

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol WHOPAR part 3
Hydrochloride 150 mg/75 mg/400 mg/275 mg
Film-coated Tablets (Macleods
Pharmaceuticals Ltd), TB168

Updated October 2018
Section 6 updated: May 2023

WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

PATIENT INFORMATION LEAFLET: INFORMATION FOR THE USER

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets¹

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 questions about the medicine, ask your health care provider.
- 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 health care provider. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets is and what it is used for
2. What you need to know before you take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets
3. How to take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets
4. Possible side effects
5. How to store Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets
6. Contents of the pack and other information

1. WHAT RIFAMPICIN/ISONIAZID/PYRAZINAMIDE/ETHAMBUTOL HYDROCHLORIDE 150 MG/75 MG/400 MG/275 MG FILM-COATED TABLETS IS AND WHAT IT IS USED FOR

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated tablets is used for the intensive phase treatment of tuberculosis in adults and children weighing more than 20kg.

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated tablets contains the active substances rifampicin, isoniazid, pyrazinamide and ethambutol.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE RIFAMPICIN/ISONIAZID/PYRAZINAMIDE/ETHAMBUTOL HYDROCHLORIDE 150 MG/75 MG/400 MG/275 MG FILM-COATED TABLETS

Do not take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets

- if you are hypersensitive (allergic) to rifampicin, isoniazid, pyrazinamide, ethambutol or any of the other ingredients of Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275mg film-coated Tablets (see section 6, What

¹ Trade names are not prequalified by WHO. This is the national medicines regulatory authority's (NMRA) responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets contains).

- if you have acute liver problems or previously have had a liver problem which was caused by drugs, including isoniazid, rifampicin or pyrazinamide
- if you have had serious side effects from isoniazid or rifampicin, such as fever, chills or swelling of the joints.
- if you have porphyria
- if you have acute gouty arthritis
- if you have severe kidney problems
- if you are taking any of the following medications:
 - voriconazole used for treating fungal infection
 - protease inhibitors used for treating HIV infection.

Do not take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets if any of the above apply to you.

If you are not sure about anything, ask your health care provider.

Take special care with Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets

Tell your health care provider if you have any of the following illnesses before taking this medicine:

- Liver problems and chronic liver disease
- Kidney problems
- Gout
- Diabetes mellitus
- Epilepsy
- HIV infection
- Tingling of the hands and feet (peripheral neuropathy) and inflammation of peripheral nerves or the optic nerve (optic neuritis)
- Eye defects
- Chronic alcoholism (drinking alcoholic beverages daily)
- Underfeeding

Also tell your health care provider if:

- you are pregnant or think you might be pregnant
- you are allergic (hypersensitive) to niacin (nicotinic acid)
- you use injection drugs (e.g. heroin).

You should not take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets if you weigh less than 30kg.

You should not interrupt treatment with Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets without checking with your health care provider.

You should use additional means of contraception (e.g. barrier method such as condoms) apart from taking

the pill as long as you take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets.

See section 4 (Possible side effects) about what you must do if you get certain side effects

Taking other medicines with Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets

Tell your health care provider if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. They may affect how well Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets works or Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets may affect the way the other medicines work.

You must not take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets with any of the following medications:

- voriconazole (a medicine used to treat fungal infections)
- HIV protease inhibitors (drugs used to treat HIV infection)

You should not take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets with any of the following medications:

- nevirapine (used for treating HIV infection)
- simvastatin (used for reducing cholesterol)
- aluminium hydroxide (used for treating stomach disorders)
- disulfiram (used in the treatment of alcoholism)

Tell your healthcare provider also if you take one of the following:

