

Package Leaflet: Information for the user

Metalcaptase® 300 mg

Enteric coated tablets

Active substance: Penicillamine

Heyly

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 Metalcaptase® 300 mg is and what it is used for
2. What you need to know before you take Metalcaptase® 300 mg
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1. WHAT METALCAPTASE® 300 MG IS AND WHAT IT IS USED FOR

Metalcaptase 300 mg contains penicillamine and is used for treatment of rheumatic diseases and as an antidote for heavy metal poisoning.

Metalcaptase 300 mg is used for the following diseases:

- Rheumatoid arthritis.
- Wilson's disease.
- Lead, mercury, copper, and zinc poisoning.
- Cystinuria with detected cystine stones when recurrence of stones cannot be prevented by other methods (methionine-free diet, hyperhydration, alkalization of urine).
- Advanced cystine stone disorders involving special risks (e.g. after nephrectomy).
- There is some evidence that scleroderma may respond to treatment with Metalcaptase 300 mg.

Explanations

Rheumatoid arthritis is a connective tissue disease, which primarily affects the joints as a rule, however internal organs may also be affected.

Scleroderma is a vessel and connective tissue disease which can lead to skin changes.

Wilson disease is an inherited copper excretion disorder.

Cystinuria is a disease characterized by an excessive excretion of cystine in the urine.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE METALCAPTASE® 300 MG

Do not take Metalcaptase 300 mg,

- if you are allergic to penicillamine or any of the other ingredients of this medicine (listed in section 6);
- if you have suffered from serious side effects during an earlier application of penicillamine particularly with effects on the kidneys or on the blood formation (toxic reaction);
- if you are hypersensitive to penicillin (penicillin allergy).

Further do not take Metalcaptase 300 mg if you suffer from

- kidney damage;

- damage to the hematogenic bone marrow;
- systemic lupus erythematosus (an illness of the immune system) or if a larger number of antibodies directed against cell nuclei have been detected;
- damage to the liver tissue and
- if you have to receive treatment with gold or chloroquine (drugs which are given at rheumatoid arthritis).

Warnings and precautions

Talk to your doctor or pharmacist before taking Metalcaptase 300 mg.

Before the beginning of treatment with Metalcaptase 300 mg blood count and nervous system must be checked in order to identify special risks. During the treatment the controls should be repeated at regular intervals.

Patients with hypersensitive tendencies (hay fevers, eczema [itching lichen], nettle-rash fever, dyspnoea attacks [asthma attacks]) require a careful monitoring.

Under certain circumstances the therapy with Metalcaptase 300 mg must be discontinued. The patient may have to be monitored by the doctor in the time following the discontinuation.

Prior to surgical interventions Metalcaptase 300 mg shall be discontinued or the dose should be reduced, if possible, for at least six weeks prior to surgery until the wound healing is completed, as D-penicillamine is able to interfere with collagen cross links and elastin tissue (connective tissue).

Follow all instructions of your doctor and attend all medical checkups your doctor arranges for you.

Other medicines and Metalcaptase 300 mg

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

The simultaneous treatment with Metalcaptase 300 mg may influence the effect of the following pharmaceutical ingredients or pharmacological groups:

- **Azathioprine** is an active substance for the inhibition of the cell division (cytostatic), used to treat rheumatoid arthritis. In combination with azathioprine the tolerability of Metalcaptase 300 mg is reduced.
- The simultaneous intake of drugs which contain **indomethacin** (an antiphlogistic active substance) can lead to increased penicillamine levels in the blood.
- The intake of **ferrous preparation** should be separated by at least two hours before or after doses of Metalcaptase 300 mg. Simultaneous intake reduces the penicillamine absorption (up to 70 %). This also applies to **magnesium or aluminum containing antacids** and to **sucralfat** (drugs for binding hydrochloric acid).

Which effect has Metalcaptase 300 mg on the vitamin metabolism?

A longer lasting medical treatment with Metalcaptase 300 mg can result in a vitamin B₆ deficiency which requires a supplementation of vitamin B₆.

Metalcaptase 300 mg with food, drink and alcohol

Take Metalcaptase 300 mg on an empty stomach, i.e. the last meal should have been taken more than two hours ago and the next meal should be taken only one hour later (see Method of administration).

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.

If Metalcaptase 300 mg is used during pregnancy in larger quantities, it may cause damage to the foetus. Therefore, women of childbearing potential must use contraceptive measures during the treatment. Metalcaptase 300 mg must not be used for the treatment of rheumatoid arthritis in the case of pregnancy. For other diseases the medical treatment with Metalcaptase 300 mg should only be continued if no other therapy with a better benefit/risk ratio is available.

