PATIENT INFORMATION LEAFLET

ORATANE causes severe birth defects. It should not be taken by pregnant women, women intending to become pregnant, or sexually active women in their childbearing ~~fertile~~ years, not using at least two methods of contraception, as severe malformations may occur during pregnancy.

SCHEDULING STATUS

S5

ORATANE 5 mg

ORATANE 10 mg

ORATANE 20 mg

ORATANE 40 mg

Soft gelatin capsules

Isotretinoin

All strengths contain sugar (sorbitol liquid (non-crystallizing)):

ORATANE 5 mg: 5 mg/capsule

ORATANE 10 mg: 7, 58 mg/capsule

ORATANE 20 mg: 24,26 mg/capsule

ORATANE 40 mg: 23,75 mg/capsule

Read all of this leaflet carefully before you start taking ORATANE capsules

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- ORATANE has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

ORATANE is not a cosmetic medicine.

- You will also receive an additional Patient Information Brochure to read.
- If you are a female patient, you will receive a Brochure on Birth Control and the Female Patient Information and Consent Form.

What is in this leaflet

1. WHAT ORATANE IS AND WHAT IT IS USED FOR

ORATANE contains isotretinoin as the active ingredient and is a dermatological product which acts by reducing the size and activity of the oil producing glands of the skin.

ORATANE is used for:

A severe type of acne called recalcitrant nodular acne. This type of acne causes hard lumps (nodules) under your skin. “Severe”, by definition, means “many” as opposed to “few or several” lumps. It should only be used in patients with severe nodular acne who have not responded to other conventional acne treatments, including antibiotics.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ORATANE

Do not take ORATANE:

Oratane must not be used by female patients who are or may become pregnant unless an effective contraceptive is used, without interruption, for one month before using Oratane, while using Oratane, and for at least one month after stopping Oratane. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking Oratane in any amount, even for short periods of time. Potentially any foetus exposed during pregnancy can be affected. You must have a negative result from a reliable pregnancy test within 11 days before you start using Oratane. Monthly repetition of pregnancy testing is strongly recommended while taking Oratane. You must start Oratane treatment only on the 2nd or 3rd day of your next normal menstrual period.

- If you are hypersensitive or allergic to isotretinoin or any of the other ingredients of ORATANE (listed in section 6: What ORATANE contains).
- ORATANE contains soya-bean oil, do not use it if you are allergic to peanuts or soya.
- If you are a woman of childbearing potential (unless all of the conditions of the Pregnancy Prevention Programme are met), pregnant, planning to become pregnant, or breastfeeding
- If you have a disease called hypervitaminosis A (too much vitamin A stored in your body). Hypervitaminosis A manifests as nausea and vomiting, headache, dizziness, blurred vision, lack of muscular coordination, abnormal liver function, and pain in weight-bearing bones and joints.
- If you have liver impairment.
- If you have excessively high triglyceride (fat-like substance) levels in your blood.
- If you have severe weight problems.
- If you are using medication from the antibiotic class, called the tetracyclines.

Warnings and precautions

Oratane is a scheduled medicine, not a cosmetic medicine. It is a criminal offence to give Oratane to or share it with any person not in possession of a valid prescription.

Take special care with ORATANE:

If you are a woman who is able to have children, you must have a pregnancy blood test within 1 week before beginning treatment with ORATANE to make sure you are not pregnant. Treatment with ORATANE will then be started within the week, on the second or third day of your next normal menstrual period. In

addition, you must have a pregnancy blood test each month while you are taking ORATANE and one month after treatment is completed.

Make sure that you are using effective forms of contraception (birth control) from at least one month before you start taking ORATANE. Contraception must be continued during the period of treatment and for one month after ORATANE is stopped. It is recommended that you use two forms of contraception.