- Medicines for HIV infection like efavirenz, zidovudine, stavudine
- Medicines to treat fungal infections like ketoconazole fluconazole and terbinafine
- Antibiotics like chloramphenicol and clarithromycin
- Medicines for malaria like atovaquone and quinine
- Medicines to suppress the immune system like ciclosporin and tacrolimus
- Medicines for heart conditions like digoxin, lidocaine and verapamil
- Medicines for blood pressure like amlodipine and atenolol
- Medicines for diabetes like glibenclamide
- Oral contraceptive pill or other hormonal contraceptives
- Medicines for gout like probenecid
- Medicines for epilepsy like carbamazepine, phenytoin and valproate
- Medicines for anxiety and sleeping disorders like diazepam
- Medicines for depression like amitriptyline and for psychiatric conditions like chlorpromazine and haloperidol
- Medicines to prevent blood clots like warfarin
- Medicines used during surgery like enflurane
- Corticosteroids like prednisolone
- Hormone treatments like thyroid hormones
- Medicines for pain like paracetamol and opioids like codeine and morphine
- Aminosalicic acid (also called para-aminosalicylic acid, a medicine for tuberculosis),
- Methadone (a medicine for heroin addicts)

Taking Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets with food and drink

Take this medicine on an empty stomach—at least one hour before a meal or two hours after a meal.

Do not drink any alcohol as long as you are taking Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets

You should avoid food which contains a large amount of tyramine (like cheese, red wine) or of histamine (like tuna fish). Taking such food while you are being treated with Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets may cause effects such as headache, pounding heartbeat, lightheadedness, sweating, itching and flushing.

Pregnancy and breast-feeding

Tell your health care provider as soon as possible if you are pregnant or think you are pregnant. Your health care provider will help you decide if it is possible to continue treatment with Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets. If you take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets during pregnancy, your health care provider should give you pyridoxine (vitamin B₆) supplements during pregnancy and vitamin K supplements during the last month of pregnancy.

This medicine goes into breast milk but the amount is too low to protect the breast-fed baby against tuberculosis. The medicine has not been reported to harm breast-fed babies of mothers taking the medicine. Tell your health care provider if you are breast-feeding or if you intend to breast-feed while taking Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets.

Driving and using machines

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150mg/75mg/400mg/275mg film-coated Tablets can cause side effects such as dizziness, confusion and blurred vision. This may make you less able to drive or do certain things like using machines.

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150mg/75mg/400mg/275mg film-coated Tablets contains Sunset Yellow and Castor oil

This medicinal product contains a colorant (sunset yellow) which may cause allergic reactions. This medicinal product also contains castor oil, which may cause stomach upset and diarrhoea.

3. HOW TO TAKE RIFAMPICIN/ISONIAZID/PYRAZINAMIDE/ETHAMBUTOL HYDROCHLORIDE 150 MG/75 MG/400MG/275MG FILM-COATED TABLETS

Always take this medicine exactly as your health care provider has told you. You should check with your health care provider if you are not sure.

These doses are for adults weighing more than 30 kg and for children weighing 21–30 kg. Children weighing less than this should not take these tablets.

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets should be taken on any empty stomach—at least 1 hour before a meal or 2 hours after a meal.

Swallow the tablets whole with a drink of water.

The dose of Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets you need to take depends on your body weight. The usual dose for an adult is as follows:

Your body weight	Dose
30–39 kg	take 2 tablets once each day
40–54 kg	take 3 tablets once each day
55–70 kg	take 4 tablets once each day
More than 70 kg	take 5 tablets once each day

For children weighing 21–30 kg the dose is 2 tablets once each day.

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets should be given only to children who can swallow whole tablets.

If you have a kidney disease, your health care provider may prescribe the ingredients of this medicine separately.

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets is not recommended for patients with a body weight below 30 kg.

Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets is usually given for 2 months at the beginning of tuberculosis treatment but your health care provider will decide on how long you need to take this medicine.

If you take more Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets than you should

If you accidentally take an extra tablet, nothing is likely to happen. If you accidentally take several tablets too many, contact your health care provider or talk to your nearest hospital casualty department immediately. If possible, take your tablets or the container with you to show the health care provider what you have taken.

Taking too many tablets can cause vomiting, stomach upset, fever, headache, dizziness, slurred speech, hallucinations and problems with vision.

If you forget to take Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets

If you forget to take a dose, take it as soon as possible. However, if your next dose is within 6 hours, skip the missed dose and take the next tablet at the usual time. You should not take a double dose to make up for a missed dose.

If you stop taking Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets

Always keep taking the tablets until the course is finished, even if you feel better. If you stop taking the tablets too soon, the infection may come back. Also, the bacteria may become resistant to the medicine, making it more difficult to treat the infection.

