

**PATIENT PACKAGE INSERT IN
ACCORDANCE WITH THE PHARMACISTS'
REGULATIONS (PREPARATIONS) - 1986**

The medicine is dispensed with a physician's prescription only

TRIENTINE RAZ 250 MG Hard Capsules

Active ingredient:

Each capsule contains trientine dihydrochloride 250 mg, equivalent to 166.67 mg of trientine base.

For the list of inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information on some of the drug ingredients".

Read the entire leaflet carefully before you start using this medicine. This leaflet contains essential information about this medicine. If you have any further questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for you. Do not pass it to others. It may harm them even if it seems to you that their medical condition is similar.

1. What is the medicine intended for?

This medicine is used for the treatment of Wilson's disease in adults, adolescents and children aged 5 years or older intolerant to D-penicillamine therapy.

Wilson's disease is an inherited condition in which the body cannot transport copper in the normal way or remove copper in the normal way as a secretion from the liver into the gut. This means that the small amounts of copper from food and drink build up to excessive levels and can lead to liver damage and problems in the nervous system.

How Trientine RAZ 250 mg works

This medicine mainly works by attaching to copper in the body which then allows it to be removed in the urine, helping to lower copper levels. It may also attach to copper in the gut and so reduce the amount taken up into the body.

The medicine controls the amount of copper in the body by binding to it, in such a way that the copper can be passed from the body.

Therapeutic group: Other alimentary tract and metabolism products, various alimentary tract and metabolism products.

2. Before using this medicine:

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient (trientine dihydrochloride) or to any of the other ingredients that this medicine contains (see section 6, "Additional information").

Special warnings regarding the use of the medicine

Talk to your doctor, pharmacist or nurse before taking Trientine RAZ 250 mg.

If you were already taking another trientine medicine, your doctor may modify your daily dose when switching to treatment with Trientine RAZ 250 mg.

Tell the doctor immediately if you notice symptoms that may indicate a problem with the nervous system: shaking, lack of coordination, slurred speech, muscle stiffness, worsening of muscle spasms. These symptoms may occur especially when starting treatment with Trientine RAZ 250 mg.

Your symptoms may initially get worse after starting the treatment. If this happens, you must tell your doctor. Your doctor will regularly check your blood and urine to ensure that you receive the right dose of Trientine RAZ 250 mg to best control your symptoms and copper levels. Regular monitoring is especially important in the following situations: at the start of treatment, in children and pregnant women and when the medicine's dose is changed. The doctor may need to change the dose of your medicine.

This medicine may also reduce the level of iron in your blood and your doctor may prescribe iron supplements (see section "Drug interactions" below).

If you have kidney or liver problems, your doctor will regularly check that the treatment dose is appropriate and does not affect the functioning of your kidney or liver.

The combination of trientine with zinc, calcium or magnesium antacids is not recommended.

Lupus-like reactions (symptoms may include persistent rash, fever, joint pain, and tiredness) have been reported in some patients switched to treatment with trientine medicine after treatment with penicillamine. However, it could not be determined if the reaction was due to trientine or to previous penicillamine treatment.

If you have difficulty swallowing, consult your doctor.

Drug interactions

If you are taking, have recently taken or may take other medicines, including non-prescription medicines and food supplements, inform your doctor or pharmacist. If you are taking iron supplements or indigestion remedies (medicines that reduce discomfort after eating), make sure that at least two hours have passed before or after taking Trientine RAZ 250 mg, since Trientine RAZ 250 mg may be less effective.

It is recommended to take Trientine RAZ 250 mg at least one hour apart from any other medicine.

Use of the medicine and food

Swallow the capsules whole with water on an empty stomach, at least one hour before the meal or two hours after the meal and at least one hour apart from any other medicine, food or milk.

Pregnancy, breast-feeding and fertility

If you are pregnant, think you might be pregnant, or are planning to become pregnant, or are breast-feeding, ask your doctor for advice before taking this medicine. You and your doctor can fully discuss the potential benefits of treatment whilst considering any possible risks that there may be with continuing treatment. Your doctor will advise you which treatment and which dose is best in your situation. Talk to your doctor if you become pregnant while taking Trientine RAZ 250 mg.

If you are pregnant and taking Trientine RAZ 250 mg, you will be monitored throughout pregnancy for any effects on the baby or changes in copper levels in your blood.

It is not known if Trientine RAZ 250 mg can pass into breast milk. It is important to tell your doctor if you are breast-feeding or plan to do so. Your doctor will then help you decide whether to stop breast-feeding or to stop taking Trientine RAZ 250 mg, considering the benefits of breast-feeding to the baby and the benefits of Trientine RAZ 250 mg to the mother. Your doctor will decide which treatment and which dose is best in your situation.

Driving and using machines

Trientine RAZ 250 mg is not expected to affect your ability to drive or operate machinery.

Important information on some of the drug ingredients This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially "sodium-free".

