Salazopyrin®
Salazopyrin® EN-tabs
enteric coated tablet

Directions for use

Prescription medicine

COMPOSITION
Each tablet, enteric-coated tablet and suppository contains:
Sulfasalazine USP 500 mg.

DESCRIPTION
Salazopyrin is used for the treatment of inflammatory bowel diseases and rheumatoid arthritis. The use of enteric coated tablets will reduce the incidence of gastrointestinal side effects. For rheumatoid arthritis only Salazopyrin EN-tabs should be used. In the colon sulfasalazine is split by intestinal bacteria into sulfapyridine and 5-aminosalicylic acid. Sulfasalazine and its metabolites have antiflammatory, immunosuppressive and antibacterial effects.

INDICATIONS
Tablets and enteric coated tablets
Ulcerative colitis
In the treatment of mild to moderate ulcerative colitis and as adjunctive therapy in severe ulcerative colitis. For maintenance of remission in ulcerative colitis.

Crohn's disease
In the treatment of active Crohn's disease, especially in patients with colonic involvement.

Enteric coated tablets
Ulcerative colitis and Crohn's disease

Rheumatoid Arthritis

Suppositories
Ulcerative proctitis

DOSAGE
Tablets and enteric coated tablets
The dosage should be adjusted according to the patient's response to treatment and tolerance to the drug. The tablets should be taken at regular intervals during the day, preferably in connection with meals. Patients not previously treated with Salazopyrin/Salazopyrin EN-tabs are recommended to increase the dose gradually during the first few weeks. The use of entric coated tablets will reduce the incidence of gastrointestinal side effects.

The enteric coated tablets should not be crushed or broken.

Inflammatory bowel diseases
Acute attacks:
Adults

Severe attacks:	2-4 tablets 3-4 times a day may be given in conjunction with steroids as part of an intensive management regime.
Moderate and mild attacks:	2 tablets 3-4 times a day.

Children
40-60 mg/kg body weight and day, divided into 3-6 doses.

Prophylaxis against relapses:
Adults
In ulcerative colitis in a state of remission a maintenance dose is recommended for keeping the patient free from symptoms, as a rule 2 tablets 2(-3) times a day. Treatment with this dosage should continue indefinitely, unless adverse effects are observed. In case of deterioration, the dosage is raised to 2(-4) tablets 3-4 times a day.

Children
20-30 mg/kg body weight and day, divided into 3-6 doses.

Enteric coated tablets
Rheumatoid Arthritis
Experience has shown that the clinical effect appears within 1-2 months' treatment.

Concurrent treatment with analgesics and/or non-steroidal anti-inflammatory agents is recommended at least until the disease-modifying effect of Salazopyrin EN-tabs is apparent. Salazopyrin EN-tabs has been shown effective and well tolerated in long term treatment.

Adults
Two enteric coated tablets twice a day, i.e. 2 grams a day. The enteric coated tablets should not be crushed or broken. When starting therapy it is advisable to increase the daily dose according to the following schedule: (Salazopyrin EN-tabs)

	Morning	Evening
1st week		1 tablet
2nd week	1 tablet	1 tablet
3rd week	1 tablet	2 tablets
4th week and after	2 tablets	2 tablets

If no response has been seen after 2 months' treatment, the dose may be increased to 3 g per day.

Children
At present no recommendation regarding treatment with Salazopyrin EN-tabs in juvenile chronic arthritis can be given.

Suppositories

Individual. 1-2 suppositories in the morning after defaecation and in the evening. After 4-5 weeks the dosage can be reduced by half. The local treatment can be combined with oral therapy with Salazopyrin/Salazopyrin EN-tabs.

SAFETY

Contraindications

Hypersensitivity to sulfonamides or salicylates. Acute intermittent porphyria.

Warnings and precautions

Patients treated with Salazopyrin/Salazopyrin EN-tabs should be under medical supervision. Bone marrow depression and leucopenia have been reported, usually within the first 3 months of starting treatment. In the vast majority of patients this has been reversible on stopping the drug. A full blood count, including differential white blood cell count, should be carried out before starting treatment and monitored closely during the first 3 months of treatment. Thereafter patients should be screened if their condition changes or if they present with symptoms infection, however mild clinically. A falling trend in the blood count is a better indication than a single value.

Red cell and platelet counts should be carried out before and periodically during therapy.

Salazopyrin/Salazopyrin EN-tabs should be used with caution in patients with reduced kidney or liver function. Liver function tests and urinalysis should be carried out before and periodically during therapy.

If serious toxic or hypersensitivity reactions occur, the drug should be discontinued immediately.

Patients with glucose-6-phosphate dehydrogenase deficiency should be closely observed for signs of haemolytic anaemia.

Use in pregnancy and lactation

Long usage and clinical studies have shown that no teratogenic hazards are associated with sulfasalazine.

The amount of sulfasalazine that passes into the milk is negligible.

The concentration of sulfapyridine in the mother’s milk is about 40% of that in serum. However, the risk of kernicterus in healthy suckling children has been assessed as low at therapeutic doses, since sulfapyridine has been shown to have a poor bilirubin displacing capacity.

Interactions

Reduced absorption of digoxin has been reported when used concomitantly with sulfasalazine. Folate deficiency may occur as sulfasalazine inhibits the absorption of folate.

Adverse reactions

It may be difficult to evaluate an adverse reaction in the individual case, since several of the untoward symptoms and signs encountered in conjunction with treatment with

Salazopyrin/Salazopyrin EN-tabs may be part of the disease.

Some side effects are dose dependent, and the symptoms can often be alleviated by reducing the dosage.

The most commonly reported adverse reactions are:
Nausea
Anorexia
Raised temperature
Erythema and pruritus
Headache

The adverse reactions listed below have only rarely been reported.

Of these the following are possibly dose-related:

Haematological reactions	Red cell abnormalities (e.g. haemolytic anaemia, macrocytosis), cyanosis
Gastro-intestinal reactions	Gastric distress and abdominal pain
CNS reactions	Dizziness and tinnitus
Renal reactions	Proteinuria, haematuria
Dermatological reactions	Yellow skin

The following reactions are probably not dose-related:

Haematological reactions	Bone marrow depression with e.g. leucopenia, agranulocytosis or thrombocytopenia
Gastro-intestinal reactions	Hepatitis, pancreatitis
CNS reactions	Peripheral neuropathy, aseptic meningitis
Dermatological reactions	Exanthema, urticaria, erythema multiforme/Stevens-Johnson syndrome, exfoliative dermatitis, epidermal necrolysis (Lyell's syndrome), photosensitivity
Pulmonary reactions	Lung complications (fibrosing alveolitis with e.g. dyspnoea, cough, fever, eosinophilia)
Other hypersensitivity reactions	Periorbital oedema, serum sickness, LE-syndrome, nephrotic syndrome
Reproductive disorders, male	Oligospermia with infertility have been described in men treated with sulfasalazine. Withdrawal of the drug will reserve the effects.

OVERDOSE
Symptoms of overdosage include nausea and vomiting.