

Patient Leaflet According to the Pharmacists' Regulations (Preparations) – 1986

This medicine is sold with a doctor's prescription only

**Colchicine 0.5 mg
Tablets**

Active ingredient:

Each tablet contains: Colchicine 0.5 mg (500 microgram).

For the list of the additional ingredients, see section 6. See also 'Important information about some of the medicine's ingredients' in section 2.

Read this 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.

Important Warning!

Do not exceed the recommended dose. Overdosing, including as a result of possible drug interactions, can lead to a life threatening, very painful and irreversible poisoning with a fatal outcome (see also sections 2-4 in this leaflet). Keep this medicine out of reach of others (before and after use).

1. What is the medicine intended for?

The medicine is intended for treatment and prevention of gout and Familial Mediterranean Fever (FMF).

Therapeutic group: alkaloid, anti-gout

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the additional ingredients the medicine contains (for the list of the additional ingredients, see section 6).
- You have a disorder in the blood composition (blood dyscrasias).
- You have severe kidney impairment.
- You have severe liver impairment.
- Pregnancy: See section 2 - 'Pregnancy, breastfeeding and fertility'.

Special warnings regarding the use of this medicine:

There is only a slight difference between the dose necessary to obtain the desired action of Colchicine and the dose that may cause symptoms of medicine poisoning; this means that even taking a dose that is slightly higher can cause acute symptoms of poisoning. If you have symptoms such as nausea, vomiting, stomach pain and diarrhea, stop taking the medicine and immediately contact your doctor. See also section 3 subparagraph - 'If you accidentally took a higher dosage' and section 4 'Side effects'.

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

- You have kidney or liver problems. See also 'Do not use the medicine if'.
- You have a heart and/or vascular disease
- You have digestive system problems.
- You are elderly or debilitated (weak). The elderly may be more sensitive to this medicine and therefore they should be medically monitored.
- You have a blood disorder (for instance abnormal blood count values). See also 'Do not use the medicine if'.

Tell your doctor also if you have suffered from these conditions in the past.

Additional warnings:

- The medicine can cause severe depression in bone marrow function, including severe shortage of certain white blood cells (agranulocytosis), shortage of blood platelets (thrombocytopenia), decrease in red blood cells (aplastic anemia). Your doctor may send you for periodic blood tests. If symptoms such as fever, inflammation of the mouth, sore throat, prolonged bleeding, bruising or skin problems develop, stop taking the medicine and contact your doctor immediately. These symptoms can be an indication of a serious blood problem and your doctor may send you for blood tests straight away. See also section 4 'Side effects'.
- Long-term use of the medicine may cause a Vitamin B12 deficiency.

Children and adolescents:

The use of Colchicine in children and adolescents is mainly for treatment of FMF: the dosage and manner of administration for children (over age 4) will be determined by the doctor according to the child's age. See also section 3.

Tests and follow-up:

during the treatment period with this medicine, the doctor may send you for blood tests.

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 not sure whether you are using one of these medicines, please consult with your doctor or pharmacist):

Medicines that might adversely affect your blood count, and/or liver and kidney functions: caution is required when taking Colchicine together with these medicines. You must consult your doctor.

Use of the following medicines during the treatment period with Colchicine, increases the probability of side effects as a result of Colchicine toxicity. These side effects can be very serious. Tell your doctor if you are taking the following medicines:

- Antibiotics from the macrolide group such as erythromycin, telithromycin, clarithromycin and azithromycin:
If possible, do not use an antibiotic of this kind during the treatment period with Colchicine. When no other treatment is possible, the doctor may lower the dose of Colchicine and monitor your condition.
- Ketoconazole, itraconazole, voriconazole (anti-fungal medicines). Do not use these medicines during the treatment period with Colchicine.
- Certain protease inhibitors used to treat HIV/AIDS such as, ritonavir, atazanavir, amprenavir, saquinavir, nelfinavir, fosamprenavir, indinavir: do not use these medicines during the treatment period with Colchicine.
- Medicines for the treatment of heart problems, such as verapamil, quinidine, diltiazem.
- Ciclosporin (medicine for the suppression of the immune system).

Taking the following medicines during the treatment period with Colchicine may cause a serious muscle disease (myopathy) and breakdown of muscle tissue, which is accompanied by muscle cramps, fever and red-brown discoloration of urine (rhabdomyolysis):

- Medicines from the statins group (such as simvastatin, fluvastatin or pravastatin) to lower cholesterol.
- Medicines from the fibrates group to lower cholesterol and certain fats in the blood.
- Digoxin (medicine used for treatment of heart problems such as heart failure and rhythm disturbances).
- Ciclosporin (medicine for the suppression of the immune system).

The following medicines might increase the effect of Colchicine:

- Cimetidine (for intestinal and gastric ulcers).

- Tolbutamide (for lowering blood sugar).

Vitamin B12 (cyanocobalamin): absorption of the vitamin from the gastrointestinal tract may decrease during the treatment period with Colchicine.

Use of the medicine and food:

Avoid eating grapefruit or drinking grapefruit juice during the treatment period, since grapefruits might raise the level of Colchicine in the blood.

Pregnancy, breastfeeding and fertility: Colchicine could harm both fertility and the fetus. See also section 4 'Side effects' regarding the effects of the medicine on the sperm.

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

Fertility:

- Treatment of Familial Mediterranean Fever (FMF): lack of treatment of FMF may also harm fertility. Your doctor will weigh the use of Colchicine against the possible risks, if required.
- Treatment of gout in men: do not impregnate a woman while you are being treated with Colchicine and for at least 6 months following termination of treatment with Colchicine. If, nevertheless, pregnancy occurs during this time period, you should go for genetic counselling. Use contraceptive means during this period.

