

APPROVED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

RISOPET film coated tablets

Rifampicin, isoniazid, pyrazinamide and ethambutol hydrochloride

RISOPET is sugarfree

Read all of this leaflet carefully before you start taking RISOPET

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- RISOPET 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.

What is in this leaflet

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

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1. What RISOPET is and what it is used for

RISOPET contains four different medicines called isoniazid, rifampicin, pyrazinamide and ethambutol hydrochloride. They all belong to a group of medicines called antituberculosis medicines. They work by killing the bacteria that cause tuberculosis (also known as TB).

RISOPET is used for the treatment and re-treatment of tuberculosis (TB) in adult patients and children.

2. What you need to know before you take RISOPET

Do not take RISOPET:

- if you are allergic (hypersensitive) to rifampicin, isoniazid, pyrazinamide, ethambutol, or to any of the ingredients of RISOPET (see section 6)
- if you have a liver disease (jaundice)
- if you have severe kidney disease
- If you have optic neuritis (inflammation of the nerves in your eye)
- if you are pregnant, planning to become pregnant or breast feeding your baby (see Pregnancy, breastfeeding and fertility)
- RISOPET should not be used in children under 13 years of age.
- if you are taking a combination of medicines called protease inhibitors, saquinavir and ritonavir (medicines used in the treatment of HIV) except ritonavir when given at full dose or 600 mg twice daily

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- if you are taking voriconazole (medicine used to treat fungal infections)
- if you have porphyria (a rare hereditary disease affecting the blood pigment with symptoms such as dark urine and extreme sensitivity of the skin to light).

Warnings and precautions

Take special care with RISOPET

- your doctor will need to check your blood before you take RISOPET. This will help your doctor to know if any changes happen to your blood after taking this medicine, as well as to check how your liver is working as each of the four components of RISOPET are known to affect the liver
- you experience any effects of hypersensitivity such as shock, kidney failure, anaemia, difficult or laboured breathing and asthma-like attacks, bleeding into the tissues, bruising, slow blood clotting after injury, fever, uncontrolled hay fever, develop eczema or if you develop any other form of rash after using RISOPET or rifampicin
- it is very important that you take RISOPET exactly as your doctor has told you.
There is a chance of you developing a severe and dangerous reaction if you do not take your tablets every day. You must keep taking this medicine until your doctor tells you to stop
- if you have a liver disease, are an elderly patient, or suffer from or have suffered from alcoholism as RISOPET may cause liver damage. Do not use RISOPET if you experience the following symptoms: yellowing of the skin or eyes, rash, fever

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- if you have any of the following conditions: neuropathy (a disease that affects the nervous system), vitamin B6 deficiency, diabetes (high blood sugar), are malnourished, an alcoholic or infected with HIV virus (AIDS) as your doctor may prescribe pyridoxine (vitamin B6) to be taken during the course of your treatment
- if you have kidney problems as your dose of RISOPET may need to be adjusted
- if you have a history with gout your doctor may need to monitor the levels of uric acid in your blood. RISOPET treatment may be discontinued should the effects of gout reappear or worsen
- do not use RISOPET if you have a blood disorder called thrombocytopenia (a condition in which there is a decreased number of circulating platelets), purpura (bleedings in the skin and mucous membranes that result in the appearance of purplish spots or patches) or shock
- you have diabetes. Your diabetes may become more difficult to control while taking this medicine
- if you have epilepsy (seizures or fits) as RISOPET may trigger fits
- if you have a psychiatric disorder
- if you experience any vision disturbances whilst taking RISOPET (e.g. blurred vision), stop taking RISOPET and immediately inform your doctor. You may be required to have an eye test done regularly during treatment
- if you are using oral birth control tablets to prevent pregnancies, you should use additional forms of birth control (see Other medicines and RISOPET)
- if you are taking antacids (for indigestion) you will need to take your dose of RISOPET an hour before taking the antacid. Preparations containing bentonite

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should be taken 8 hours after taking RISOPET (see Other medicines and RISOPET)

- be aware that rifampicin as contained in RISOPET may stain soft contact lenses irreversibly. The use of soft contact lenses when taking RISOPET is not recommended
- RISOPET treatment may lead to reddish-orange colouration of faeces, saliva, urine, tears and sweat.

Other medicines and RISOPET

Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

The active ingredients contained in RISOPET may increase or decrease the effects of some medicines or cause unwanted side effects if taken at the same time.

Do not take RISOPET if:

- you are taking voriconazole (to treat fungal infections) or protease inhibitors (used in the treatment of HIV) as the combination may result in liver damage (see Do not take RISOPET). Taking the combination of saquinavir (used in the treatment of HIV) and ritonavir whilst taking RISOPET may result in liver damage, therefore RISOPET should not be taken with these medicines.