During the medical treatment with Metalcaptase 300 mg breast feeding should not be carried out.

Driving and using machines

No consequences are known to this day.

3. HOW TO TAKE METALCAPTASE® 300 MG

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 active ingredient of Metalcaptase 300 mg is penicillamine.

The high daily dose should be divided into 2 to 3 single doses per day.

The recommended dose is:

Rheumatoid arthritis

Metalcaptase 300 mg is not suitable for the start of the therapy and for the gradual dose increase/dose reduction in patients with rheumatoid arthritis, since the content of the active ingredient is too high. For the start of the therapy tablets with a lower content of the active ingredient are available.

After the onset of action, the individual daily maintenance dose is 1 to 2 tablets (300 to 600 mg of penicillamine) for adults.

If you are free of symptoms over a longer period, then the therapy with Metalcaptase 300 mg can be discontinued, if your doctor regards this as acceptable.

Metalcaptase 300 mg is not suitable for the treatment of rheumatoid arthritis in children and adolescents since the active ingredient content is too high. For children and adolescents tablets with a lower content of the active ingredient are available.

Wilson's disease

Adults, children and adolescents with Wilson's disease take 10 to 20 mg of penicillamine per kg of body weight daily (e.g. 2 tablets daily per 60 kg or 1 tablet Metalcaptase 300 mg daily per 20 kg of body weight).

Heavy metal poisoning

At the beginning adults with heavy-metal poisonings take 1 tablet Metalcaptase 300 mg (300 mg of penicillamine) 4 times per day. The daily intake should not exceed 40 mg of penicillamine per kg of body weight when a longer period of treatment is required (e.g. 4 times 2 tablets daily per 60 kg of body weight).

Children and adolescents should take up to 100 mg of penicillamine per kg of body weight daily for heavy metal poisonings (e.g. 3 tablets daily per 9 kg of body weight). The daily maximum dose is 1,050 mg of penicillamine.

Cystinuria

Patients with cystinuria take 4 to 6 tablets of Metalcaptase 300 mg daily, divided into 4 - 6 single doses, depending on the excreted amount of cystine.

Route and method of administration

The tablets should be swallowed whole with plenty of water (this applies particularly to the treatment of cystinuria) and on an empty stomach, i.e. one hour before or two hours after meals.

To preserve the gastric acid resistant coating, coated tablets may not be split or chewed.

Duration of treatment

Your doctor will make a decision on the length of treatment based on the course of the disease.

If you take more Metalcaptase 300 mg than you should

If you have accidentally taken twice your prescribed dose, this does not have any effects on the further intake, i.e. you take Metalcaptase 300 mg after that as usual.

In the event of substantial overdose please call a doctor to help since gastric lavage can be necessary. Further measures are normally not required.

If you forget to take Metalcaptase 300 mg

A forgotten dose does normally not lead to any disease symptoms. The medication should be continued as usual. Do not take a double dose to make up for a forgotten dose. However, please take into account that Metalcaptase 300 mg only can work safely and sufficiently if it is taken regularly.

If you stop taking Metalcaptase 300 mg

In cases of unpleasant side effects your doctor will discuss with you, which countermeasures are possible and whether other drugs are worth considering for the 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.

Some side effects can be severe. Consult the next available doctor immediately in the following case:

Common: may affect up to 1 in 10 people

- damage of the hematogenic bone marrow with reduction of white blood cells (leukocytopenia), erythrocytes (anemia) and blood platelets (thrombocytopenia). There is a risk for developing agranulocytosis or panmyelopathy (very strong reduction of certain white blood cells or all blood cells). Symptoms are: high fever, chill and ulcers on oral mucosa, palatine tonsils, anus and genitals. In these cases Metalcaptase 300 mg must be discontinued immediately. Self medication with painkillers and antipyretics (fever reducers) should be abstained from. Since agranulocytosis (absence of certain white blood cells) may develop quickly within a few hours, blood counts should be performed promptly.

If you recognise one of the symptoms described above in yourself, please consult the next available doctor immediately.

Further possible side effects

Very common: may affect more than 1 in 10 people

- reduction or loss of the taste (hypogeusia or ageusia). These effects are reversible and will go away when the dose of Metalcaptase 300 mg is decreased;
- gastrointestinal complaints like gastric intolerance, loss of appetite, sick feeling, nausea and less often diarrhoea;
- skin symptoms of different forms, mostly due to a hypersensitivity to Metalcaptase 300 mg. Fever occurs occasionally;
- excretion of proteins in the urine (proteinuria) which is sometimes accompanied by excretion of blood in the urine (hematuria). These are symptoms of kidney damage caused by antibodies (immune complex nephritis). The kidney damage can develop into a nephrotic syndrome at any time (it results in an increase of blood fats and in protein excretion, leading to abnormal accumulation of tissue fluid in the lower legs and, subsequently, in the abdomen and pleural fissure).

