

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

The medicine is dispensed with a doctor's prescription only

Rafassal[®] 1 gram Enema

Rafassal[®] 4 gram Enema

Active ingredient:

Each Rafassal 1 gram Enema contains: mesalazine 1 gram.

Each Rafassal 4 gram Enema contains: mesalazine 4 gram.

The active ingredient is also called mesalamine or 5-aminosalicylic acid.

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 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 the 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 intended for treatment and prevention of ulcerative colitis (ulcerative inflammation of the large intestine) and 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 the additional ingredients, see section 6).
- You suffer from severe impairment of liver or kidney function.

Special warnings regarding the use of the medicine:

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

- You suffer or have suffered in the past from lung problems, particularly if you suffer from asthma (bronchial).
- You suffer or have suffered in the past from allergy to a substance named sulphasalazine, which is a substance related to the active ingredient mesalazine. In such a case, close medical supervision will be required. (If acute symptoms of intolerance appear, for instance abdominal pain or cramps, 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, blistering and/or mouth sores after using medicines containing mesalazine (the active ingredient in Rafassal).

The active ingredient (mesalazine) may discolor the urine red-brown upon contact with the bleaching agent sodium hypochlorite, for instance in the toilet water. This is a chemical reaction which is harmless for 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 with use of the medicine. Symptoms may include pain in sides of abdomen and blood in the urine. Take care to drink a sufficient amount of liquids during the treatment with the medicine.
- Serious skin reactions have been reported, 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 (see detailed symptoms described in section 4 'Side effects').

Children and adolescents: there is little experience in use with children. The use in children and adolescents aged 6 to 18 years is as instructed by the doctor and will be determined according to their condition and body weight.

Tests and follow up: before and during the 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 any other medicines, including non-prescription medicines and nutritional supplements, please tell your doctor or pharmacist. Especially inform the 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 with the doctor or pharmacist):

- Certain anticoagulant medicines (e.g. warfarin).
- Azathioprine, 6-mercaptopurine, thioguanine (medicines used to treat 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 on the use of Rafassal in pregnant women. Use of Rafassal during pregnancy will be only upon the decision and guidance of your doctor.
- **Breastfeeding:** there is insufficient information on the use of Rafassal in breastfeeding women. The medicine passes into the breast milk. There may be hypersensitivity reactions such as diarrhea in the breastfed baby. Therefore, the use of Rafassal will be only upon the decision and guidance of your doctor. If your doctor allowed you to breastfeed, and the baby develops diarrhea, stop the breastfeeding.

Driving and operating machinery: The use of this medicine is not expected to affect your 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). Caution should be employed in patients with a decrease in kidney function or in patients with 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 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 the manner of treatment with the medicine.

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

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

In the absence of any other instruction by the doctor, use the enema at bedtime.

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

Do not exceed the recommended dose.

Attention:

Not to be swallowed! This medicine is intended for use through the anus.

Shake well before use!

Manner of use: see instructions for use and illustrations in section 7.

If you accidentally used a higher dosage:

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

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

Adhere to the treatment as recommended by the doctor. In order to obtain the maximum benefit from the medicine, take it regularly and consistently, both during acute episodes of inflammation and as a preventive treatment during remission.

If you stop taking the medicine: abrupt stopping of the medicine is not recommended.

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

Do not take or use 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 Rafassal enema 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 refer to a doctor immediately in the following cases:

- **General allergic reactions.** Symptoms of an allergic reaction may include: fever, skin rash, joint pains and/or breathing difficulties, Lupus Erythematosus or general inflammation of the large intestine (causing severe diarrhea and/or severe abdominal pain). These severe reactions are very rare.

- Generally unwell feeling (deterioration in your general health), especially if accompanied by fever and/or sore mouth and/or throat. These symptoms can, very rarely, indicate a decrease in the number of white blood cells (**agranulocytosis**), a condition which may make you more prone to developing a serious infection. Other blood cells might be affected (for instance platelets or red blood cells, causing **aplastic anemia or thrombocytopenia**) and may therefore cause symptoms such as unexplained bleeding, purple spots or spots under the skin and anemia (feeling of tiredness, weakness and a pale look, particularly in the lips and nails). A blood test can check whether these symptoms are due to the effect of the medicine on your blood. These reactions are very rare.
- **Serious skin reactions** such as reddish non-elevated, target-like or circular patches, often with central blisters, skin peeling, ulcers of 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 reactions occur in an unknown number of patients (unknown frequency).
- Chest pain, shortness of breath or swelling of limbs which might indicate **hypersensitive reactions in the heart** (including inflammation of the heart muscle or the heart membrane). These reactions are rare.
- **Kidney function problems** (can occur very rarely). For instance change in the urine color or amount of urine produced and swelling of the limbs or sudden pain in the hip area (caused by a kidney stone). This occurs in an unknown number of patients (unknown frequency).

Additional side effects:

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

- Rash, itching

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

- Abdominal pain, diarrhea, wind (flatulence), nausea, vomiting, constipation.
- Headache, dizziness.
- Photosensitivity, which is increased sensitivity of the skin to the sun and to ultraviolet (UV) light.

Very rare side effects (appear in less than 1 user out of 10,000):

- Inflammation of the pancreas which can be manifested in severe abdominal pain.
- Allergic and/or inflammatory reaction of the lungs which can be manifested, inter alia, in shortness of breath, cough, wheezing, lung shadow seen on an x-ray.
- Muscle and/or joint pains.
- Liver and/or bile flow impairments which may cause abdominal pain and/or jaundice (which may be manifested in yellowing of the skin and the white of the eye).
- Liver function problems (including inflammation of the liver, increase in liver enzyme levels).
- Hair loss, development of baldness.
- Numbness and tingling in the hands and feet (peripheral neuropathy).
- Reversible decrease in semen production.

If a side effect appears, if any of the side effects worsens, or when you suffer from a side effect not mentioned in the leaflet, consult 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) stated on the package. The expiry date refers to the last day of that month.
- Storage conditions: store below 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 gram each.

7. Instructions on how to use the enema:

The best results will be obtained if the enema is used immediately after bowel emptying.

1) Preparation of the medicine for use:

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

2) Correct position of the body:

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

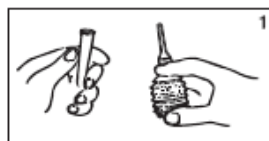
3) Administration of the enema:

- a) Thoroughly clean and dry the rectal area (anus).
- b) Gently insert the applicator, which is already lubricated, into the anus (rectum) while directing it towards the navel.
- c) Hold the bottle firmly and tilt it slightly, so that the applicator tip 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.

After the use, discard the used bottle.

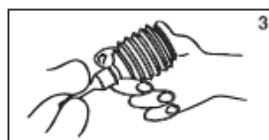
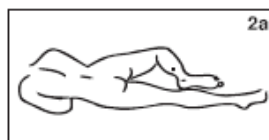
- d) Stay in this position for at least the minutes to enable complete spreading medicine in the intestine.

If possible, use the enema at bedtime and night long.



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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 gram Enema: 0295825321

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