The following combinations are not recommended with RISOPET:

- nevirapine, ritonavir (to treat HIV infection), simvastatin (used in patients with high

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cholesterol) and oral contraceptives

- halothane (used in anaesthetics).

Your doctor may either change or adjust your dose of the following medicines:

- paracetamol, alfentanil, methadone, morphine etoricoxib, rofecoxib (painkillers)
- atovaquone (used for pneumonia), quinine (anti-malaria medicines)
- ciclosporin, tacrolimus and azathioprine (immunosuppressant medicines used in organ transplantation and in the treatment of autoimmune diseases such as rheumatoid arthritis - inflammation of the joints and surrounding tissues), pemphigus (a disease characterised by blistering of the skin and mucous membranes), Crohn's disease (a type of inflammatory bowel disease, affecting the small intestines), ulcerative colitis (a type of inflammatory bowel disease affecting the large intestine and rectum) and multiple sclerosis (a disease that affects the brain and spinal cord)
- chloramphenicol, doxycycline, cycloserine, clarithromycin, telithromycin, linezolid and fluoroquinolones (antibiotics used to treat certain infections)
- anti-cancer medicines including irinotecan, imatinib, gefitinib
- cimetidine (used in the treatment of heartburn and peptic ulcers)
- clofibrate and statins (used to treat high cholesterol), corticosteroids (anti-inflammatory)
- coumarin anticoagulants (e.g. warfarin used to prevent blood clots), ciclosporin (used to reduce the risk of organ rejection after organ transplant)
- dapsone, clofazimine, co-trimoxazole (used to treat certain infections)

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- benzodiazepines (e.g. diazepam, triazolam) and benzodiazepine-related medicines (used to treat anxiety, convulsions [seizures/fits], sleeping disturbances and muscle spasms), including zopiclone and zolpidem
- azole antifungals, such as voriconazole, fluconazole, itraconazole, ketoconazole (used to treat fungal infections)
- haloperidol, clozapine, aripiprazole (used in psychiatric disorders)
- oral medicines used to treat diabetes (high blood sugar)
- phenytoin, carbamazepine, primidone, ethosuximide (used to treat seizures or fits)
- sulfasalazine (used as an anti-inflammatory agent in the treatment of inflammatory bowel disease as well as for rheumatoid arthritis – it is not a pain killer)
- thyroxine (used in the treatment of an inactive thyroid gland)
- theophylline (used in therapy for respiratory diseases such as asthma)
- antiretroviral medicines, such as zidovudine, delavirdine, indinavir, efavirenz, nevirapine and protease inhibitors (used in the treatment of HIV infection (AIDS))
- medicines to help you sleep (barbiturates, e.g. hexobarbitone)
- beta-blockers such as those used for the management of cardiac dysrhythmias (abnormal electrical activity in the heart), protection of the heart after a heart attack, and hypertension)
- digoxin, antidysrhythmic medicines (such as disopyramide, mexiletine, quinidine, propafenone, tocainide and verapamil), calcium channel blockers (such as diltiazem, nifedipine, verapamil, nimodipine, isradipine, nicardipine, nisoldipine,

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amlodipine), used to treat cardiac disease and losartan, eplerenone (used to treat water retention and cardiac disease)

- female hormonal medicines that reduce estrogen levels and are also used for treating breast cancer, such as tamoxifen, gestrinone and toremifene
- birth control tablets (containing estrogens) used to prevent unwanted pregnancies
- chlorzoxazone (used to treat muscle spasms)
- allopurinol, colchicine, probenecid, sulfinpyrazone (used in the therapy of gout)
- hormonal preparations used to treat thyroid (goitre) problems, such as levothyroxine
- ondansetron, used for the treatment of nausea
- enalapril (to treat high blood pressure)
- disulfiram (to treat alcohol abuse)
- enflurane (general anaesthetic)
- antacids containing aluminium (see Take special care)
- other antituberculosis medicines (e.g. cycloserine, para-aminosalicylic acid (PAS))
- tricyclic antidepressants (e.g. amitriptyline).

Avoid alcohol consumption when taking RISOPET (see Take special care).

RISOPET may interfere with the results of certain medical tests, including blood tests for folate and vitamin B12 and copper sulphate urine glucose test.

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Tell your healthcare professional, who performs such tests that you are taking
RISOPET.

This medicine may influence contrast media used for gallbladder tests, therefore, these
tests should be performed before the morning dose of RISOPET.

RISOPET with food and drink

RISOPET should be taken with a full glass of water 1 hour before or 2 hours after a meal.

If you experience stomach disturbances, the tablet may be taken with food.

If you are taking antacids containing aluminium, use RISOPET 1 hour after taking antacids
(see Take special care and Other medicines).