If you have any further questions on the use of this product, ask your health care provider.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets can cause side effects, although not everybody gets them. Tell your health care provider about any change in your health.

Serious side effects

If you have any of the following symptoms of a severe allergic reaction, stop taking this medicine and **tell your healthcare provider immediately** or go to the casualty department at your nearest hospital:

- Sudden difficulty in breathing, speaking and swallowing
- Swelling of lips, tongue, face or neck
- Extreme dizziness or collapse
- Severe or itchy skin rashes, especially if this shows blistering and there is soreness of the eyes, mouth or genital organs

If you get any of the following side effects **contact your healthcare provider as soon as possible**:

- Diarrhoea that is serious, lasts a long time or has blood in it with stomach pain or fever: This can be a sign of serious bowel inflammation.
- Bruising or unusual bleeding; if you continue taking Rifampicin /Isoniazid /Pyrazinamide /Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets, you are at risk of brain haemorrhage (bleeding)
- Yellowing of the skin or whites of the eyes, or urine getting darker and stools paler, fatigue, weakness, loss of appetite, nausea or vomiting—these are signs of liver problems (hepatitis).
- Inflammation of the pancreas, which causes severe pain in the abdomen and back (pancreatitis).
- Vision disturbances like blurred vision, eye pain, red-green colour blindness or even loss of vision.
- Reduced white blood cells, accompanied by sudden high fever, severe sore throat and ulcers in the mouth (agranulocytosis).

These are all serious side effects. You may need urgent medical attention. Serious side effects are rare (affect fewer than 1 in 1000 people) or very rare (affect fewer than 1 in 10000 people).

Other common side effects

(These can affect at least 1 in every 100 patients treated, but fewer than 1 in every 10 patients treated)

- Tiredness, drowsiness, headache, lightheadedness, dizziness
- Tingling, pricking or numbness (peripheral neuropathy)—your doctor or healthcare provider may prescribe pyridoxine (vitamin B6) to prevent these effects
- Reddish discoloration of body fluids and secretions like urine, tear fluid, sweat, sputum, stools and saliva
- Reddening of the eyes, permanent discoloration of soft contact lenses
- Nausea, vomiting, loss of appetite, abdominal discomfort and pain, bloatedness
- Flushing, itching with or without skin rash, nettle rash
- Allergic or other reactions like skin rash, fever, muscle or joint pain
- Loss of appetite, nausea, vomiting, fatigue, malaise and weakness—indicating liver problems
- Blood test showing increase in liver enzymes
- Increase in blood uric acid, acute gouty arthritis (chills, pain and swelling of joints, especially big toe, ankle or knee)

Uncommon side effects

(These can affect at least 1 in every 1000 patients treated, but fewer than 1 in every 100 patients treated)

- Hallucinations, disorientation, confusion, malaise

Rare side effects

(These can affect at least 1 in every 10 000 patients treated, but less than 1 in every 1000 patients treated)

- Changes of white and red blood cell count, changes of platelet count, anaemia, disorders of blood clotting, swelling of spleen,
- Oedema or swelling because of water retention
- Breathing difficulty and inflammation of the lungs
- Metallic taste, diarrhoea, flatulence
- Menstrual disturbances, swelling of breast tissue in men, early puberty, difficulties in diabetes control, high blood sugar, Cushing's syndrome (disease caused by increase of corticosteroid hormones), induction of crisis in Addison's patients (patients with a special form of hormonal disorder)
- Psychosis, hyperactivity, euphoria, sleeplessness, convulsions
- Muscle weakness, problems with co-ordination of movement (ataxia), increase in seizure frequency in patients with epilepsy
- Disturbances of vision, damage to the optic nerve (optic neuritis)
- Gastritis, jaundice, enlargement and inflammation of the liver (in rare cases severe)
- Allergic and other reactions like dry mouth, heartburn, urination disorders, rheumatic syndromes and symptoms
- Pellagra (characterised by gastrointestinal disturbances, reddening of skin, nervous and mental disorders), swelling of lymph nodes, acne, skin rash, light sensitivity
- Raised kidney enzymes, acute kidney failure, inflammation of the kidney, problems with urination
- Induction of porphyria (a group of disorders characterised by sensitivity to light, skin lesions, anaemia, psychosis and acute abdominal pain)

If you start taking Rifampicin /Isoniazid /Pyrazinamide /Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets again after interrupting treatment, a so-called influenza-like syndrome may occur. It is characterised by fever, shivering and possibly headache, dizziness, bone and muscle pain. In rare cases bleeding into the skin, breathing difficulties, asthma-like attacks, anaemia, shock and kidney failure might develop.

