# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Salofalk 250 mg Suppositories

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains 250 mg of mesalazine.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Suppository
White to creamy coloured suppository.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

As an anti-inflammatory in the management of ulcerative colitis, alone or, particularly in the acute phase, with corticosteroids.

### 4.2 Posology and method of administration

Posology
*Adults and elderly*
Unless prescribed otherwise, for acute inflammatory symptoms, 2 Salofalk 250 Suppositories are to be introduced rectally morning, noon and evening. In severe cases of the disease, the dosage may be doubled. For long-term treatment and prevention of recurrences, one suppository to be introduced rectally morning, noon and evening.
Treatment with Salofalk 250 Suppositories, whether during an acute inflammatory stage or in long-term treatment of patients, must be faithfully and strictly adhered to, as this is essential if the desired therapeutic success is to be obtained.

*Paediatric population*
There is little experience and only limited documentation for an effect in children.

*Duration of treatment*
The duration of use is determined by the physician.

Method of administration
Salofalk suppositories are for rectal administration.

### 4.3 Contraindications

Salofalk is contraindicated in cases of:
Hypersensitivity to the active substance to salicylates or any of the excipients listed in section 6.1
Severe impairment of hepatic or renal function.

### 4.4 Special warnings and precautions for use

Blood tests (differential blood count; liver function parameters such as ALT or AST; serum creatinine) and urinary status (dip sticks) should be determined prior to and during treatment, at the discretion of the treating physician. As a guideline, follow-up tests are recommended 14 days after commencement of treatment, then a further two to three tests at intervals of 4 weeks.

If the findings are normal, follow-up tests should be carried out every 3 months. If additional symptoms occur, these tests should be performed immediately.

Caution is recommended in patients with impaired hepatic function.

Mesalazine should not be used in patients with impaired renal function.

Mesalazine-induced renal toxicity should be considered if renal function deteriorates during treatment. If this is the case, Salofalk 250mg Suppositories should be discontinued immediately.

Cases of nephrolithiasis have been reported with the use of mesalazine including stones with a 100% mesalazine content. It is recommended to ensure adequate fluid intake during treatment.

Mesalazine may produce red-brown urine discoloration after contact with sodium hypochlorite bleach (e.g., in toilets cleaned with sodium hypochlorite contained in certain bleaches).

Serious blood dyscrasias have been reported very rarely with mesalazine. Hematological investigations should be performed if patients suffer from unexplained haemorrhages, bruises, purpura, anaemia, fever or pharyngolaryngeal pain. Salofalk 250mg Suppositories should be discontinued in case of suspected or confirmed blood dyscrasia.

Cardiac hypersensitivity reactions (myocarditis, and pericarditis) induced by mesalazine have been rarely reported.
Salofalk 250mg Suppositories should then be discontinued immediately.

Patients with pulmonary disease, in particular asthma, should be very carefully monitored during a course of treatment with mesalazine.

Severe cutaneous adverse reactions
Severe cutaneous adverse reactions (SCARs), including drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in association with mesalazine treatment.

Mesalazine should be discontinued, at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

Idiopathic intracranial hypertension
Idiopathic intracranial hypertension (pseudotumor cerebri) has been reported in patients receiving mesalazine. Patients should be warned for signs and symptoms of idiopathic intracranial hypertension, including severe or recurrent headache, visual disturbances or tinnitus. If idiopathic intracranial hypertension occurs, discontinuation of mesalazine should be considered.

Patients with a history of adverse drug reactions to preparations containing sulfasalazine should be kept under close medical surveillance on commencement of a course of treatment with mesalazine. Should Salofalk suppositories cause acute intolerance reactions such as abdominal cramps, acute abdominal pain, fever, severe headache and rash, therapy should be discontinued immediately.

**4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed.

In patients who are concomitantly treated with azathioprine, 6-mercaptopurine or thioguanine, a possible increase in the myelosuppressive effects of azathioprine, 6-mercaptopurine or thioguanine should be taken into account.

There is weak evidence that mesalazine might decrease the anticoagulant effect of warfarin.

**4.6 Fertility, pregnancy and lactation**

Pregnancy
There are no adequate data from the use of mesalazine in pregnant women.

However, data on a limited number of exposed pregnancies indicate no adverse effect of mesalazine on pregnancy or on the health of the foetus/newborn child. To date no other relevant epidemiologic data are available. In one single case after long-term use of a high dose mesalazine (2-4g, orally) during pregnancy, renal failure in a neonate was reported.

Animal studies on oral mesalazine do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development.

Salofalk suppositories should only be used during pregnancy if the potential benefit outweighs the possible risk.

Breastfeeding
N-acetyl-5-aminosalicylic acid and to a lesser degree mesalazine are excreted in breast milk. Only limited experience during lactation in women is available to date. Hypersensitivity reactions such as diarrhoea in the infant cannot be excluded. Therefore, Salofalk suppositories should only be used during breast-feeding if the potential benefit outweighs the possible risk. If the infant develops diarrhoea, breast-feeding should be discontinued.

**4.7 Effects on ability to drive and use machines**

Mesalazine has no or negligible influence on the ability to drive and use machines.