Tell your doctor or health care provider before taking ORATANE

- ORATANE contains sugar (sorbitol, which is a source of fructose). Patients with the rare hereditary fructose intolerance (HFI) should not take ORATANE.
- If you have a history of depression. Oratane may worsen depression, cause anxiety, aggressive tendencies, alter your mood and bring on ideation of suicide. Your doctor will monitor you for any of these symptoms.
- If you have high cholesterol.
- If you have a disease called diabetes mellitus (high blood sugar).
- If you have a liver disease. Your doctor will send you for blood tests before treatment and monthly to confirm that your liver function is not affected.
- If you use contact lenses. ORATANE may cause dryness of the eyes and scarring of your cornea. Therefore, if you wear contact lenses, your eyes may be more sensitive to them during the time you are taking ORATANE and for up to about 2 weeks after you stop taking it. This may necessitate you to wear glasses during treatment. To help relieve dryness of the eyes, check with your doctor about using an eye lubricating solution, such as artificial tears. If eye inflammation occurs, check with your doctor.
- If you drive or operate machines at night as Oratane may cause decreased vision at night.
- Do not donate blood during the use of ORATANE and up to one month after stopping treatment as blood donated to a pregnant person may negatively affect their baby.
- Avoid excessive dermabrasion (removal of superficial layers of skin) and waxing whilst taking Oratane and for a period of 5 to 6 months after treatment, because of the risk of scarring.
- Avoid too much direct sunlight, wind or cold weather. Your skin will be more prone to sunburn, dryness, or irritation, especially during the first 2 or 3 weeks of treatment. Use an effective sunscreen or sun-block regularly, as well as protective clothing, such as hats. You should not stop taking ORATANE unless the skin irritation becomes too severe. Please consult with your doctor first.

- High Risk Patients: In patients with diabetes, obesity, alcoholism or a lipid metabolism disorder, more frequent checks of serum values for lipids and/or blood glucose may be necessary. Increased fasting blood sugars have been reported, and new cases of diabetes have been diagnosed during ORATANE therapy.

If you have any of these conditions, you may need a dose adjustment or special tests to safely take ORATANE.

Tell your doctor, pharmacist or professional healthcare provider if any of these apply to you.

Children

The safety and effectiveness of Oratane in children under 12 has not been demonstrated. Oratane should therefore not be used in children under 12 years of age.

Other medicines and ORATANE

Always tell your health care provider if you are taking any other medicine.

(This includes all complementary or traditional medicines.)

Do not take any medication or supplements which contain vitamin A. This may include your daily multivitamin supplement. These medicines may cause toxic levels of vitamin A in your body.

Do not take medication from the antibiotic class, called the tetracyclines as taking these with Oratane may increase the pressure around your brain.

Do not use preparations that soften, remove or exfoliate the outer skin.

Do not undergo any form of radiation or UV (ultra-violet) treatment, such as sun-beds.

Pregnancy, breastfeeding and fertility:

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning or are able to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking ORATANE (see section: Do not take ORATANE).

DO NOT use ORATANE if you are pregnant or suspect that you are pregnant as it may result in very severe malformations of the foetus. Contact you doctor immediately.

DO NOT use ORATANE during breastfeeding as it may pass into the breast milk and result in side effects for the infant.

Oratane does not affect fertility for men that are on treatment.

Driving and using machines:

ORATANE may make you drowsy and dizzy which may impair your ability to drive and use machinery.

ORATANE may impair your ability to drive and use machinery at night as it affects night vision. The impact on night vision may continue even after you have stopped treatment with Oratane.

It is not always possible to predict to what extent ORATANE may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which ORATANE affects them.

ORATANE contains sorbitol and soya oil

Sorbitol is a source of fructose. If your doctor has told you that you (or your child) have an intolerance to some sugars, talk to your doctor before you (or your child) take or receive Oratane.

Sorbitol may cause gastrointestinal discomfort and mild laxative effect if taking 140 mg/kg/day or more per day.

Care should be taken when taking other medicines or foods containing sorbitol or fructose as these may increase the effects.

Soya oil is contraindicated in patients allergic to peanuts or soya. If you are allergic to peanut or soya, do not use Oratane.

3. HOW to take ORATANE

Do not share medicines prescribed for you with any other person.

It is a criminal act to give Oratane to any person who does not have a valid prescription.

Always use ORATANE exactly as your doctor or pharmacist has told you.

Check with your doctor or pharmacist or nurse if you are not sure.

The dose required varies from person to person. It is based on your weight. Your doctor will prescribe and/or adjust the correct dose of ORATANE for your condition and the side-effects you may develop.

Your doctor will also tell you whether you should take it as a once daily or twice daily dose. In order to achieve the correct dose, your doctor may prescribe two different strength capsules to be taken as a single dose. Ensure that you do not confuse the capsules and take two of the same strength at one time, unless specifically instructed to do so.

