

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

The medicine is dispensed with a doctor's prescription only

**Minocycline 50 mg
Minocycline 100 mg
Capsules**

Active ingredient:

Each capsule of Minocycline 50 mg contains:

Minocycline 50 mg (as Hydrochloride)

Each capsule of Minocycline 100 mg contains:

Minocycline 100 mg (as Hydrochloride)

For the list of the additional ingredients, see section 6.

Read the entire leaflet carefully before using the medicine.

This leaflet contains concise information about the medicine. If you have any further questions, please refer to your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is the medicine intended for?

The medicine is active against bacteria susceptible to minocycline, e.g.: acne.

Therapeutic Group: antibiotic medicine belonging to the tetracycline group.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient, to other antibiotics of the tetracycline group (such as tetracycline, doxycycline), or to any of the additional ingredients the medicine contains (for the list of the additional ingredients, see section 6).
- You have Systemic Lupus Erythematosus (SLE).
- You are pregnant or breastfeeding.
- You suffer from kidney failure.
- Do not use in children under 12 years of age.

Special warnings regarding the use of this medicine:

Before (and during) the treatment with Minocycline, tell your doctor if:

- You suffer from myasthenia gravis (a condition manifested by muscular weakness, difficulty chewing and swallowing and impaired speech).
- You suffer or have suffered in the past from impaired function of the liver or kidneys.
- You have systemic lupus erythematosus, a condition characterized by a rash (especially on the face), hair loss, fever, a feeling of general discomfort and illness, joint pain - see 'Do not use the medicine if'.
- You suffer from increased pressure in the skull (intracranial hypertension).
- You are sensitive to sunlight or artificial light (e.g. sunbeds).

Additional warnings:

- **Sensitivity to light (photosensitivity):** the medicine may cause hypersensitivity when you are exposed to light; therefore avoid direct exposure to natural or artificial light. Refer to your doctor if you experience photosensitivity symptoms. It may be recommended to stop the treatment. See also section 'Side effects'.
- **Hyperpigmentation:** change in the skin color, secretions and other organs in the body (see section 'Side effects') may occur especially in long-term use. In this case refer to your doctor who will decide on the continuation of the treatment.

Children and adolescents: this medicine is not intended for babies and children under 12 years of age, since it may cause permanent discoloration and underdevelopment of tooth enamel.

Tests and follow-up:

- Tell your doctor or nurse that you are taking Minocycline before performing a urine test as the medicine may affect the results.
- If the treatment lasts for longer than 6 months you should perform blood tests every 3 months to check whether systemic lupus erythematosus is developing and also to check your liver functions.
- The doctor may decide to carry out additional monitoring, for instance kidney functions.

Drug interactions:

If you are taking, or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, please tell your doctor or pharmacist. Especially inform your doctor or pharmacist if you are taking the following medicines (it should be noted that the following list indicates the active ingredients in the medicines. If you are unsure whether you are using one of these medicines, please consult your doctor or pharmacist):

- Antibiotics from the penicillin group such as phenoxymethylpenicillin: do not use concomitantly with penicillin.
- Medicines that may affect liver function (check the medicines that you are taking with the doctor or pharmacist).
- Retinoids such as isotretinoin (for the treatment of acne): avoid using them for a short time before the treatment with Minocycline, during the treatment with Minocycline and for some time after the treatment with Minocycline, since both of the medicines are associated with increased risk of benign intracranial hypertension.
- Quinapril (ACE inhibitor used inter alia for treatment of heart problems): reduces the Minocycline absorption.
- Anticoagulants (to thin the blood e.g. warfarin): reduced dosages of the anticoagulants may be required.
- Diuretics (e.g. furosemide): may exacerbate kidney toxicity.
- Ergometrine (for inducing contractions or birth), ergotamine (for treatment of migraines).
- Kaolin (for treatment of diarrhea), antacids (for digestive problems such as heartburn) or additional medicines containing aluminium, calcium, iron, magnesium, zinc: do not take at the same time with Minocycline, as absorption of minocycline may be reduced. If there is a need to take them concomitantly, it is recommended to take them as far apart from each other as possible.
- Sucralfate (for treatment of ulcers), bismuth (for the relief of abdominal pain): reduce Minocycline absorption.
- Contraceptive pills: both medicines may cause hyperpigmentation.

Use of this medicine and food:

- Food and moderate milk consumption do not impair the absorption of the medicine, so the medicine may be taken regardless of mealtimes.

Use of the medicine and alcohol consumption:

Consult your doctor about drinking alcohol, as the combination might negatively affect the liver.

