Package Leaflet: Information for the user

FATOL

RIEMSER

PETEHA

Film-coated tablets
Active ingredient: prothionamide

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist

In this leaflet:

The pharmaceutically active ingredient is prothionamide.

1 film-coated tablet contains 250 mg prothionamide (PTH).

Excipients: croscarmellose sodium, copovidone, crospovidone, magnesium stearate, colloidal anhydrous silica, macrogol 6000, hypromellose, microcrystalline cellulose, colourants E171, E110, lactose monohydrate.

PETEHA is available in packs containing 50, 100 and 250 film-coated tablets.

1. WHAT PETEHA IS AND WHAT IT IS USED FOR

1.1 PETEHA is a medicine used to treat tuberculosis, diseases caused by atypical mycobacteria, and leprosy.

1.2 Marketing Authorization Holder

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1.3 PETEHA is taken

- in the treatment of all forms and stages of pulmonary and extra pulmonary tuberculosis as a secondary medicine, in cases of proven multidrug resistance of pathogens toward primary medicines,
- in the treatment of diseases which are caused by so-called non tuberculous mycobacteria,
- in the treatment of leprosy in the scope of modified therapy regimes.

PETEHA is always applied in combination with medicines acting effectively against the pathogen and only if the pathogen‘s sensitivity to prothionamide has been ascertained.

2. BEFORE YOU TAKE PETEHA

2.1 Do not take PETEHA,

- if you are hypersensitive (allergic) to Prothionamide, yellow-orange S (E110), or one or more of the excipients,
- if you have a severe liver disease or an acute inflammation of the liver (hepatitis),
- if you are known to suffer from cerebral seizures or psychosis,
- during pregnancy and lactation (see Section 2.2).

2.2 Take special care with PETEHA,

- because of the liver-damaging action of prothionamide and other possible combinative agents administered in the scope of the chosen therapy regime.
  Close monitoring of functional liver parameters is therefore necessary. These values must be checked prior to the onset of treatment and in regular time intervals afterwards.
- if you consume alcohol regularly. In case of regular alcohol consumption the benefit of the treatment with PETEHA must be weighed against the risks.
  Note that alcohol tolerance is reduced during treatment with PETEHA. You must abstain from drinking alcohol while treatment with PETEHA is in progress.
- if you have diabetes. The blood sugar level must be monitored in short intervals. Adjustment of the blood sugar level might be more difficult during treatment with PETEHA.
- if you develop skin reactions, particularly when the mucous membranes are involved. These may be side effects with signs similar to pellagra, which are caused by nicotinic acid or vitamin B deficiency. They are to be considered as warning symptoms which should normally lead to the cessation of PETEHA treatment.
- if you suffer from depression or other psychiatric illnesses or a serious impairment of kidney function. In case of impaired kidney function the dose must be adjusted accordingly (see under Section 3. How to take PETEHA).
- if you have been found to have acute gastritis, a stomach ulcer, or an ulcer of the duodenum, or if you are coughing up blood.
- if you are known to have a blood coagulation disturbance. The very rare occurrence of an effect on prothrombin and fibrinogen has been observed.

a) Pregnancy
There is no adequate information for the use of prothionamide, the active substance of PETEHA, in pregnant women. In animal studies malformations due to prothionamide occurred. Since the possibility for causing malformations in humans cannot be excluded, your doctor must prescribe PETEHA only after weighing all risks connected with the application and if treatment is considered as inevitable (vital indication).

Ask your doctor or pharmacist for advice before taking any medicine.

b) Breast-feeding
It is currently unknown if prothionamide, the active substance of PETEHA, passes into the mother`s milk. If your doctor considers a treatment with PETEHA as inevitable during breastfeeding, the mother should wean her baby.

Ask your doctor or pharmacist for advice before taking any medicine.

c) Driving and using machines
Even when taken properly, PETEHA may reduce your reaction capabilities to a degree that, for example, affects your ability to move safely in traffic or operate machines. This applies to a greater degree in combination with alcohol consumption.

d) Important warnings and precautions concerning the excipients of PETEHA
This medicine contains lactose. Please take PETEHA only after consulting your doctor, if you are aware that you suffer from sugar intolerance.

2.3 Taking other medicines

Please inform your doctor or pharmacist if you are taking/applying or have recently taken/applied any other medicine. This also applies to medicine not on prescription

Other medicines or groups of medicines mentioned in the following may affect treatment with PETEHA when they are applied concomitantly.