The daily dose should be taken with meals and a full glass of liquid, such as milk or water.

The capsule should not be crushed, chewed or sucked, but should be swallowed whole with meals.

Taking ORATANE at the same time each day will have the best effect. It will also help you remember when to take your medicine.

Your doctor will tell you how long your treatment with ORATANE will last and if or when you need a second course.

Your acne may be worsened at first. Do not stop taking ORATANE as it is essential that you continue treatment during this phase.

If you have the impression that the effect of ORATANE is too strong or too weak, tell your doctor or pharmacist.

If you take more ORATANE than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Always take the labelled medicine package with you, whether there are any ORATANE tablets left or not.

The signs and symptoms of an overdose will resemble those of vitamin A toxicity which include headache, nausea or vomiting, drowsiness, irritability, and itching.

If you forget to take your ORATANE:

If you miss a dose of Oratane, take the missed dose as soon you remember. However, if it is almost time for you next dose, continue to take the next dose at the usual time.

Do not take a double dose to make up for the forgotten individual dose.

If you stop using ORATANE

Do not stop taking ORATANE without first talking to your doctor, pharmacist or professional healthcare provider.

4. POSSIBLE SIDE EFFECTS

ORATANE can have side effects.

Not all side effects reported for ORATANE are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while taking ORATANE, please consult your health care provider for advice.

Every patient should be warned about the possible occurrence of side effects.

Most of the side effects of Oratane are dose-related.

If any of the following happens, stop taking ORATANE and tell your doctor immediately or go to the casualty department at your nearest hospital:

- serious allergic reactions with swelling of your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- allergic reactions including rash or itching

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to ORATANE.

You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- infections
- depression or increased depression, aggressive tendencies, anxiety, mood alterations, psychotic disorders, abnormal behaviour
- severe or frequent headaches, often along with nausea or vomiting, double vision, loss of vision as these could be symptoms of high pressure around the brain (benign intracranial hypertension)
- difficulty in breathing (bronchospasm), particularly in patients with asthma
- pain or discomfort of your intestines or bloody diarrhoea
- fainting
- depression, suicide attempt, suicidal thoughts, mood or mental changes (psychotic disorders)
- seizures (fits or epilepsy) or sudden, violent, irregular movement of the body, caused by involuntary contraction of muscles (convulsions)
- yellow skin and eyes (also called jaundice) or abdominal tenderness, could be signs of hepatitis.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following side-effects reported for ORATANE:

Frequent side-effects:

- weakness, tiredness, pale skin (anaemia)
- other changes in your blood, like too little platelets (thrombocytopenia), too many platelets (thrombocytosis), red blood cell sedimentation rate increased and low levels of white blood cells (neutropenia).
- headache

- inflammation of the eyelids in which they become red, irritated and itchy with dandruff-like scales that form on the eyelashes (blepharitis),
- pink eye (conjunctivitis), dry eyes, eye irritation
- a common cold (nasopharyngitis), nose bleeding (epistaxis), dry nose
- high levels of transaminase in your blood
- itchy or an unpleasant sensation of the skin (pruritis)
- skin rash (erythematous)
- itchy, dry skin or a rash on swollen, reddened skin (dermatitis)
- dry lips (cheilitis), dry skin, flaking of the skin (localised exfoliation)
- thinning or easy bleeding skin (skin fragility) with risk of frictional trauma
- joint pain (arthralgia), muscle pain (myalgia) or back pain (particularly in adolescent patients)
- changes to your blood and urine shown by blood or urine tests, like higher levels of triglycerides, lower levels of high density lipoprotein, higher levels of blood cholesterol and glucose, blood in your urine (haematuria), higher levels of protein in the urine (proteinuria)

Less frequent side-effects:

- bacterial infections
- disease of the lymph nodes (lymphadenopathy)
- severe allergic reactions (anaphylactic reactions)
- hypersensitivity of the skin (e.g. sensitivity to sunlight)
- allergic skin reaction
- high blood sugar (diabetes mellitus) with signs like thirst, frequent urination, extreme hunger, unexplained weight loss, tiredness, slow-healing sores
- high uric acid levels in the blood (hyperuricaemia) with signs like pain and stiffness of joints
- depression or more severe depression
- suicide, suicide attempt or thinking of committing suicide
- other psychotic disorders, including getting aggressive more likely, anxiety (fear), mood changes, abnormal behaviour