**4.8 Undesirable effects**

| Organ Class System | Frequency according to MedDRA convention | | | |
|---|---|---|---|---|
| | Common (≥1/100; <1/10) | Rare (≥1/10,000; < 1/1,000) | Very rare (< 1/10,000) | Not known (cannot be estimated from the available data) |
| Blood and lymphatic system disorders | | | Altered blood counts (aplastic anaemia, agranulocytosis, pancytopenia, neutropenia, leukopenia, thrombocytopenia) | |
| Nervous system disorders | | Headache, dizziness | Peripheral neuropathy | Idiopathic intracranial hypertension (see section 4.4) |
| Cardiac disorders | | Myocarditis, pericarditis | | |
| Respiratory, thoracic and mediastinal disorders | | | Allergic and fibrotic lung reactions (including dyspnoea, cough, bronchospasm, alveolitis, pulmonary eosinophilia, lung infiltration, pneumonitis) | |
| Gastrointestinal disorders | | Abdominal pain, diarrhoea, flatulence, nausea, vomiting, constipation | Acute pancreatitis | |
| Renal and urinary | | | Impairment of renal function | Nephrolithiasis* |

| | | | | |
|---|---|---|---|---|
| disorders | | | including acute and chronic interstitial nephritis and renal insufficiency | |
| Skin and subcutaneous tissue disorders | Rash, pruritus | Photosensitivity | Alopecia | Drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) |
| Musculoskeletal and connective tissue disorders | | | Myalgia, arthralgia | |
| Immune system disorders | | | Hypersensitivity reactions such as allergic exanthema, drug fever, lupus erythematosus syndrome, pancolitis | |
| Hepatobiliary disorders | | | Changes in liver function parameters (increase in transaminases and parameters of cholestasis), hepatitis, cholestatic hepatitis | |
| Reproductive system disorders | | | Oligospermia (reversible) | |

* see section 4.4 for further information
Severe cutaneous adverse reactions (SCARs), including drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in association with mesalazine treatment (see section 4.4).

Photosensitivity
More severe reactions are reported in patients with pre-existing skin conditions such as atopic dermatitis and atopic eczema.

Reporting of suspected adverse reactions
Reporting of suspected reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

HPRA Pharmacovigilance
Website: www.hpra.ie

**4.9 Overdose**

There are rare data on overdosage (e.g. intended suicide with high oral doses of mesalazine), which do not indicate renal or hepatic toxicity. There is no specific antidote and treatment is symptomatic and supportive.

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Intestinal anti-inflammatory agent

ATC Code: A07EC02

The mechanism of the anti-inflammatory action is unknown. The results of *in vitro* studies indicate that inhibition of lipoxygenase may play a role.

Effects on prostaglandin concentrations in the intestinal mucosa have also been demonstrated. Mesalazine (5-aminosalicylic acid/5-ASA) may also function as a radical scavenger of reactive oxygen compounds.

On reaching the intestinal lumen, rectally administered mesalazine has largely local effects on the intestinal mucosa and sub mucosal tissue.

**5.2 Pharmacokinetic properties**

General considerations of mesalazine:

*Absorption:*
Mesalazine absorption is highest in proximal gut regions and lowest in distal gut areas.

*Biotransformation:*
Mesalazine is metabolised both pre-systemically by the intestinal mucosa and the liver to the pharmacologically inactive N-acetyl-5-aminosalicylic acid (N-Ac-5-ASA). The acetylation seems to be independent of the acetylator phenotype of the patient. Some acetylation also occurs through the action of colonic bacteria. Protein binding of mesalazine and N-Ac-5-ASA is 43 % and 78 %, respectively.

*Elimination:*
Mesalazine and its metabolite N-Ac-5-ASA are eliminated via the faeces (major part), renally (varies between 20 and 50 %, dependent on kind of application, pharmaceutical preparation and route of mesalazine release, respectively), and biliary (minor part). Renal excretion predominantly occurs as N-Ac-5-ASA. About 1 % of total orally administered mesalazine dose is excreted into the breast milk mainly as N-Ac-5-ASA.

**5.3 Preclinical safety data**

With the exception of a local tolerance study in dogs, which showed good rectal tolerance, no preclinical studies have been performed with Salofalk suppositories.

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity, carcinogenicity (rat) or toxicity to reproduction.

Kidney toxicity (renal papillary necrosis and epithelial damage in the proximal convoluted tubule or the whole nephron) has been seen in repeat-dose toxicity studies with high oral doses of mesalazine. The clinical relevance of this finding is unknown.

**6 PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Hard fat

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

3 years.

**6.4 Special precautions for storage**

Do not store above 25°C.
Keep in the original package in order to protect from light.

**6.5 Nature and contents of container**

Cardboard box containing 10 or 30 suppositories sealed in blister packs which consist of PVC/PE films.
Not all pack sizes may be marketed.

**6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

No special requirements.

**7 MARKETING AUTHORISATION HOLDER**

Dr. Falk Pharma GmbH
Leinenweberstrasse 5
79108 Freiburg
Germany

**8 MARKETING AUTHORISATION NUMBER**

PA0573/004/002

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 08 February 1989

Date of last renewal: 08 February 2009

**10 DATE OF REVISION OF THE TEXT**

May 2025