

PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Rafassal® 1 gram Enema

Rafassal® 4 grams Enema

Active ingredient:

Each Rafassal 1 gram Enema contains: 1 gram mesalazine.
Each Rafassal 4 grams Enema contains: 4 grams mesalazine.
The active ingredient is also called mesalamine or 5-aminosalicylic acid.
For the list of additional ingredients see section 6. See also "Important information about some of the medicine's ingredients" in section 2.

Read the entire leaflet carefully before using the medicine.

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

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

1. What is the medicine intended for?

The medicine is intended for treatment and prevention of ulcerative colitis and of Crohn's disease.

Therapeutic group: anti-inflammatory medicine from the salicylate group.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient, to salicylic acid, to salicylates such as acetylsalicylic acid (aspirin), or to any of the additional ingredients the medicine contains (for the list of additional ingredients, see section 6).
- You suffer from a severe liver or kidney function impairment.

Special warnings regarding the use of the medicine:

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

- You suffer or have suffered in the past from lung problems, especially if you suffer from (bronchial) asthma.
- You suffer or have suffered in the past from an allergy to a substance called sulphasalazine, which is a substance related to the active ingredient mesalazine. In this case, close medical supervision is required. (If acute symptoms of intolerance occur, such as: abdominal pain or spasms, fever, severe headache, rash – stop the treatment immediately).
- You suffer or have suffered in the past from liver problems.
- You suffer or have suffered in the past from kidney problems.
- You have ever developed a severe skin rash or skin peeling, blisters and/or mouth ulcers after using medicines containing mesalazine (the active ingredient in Rafassal).

The active ingredient (mesalazine) may cause red-brown urine discoloration after contact with the bleaching agent sodium hypochlorite, for example in the toilet water. This is a chemical reaction which is harmless to the patient.

Additional warnings:

- During the treatment with the medicine, the doctor may decide on close medical supervision (see "Tests and follow-up").
- Kidney stones may develop due to the use of this medicine. The symptoms may include pain in the sides of the abdomen and blood in the urine. Make sure to drink a sufficient amount of liquids during treatment with the medicine.
- Serious skin reactions including DRESS syndrome (drug reaction with eosinophilia and systemic symptoms), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis have been reported in association with mesalazine treatment. Stop using the medicine and refer to the doctor immediately if you notice these serious skin reactions (for the list of symptoms see section 4 "Side effects").
- If you experience strong or recurrent headache, disturbance of vision, or ringing/buzzing in the ears refer to your doctor immediately.

Children and adolescents: there is not much experience with the use in children. The use in children and adolescents aged 6 to 18 years is according to the doctor's instructions and will be determined according to their condition and body weight.

Tests and follow-up: before starting treatment and during treatment, you may need to undergo blood and urine tests, liver and kidney function tests.

Drug interactions: if you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist. In particular, inform the doctor or pharmacist if you are taking the following medicines (note that the following list mentions the active ingredients in the medicines. If you are not sure whether you are using any of these medicines, please consult the doctor or pharmacist):

- Certain anticoagulant medicines (such as warfarin).
- Azathioprine, 6-mercaptopurine, thioguanine (medicines used for treatment of immune system disorders).

Pregnancy and breastfeeding:

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

- Pregnancy:** there is insufficient information regarding the use of Rafassal in pregnant women. Rafassal should be used during pregnancy only at the doctor's discretion and under his guidance.
- Breastfeeding:** there is insufficient information regarding the use of Rafassal in breastfeeding women. The medicine passes into breast milk. There may be hypersensitivity reactions in the breastfed baby, such as diarrhea. Therefore, Rafassal should only be used at the doctor's discretion and under his guidance. If the doctor has allowed you to breastfeed, and the baby develops diarrhea, you should stop breastfeeding.

Driving and use of machinery: the use of the medicine is not expected to affect the ability to drive or operate machinery.

Important information about some of the medicine's ingredients:

- The enema contains sodium benzoate (60 mg per bottle) which may cause local irritation.
- The enema contains potassium metabisulfite (281 mg per bottle) which may rarely cause severe hypersensitivity reactions and bronchospasm.
- The enema contains potassium (about 200 mg per bottle). Be aware in patients with decreased kidney function or in patients on a potassium-controlled diet.
- The enema contains sodium (about 27 mg per bottle). This amount constitutes about 1.4% of the maximum recommended daily intake in adults, which is 2 grams.

3. How to use the medicine?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and manner of treatment with the medicine.

The standard dosage is usually: the dosage, treatment regimen and duration of treatment will be determined only by the doctor.

The dosage will be personally adjusted for you by the doctor, depending on your condition and your response to the treatment, which will be examined in periodic medical follow-ups and periodic tests.

Unless otherwise instructed by the doctor, use the enema before bedtime. This medicine should be used at set intervals as determined by the attending doctor.

Do not exceed the recommended dose.

Note:

Do not swallow! This medicine is intended for anal use.

Shake well before use.

Method of use: see instructions for use and figures in section 7.

If you accidentally used a higher dosage:

- If you used a higher dose, refer to a doctor who will advise you what to do.
- If a child or any person accidentally swallowed the medicine, refer immediately to a doctor or to a hospital emergency room, and bring the package of the medicine with you.

If you forgot to use the medicine: if you forgot to use the enema at the scheduled time, continue treatment according to the prescribed dosage. Do not use a larger dose in order to compensate for the forgotten dose.

Adhere to the treatment as recommended by the doctor. In order to get the maximum benefit from the medicine, it should be taken regularly and consistently, both during periods of inflammation flare-ups and as a preventive treatment during remission.