- increased pressure in your skull (benign intracranial hypertension), with early signs and symptoms like swelling of your eye disc (papilloedema), headache, nausea, vomiting and visual disturbances or ringing sound in ears and can cause neck, shoulder or back pain and dizziness
- convulsions (seizures, fits or epilepsy)
- drowsiness and dizziness
- visual disturbances (including cataract in your eye, colour blindness (colour vision deficiencies), contact lens irritation, corneal opacity (white or clouded front of the eye), decreased night vision, inflammation of the cornea (keratitis), extreme sensitivity to light (photophobia), blurred vision
- hearing disturbances
- vasculitis (for example Wegener's (eosinophilic) granulomatosis, allergic vasculitis) – inflammation of the veins
- bronchospasm (particularly in patients with asthma) – tightness of the chest
- hoarseness
- bowel disturbances such as inflammatory bowel disease, inflammation of the colon (colitis), ileum (ileitis), pancreas (pancreatitis), gastrointestinal bleeding, bloody diarrhoea, nausea, dry throat
- inflammation of the liver (hepatitis)
- hair loss (alopecia), and other hair disorders such as abnormal growth of hair (hirsutism)
- acute, painful, ulcerating and bleeding acne (Acne fulminans)
- more severe acne (acne flare), redness of the skin on your face (erythema (facial))
- irritable skin rash (exanthema)
- nails changing form (dystrophy), nail infections (paronychia)
- sensitivity reactions to sunlight (photosensitivity)
- increased number of the small blood vessels in the skin with signs like shiny red lumps (pyogenic granuloma),
- darkening of the skin (hyperpigmentation)
- sweating more than usually
- inflammation of the joints (arthritis) withs signs like stiffness and painful, red joints
- formation of calcium deposits in soft tissue (calcinosis) with signs like painful bumps

- too early closure of the end part of a long bone, initially growing separately from the shaft (epiphyses) (premature fusion)
- excessive growth of bone on top of existing bone (exostosis (hyperostosis))
- reduced bone density
- inflammation of tendons (tendonitis) with signs such as joint pain and stiffness, which often affects the elbow, wrist, finger, thigh, and other parts of the body
- inflammation of the tiny filters in your kidney (glomerulonephritis) with signs such as blood in the urine, foamy urine and swelling of the face, eyes, ankles, feet, legs, or abdomen
- increased formation of new connective tissue and microscopic blood vessels (granulation tissue) that form on the surfaces of wounds during the healing process
- weakness or not feeling well (malaise)
- higher levels of creatine phosphokinase (an enzyme) in your blood) shown by blood tests

Unknown frequency side-effects:

- skin immune reactions with signs such as bulging, rash-like lesions that are red, pink, purple, or brown (Erythema multiforme)
- serious disorder of the skin and mucous membranes, usually a reaction to medication that starts with flu-like symptoms, followed by a painful rash that spreads and blisters (Stevens-Johnson Syndrome)
- serious skin conditions with signs like severe skin peeling and blistering (toxic epidermal necrolysis)
- serious syndrome due to a breakdown of muscle fibres with signs like weakness and not feeling well (rhabdomyolysis).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

By reporting side effects, you can help provide more information on the safety of ORATANE.

5. HOW TO STORE ORATANE

- Store at or below 30 °C.
- Protect from light.
- Keep blisters in outer carton until required for use.
- Do not refrigerate or freeze the product.
- Do not take ORATANE after the expiry date stated on the blister strip and carton.
- Return all unused medicine to your pharmacist for safe disposal.

  Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).
- KEEP ALL MEDICINE OUT OF THE REACH AND SIGHT OF CHILDREN.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What ORATANE contains

ORATANE 5 mg:

*The active substance is***:** Each soft gelatin capsule contains 5 mg isotretinoin.

The other ingredients are:

Capsule Fill: all-rac-alpha-tocopherol*,* beeswax, yellow, butylhydroxyanisole, disodium edetate (as dihydrate), hydrogenated vegetable oil, soya-bean oil, partly hydrogenated , soya-bean oil, refined.

ORATANE 10 mg:

The active substance is: Each soft gelatin capsule contains 10 mg isotretinoin.

