Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Salazopyrin®
Tablets

Salazopyrin® EN
Enteric-coated tablets

Each tablet contains sulfasalazine 500 mg

Inactive ingredients and allergens: See section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Further information'.

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

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

1. WHAT IS THIS MEDICINE INTENDED FOR?

- Treatment of ulcerative colitis and Crohn's disease.
- Salazopyrin EN enteric-coated tablets are also used for treatment of rheumatoid arthritis and inflammatory skin ulcers (pyoderma gangrenosum).

Therapeutic group:
Anti-inflammatory drug of aminosalicylic acid type.

2. BEFORE USING THIS MEDICINE

Do not use the medicine:

- If you are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (see section 6), to salicylates (such as aspirin) or to sulfonamides (a certain type of antibiotic).
- If you have a disease known as porphyria (a rare blood system disorder).
- **In children under the age of two years.**

Special warnings regarding the use of the medicine

Before treatment with Salazopyrin, tell your doctor:

- If you have a deficiency of the G6PD enzyme which is responsible for normal function of red blood cells.
- If you have or have ever had asthma.
- If you have or have ever had impaired function of the liver or the kidney.
- If you have or have ever had impaired function of the blood system (such as coagulation).
- If you have or have ever had an acute allergy.
- In case of rheumatoid arthritis in children.
- If you have a history of recurring chronic infections or an underlying condition which may predispose you to infections.

Potentially life-threatening skin rashes (exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis) have been reported with the use of the medicine, appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. Additional signs to look for include ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These potentially life-threatening skin rashes are often accompanied by flu-like symptoms. The rash may progress to widespread blistering or peeling of the skin. The highest risk for occurrence of serious skin reactions is within the first weeks of treatment.

If you have developed exfoliative dermatitis, Stevens-Johnson syndrome or toxic epidermal necrolysis with the use of the medicine, you must not be re-started on the medicine at any time. If you develop a rash or these skin symptoms, stop taking the medicine, seek immediate advice from a doctor and tell your doctor that you are taking this medicine.

Severe, life-threatening allergic reactions such as Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) have been reported in patients taking various drugs including the medicine. It is important to note that early signs of severe allergy, such as fever or swollen lymph nodes, may be present even though rash is not evident. If such signs or symptoms are present, you should seek immediate advice from a doctor. The medicine should be discontinued if an alternative cause for the signs or symptoms cannot be established.

The medicine inhibits the absorption and metabolism of folic acid and may lead to a deficiency in folic acid, which could lead to serious blood disorders (for example, abnormally large red blood cells and a lower than normal number of red and white blood cells and platelets). These can be normalized by taking folic acid.

As the medicine causes crystals in urine and the development of kidney stone, adequate fluid intake should be ensured during treatment.

Children and adolescents
Administration of the medicine is not recommended if you have systemic-onset juvenile rheumatoid arthritis (Stills disease).

Tests and follow-up
- The doctor will refer you to complete blood test and liver function test before you start treatment with the medicine and once in two weeks during the first three months of treatment, once a month during the next three months of treatment and afterwards, every three months and as required.
- Urine analysis and an assessment of kidney function should also be done in all patients initiating treatment with the medicine. For patients with baseline renal impairment, treatment with the medicine should only be initiated if the benefits are considered to outweigh risk. Thereafter, periodic renal function monitoring, especially in the early months of treatment, should be conducted. Treatment should be discontinued if renal function deteriorates.

Drug interactions
If you are taking or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
- medicines for treatment of high blood sugar levels/diabetes. This may result in a decrease in sugar level; patients taking these medicines should be under medical supervision.
- methenamine, an antibiotic for treatment of urinary tract infections.

- digoxin, for treatment of heart disease. This may result in reduced medical efficacy of digoxin.
- folate (such as folic acid) given during pregnancy.
- azathioprine and mercaptopurine – used after organ transplantation and in chronic inflammations such as rheumatoid arthritis.
- methotrexate (to treat rheumatoid arthritis). This may result in an increased frequency of gastrointestinal side effects, especially nausea.

Using this medicine and food
The medicine should be taken with or after food.

Pregnancy, breast-feeding, and fertility
Pregnancy and breast-feeding
If you are pregnant or breast-feeding, planning to become pregnant or to breast-feed, you must ask your doctor for advice before taking this medicine.
The doctor will advise you on whether you may take or continue to take this medicine.
You should avoid breast-feeding the baby during treatment with the medicine. There have been reports of diarrhea or bloody stools in babies of breast-feeding mothers taking the medicine.
If this happens, you must stop taking the medicine and contact your doctor as soon as possible.
There have been reports of babies with birth defects of the brain, spine or spinal cord born to mothers who were exposed to the medicine during pregnancy, although the effect of the medicine on these defects has not been established.

Low sperm count and infertility may occur in men treated with the medicine. Discontinuation of the medicine appears to reverse these effects within 2 to 3 months.

Fertility
The medicine may cause a disorder in sperm production and temporary male infertility. This effect is reversible within two to three months of discontinuation of the treatment with the medicine.

Driving and using machines
Use of the medicine is unlikely to affect the ability to drive or use of machines.

Important information about some of this medicine's ingredients
Salazopyrin EN contains 5 mg propylene glycol in each Enteric-coated tablet.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine.
The dosage and treatment regimen will be determined by your doctor only.

Do not exceed the recommended dose.

Swallow the medicine whole with a glass of water.
Do not crush/split/chew the tablets:
Since the tablets are film-coated (Salazopyrin EN).
Since the effects of these modes of administration has not been examined (Salazopyrin).