If any of the side effects get serious or if you notice any side effects not listed in this leaflet tell your health care provider.

5. HOW TO STORE RIFAMPICIN/ISONIAZID/PYRAZINAMIDE/ETHAMBUTOL HYDROCHLORIDE 150 MG/75 MG/400 MG/275 MG FILM-COATED TABLETS

Keep out of the sight and reach of children.

For bulk HDPE bottle pack: Store at temperature not exceeding 25°C in a dry place Protect from light.

For amber colour Alu-PVC/PE/PVDC and Alu-PVC/PVDC blister packs: Store at a temperature not exceeding 25°C. Protect from light

For Alu-Alu strip pack: Store at a temperature not exceeding 30°C. Protect from light

Do not use Rifampicin /Isoniazid /Pyrazinamide /Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets after the expiry date stated on the carton. 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 protect the environment

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets contains

The active ingredients are 150 mg rifampicin, 75 mg isoniazid, 400 mg pyrazinamide and 275 mg ethambutol hydrochloride

The other ingredients are:

Tablet core: Calcium stearate, colloidal anhydrous silica, croscarmellose sodium, crospovidone, disodium edetate, maize starch, povidone, purified talc and shellac.

Film coating: Copovidone, purified talc, castor oil, colour lake of sunset yellow, diethyl phthalate, hypromellose, magnesium stearate, purified talc and titanium dioxide.

(see section 2, "Rifampicin/Isoniazid/Pyrazinamide/Ethambutol 150 mg/75 mg/400 mg/275 mg film-coated Tablets contains Sunset Yellow and Castor oil").

What Rifampicin/Isoniazid/Pyrazinamide/Ethambutol Hydrochloride 150 mg/75 mg/400 mg/275 mg film-coated Tablets looks like and contents of the pack

Light buff coloured biconvex capsule shaped film-coated tablets, plain on both sides.

The tablet should not be divided.

Transparent LDPE bag, packed in a triple laminated aluminium sachet which is further packed in an HDPE bottle along with a leaflet. Each bottle is sealed with an aluminium tagger and closed with a screw cap. Pack sizes: 500 and 1000 tablets.

Al/PVC/PVDC blister of 10 tablets. Such 10 blisters per box. Pack size: 100 tablets.

Al/PVC/PVDC blister of 28 tablets. Such 3 or 24 blisters per box. Pack sizes: 84 (28x3) and 672 (28x24) tablets.

Al/Al strip of 10 tablets. Such 10 strips in a carton. Pack sizes: 100 (10x10) tablets.

Al/Al strip of 14 tablets. Such 12 strips in a carton. Pack sizes: 168 (14x12) tablets.

Al/Al strip of 28 tablets. Such 3 or 24 strips in a carton. Pack sizes: 84 (28x3) and 672 (28x24) tablets.

Al/PVC/PE/PVDC blister of 10 tablets. Such 10 blisters per box. Pack size: 100 (10x10) tablets.

Al/PVC/PE/PVDC blister of 7 tablets. Such 10 blisters per box. Pack size: 70 (10x7) tablets

Al/PVC/PE/PVDC blister of 28 tablets. Such 3, 6 or 24 blisters per box. Pack sizes: 84 (28x3), 168(28x6) and 672(28x24) tablets.

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Rifampicin/Isoniazid/Pyrazinamide/Ethambutol WHOPAR part 3
Hydrochloride 150 mg/75 mg/400 mg/275 mg
Film-coated Tablets (Macleods
Pharmaceuticals Ltd), TB168

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Detailed information on this medicine is available on the World Health Organization (WHO) web site:
<https://extranet.who.int/prequal/>