The other ingredients are:

Capsule fill: all-rac-alpha-tocopherol, beeswax (yellow), butylhydroxyanisole, disodium edetate (as dihydrate), hydrogenated vegetable oil, soybean oil (partly hydrogenated), soybean oil (refined)

Capsule shell: gelatin, glycerol, purified water, sorbitol liquid (non-crystallizing), titanium dioxide. iron oxide black, Ponceau 4R,

ORATANE 20 mg:

The active substance is: Each soft gelatin capsule contains 20 mg isotretinoin.

The other ingredients are:

Capsule fill: all-rac-alpha-tocopherol, beeswax (yellow), butylhydroxyanisole, disodium edetate (as dihydrate), hydrogenated vegetable oil, soya-bean oil (partly hydrogenated), soya-bean oil (refined)

Capsule shell: gelatin, glycerol, purified water, sorbitol liquid (non-crystallizing), titanium dioxide, Indigotine lacquer, Ponceau 4R

ORATANE 40 mg:

The active substance is: Each soft gelatin capsule contains 40 mg isotretinoin.

The other ingredients are:

Capsule fill: all-rac-alpha-tocopherol, beeswax (yellow), butylhydroxyanisole, disodium edetate (as dihydrate), soya-bean oil (hydrogenated), soya-bean oil (partly hydrogenated), soya-bean oil, refined

Capsule shell: gelatin, glycerol, sorbitol liquid (non-crystallizing), Sunset yellow E110, titanium dioxide.

All strengths contain DL-alpha-tocopherol 1,56 % *w/w* and butylhydroxyanisole 0,06 % *w/w* as antioxidants.

What ORATANE looks like and contents of the pack

ORATANE 5 mg: Faint pinkish-cream to cream coloured, oval, soft gelatin capsule, containing a yellow/orange, opaque viscous liquid.

Capsules are packed into PVC/PVDC film with Aluminium backing blister strips of 30 capsules within an outer carton.

ORATANE 10 mg: Light violet coloured, oval, soft gelatin capsule, containing a yellow/orange opaque viscous suspension.

Capsules are packed into PVC/PVDC/Aluminium blister strips containing, 15 capsules, packed in pack size of 60 capsules within an outer carton.

ORATANE 20 mg: Maroon coloured, oval, soft gelatin capsule, containing a yellow/orange opaque viscous suspension.

Capsules are packed into PVC/PVDC/Aluminium blister strips containing 15 capsules, packed in pack size of 60 capsules within an outer carton.

ORATANE 40 mg: A light orange coloured, oval, soft gelatin capsule, containing a yellow/orange, opaque, viscous liquid.

Capsules are packed into PVC/PVDC film or PVC/PCTFE film blister strips sealed with aluminium foil containing 10 capsules, packed in pack size of 30 capsules within an outer carton.

Holder of Certificate of Registration

Acino Pharma (Pty) Ltd

106 – 16th Road

Midrand

1685

This leaflet was last revised in

Date of current approved patient information leaflet: 29 November 2022.

Registration numbers

ORATANE 5 mg: 43/13.4.2/0746

ORATANE 10 mg: 35/13.4.2/0375

ORATANE 20 mg: 35/13.4.2/0376

ORATANE 40 mg: 42/13.4.2/0460

Prescription Only Medicine

ORATANE 10 mg:

Registration numbers per country:	
Ghana: FDA/SD.193-11981 Kenya: Mauritius: R9944/02/14 Namibia: 04/13.4.2/1717: Scheduling status: NS3	Nigeria: Tanzania: TAN 20 HM 0430 Uganda: Botswana: BOT1402526: Scheduling status: S2

ORATANE 20 mg:

Registration numbers per country:	
Ghana: FDA/SD.193-11982 Kenya: Mauritius: R9945/02/14 Namibia: 04/13.4.2/1718: Scheduling status: NS3	Nigeria: Tanzania: TAN 20 HM 0443 Uganda: Botswana: BOT1402527: Scheduling status: S2

ORATANE 40 mg:

Registration numbers per country:	
Ghana: FDA/SD.193-11983	Nigeria:

Kenya: Mauritius: E13091/03/2019 Namibia: 18/13.4.3/0016: Scheduling status: NS3	Tanzania: TAN21 HM 0038 Uganda: