Package leaflet: Information for the user

PETEHA, 250 mg, film-coated tablets

Active substance: Protionamide

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. See section 4.

What is in this leaflet

1. What PETEHA is and what it is used for

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

PETEHA is taken

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

PETEHA is always applied in combination with other medicines effective against the pathogen and only if the pathogen's sensitivity to protionamide has been proven.

2. What you need to know before you take PETEHA

Do not take PETEHA:

- if you are allergic to protionamide, Sunset Yellow FCF (E110) or any of the other ingredients of this medicine (listed in section 6),
- if you have a severe liver disease or an acute inflammation of the liver (hepatitis),
- if you are known to suffer from cerebral seizures (cerebral seizures) or psychoses,
- during pregnancy and lactation (see Section “Pregnancy and Lactation”).

Warnings and precautions
Talk to your doctor or pharmacist before taking PETEHA.

Take special care with PETEHA

- because of the liver-damaging action of protionamide and further 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 start of treatment and at regular intervals thereafter.
- 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 at short intervals. Adjustment of the blood sugar level may 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 a deficiency nicotinic acid and vitamin B. They are to be considered as warning symptoms which should normally lead to the cessation of treatment with PETEHA.
- if you suffer from depression or other psychiatric illnesses or a serious impairment of kidney function, the dose must be adjusted accordingly (see 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.

Children
The specific dose recommendations for children are to be observed (see section 3. “How to take PETEHA®?).

Other medicines and PETEHA
Tell your doctor or pharmacist if you are taking/using or have recently taken/used or might take/use any other medicines.

The effect of the medicines or groups of medicines stated below may be influenced in concomitant treatment with PETEHA.

Enhancement of effect, going as far as an increased risk of side effects:

- In the course of the therapeutic regime to treat tuberculosis, the additive nature of liver-damaging effects of the individual medicines must be taken into account. This particularly applies to the combination of PETEHA with isoniazid, rifampicin and/or pyrazinamide.
- Also when PETEHA and hormonal birth control (hormonal contraceptives) are taken, a potential additive liver-damaging effect must be taken into account.
- Stimulatory effects on the nervous system/ neurotoxic effects are enhanced by administration of isoniazid and/or medicines having an effect on mental functions, such as cycloserine or terizidone. Also, tolerance to alcohol and medicines with sedative effects may be reduced.
- Consumption of alcohol enhances the stimulatory effect on the central nervous system.
- PETEHA decelerates decomposition of isoniazid and barbiturates (medicines with a centrally sedative effect).

PETEHA is influenced as follows:

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

Other possible interactions:

- The dose of insulin or orally administered agents to reduce blood sugar levels must be reduced.

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

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:
There is no adequate information for the use of protionamide, the active substance in PETEHA, in pregnant women. In animal studies, a damaging effect on the breed was seen. As the possibility of an embryo-damaging effect in humans cannot be ruled out, your doctor may only prescribe PETEHA for you if he thinks it is absolutely necessary, weighing up all the risks (vital indication).

Breast feeding:
It is not known whether protionamide, the active substance in PETEHA, passes into the mother`s milk. If your doctor considers treatment with PETEHA to be absolutely necessary during breast feeding, you should wean your baby.

Driving and using machines
Even when taken as intended, PETEHA may reduce your reaction capabilities to such a degree that, for example, it affects your ability to move safely in road traffic or operate machines. This applies to an increased extent in combination with alcohol consumption.

PETEHA contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take PETEHA?

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

For treatment of tuberculosis and illnesses caused by atypical mycobacteria:

Adults:
The dose of protionamide depends on your body weight. Adults are given 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 in a dose of 15 mg PTH/kg body weight can be seen from 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 ½**
30	**450**	**2**
35	**525**	**2**
40	**600**	**2 ½**
45	**675**	**2 ½**
50	**750**	**3**
55	**825**	**3 ½**
60	**900**	**3 ½**
65	**975**	**4**
≥ 70	**1000**	**4**

If PETEHA is administered with isoniazid, in the course of a combination therapy, the daily dose of PETEHA must be reduced by half. The maximum daily dose should then not exceed 500 mg protionamide (equivalent to 2 PETEHA film-coated tablets).

Children:
Depending on their body weight, children are given 7.5 – (15) mg PTH/kg body weight as a daily dose. The maximum daily dose must not exceed 500 mg protionamide.

Dosage in cases of impaired renal function:
Patients with a glomerular filtration rate (GFR) below 30 ml/min and dialysis patients are given 250 – 500 mg protionamide (equivalent to 1 to 2 PETEHA film-coated tablets) daily depended on their body weight. In patients with a severe impairment of the kidney function, the levels of active substance in the blood are to be monitored and the dose adapted if necessary.

For treatment of leprosy:
In the treatment of leprosy, PETEHA is applied in the scope of modified therapy regimes in

accordance with the dosage recommendations stated.

Method of administration
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, may be attenuated as a result.
PETEHA is a secondary medicine (reserve medicine) for treatment of tuberculosis and illnesses caused by so-called ubiquitous (atypical) mycobacteria. It is always administered with other antimycobacterial medicines as part of a combination therapy if sensitivity of the pathogen to the active substance protionamide is known. The choice of the therapy regime depends on the detection of the pathogen sensitivity in the samples from the patient. For treatment of leprosy, protionamide is used in the scope of a modified therapy regime.

Duration of administration
Treatment of tuberculosis:
PETEHA should always be applied in combination with other antimycobacterial medicines. In case of tuberculosis, application in a 3 to 4-fold combination therapy in the initial phase and continuation with a reduced amount in the continuity phase is recommended.
The duration of therapy depends on the treatment regime chosen. It may last from 9 months to up to 2 years.

Treatment of leprosy:
The duration of therapy depends on the treatment regime chosen.

Please consult your doctor or pharmacist if you have the impression that the effect of PETEHA is too strong or not strong enough.

If you take more PETEHA than you should
If you have accidentally taken more PETEHA, the side effects mentioned in Section 4. “Possible side effects” may become more pronounced. Contact your doctor immediately if you suspect that you have taken an overdose so that he can decide on the necessary measures in accordance with the severity of the case, if required.

If you forget to take PETEHA
Do not take a double dose to make up for a forgotten dose.

If you stop taking PETEHA
Pathogens (mycobacteria) may become resistant to the 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.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
The reported incidence rates of the side effects stated below vary considerably in underlying literature references. Meaningful studies with sufficient number of patients are not available.
The incidence rates of side effects are based on the following categories:

Very common:	may affect more than 1 in 10 people
Common:	may affect up to 1 in 10 people
Uncommon:	may affect up to 1 in 100 people
Rare:	may affect up to 1 in 1,000 people
Very rare:	may affect up to 1 in 10,000 people
Not known:	frequency cannot be estimated from the available data

Possible side effects:

Blood and lymphatic system disorders:
Disorders of the red blood cells (anemia, methemoglobinemia), functional disorders of blood coagulation (hypoprothrombinaemia and hypofibrinogenemia).

Immune system disorders:
Individual cases: allergic reactions

Endocrine (hormonal) disorders:
Rare: Increase of mammary gland tissues in males (gynaecomastia), menstrual cycle disorders in women (dysmenorrhea, amenorrhoea), reduced function of the thyroid gland (hypothyreosis)

Metabolism and nutritional disorders:
Rare: Blood sugar fluctuations and reduction of the blood sugar level in diabetics

Psychiatric disorders:
Uncommon: Concentration disorders, states of confusion, psychiatric disorders such as depression, excitation, psychoses
Individual cases: suicide attempts

Nervous system disorders:
Common: Dizziness, headaches
Rare: Seizures, sleep disorders
Optic nerve (Nervus opticus) damage with clouded vision, eye muscle paralysis and disorders of visual acuity (accommodation disturbances) have been reported.