From an enhancement of effects to an increased risk of side effects:

- In the scope of the therapeutic regime to treat tuberculosis, the additive nature of liver-damaging effects of the individual medicines must be taken into account. This applies particularly to the combination of PETEHA with isoniazid, rifampicin and/or pyrazinamide.
- When PETEHA and hormonal birth control (hormonal contraceptives) are combined, a potential additive liver-damaging effect must also be considered.
- Stimulatory effects on the nervous system / neurotoxic effects will be enhanced by the administration of isoniazid and/or medicines having an effect on mental functions, such as cycloserine or terizidone. The tolerance to alcohol and medicines inducing sedative effects might be reduced.

- Consumption of alcohol enhances the stimulatory effect on the central nervous system.
- PETEHA reduces the metabolic decomposition rate of isoniazid and barbiturates (medicines eliciting a depressive central nervous effect).

PETEHA is subject to influences as described in the following:

- The levels of prothionamide in blood are increased by the administration of isoniazid. The dose of prothionamide should therefore be reduced (see under Section 3. How to take PETEHA).

Other possible interactions:

- The dose of insulin or other, orally administered agents that reduce blood-sugar levels must be lowered.

2.4 Taking PETEHA with food and drink

You must not drink any alcohol while being treated with PETEHA.

3. HOW TO TAKE PETEHA

Always take PETEHA according to your doctor‘s instructions. Please ask your doctor or pharmacist if you are not sure.

3.1 Form of application

Oral use

Take a total daily dose of PETEHA determined for you as a single dose during a meal or shortly before going to bed. The awareness of side effects, in particular, gastrointestinal complaints can be thus attenuated.

PETEHA is a secondary medicine (reserve medicine) to treat tuberculosis and diseases which are caused by nontuberculous mycobacteria. It is invariably administered together with other antimycobacterial medicines in the scope of a combination therapy, if a sensitivity of the pathogen to the active ingredient prothionamide is given. The choice of the therapeutic regime depends on the positive determination of pathogenic sensitivity in samples derived from the patient. In the treatment of leprosy, prothionamide is applied in the scope of a modified therapeutic regime.

3.2 If not prescribed otherwise by your doctor, the normal daily dose to treat tuberculosis and diseases caused by nontuberculous mycobacteria is as follows:

Adults:
The dose of prothionamide depends on your body weight. Adults receive a daily dose of 15 mg/kg body weight.

A maximum daily dose of 1000 mg should not be exceeded.

The number of film-coated tablets that make up a dose of 15 mg PTH/kg body weight is summarized in the following table. The maximum daily dose must not be exceeded.

Body Weight	Daily Dose	
[kg]	Dose in [mg]	Number of PETEHA film-coated tablets
< 25	250	1
25	375	1 1/2
30	450	2
35	525	2
40	600	2 1/2
45	675	2 1/2
50	750	3
55	825	3 1/2
60	900	3 1/2
65	975	4
≥ 70	1000	4

In case PETEHA is administered in the scope of a combination drug therapy including isoniazid, the daily dose of PETEHA must be reduced by 50 percent. The maximum daily dose should then not exceed 500 mg prothionamide (equivalent to 2 film-coated PETEHA tablets).

Children:
Depending on their body weight children receive a daily dose of 7.5 – (15) mg PTH/kg body weight. The maximum daily dose should not exceed 500 mg prothionamide.

Dosage in cases of impaired renal function:

Patients with a glomerular filtration rate (GFR) of less than 30 ml/min. and dialysis patients receive 250 – 500 mg prothionamide daily depending on their body weight (equivalent to 1 to 2 film-coated PETEHA tablets). In patients with a severe kidney insufficiency the levels of active ingredient in the blood must be monitored and the dose adjusted accordingly.

Duration of application

PETEHA should invariably be applied with other antimycobacterial medicines. In case of tuberculosis, it is recommended to apply this medicine during the initial phase in a 3 to 4-fold combination therapy, and to continue treatment applying a reduced regime in the continuity phase.

The duration of therapy depends on the treatment regime selected. It may last from 9 months to up to 2 years.

Treatment of leprosy

In the treatment of leprosy, PETEHA is applied in the scope of modified therapy regimes in accordance with the mentioned dosage recommendations. The duration of application depends on the therapy regime selected.

3.3 If you take more PETEHA than you should

If you have accidentally taken more PETEHA than stated in this leaflet, or more than your doctor has prescribed, the side effects mentioned in Section 4.1 might become more pronounced. Contact your doctor immediately if you believe to have taken an overdose, so that he can decide on taking necessary measures, if required, in accordance with the severity of the case.