Ingestion of certain types of cheese (e.g. Swiss or Cheshire), or fish (e.g. tuna, skipjack,
other tropical fish, salmon, mackerel), red wine or beer may result in itching of the skin,
rapid or pounding heart, sweating, flushing, low blood pressure, chills or headache. These
foods should be avoided while taking RISOPET.

Using alcohol while you are being treated with RISOPET can increase your risk of
developing liver disease or problems.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning
to have a baby, please consult your doctor, pharmacist or other healthcare provider for
advice before using RISOPET.

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DO NOT take RISOPET if you are pregnant or suspect that you are pregnant.

DO NOT take RISOPET if you are breastfeeding your baby.

Driving and using machines

RISOPET can cause dizziness and drowsiness and impair your ability to drive and use machinery.

Do not drive, operate machinery, or do anything else that could be dangerous until you know how RISOPET affects you.

It is not always possible to predict to what extent RISOPET 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 RISOPET affects them.

3. How to take RISOPET

Do not share medicines prescribed for you with any other person. Always use RISOPET exactly as your doctor has told you. You should check with your doctor or pharmacist if you are unsure.

Take RISOPET tablets with a full glass of water 1 hour before, or 2 hours after a meal. However, if stomach irritation occurs, the tablets may be taken with food.

If you are taking antacids containing aluminium, take RISOPET 1 hour after the antacids (see Take special care and Other medicines).

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The recommended treatment dosages, based on your body weight, given daily for the 2-month starting-phase treatment in adults and children over 13 years of age are as follows:

- 30 - 37 kg 2 tablets
- 38 - 54 kg 3 tablets
- 55 - 70 kg 4 tablets
- 71 kg and over 5 tablets.

Your doctor will tell you how long your treatment with RISOPET will last. Do not stop treatment early because you may experience withdrawal symptoms (see If you stop taking RISOPET).

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

If you take more RISOPET than you should

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

Symptoms of overdose may include:

- diarrhoea, nausea, vomiting, abdominal cramps, severe weight loss (anorexia), reddish-orange colour of saliva or tears, muscle pain and weakness, tingling or numbness, movement disorders, constipation, dry mouth, joint pain, gout, jaundice and liver problems, rash, fever, visual disturbances, low blood pressure, irregular

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heartbeat, seizures, heart attack, dizziness, slurred speech, hallucinations,
breathing problems, coma, gout.

If you forget to take RISOPET

Take the missed dose as soon as you remember. If it is almost time for your next dose, skip the missed dose and take the medicine at the next regularly scheduled time. Do not take a double dose to make up for forgotten individual doses.

If you stop taking RISOPET

Do not stop taking RISOPET until the course of treatment is complete as stopping and restarting treatment may cause serious side effects.

4. Possible side effects

RISOPET can have side effects.

Not all side effects reported for RISOPET are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using RISOPET, please consult your healthcare provider for advice.

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

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching

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- fainting.

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

- yellowing of the skin and eyes, also called jaundice
- decreased blood pressure (feeling dizzy)
- diarrhoea that is serious, lasts a long time or has blood in it with stomach pain or fever as this can be a sign of serious bowel inflammation
- bleeding into the skin, bruising and slow blood clotting after an injury (thrombocytopenia)
- shortage of white blood cells, accompanied by sudden high fever, severe sore throat and ulcers in the mouth (agranulocytosis)
- hepatitis (swelling and inflammation of the liver, characterised by symptoms such as, abdominal pain or distension, dark urine and pale or clay-coloured stools, fatigue, fever, general itching, yellowing of the skin or eyes, loss of appetite, nausea and vomiting)
- inflammation of the pancreas, which causes severe pain in the abdomen and back (pancreatitis)
- weakness, fatigue, weight loss, headache (symptoms of a condition called vasculitis)
- vision disturbances like blurred vision, eye pain, red-green colour blindness or even

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loss of vision, swelling of the optic nerve, bleeding in the eye, blind spot

- confusion, disorientation, hallucinations (strange visions or sounds), convulsions (fits)
- delusions, memory loss, mood changes, altered mental state
- Stevens-Johnson syndrome (a life-threatening skin disorder with symptoms such as a red-purplish rash and blisters)
- swelling in any part of the body
- sensitivity of the skin to sunlight (photosensitivity)
- changes in kidney function and passing of urine, including the amount, frequency and colour of the urine, kidney failure
- severe extensive skin damage, e.g. separation of the epidermis and superficial mucous membranes (known as toxic epidermal necrolysis)
- shortness of breath, wheezing, laboured breathing, non-productive cough, fever, severe hypoxia (blue tinge to skin due to oxygen deprivation), chest pain
- fever, unexplained tiredness or shortness of breath, cough, swollen glands, muscle pains, diarrhoea, a full feeling quickly while eating or a rash or itching, or liver problems (these may be symptoms of 'DRESS syndrome', a medicine hypersensitivity reaction which affects your internal organs, and increase the white cells in your blood)
- blistering, peeling, bleeding, scaling or fluid-filled patches on any part of your skin. This includes your lips, eyes, mouth, nose, genitals, hands or feet. You may have a serious skin problem (pemphigoid)
- a sudden severe headache, this could be a sign of bleeding in the brain

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- abnormal blood clotting (signs may be chest pains, shortness of breath, leg pains or problems speaking) or bleeding from your nose, ear, gums, throat, skin or stomach (signs may include a feeling of tenderness and swelling in your stomach, purple spots on your skin and black or tar-like stools).

