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

This medicine is sold with a doctor's prescription only

Rafassal Granules

1 gram, 1.5 gram, 3 gram

Sachets containing prolonged-release gastro-resistant granules

Active ingredient:

Each Rafassal 1 gram Granules sachet contains: mesalazine 1 gram.

Each Rafassal 1.5 gram Granules sachet contains: mesalazine 1.5 gram.

Each Rafassal 3 gram Granules sachet contains: mesalazine 3 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 leaflet carefully in its entirety 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 intended for the treatment of acute episodes of ulcerative colitis (inflammation of the large intestine).

The medicine is also intended for maintenance treatment during remission of the inflammation.

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

Special warnings regarding the use of this medicine:

Before (and during) the 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).

Additional warnings:

- During treatment with this medicine your doctor may decide to keep you under close medical supervision (See also 'Tests and follow-up').
- Kidney stones may develop with use of the medicine. Symptoms may include pain in sides of abdomen and blood in urine. Take care to drink a sufficient amount of liquids during treatment with the medicine.
- Serious skin reactions including Stevens-Johnson syndrome 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, as well as 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 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 with your doctor or pharmacist):

- Azathioprine, 6-mercaptopurine, thioguanine (medicines used to treat immune system disorders).
- Certain anticoagulant medicines (e.g. warfarin).
- Lactulose (medicine used to treat constipation) or any other medicine that can change the acidity of the stools.

Pregnancy and breastfeeding:

If you are pregnant, think you are pregnant, are planning a pregnancy or if you are breastfeeding, consult your doctor before taking 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 instruction 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 instruction 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 medicine contains the sweetener aspartame. Aspartame is a source of phenylalanine, which may be harmful if you have phenylketonuria.
  A Rafassal 1 gram sachet contains 2 mg aspartame, a Rafassal 1.5 gram sachet contains 3 mg aspartame, a Rafassal 3 gram sachet contains 6 mg aspartame.
- The medicine contains a tiny amount of sucrose. If you suffer from intolerance to certain sugars, consult your doctor before taking this medicine.
  A Rafassal 1 gram sachet contains 0.04 mg sucrose, a Rafassal 1.5 gram sachet contains 0.06 mg sucrose, a Rafassal 3 gram sachet contains 0.12 mg sucrose.
- Each sachet contains less than 23 mg sodium (1 mmol) and is therefore considered sodium-free.

3. How to use this medicine?

Always use according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and the treatment regimen with the medicine.
The standard dosage is usually: the dosage, the treatment regimen 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.
Use this medicine at set times as determined by your attending doctor.

Do not exceed the recommended dose.

Manner of use:

The medicine is intended to be administered orally only.

Do not chew or crush the granules since this may impair the activity of the medicine.

Place the granules directly on your tongue and then swallow them with plenty of water.
Instructions for opening the sachet: hold the sachet at the top edge next to the marked arrow and gently shake so that the granules go beneath the arrow. Then cut the sachet according to the marking (you can use scissors).

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

If you forgot to take the medicine at the designated time, do not take a larger dose at the next time to compensate for the forgotten dose, but continue the treatment with the prescribed dosage.

Adhere to the treatment as recommended by your doctor. In order to obtain the maximum benefit from the medicine, you must take it regularly, and consistently both during acute episodes of inflammation and as preventive treatment during remission.
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 a 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, use of Rafassal 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 contact a doctor immediately in the following cases:

- If an allergic reaction occurs. Any medicine can cause an allergic reaction although a serious allergic reaction is very rare. Symptoms of an allergic reaction may include: fever, skin rash, breathing difficulties.
- If you suffer from a 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 fall in the number of white blood cells (agranulocytosis), a condition which may make you more prone to developing a serious infection. A blood test can confirm whether these symptoms are due to the effect of this medicine on your blood.
- If you notice any of the following symptoms: reddish non-elevated, target-like or circular patches, often with central blisters, skin peeling, ulcers of the mouth, throat, nose, genitals and eyes. These serious skin reactions can be preceded by fever and flu-like symptoms. See also 'Additional warnings' in section 2.

<u>Additional side effects</u>:

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

- Headache.

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

- Abdominal pain, diarrhea, indigestion, wind (flatulence), nausea, vomiting.
- Inflammation of the pancreas which can be manifested in severe abdominal pain.
- Changes in liver function parameters (for instance an increased level of liver enzymes), changes in pancreatic enzymes.
- Changes in the number of white blood cells.

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

- Dizziness.
- Chest pain, breathlessness or swollen limbs because of an effect on the heart (including inflammation of the heart muscle or heart membrane).
- Liver and/or bile flow disorders which may cause abdominal pain and/or jaundice (which may be manifested in yellowing of the skin and the white of the eye).
- Photosensitivity, which is increased sensitivity of the skin to sun and ultraviolet (UV) light.
- Joint pain.
- Feeling weak or tired.

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

- Fever, sore throat, malaise due to blood count changes.
- Skin rash or inflammation; allergic reaction which causes joint pain, skin rashes and fever, lupus erythematosus syndrome.
- Severe diarrhea and/or severe abdominal pain because of inflammation or an allergic reaction of the bowel.
- Numbness and tingling in the hands and feet (peripheral neuropathy).
- Allergic and/or inflammatory reaction of the lungs which can be manifested, inter alia, in shortness of breath, cough, wheezing, lung shadow seen on x-ray.

- Hair loss, development of baldness.
- Muscle pains.
- Changes in kidney functions, sometimes accompanied by swelling of the limbs or flank pain.
- Reversible decrease in semen production.
- Liver inflammation (hepatitis).

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

- Kidney stones and associated kidney pain (see also warnings in section 2).

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 30°C.

6. Additional information

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

Aspartame, Carmellose sodium, Citric acid anhydrous, Silica colloidal anhydrous, Hypromellose, Magnesium stearate, Methacrylic acid-methyl methacrylate copolymer 1:1 (Eudragit L 100), Methylcellulose, Cellulose microcrystalline, Eudragit NE 40 D (Polyacrylate dispersion 40% contains 2% Nonoxynol), Povidone K 25, Simeticone, Sorbic acid, Talc, Titanium dioxide, Triethyl citrate, Vanilla custard flavoring (containing sucrose).

For information on **the aspartame and the sucrose content** see section 2, 'Important information about some of the medicine's ingredients'.

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

The sachets contain white-gray granules. Each package contains 30, 50 or 100 sachets. Not all package sizes may be marketed.

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 Granules: 151 72 33698
Rafassal 1.5 gram Granules: 151 73 33700
Rafassal 3 gram Granules: 151 74 33701

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