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

In particular after simultaneous administration of isoniazid, visual disorders, inflammatory disease of the nervous system (polyneuropathies) with sensation disorders (paraesthesia), muscular weakness and disorders of the course of movement (ataxia) have been reported.

Eye disorders:
See also Nervous system disorders.
Vision disorders, inter alia double vision (diplopia)

Ear and labyrinth disorders
Individual cases: Loss of hearing, ear noises (tinnitus)

Respiratory, thoracic and mediastinal (central area of the thorax) disorders:
Individual cases: Coughing up blood (hemoptysis)

Gastrointestinal disorders (stomach/intestinal tract):
Very common: Metallic or sulfurous taste, mouth dryness, but also an increased salivary flow, loss of appetite, emaciation (anorexia), nausea
Uncommon: Vomiting, heartburn, abdominal pains, feeling of fullness, diarrhea or constipation, flatulence (meteorism)

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

Swelling of the salivary gland (parotis) has been reported.
Hepatobiliary disorders
An increase of liver enzyme activity (transaminases) is common in therapy with PETEHA, receding after discontinuance, but *rarely* results in a pronounced hepatic function disorders with jaundice (icterus). The liver-damaging effect decisively depends on the prior damage of the liver function (for example alcoholism, post-hepatic liver function disorder) and is frequently in combination with other potentially liver-damaging medicines (isoniazid, rifampicin, pyrazinamide).
Severe inflammations of the liver with jaundice have been reported as has an individual case of liver failure.

Skin and subcutaneous tissue disorders
Skin rash (pellagra-like reactions), light sensitivity of the skin (photodermatoses), skin fissures (rhagades), inflammations of the oral mucous membranes (stomatitis), acne, inflammation of the lips (cheilitis), inflammation of the tongue (glossitis), loss of hair (alopecia).

Musculoskeletal and connective tissue disorders
Joint pain (arthralgias), joint inflammations (arthritis), muscle weakness

Renal and urinary disorders
Formation of bladder stones (urolithiasis)

Sunset Yellow FCF (E 110) may cause allergic reactions.

Countermeasures
If you notice the occurrence of pronounced side effects, get in touch with a doctor so that he can initiate the necessary measures.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

Bundesinstitut für Arzneimittel und Medizinprodukte
(Federal Institute for Drugs and Medical Devices)
Abt. Pharmakovigilanz
(Department of Pharmacovigilance)
Kurt-Georg-Kiesinger-Allee 3
53175 Bonn
Website: www.bfarm.de

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store PETEHA

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the blister or the label of the plastic container and the folding box after "Expiry date:". The expiry date refers to the last day of that month.
Use the medicinal product within 2 months after first opening of the plastic container. Keep the container tightly closed.
Do not throw away any medicines via wastewater (e.g. do not use the toilet or washbasin). Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment. Further information can be found under www.bfarm.de/arzneimittelentsorgung.

6. Contents of the pack and other information

What PETEHA contains
-The active substance is: protionamide.
One film-coated tablet contains 250 mg protionamide.

-The other ingredients are: croscarmellose sodium, copovidone, crospovidone (Type A, Ph. Eur.), magnesium stearate (Ph. Eur.) [vegetable], silica colloidal anhydrous, macrogol 6000, hypromellose, cellulose microcrystalline, titanium dioxide (E 171), Sunset Yellow FCF (E 110), lactose monohydrate.

What PETEHA looks like and contents of the pack
PETEHA is an orange, round, biconvex film-coated tablet with a breakline on one side.

PETEHA, film-coated tablets are available in the following packs:
PVC/Aluminium blister packs:

Original pack containing 50 film-coated tablets
Original pack containing 100 film-coated tablets

Plastic container made of polypropylene (PP) with LDPE closure:

Original pack containing 100 film-coated tablets

Not all pack sizes may be marketed.

Marketing Authorization Holder and Manufacturer

Marketing Authorization Holder

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