems

If you experience yellowing of the skin or eyes with tiredness, stop taking your medication as soon as possible and contact your doctor. Very rarely patients have developed serious liver problems (hepatitis).

##### Kidney problems

In very rare cases, patients may experience inflammation of their kidneys. Symptoms include feeling excessively tired, difficulty urinating as well as swollen and puffy eyelids. If this occurs while you are taking your medicine, stop the therapy and contact your doctor.

#### 6. Contents of the pack and other information

##### What A-cnotren contains

The active substance is Isotretinoin .

Each soft capsule contains 10 mg of isotretinoin.

The other ingredients are: Each soft capsule also contains: Refined soya bean oil, yellow beeswax, hydrogenated soya bean oil, partially hydrogenated soya bean oil.

The capsule shell contains: Gelatin, glycerol, the colours titanium dioxide (E171), yellow and red iron oxide (E 172).

##### What A-cnotren looks like and contents of the pack

A-cnotren 10 mg capsules are oval, red/orange (size 3)

Pack sizes: 30, 50, 60, 100

Not all pack sizes may be marketed.

#### THIS IS A MEDICAMENT

- A Medicament is a product, which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medication.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription, without consulting your doctor.

**Keep all medicaments out of the reach of children.**

##### Marketing Authorisation Holder in Greece:

Pharmathen Hellas S.A., 144, Marathonos Avenue, 15351 Pallini, Attiki, Greece

##### Responsible for exports:

Pharmathen S.A., Dervenakion 6, 15351 Pallini, Attiki, Greece

##### Manufacturer:

G.A. Pharmaceuticals S.A., 46 Agisilaou Str., Agios Dimitrios Attiki, 17341 Greece

##### Packagers & Batch releasers:

Pharmathen International S.A., Industrial Park Sapes, Rodopi Prefecture, Block No 5, Rodopi 69300, Greece

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*Handwritten signatures and dates:*  
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Skin and hair problems – Unknown frequency  
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).

If you develop a rash or these skin symptoms, stop taking A-cnotren and contact your doctor immediately.

#### Other side effects

Very common: >1/10

Decreased liver function (increased activity of transaminase in blood) anaemia, blood disorders (thrombocytopenia, thrombocytosis), inflammation of the eyelid area (blepharitis) and the eye (conjunctivitis), dry eyes, eye irritation, inflamed lips, inflamed skin (dermatitis), dry skin, peeling of the skin, itching, blushing rash, fragile skin, joint and muscle pain, back pain (particularly in children and adolescent patients), increased blood levels of fat-like substances.

Common: >1/100 and <1/10

Blood disorders (neutropenia), headache, nose bleeding, dryness of the nose, common cold, increase of blood levels of cholesterol, glucose, protein, and uric acid.

Rare: >1/10 000 and <1/1000

Allergic reactions, hypersensitivity, severe hypersensitivity reactions (anaphylactic reactions), loss of hair.

Very rare: <1/10 000 including isolated cases

Bacterial infections, lymph glands disorders (lymphadenopathy), diabetes mellitus, hyperuricaemia, convulsions, drowsiness, dizziness, blurred vision, corneal opacities, cataracts, colour blindness, discomfort in wearing contact lenses, keratitis, decreased night vision, photophobia, visual disturbances, vasculitis, decreased hearing, dryness of the throat, nausea, worsening and increasing of the acne, facial erythema, increase of hair (hirsutism), changes in the nails, infection in the tissue around the base of the nails, sensitivity to light, rash (exanthema), inflammation of the skin, increased pigmentation, excessive sweating, arthritis, bone disorders, calcification in soft tissues, soreness of the tendons, muscle tissue (rhabdomyolysis), increase of granulation tissue, malaise (feeling of being unwell), increased level of muscle degradation product (creatine phosphokinase activity) in the blood.

Metabolism and nutrition disorders: Diabetes mellitus.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

#### 5. How to store A-cnotren

Keep this medicine out of the sight and reach of children. Do not store above 30° C. Store in the original container. Keep the container tightly closed in order to protect from light.

Do not use this medicine after the expiry date which is stated on the carton.

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

Do not throw 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.