Pregnancy

- Treatment of Familial Mediterranean Fever (FMF): lack of treatment of FMF may also adversely affect the pregnancy. The doctor will weigh the use of Colchicine against the possible risks, if required.
- Treatment of gout in men: do not use Colchicine if you are pregnant or if you might become pregnant. Women of childbearing age and might become pregnant, need to use contraception while being treated with Colchicine, and for at least 3 months following termination of treatment with Colchicine. If, nevertheless, pregnancy occurs during the treatment period or within 3 months after its termination, you should go for genetic counselling.

Breastfeeding:

Colchicine passes into the breastmilk. Do not use Colchicine if you are breastfeeding. Consult your doctor about the benefits of breastfeeding for the child versus the benefit of treatment for the mother.

Driving and use of machinery: before driving and/or using machinery make sure you do not feel sleepy or dizzy which could adversely affect your ability to drive and use of machinery.

Important information about some of the medicine's ingredients:

Colchicine contains lactose. If you have intolerance to certain sugars, consult your doctor before taking the medicine.

3. How to use this medicine?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and manner of treatment with the medicine.

Do not exceed the dose prescribed by the doctor since too high of a dose of Colchicine could be toxic.

If you feel that the dosage is not right for you, contact your doctor.

The generally recommended dosage is: the dosage and manner of treatment will be determined by the doctor only. The dosage will be adjusted to each patient individually depending on the reason for taking the medicine, the patient's age, liver functions, kidney functions, and concomitant use of other medicines. If you need a dosage other than 0.5 mg (tablet), or multiples of 0.5 mg, consult your doctor.

The generally recommended dosage for treatment of gout is usually: start with the treatment prescribed by the doctor, and then continue to take additional tablets according to the doctor's

instructions until relief of the pain or until the occurrence of side effects (such as nausea, vomiting or diarrhea). Recommended to keep Colchicine tablets within reach, so you can start the treatment according to the doctor's instructions if you experience symptoms of a flare attack.

The generally recommended dosage for treatment of FMF is usually: the doctor will usually adjust/adapt the dosage gradually. The daily dose may be taken once a day or as divided doses twice a day. If side effects appear, consult your doctor who may adjust the dosage for you.

Do not exceed the recommended dose.

Manner of use:

Do not halve the tablet since there is no scored line.

There is no information regarding crushing/chewing of the tablets.

Swallow the medicine with a glass of water.

If you accidentally took a higher dosage: if you took an overdose, or if a child has accidentally swallowed the medicine, there is a risk of poisoning therefore proceed immediately to a doctor or to a hospital emergency room, and bring the package of the medicine with you. Overdose symptoms include:

- After swallowing a high dose, early symptoms of overdose can occur even after a few hours and include: a burning sensation in throat, stomach and skin; nausea, vomiting, abdominal cramps/pain, bloody diarrhea which may lead to low pH value of the blood (high blood acidity), abnormal electrolyte values in the blood, leukocytosis (increase in white blood cells), dehydration, lowering of blood pressure, shock.
- 24 to 72 hours after swallowing a high dose, the following life-threatening systemic complications may occur: consciousness disorder, confusion, delusions, coma, nerve damage (can be manifested in paralysis, numbness), respiratory depression, fluid retention in the lungs, kidney damage, decrease in blood cells and other blood problems (such as clotting problems), heart rhythm problems, cardiac arrest, death.
- About 7 days after swallowing a high dose: temporary increase of white blood cells (leukocytosis) and hair loss.

If you forgot to take the medicine: if you forgot to take the medicine at the set time, take a dose as soon as you remember. If it is almost time for the next dose, do not take the forgotten dose, and continue taking the medicine at the times set by the doctor. Under no circumstances take a double dose to make up for the forgotten dose. Check with your doctor if you are not sure.

Adhere to the treatment as recommended by your doctor. Even if your state of health improves, do not stop the treatment with the medicine without consulting your doctor.

If you stop taking the medicine: if you stop taking the medicine before the time determined by the doctor, the symptoms from which you suffered before the treatment may return.

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 the doctor or pharmacist.

4. Side effects

As with any medicine, the use of Colchicine 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 treatment and seek immediate medical assistance if the following side effects appear:

- Nausea, vomiting, abdominal cramps/pain, diarrhea. These side effects are common (affect up to 1 out of 10 people).
- Weakness of the muscles (myopathy), redbrown discoloration of the urine (rhabdomyolysis), muscles pain, fatigue. These side effects are uncommon (affect up to 1 out of 100 people).
- Infection with symptoms such as high fever, severe sore throat, sore mouth, serious form of anemia (aplastic anemia), decrease in blood platelets. These side effects are rare (affect up to 1 out of 1000 people). See also section 2, 'Additional warnings' regarding bone marrow suppression (agranulocytosis, thrombocytopenia, aplastic anemia).

Additional side effects:

Side effects of unknown frequency (effects whose frequency has not yet been determined).

- Hair loss, rash
- Reduction of the number of sperm cells in the seminal fluid or absence of sperm cells in the seminal fluid
- Sore throat
- Neuropathy (nerve disease), inflammation of the nerves which can cause pain, numbness and sometimes impaired nerve function
- Absence of menstrual periods during a period of 6 months or longer and pain and/or cramps during menstruation
- Vitamin B12 deficiency
- Liver damage
- Drowsiness, dizziness

If a side effect occurs, 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 infants, 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 below 25°C. Protect from light.

6. Additional information

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

Lactose, corn starch, povidone K25, magnesium stearate.

Each tablet contains about 80 mg of lactose.

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

Round white tablets. The tablets are packaged in blisters, 30 tablets per box.

Manufacturer and registration holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301.

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

0167324811

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