Pregnancy and breastfeeding:

If you are pregnant, think you are pregnant, are planning a pregnancy or are breastfeeding, consult your doctor before taking the medicine.

- Do not use the medicine if you are pregnant or planning a pregnancy, as it can affect the development of the fetus (including affecting the bones and teeth).
- Do not breastfeed while using the medicine, as the medicine passes into the breastmilk and might affect the baby.

Driving and use of machinery: Use of this medicine may cause dizziness, headaches, vertigo (a spinning sensation), light-headedness, sight or hearing disturbances (including ringing in the ears) that might affect your ability to drive or operate machinery. Do not drive if you feel these effects.

3. How to use this medicine

Always use according to the doctor's instructions. You should check with your doctor or pharmacist if you are not sure regarding the dosage and manner of treatment.

The dosage and manner of treatment will be determined by the doctor only.

Use this medicine at set times as determined by the attending doctor.

The standard dosage is usually: The dosage will be determined by the doctor according to the treatment goal and the type of infection and also according to your age and medical condition.

If you suffer from impaired kidney function, the doctor may give you a lower dosage.

If the treatment is intended for acne, it will generally last for at least 6 weeks.

Do not exceed the recommended dose.

Do not chew! It is forbidden to open the capsules and spread their contents (as the medicine may cause irritation and/or ulcerations in the esophagus (food pipe). Swallow the capsules whole with a glass of water.

Take the medicine while standing (or sitting erect). **Do not take the medicine when lying down.**

If you have accidentally taken a higher dosage: if an overdose was taken or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or hospital emergency room and bring the package of the medicine with you. Overdose symptoms include dizziness, nausea and vomiting.

If you forgot to take the medicine: if you forgot to take this medicine at the set time, take a dose as soon as you remember, and then take the next dose at the set time. Do not take a double dose to make up for the forgotten dose.

Adhere to the treatment and complete it as recommended by the doctor.

Even if your state of health improves, do not stop the treatment with the medicine without consulting your doctor.

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

If you have further questions concerning the use of the medicine, consult your doctor or pharmacist.

4. Side Effects

As with any medicine, the use of minocycline 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.

Stop the treatment and proceed to a doctor or hospital emergency room immediately, if the following side effects appear:

Rare side effects (appear in up to 1 in 1000 users):

- **Allergic reactions (such as hypersensitivity, anaphylactic reaction, shock) that can be manifested in the following symptoms:** skin rash, flaking, red, itchy and swollen skin, joint pain, swelling of the face, lips, mouth, tongue or throat, breathing difficulties, high levels of white blood cells and one or more of the following: inflammation of the liver (hepatitis), inflammation of the lungs, inflammation of the kidneys, inflammation of the heart muscle (myocarditis) or membrane around the heart (pericarditis). You may also have a fever and swollen lymph glands. In severe cases the reactions may be life-threatening.
- Severe headaches with eyesight disturbances such as loss of vision, blurred vision or double vision. These symptoms can be a sign of intracranial hypertension.

- Reduction in types of blood cells such as leucopenia resulting in frequent or recurrent infections causing fever, severe chills, mouth ulcers or chest infection; thrombocytopenia that causes unexplained bruising or bleeding for a longer time period than usual.
- Shortness of breath upon exertion/ during exercise, fatigue, chest pain or pressure. These symptoms can be a sign of an inflamed heart muscle (myocarditis).
- Sudden and sharp chest pain made worse by coughing or deep breathing. These symptoms can be a sign of inflammation of the membranes around the heart (pericarditis).
- Yellowing of the skin or whites of the eyes (jaundice), dark urine, pale stools, loss of appetite, abdominal pain. These symptoms can be a sign of severe liver problems.
- Lupus-like syndrome that can be manifested by the presence of certain antibodies in the blood; pain, inflammation, stiffness or swelling of the joints with one or more of the following symptoms: fever, muscle pain, inflammation of the liver (hepatitis), rash, inflammation of blood vessels. In serious cases the syndrome may be life-threatening.
- Producing little or no urine, pain or discomfort passing urine, cloudy or dark urine with lower back pain. These symptoms can be a sign of serious kidney problems.
- Inflammation of the tongue, mouth or female genitals, inflammation of the intestines causing severe nausea and vomiting, stomach cramps or diarrhea, itching of the anus. These symptoms can be a sign of growth of tetracycline-resistant bacteria.
- Painful purple lumps on the skin (erythema nodosum).
- Patches/areas of darker or red skin.
- Sensitivity to sunlight or artificial light (e.g. tanning lamps). The symptoms include tingling, burning or redness of the skin. If you experience these symptoms, avoid direct exposure to sunlight or artificial light.