Make sure that you are drinking a sufficient amount of fluids while taking the medicine to avoid kidney problems.

Refer to a doctor if the film-coated tablet (Salazopyrin EN) remained intact in stool, since in such case the active ingredient has not been absorbed.

If you have accidentally taken a higher dosage
The most common symptoms of overdose are nausea and vomiting.

If you experience any of these symptoms or if you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine
If you forget to take the medicine at the scheduled time, take the next dose at the usual time. Do not take a double dose to make up for the forgotten dose.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of the medicine may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Stop taking this medicine and contact your doctor immediately if you experience any of the following symptoms after taking the medicine. Although these symptoms are very rare, they may be serious.

- An allergic reaction including wheezing, difficulty breathing, swelling of eyelids, face or lips, rash or itching (especially when affecting the whole body).
- If you develop a severe skin rash that causes blistering (this may affect the mouth and tongue). Potentially life-threatening skin rashes (exfoliative dermatitis, Stevens-Johnson syndrome, or toxic epidermal necrolysis) have been reported very rarely. See section ‘Special warnings regarding the use of the medicine’. The doctor will stop the treatment in these cases.
- If you have serious skin problems with a rash (sometimes confined to the cheeks and bridge of the nose), peeling skin or blistering. It may be triggered or aggravated by sunlight. Should this occur, **stop taking this medicine, avoid strong sunlight and refer to a doctor immediately.**
- If you are generally feeling unwell, have a fever, have pain in your joints, hives, swollen glands, rash and itching. These may be signs of a condition known as serum sickness. The doctor will stop the treatment in these cases.
- If you are breast-feeding, **stop taking this medicine** once you notice blood in stools or diarrhea in the newborn.

Tell the doctor immediately if you experience any of the following symptoms after taking this medicine, as he may stop treatment in the following cases:

- If you notice any unexplained bleeding.
- If you notice bruising, fever, rash, pallor, a severe sore throat or tiredness.

These may be the first signs of a blood problem, including decrease in the number of red blood cells, white blood cells and platelets. Your doctor will perform routine blood tests to check for these effects.
Discontinue treatment with the medicine while waiting for the blood test results.

Additional side effects that may occur are:

Very common side effects (may appear in more than 1 in 10 people):

- Indigestion, heartburn

- Nausea

Common side effects (may appear in up to 1 in 10 people):

- Dizziness
- Difficulty sleeping
- Headache
- Changes in taste
- Abdominal pain
- Diarrhea
- Vomiting
- Ringing in the ears
- Bloodshot eyes
- Inflamed oral mucosa (stomatitis)
- Cough
- Itching of the skin
- Purple discolorations on the skin
- Joint pain
- Protein in urine
- Fever

Uncommon side effects (may appear in up to 1 in 100 people):

- Depression
- Convulsions, involuntary movements
- Loss of balance
- Shortness of breath
- Hair loss
- Hives
- Puffiness around the eyes and in the face
- Yellowing of the skin or whites of the eyes (jaundice)

Side effects of unknown frequency (the frequency of these effects has not been established yet):

- Inflammation of the lining of the brain (Meningitis)
- Severe diarrhea
- Blood system disorders including anemia, enlarged lymph nodes, glandular fever, persistent sore throat
- Blood vessel inflammation
- Loss of appetite
- Hallucinations
- Changes in mental state
- Disorders in sense of smell
- Inflammation of the sac surrounding the heart (pericarditis)
- Inflammation of the heart muscle (myocarditis)
- Bluish tint or paleness of the skin due to poor circulation
- Lung complications with shortness of breath
- Inflammation of the salivary glands on both sides of the face
- Kidney inflammation and kidney pain, kidney stones
- Liver disease (hepatitis)
- Inflammation of pancreas (accompanied by severe pain in the abdomen and face)
- Rash, reddening or blistering of the skin, eczema, swelling of the skin
- Tingling, numbness, pain in the hands and feet
- Blood and crystals in urine

- Urine or stool may become yellow/orange, which is normal and harmless
- Decrease (reversible) in sperm concentration and infertility in men. This effect resolves when treatment with the medicine is stopped. Use of contraception should be continued
- Dryness of the mouth and eyes
- Deficiency in folic acid (may cause fatigue)

Very rarely, this medicine may cause discoloration of soft contact lenses.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This and any other medicine should be kept in a closed place, out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- Store the medicine below 25°C.
- In a bottle pack, after first opening, the medicine can be used for 6 months while stored at room temperature below 25°C.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Salazopyrin:
Starch pregelatinized, povidone, magnesium stearate, silica colloidal anhydrous.
Salazopyrin EN:
Starch pregelatinized, povidone, magnesium stearate, silica colloidal anhydrous, cellulose acetate phthalate, propylene glycol (E1520), talc, macrogol, carnauba wax, glyceryl monostearate, beeswax white.

What the medicine looks like and contents of the pack:
Salazopyrin: A round yellow-orange tablet with "Kph" embossed on one side and "101" on the other side.
Salazopyrin EN: A film-coated elliptical yellow-orange tablet with "Kph" embossed on one side and "102" on the other side.

The medicine is marketed in packs of bottles containing 100 or 300 tablets or in blisters containing 30 or 100 tablets.

Not all pack sizes may be marketed.

Registration holder and address: Pfizer PFE Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

Registration number of the medicine in the Ministry of Health's National Drug Registry:
Salazopyrin: 113-35-21579
Salazopyrin EN: 113-34-20570

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