3.4 If you forget to take PETEHA

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

3.5 Consequences of discontinued PETEHA treatment

Pathogens (mycobacteria) might become resistant to this medicine as a result of irregular uptake and/or premature discontinuance of treatment. This puts your chance of recovery at risk and has negative effects on subsequent options of treatment.

4. POSSIBLE SIDE EFFECTS

Like all medicines, PETEHA can have side effects.

The reported incidence rates of the side effects mentioned in the following vary considerably in the underlying literature references. Reliable studies including a sufficient number of patients are not available.

The evaluation of side effects is based on incidence rates as follows:

4.1 Side effects

very common: occurring in more than 1 per 10 patients treated	**common:** occurring in more than 1 per 100 patients treated
uncommon: occurring in more than 1 per 1,000 patients treated	**rare:** occurring in more than 1 per 10,000 patients treated
very rare: occurring in 1 or less per 10,000 patients treated including singular incidences	

Blood

Disorders relating to the functioning of the red blood cells (anemia, methemoglobinemia), blood coagulation disturbances (hypoprothrombinemia and hypofibrinogenemia).

Hypersensitivity reactions

Single cases: allergic reactions

Metabolism

Rare: Increase of mammary gland tissue in males (gynecomastia), menstrual cycle disorders in women (dysmenorrhea, amenorrhea), decreased functional activity of the thyroid gland (hypothyroidism), instable blood sugar levels and a reduction of blood sugar levels in diabetics.

Central and peripheral nervous system

Common: vertigo, headaches
Rare: cramp seizures, sleeping disorders
Uncommon: Concentration disturbances, states of confusion, men-

tal disorders such as depression, excitation, psychoses
Single cases: suicide attempts
Optic nerve (Nervus opticus) damage including clouded vision, eye-muscle paralysis and visual acuity disturbances (accommodation disturbances) have been reported.

A shoulder-hand-syndrome in the sense of an algodystrophia (painful sensations in numerous joints) has also been reported.

Disturbances of vision, inflammatory disease of the nervous system (polyneuropathies) including disturbances of sensation (paraesthesias), muscular weakness and disturbed locomotor coordination (ataxia) have been reported particularly after a concomitant administration of isoniazid.

Eyes

Also see under central and peripheral nervous system disturbance of vision, for example, double vision (diplopia)

Ear and vestibular organ

Single cases: Deterioration of hearing capabilities, ear noises (tinnitus)

Airways and respiratory organs

Single cases: Coughing up blood (hemoptysis)

Gastrointestinal tract

Very common: Metallic or sulfurous taste in the mouth, but also an increased salivary flow, loss of appetite, emaciation (anorexia), nausea
Uncommon: Vomiting, heartburn, stomach ache, feeling of fullness, diarrhea or constipation, flatulence (meteorism):

These side effects disappear quickly and completely after discontinuance of PETEHA treatment. Tolerance might be improved by a gradually increasing dose regimen. A reduction of the dose and/or a combination with an agent acting against nausea (antiemetic) has also proven to be beneficial.

The swelling of the salivary gland (parotis) has been reported.

Liver

An increase of liver enzyme activity (transaminases) is common under PETEHA therapy which recedes after the discontinuance of treatment, but rarely results in a pronounced functional disturbance of the liver with jaundice (icterus). The liver-damaging effect decisively depends on a preceding damage of liver function (for example, alcohol abuse, post-hepatic liver disorder) and occurs predominantly in combination with other medicines which elicit potential liver-damaging effects (isoniazid, rifampicin, pyrazinamide).

Severe inflammations of the liver including jaundice have been reported as well as a single case of liver failure.

Skin and cutaneous appendages

Skin rash (responses similar to pellagra), light sensitivity of the skin (photodermatoses), skin fissures (rhagades), inflammations of the mucous membranes (stomatitis), acne, inflammation of the lips (cheilitis), inflammation of the tongue (glossitis), loss of hair (alopecia).

Muscles and skeletal system

Joint pain (arthralgias), inflammations of the joints (arthritis), muscular weakness

Kidneys

Formation of bladder stones (urolithiasis)

Yellow-orange S (E110) may cause allergic reactions.

4.2 Countermeasures

If you notice the occurrence of pronounced side effects, notify your doctor so he can take the necessary measures.

4.3 Inform your doctor or pharmacist,

if you notice any side effects not mentioned in this leaflet

5. HOW TO STORE PETEHA

Keep medicines out of the reach of children.

Do not use after the expiry date which is stated on the blister package and the carton and/or on the label.

Do not store above 25 °C.

Revision

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