Package leaflet: Information for the patient

CUPROS L 250 mg capsules

D-Penicillamine

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 CUPROS L is and what it is used for

What CUPROS L is
CUPROS L contains the active substance 'penicillamine' and is used for treatment of rheumatic diseases and as an antidote for heavy metal poisoning.

What CUPROS L is used for
CUPROS L is used in adults for:
- Rheumatoid arthritis, including juvenile manifestations, when the disease is resistant to other treatments
- Wilson's disease
- Heavy metals intoxication
- Cystinuria

How CUPROS L works
Penicillamine belongs to a group of medicines called disease modifying anti-rheumatic drugs (DMARDS).
Penicillamine works by reducing the body's immune response and relieving pain, swelling and stiffness caused by rheumatoid arthritis.
Penicillamine is also a chelating agent. This means that it binds to certain metals in your body, including lead and copper, to help to remove them from your body.

2. What you need to know before you take CUPROS L

You must read the package leaflet of all medicinal products to be taken in combination with CUPROS L before starting treatment with CUPROS L.

Do not take CUPROS L :
- 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 allergic hypersensitive to penicillin (penicillin allergy).

Further do not take CUPROS L 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

Before the beginning of treatment with CUPROS L 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.

Prior to surgical interventions CUPROS L 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 CUPROS L
Tell your doctor or pharmacist if you are taking or have recently taken any other medicines.

CUPROS L may increase the risk of side effects if you also take the following medicines:
- gold (used to treat rheumatoid arthritis)
- NSAIDs (non-steroidal anti-inflammatory drugs) e.g. ibuprofen or naproxen (used to treat arthritis and for pain relief) as there is an increased risk of damaging your kidneys
- clozapine (used to treat schizophrenia) as taking Penicillamine with clozapine may increase the potential side effects on the bone marrow.

The simultaneous treatment with CUPROS L 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 CUPROS L 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 CUPROS L. 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 CUPROS L on the vitamin metabolism?
A longer lasting medical treatment with CUPROS L can result in a vitamin B6 deficiency which requires a supplementation of vitamin B6.

CUPROS L with food, drink and alcohol
Take CUPROS L 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 CUPROS L 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. CUPROS L must not be used for the treatment of rheumatoid arthritis in the case of pregnancy. For other diseases the medical treatment with CUPROS L should only be continued if no other therapy with a better benefit/risk ratio is available.
During the medical treatment with CUPROS L breast feeding should not be carried out.

Driving and using machines
Do not drive or operate machines if you feel dizzy, tired, sleepy, have vertigo or blurred vision after taking CUPROS L.

3. How to take CUPROS L

Always take CUPROS L exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

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

The recommended dose is:

<u>Rheumatoid arthritis</u>
It is recommended to administer small doses at the beginning of treatment to gradually increase them later.

Adults: Normally, the dosage in adults should not exceed 125-250 mg per day during the first four weeks of treatment, then increasing progressively (every 4-8 weeks) until improvement occurs. The normal dose ranges between 500-700 mg/day, being able to reach even 1,000mg/day. Always stick to the lowest effective dose.
Children: Administration in the form of 50 mg capsules is recommended, starting with 1 or 2 capsules per day and then progressively increasing according to the weight of the child up to 10-20 mg/kg/day.
As in the adult, stick to the lowest effective dose.

Wilson's disease
In Wilson's disease the dose must be adjusted individually taking as parameters the amount of copper excreted in the urine.
As a guideline value, doses of, respectively, 2,000-1,000 mg/day in adults and about 20 mg/kg/day in children are recommended. Due to the effects of penicillamine on collagen, it is advisable to discontinue treatment, or reduce the dose to 250 mg daily, if the patient is to undergo surgery. Treatment should be reinstituted only when the wound is completely healed.

Heavy metals intoxication
In poisoning by lead or other heavy metals, for adults doses of 500-1,000 mg/day are recommended. The daily intake should not exceed 40 mg of penicillamine per kg of body weight when a longer period of treatment is required

Cystinuria
In cystinuria, the dose must be adjusted individually taking as parameters the amount of cystine excreted in the urine. Patients with cystinuria take 4 times per day 1,200 - 1,800 mg penicillamine, depending on the excreted amount of cystine.

Route and method of administration
The capsules 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.

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 CUPROS L 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 CUPROS L after that as usual.

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

If you forget to take CUPROS L
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 CUPROS L only can work safely and sufficiently if it is taken regularly.

If you stop taking CUPROS L
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.

Side effects can be lessened in frequency and severity if the dosage is progressive and the maintenance doses are low.
The most common are maculopapular or erythematous-type reactions, occasionally accompanied by fever, arthralgia, or lymphadenopathy. Sometimes hives occur.
Cases of therapy-related nephrotic syndrome and membranous glomerulonephritis have been reported. Sometimes proteinuria appears as the first symptom. In case of persistent proteinuria unrelated to another organic cause, treatment should be discontinued. Recovery is slow, but fully achieved.
Penicillamine causes an increase in soluble collagen, which is probably the cause of the increased friability of the skin in places subject to friction that is sometimes observed during treatment. Blood extravasations may occur under these circumstances.
Loss of taste sensitivity may occur, related to copper deficiency. It does not occur, therefore, in patients with Wilson's disease and in other cases it reverts with the end of treatment, or it can be corrected during treatment by adding 5 or 10 mg of copper ion daily to the diet.

Other side effects described are:
- gastrointestinal disorders
- anorexia
- nausea
- vomiting
- diarrhea
- agranulocytosis
- thrombocytopenia
- hemolytic anemia
- purpura
- leukopenia.

All of them reversible with the suspension of the treatment.
If you notice any other adverse reaction not described above, consult your doctor or pharmacist.

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

5. How to store CUPROS L

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 carton after "EXP". The expiry date refers to the last day of that month.

This product does not require any special storage conditions.

Do not use this medicine if you notice any damage or signs of tampering to the pack.

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 CUPROS L contains

The active substance is D-penicillamine. Each capsule contains 250 mg of D-penicillamine.
The other ingredients are: magnesium stearate.

What CUPROS L looks like and contents of the pack

CUPROS L 250 mg capsules have yellowish pink cap and body, with the capsule shell size No. 1.

Carton box containing a plastic bottle with 50 capsules.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
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