Common: may affect up to 1 in 10 people

- ulcer formation on buccal and tongue mucosa;

Uncommon: may affect up to 1 in 100 people

- premature fatigue of the voluntary muscles (particularly the ocular muscles), which increases under exertion and decreases at rest (myasthenic syndrome);
- an increased amount of antibodies in the blood which are directed against nuclei. This is an indication of possible damage resulting from the body's immune system attacking normal body components (clinically latent, humoral, antinuclear antibody syndrome as an indicator of the risk of induction of autoimmune damage);
- Stomach and intestinal bleedings;
- excessive hairiness in females (hirsutism);
- alopecia.

Very rare: may affect up to 1 in 10,000 people

- severe skin changes like pemphigus (vesicular detachment of the skin);
- inflammation of the optic nerve (neuritis nerves optici);
- reversible pulmonary infiltrates;
- chronically progressive lung changes (chronic inflammation with hardening of connective tissue in the lung);
- pseudoxanthoma elasticum, Elastosis perforans serpiginosa (alteration in the elastic tissue of skin and mucosa with increased vulnerability);
- lichen planus (red to brownish, usually itching nodules on the skin);
- polymyositis and dermatomyositis (illnesses associated with muscle pains, muscle weakness, muscle wasting and skin changes);
- ulcerative colitis (long-lasting inflammatory illness of colon and often rectum with mucous bloody diarrheas, intestinal ulcers and scarred narrowings of the intestine);
- systemic lupus erythematosus (an illness of the immune system);
- intrahepatic cholestasia;
- mammary enlargement;
- yellow colouring of the nail;
- possible aggravation of neurological symptoms at patients with Wilson's disease. In this case, the treatment with penicillamine should be discontinued (even after discontinuing therapy the deterioration in symptoms may be irreversible in some cases).

At high doses of Metalcaptase 300 mg, bloody blisters may occur in the area of bruised skin after blunt skin injury.

Damage of the kidneys, skin (pemphigus) or bone marrow usually take a benign course if detected early enough and immediate discontinuation of the medication with Metalcaptase 300 mg. However, in the rare cases when the damages go unrecognised, they may take a severe course leading, under certain circumstances, to death.

Contact your attending doctor at your earliest convenience if you recognize one of the symptoms described above.

Please inform your doctor if you are suffering from diarrhea since this may decrease the absorption and the effectiveness of Metalcaptase 300 mg.

Stop taking Metalcaptase® 300 mg and contact your doctor if you experience signs of a hypersensitivity (allergic) reaction. If you experience severe hypersensitivity reactions, see a doctor immediately!

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 to Bundesinstitut für Arzneimittel und Medizinprodukte, Abt. Pharmakovigilanz, Kurt-Georg-Kiesinger Allee 3, D-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 METALCAPTASE® 300 MG

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on each blister and carton after "expiry date:". The expiry date refers to the last day of that month.

Do not store above 25 °C.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Metalcaptase 300 mg contains

The active substance is penicillamine.

1 enteric coated tablet contains 300 mg penicillamine.

The other ingredients are: Calcium behenate, calcium hydrogen phosphate dihydrate, cellulose (microcrystalline and powder), copovidon, dimeticon, macrogol 6000, cornstarch, poly(methacrylic acid-co-methylmethacrylate)(1:1), triacetin, methacrylic acid-ethylacrylate-copolymer(1:1), polysorbate 80, hydrogenated castor oil, highly disperse silicon dioxide, talc, titanium dioxide.

What Metalcaptase 300 mg looks like and contents of the pack

Metalcaptase 300 mg is a white round tablet and available in packages with 50 enteric coated tablets or 100 enteric coated tablets.

Marketing authorization holder

Heyl Chem.-pharm. Fabrik

GmbH & Co. KG

or

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This drug is approved under the following names in the member states of the European Economic Area (EEA):

Federal Republic of Germany: Metalcaptase® 300 mg

Czech Republic and Slovak Republic: Metalcaptase® 300

This leaflet was last revised in December 2014.

The following information is intended for medical healthcare professionals only:

Treatment of overdose

No reports on acute symptoms of poisoning are available. If penicillamine has already been absorbed, the excretion can be accelerated by forced diuresis or dialysis.