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- headache, numbness, tiredness, drowsiness, light-headedness, dizziness, lack of co-ordination
- eye irritation, blurred vision, conjunctivitis
- nausea, vomiting, diarrhoea
- reddish-orange discoloration of urine, faeces, saliva, sputum, sweat and tears, fever, chills
- blood tests may show changes in the way your liver or kidneys are working
- tingling sensation in your hands, feet or lips ("pins and needles), feeling unwell
- limb weakness or numbness, loss of memory, vision, and/or intellect, uncontrollable obsessive and/or compulsive behaviours, delusions, headache, cognitive and behavioural problems and sexual dysfunction (symptoms of neurotoxicity)
- polyneuritis (paralysis and loss of reflexes, usually in the leg)
- constipation, dry mouth, stomach cramps, loss of weight, anorexia, metallic taste
- pain or inflammation in the large and small joints, bone pain, muscle pain, twitching or weakness

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- fever, a general feeling of discomfort, illness, or unease.

Less frequent side effects:

- sore mouth or tongue (due to fungal infection such as thrush)
- blood tests showing low white blood cell count
- low blood pressure, low blood levels of sugar and high blood levels of potassium in Addison patients
- skin rashes or other skin conditions, such as flushing, hives, itching, acne, hair loss
- angioedema (painless swelling under the skin)
- gouty arthritis (chills, pain and swelling of joints, especially big toe, ankle or knee, tense hot skin over affected joints).

The following side effects have been reported but the frequency for them to occur is not known:

- flu-like symptoms (chills, difficult breathing, dizziness, fever, headache, muscle and bone pain, fatigue and shivering)
- decreased appetite
- permanent discolouration of soft contact lenses
- tooth discolouration
- muscle weakness, bone pain, muscle pain
- severe vaginal bleeding after childbirth, transfer of foetal blood into the maternal circulation during pregnancy
- painful or abnormal menstruation

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- worsening of porphyria
- Cushing syndrome (fatty hump between the shoulders, a rounded face and pink or purple stretch marks), early puberty, difficult controllable diabetes
- pellagra (a disease caused by low levels of niacin, also known as vitamin B3 with symptoms such as dementia, diarrhoea, and dermatitis), hyperglycaemia (high blood glucose), metabolic acidosis (too much acid in the body)
- increased seizure frequency in epileptics, hyperactivity, euphoria, insomnia, delusions, dulled or completely suspended sense or sensibility
- ringing in the ears (tinnitus), loss of balance (vertigo)
- enlargement of a man's breasts
- swelling of the lymph glands
- aggravation of peptic ulcer
- painful or difficult urination
- urine tests showing excess uric acid in the urine.

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, pharmacist or nurse. You can also report side effects to SAHPRA via the online service for adverse drug reaction reporting by following the link: <https://www.sahpra.org.za/Publications/Index/8>.

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By reporting side effects, you can help provide more information on the safety of RISOPET. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

5. How to store RISOPET

Store all medicines out of reach of children.

Store in a cool place, at or below 25 °C in a well closed container.

Protect from light.

Do not remove blisters from outer container until required for use.

Do not use after the expiry date stated on the carton.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What RISOPET contains

The active ingredients are rifampicin, isoniazid, pyrazinamide and ethambutol hydrochloride.

Each tablet contains: 150 mg rifampicin, 75 mg isoniazid, 400 mg pyrazinamide and 275 mg ethambutol hydrochloride

The other ingredients are:

Tablet cores:

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Ascorbic acid (as antioxidant), gelatin, colloidal silicon dioxide, croscopovidone, magnesium stearate, microcrystalline cellulose, pre-gelatinised starch.

Film coating

Iron oxide red, lecithin (soya), polyvinyl alcohol-part hydrolysed or polyvinyl alcohol, talc, titanium dioxide, xanthan gum.

What RISOPET looks like and contents of the pack

Brown coloured, capsule shaped film coated tablets with a break line on one side and plain on the other side.

Amber PVC/ACLAR & ALU/ALU blister packs of 28, 56, 84 and 112 tablets, packed into an outer cardboard carton.

Holder of Certificate of Registration

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Pharma Dynamics (Pty) Limited
RISOPET tablets

Each film coated tablet contains
rifampicin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg,
ethambutol 275 mg
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