Very rare side effects (appear in up to 1 in 10,000 users):

- Reduction in red blood cells that causes pale/yellowish skin and weakness or shortness of breath (hemolytic anemia).
- Breathing problems such as shortness of breath at rest, wheezing, coughing with chest tightness or worsening of asthma.
- Watery diarrhea at times with blood, loss of appetite, stomach cramps, nausea, vomiting. These symptoms can be a sign of inflammation in the intestines.
- Severe stomach pain which radiates to the back. These symptoms can be a sign of an inflamed pancreas.
- Severe skin reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis), blistering of the skin, mouth, eyes and genitals, flaking or peeling of the skin.
- Development or worsening of systemic lupus erythematosus. Symptoms include: large areas of red scaly patches on the face, hair loss, weight loss, joint pain and fever.

Side effects of unknown frequency:

- Seizures.
- A disease in which the body's immune system attacks the liver cells, causing inflammation of the liver (autoimmune hepatitis).
- Drug-induced allergic reaction that includes fever, rash, and blood abnormalities (DRESS syndrome - drug rash with eosinophilia and systemic symptoms).
- A reduction in white blood cells causing high temperature and ulcers in the mouth and throat (agranulocytosis).
- Fever, rash (including itchy rash, urticaria); pain, inflammation, stiffness or swelling of the joints, increase in the number of white blood cells. These symptoms can be a sign of a serum sickness-like syndrome. In serious cases the syndrome could be life-threatening.

Additional side effects:

Common side effects (appear in 1-10 users out of 100): dizziness.

Uncommon side effects (appear in 1-10 users out of 1,000): fever.

Rare side effects (appear in 1-10 users out of 10,000): increase in number of certain white blood cells which can be seen in a blood test; feeling of spinning when standing or sitting still (vertigo), ringing in ears, other hearing problems; loss of appetite, diarrhea, nausea, vomiting; headache, cough, breathing difficulties; feeling of pins and needles in the hands and feet or a reduction in the sense of touch; change in the color of the teeth; increase in levels of liver enzymes or urea levels which can be seen in a blood test; red round lumps under the skin particularly below the knee; skin reaction that keeps appearing in the same area every time you take the medicine; hair loss, skin itching, skin rash, urticaria; change in skin color; redness or pain, swelling or tenderness around a vein (vasculitis/blood vessel inflammation); joint pain, muscle pain.

Very rare side effects (appear in less than one user out of 10,000): bulging fontanelle (the spot soft to touch on the head of babies-for whom the use is forbidden); fungal infection in the mouth or genital area ; abnormal thyroid gland function; indigestion, swallowing difficulties, inflammation or ulcers in your esophagus, inflammation of the tongue; problems with the tooth enamel; high levels of bilirubin which can be seen in blood tests; flaky/peeling skin (exfoliative dermatitis); change in color of the nails, teeth, mucous membrane of the mouth, bones, thyroid gland, eyes, secretions including breastmilk, tears or sweat (hyperpigmentation); swelling or stiffness of joints, inflammation of joints (arthritis); inflammation of the head of the penis.

Side effects of unknown frequency (effects whose frequency has not yet been determined): rash of small red or purple spots; increase in the number of white blood cells and substances in the lungs which can be seen in an x-ray, inflammation of the lungs caused by an infection (pneumonitis); drowsiness.

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 with your doctor.

Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads to an online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il/>

5. How to store the medicine?

- Avoid poisoning! This medicine, and any other medicine, must be stored in a closed place out of the reach and sight of children and/or babies, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Storage conditions: Store in the original package below 25 °C.

6. Additional information

In addition to the active ingredient, the medicine also contains:

Pregelatinized maize starch, magnesium stearate, silicon dioxide colloidal, gelatin, titanium dioxide (E171), yellow iron oxide (E172), red iron oxide (E172), erythrosine (FD&C red 3), indigo carmine (FD&C blue 2).

What does the medicine look like and what does the package contain?

Minocycline 50 mg: orange capsules, containing a yellow powder, in blister packs of 30 capsules.
Minocycline 100 mg: orange/blue capsules, containing a yellow powder, in blister packs of 10 capsules.

Registration holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301.

Medicine registration number in the National Medicines Registry of the Ministry of Health:

Minocycline 50 mg: 0649827129

Minocycline 100 mg: 1167327128

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