If you stop using the medicine: abrupt discontinuation of the medicine is not recommended.

Even if there is an improvement in your state of health, do not stop treatment with the medicine without consulting the doctor.

Do not use or take medicines in the dark! Check the label and the dose every time you take a medicine.

Wear glasses if you need them.

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

4. Side effects

As with any medicine, using Rafassal Enema may cause side effects in some users. Do not be alarmed when reading the list of side effects, you may not suffer from any of them.

Stop the treatment and refer to the doctor immediately in the following cases:

- General allergic reactions:** symptoms of an allergic reaction can include: fever, skin rash, joint pain and/or breathing difficulties. Lupus erythematosus syndrome or general inflammation of the large bowel (causing severe diarrhea and/or severe abdominal pain). These reactions are very rare.
- General malaise (worsening of your general health), especially one accompanied by fever and/or pain in the mouth and/or throat. These symptoms can very rarely indicate a drop in the number of white blood cells (**agranulocytosis**), a condition which may make you more susceptible to the development of a severe infection. Other blood cells may be affected (e.g. platelets or red blood cells, thereby causing **aplastic anemia or thrombocytopenia**) and may cause symptoms such as unexplained bleeding, purple spots or blotches under the skin and anemia (feeling of tiredness, weakness and pale appearance, especially of the lips and nails). A blood test can check whether these symptoms are caused by the medicine's effect on your blood. These effects are very rare.
- Serious skin reactions** such as reddish, non-elevated, round or target-like patches, often with central blisters, skin peeling, ulcers in the mouth, throat, nose, genitals and eyes, widespread rash, high fever and enlarged lymph nodes. These serious skin reactions can be preceded by fever and flu-like symptoms. See also "Additional warnings" in section 2. These effects occur in an unknown number of patients (unknown frequency).
- Chest pain, shortness of breath or swelling of the limbs which may indicate **hypersensitivity reactions in the heart** (including inflammation of the heart muscle or heart membrane). These effects are rare.
- Kidney function problems** (can occur very rarely), e.g., change in the color of the urine or in the amount of urine produced and swelling of the limbs or sudden pain in the waist area (caused by a kidney stone). Occur in an unknown number of patients (unknown frequency).
- Strong or recurrent headache, disturbance of vision, or ringing/buzzing in the ears.** These can be symptoms of increased pressure inside your skull (idiopathic intracranial hypertension) (unknown frequency).

Additional side effects:

Common side effects (occur in 1-10 users out of 100):

- Rash, itching

Rare side effects (occur in 1-10 users out of 10,000):

- Abdominal pain, diarrhea, wind (flatulence), nausea, vomiting, constipation.
- Headache, dizziness.
- Photosensitivity, which is an increased sensitivity of the skin to the sun and to ultraviolet (UV) light.
- Very rare side effects (occur in less than one user out of 10,000):*
- Inflammation of the pancreas, which can manifest by severe abdominal pain.
- An allergic and/or inflammatory reaction of the lungs, which can manifest, among other things, by shortness of breath, cough, wheezing or a shadow in the lungs, seen in an x-ray.
- Muscle and/or joint pain.
- Liver and/or bile flow impairments, which may cause abdominal pain and/or jaundice (which can be manifested by yellowing of the skin and of the white of the eye).
- Liver function impairment (including inflammation of the liver, an increase in liver enzyme levels).
- Hair loss, balding.
- Numbness and tingling in the hands and feet (peripheral neuropathy).
- Reversible decrease in sperm production.

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 the doctor.

Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which leads to the online form for reporting side effects, or by clicking on the link: <https://sideeffects.health.gov.il/>

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- Storage conditions: store at a temperature lower than 25°C.

6. Additional information

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

Potassium metabisulfite, potassium acetate, xanthan gum, sodium benzoate, disodium edetate, carbomer 934P, purified water.

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

Beige/light brown suspension in a squeeze bottle.

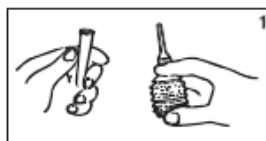
Each box contains 7 enemas of 60 grams each.

7. Instructions for using the enema:

The best results will be achieved if the enema is performed immediately after emptying the bowels.

1) Preparing the medicine for use:

- Shake the bottle well to ensure the homogeneity of the liquid.
- Remove the protective cap from the applicator and hold the bottle by its neck to prevent leakage (Figure 1).



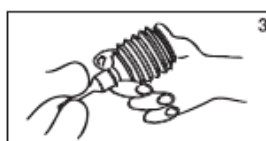
2) The correct body position:

- The best results are achieved when lying down on the left side, with the left leg straight and the right leg bent forward for balance (Figure 2a).
- The other option is: "knee-chest" position (Figure 2b).



3) Administration of the enema:

- Thoroughly clean and dry the rectum (anus) area.
- Gently insert the applicator, which is already lubricated, into the anus (rectum) while directing it towards the navel.
- Hold the bottle firmly and slightly tilt it so that the tip of the applicator is directed towards the back, and then slowly squeeze the bottle to insert the liquid inwards (Figure 3). Steady pressure of the hand will release most of the liquid. Discard the used bottle after use.



- Remain in this position for at least the next 30 minutes, to allow complete distribution of the medicine in the intestine.

If possible, use the enema before bedtime and hold the liquid inside for the entire night.

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

Medicine registration number in the national medicines registry of the Ministry of Health:

Rafassal 1 gram Enema: 1203926001

Rafassal 4 grams Enema: 0295825321

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