3. How should you use the medicine?

Always use the medicine according to the doctor's instructions. You should check with the doctor or the pharmacist if you are unsure about the drug dosage and treatment regimen.

The Dosage treatment regimen will be determined by the doctor only.

The usual recommended dose is:

In adults of all ages including the elderly

The recommended total daily dose is between 4 and 8 capsules per day (making a total of 0.67-1.34 grams trientine base), to be taken orally. This daily total dose will be divided into 2 to 4 smaller doses to be taken during the day. Your doctor will tell you how many capsules you should take and how often in the day.

Children

The dose that you will give your child is usually lower than for an adult and depends on the age and body weight of your child. The total daily dose varies between 2 and 5 capsules, to be taken orally. This daily total dose will be divided into 2 to 4 small doses to be taken during the day. Your doctor will tell you how many capsules you should give your child and how often in the day.

Once the treatment has started, the attending doctor may adjust the dose based on the response to treatment.

Do not exceed the recommended dose.

Method of administration

Swallow the capsules whole with water on an empty stomach, at least one hour before the meal or two hours after the meal and at least one hour apart from any other medicine, food or milk.

There is no information about opening, dispersing and chewing the capsule.

If you take iron supplements, take them at least two hours after taking a dose of Trientine RAZ 250 mg.

If you have accidentally taken a higher dose

Take Trientine RAZ 250 mg only as it is prescribed for you. If you think you may have taken more Trientine RAZ 250 mg than you were told to, immediately contact your doctor or pharmacist. If you have accidentally taken a higher dose, you may feel dizziness, nausea, or a desire to vomit.

If you have accidentally taken an overdose or if a child has accidentally swallowed the medicine, immediately contact a doctor or go to a hospital emergency room and take the medicine package with you.

If you forget to take the medicine

If you forget to take one or more doses, take another dose as soon as possible, then take the next dose as per your regularly scheduled time. Do not take a double dose to make up for a forgotten dose.

Adhere to the treatment as recommended by the doctor. Even if your medical condition has improved, do not stop the drug treatment without consulting your doctor.

Do not take medicines in the dark! Check the label and the dose every time you take the medicine. Wear glasses if you need them.

If you have any further questions regarding the use of this medicine, consult the doctor or the pharmacist.

4. Side effects

Like any medicine, the use of Trientine RAZ 250 mg may cause side effects in some users. Do not be alarmed while reading the list of side effects. You may not suffer from any of them. Occasionally, treatment with trientine can cause inflammation of the small intestine or colon.

If you experience any of the following side effects, contact your doctor immediately:

- severe stomach pains (duodenitis)
- persistent diarrhoea (colitis)
- nervous system problems such as shaking (tremor), lack of coordination, slurred speech (dysarthria), muscle stiffness, worsening of muscle spasms (dystonia)

Other side effects may include:

Common side effects (may affect up to 1 in 10 people)

- feeling sick (nausea), especially when starting treatment

Uncommon side effects (may affect up to 1 in 100 people)

- skin rashes
- anaemia (you may feel unusually tired)

Side effects whose frequency is not known (frequency cannot be estimated from available data)

- lupus-like syndrome (symptoms may include: persistent rash, fever, joint pain and tiredness)
- inflammation of the kidneys (lupus nephritis).

If a side effect appears, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult a doctor.

Reporting of side effects

You can report side effects to the Ministry of Health by clicking the "report side effects due to medication" in the homepage of the Ministry of Health (www.health.gov.il) referring to an online form for reporting side effects, or by clicking the link: <https://sideeffects.health.gov.il>.

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use this medicine after the expiry date (EXP:) which appears on the package. The expiry date refers to the last day of that month.
- Store below 25°C and keep the bottle tightly closed in order to protect from moisture.
- Shelf life and storage conditions after opening (relevant only when the medicine is marketed in a bottle package) The product can be used for 100 days after first opening when stored at temperature of 2-8°C. or up to 60 days after first opening when stored at temperature of 15-30°C.
- 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. Additional information:

In addition to the active ingredient the medicine also contains:

Capsule content: stearic acid, anhydrous colloidal silica

Capsule shell:

Gelatin, Titanium Dioxide (E171), yellow iron oxide (E172), sodium lauryl sulphate, red iron oxide (E172), printing ink: shellac, black iron oxide (E172), propylene glycol, potassium hydroxide.

What does the medicine look like and what is the content of the package:

Hard gelatin capsule filled with white to pale yellow powder. Capsule cap and body are brown opaque and imprinted with "HP551" in black ink.

Trientine RAZ 250 mg capsules are available in white opaque HDPE bottle with a PP child-resistant closure, or in a blister pack in a carton box. The bottle contains 100 capsules. The carton pack (blisters) contains 30, 72, 96, 100, 240, or 300 capsules in a pack. Not all pack sizes may be marketed.

Marketing Authorization Holder and importer and its address
RAZ Pharmaceuticals Ltd., 31 Gesher Ha'Etz, Emek Hefer Industrial Park, Israel.

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