Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Salofalk 1g/Actuation Rectal Foam

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 actuation contains: Mesalazine 1.0g

Excipients with known effect:
Each actuation of Salofalk rectal foam contains 3.44 g propylene glycol, 50 mg sodium metabisulphite and 9.1 mg cetostearyl alcohol.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Rectal foam.
White-greyish to slightly reddish-violet, creamy firm foam.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of active, mild ulcerative colitis of the sigmoid colon and rectum.

4.2 Posology and method of administration

Posology
Adults and elderly:
Two administrations once a day at bedtime. Salofalk rectal foam should be used at room temperature (between 20°C and not more than 30°C; see also section 6.4. The canister is first fitted with an applicator and then shaken for about 20 seconds before the applicator is inserted into the rectum as far as comfortable. To administer a dose of Salofalk, the pump dome is fully pushed down and released. Note that the spray will only work properly when held with the pump dome pointing down. Following the first or second activation depending upon need (see below) the applicator should be held in position for 10-15 seconds before being withdrawn from the rectum. If the patient has difficulty in holding this amount of foam, the foam can also be administered in divided doses: one at bedtime and the other during the night (after evacuation of the first single dose) or in the early morning. The best results are obtained when the intestine is evacuated prior to administration of Salofalk rectal foam.

In general, an acute episode of a mild ulcerative colitis subsides after 4-6 weeks. It is recommended to continue the maintenance therapy with an oral mesalazine preparation e.g., Salofalk prolonged release granules at a dosage recommended for this preparation.

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
rectal.

4.3 Contraindications

Salofalk is contraindicated in cases of:
- known hypersensitivity to salicylates or to any of the excipients listed in section 6.1

- severe impairment of hepatic or renal function

Caution:
Asthmatics should be treated with care with Salofalk since sulphite contained in the foam may cause hypersensitivity reactions.

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 rectal foam 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 rectal foam 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 rectal foam 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 sulphasalazine should be kept under close medical surveillance on commencement of a course of treatment with mesalazine. Should Salofalk cause acute intolerance reactions such as abdominal cramps, acute abdominal pain, fever, severe headache and rash, therapy should be discontinued immediately.

This medicinal product contains 3.44 g propylene glycol in each actuation of Salofalk rectal foam. Propylene glycol may cause skin irritation.

This medicinal product contains sodium metabisulphite and cetostearyl alcohol.
Sodium metabisulphite may rarely cause severe hypersensitivity reactions and bronchospasm.
Cetostearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

Specific interaction studies have not 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 on 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 of mesalazine (2-4g, orally) during pregnancy, renal failure in a neonate was reported.

No animal studies with Salofalk rectal foam have been performed.
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 rectal foam 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 rectal foam 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

System organ class	Frequency According to MedDRA Convention				
	Common (³1/100, <1/10)	Uncommon (³1/1,000, <1/100)	Rare (³1/10,000, <1/1,000)	Very rare (<1/10,000)	Not known (cannot be estimated from the available data)
General disorders and administration site conditions	Abdominal distension	Anal discomfort; application site irritation, painful rectal tenesmus			
Blood and lymphatic system				Altered blood counts (aplastic anaemia,	

disorders				agranulocytosis, pancytopenia, neutropenia, leukopenia, thrombocytopenia)	
Nervous system disorders			Headaches, 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	Acute pancreatitis	
Renal and urinary disorders				Impairment of renal function including acute and chronic interstitial nephritis and renal insufficiency	Nephrolithiasis*
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 suspected adverse 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 the national reporting system:
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 agents: aminosalicylic acid and similar agents
ATC Code: A07EC02.

Mechanism of action:
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 may also function as a radical scavenger of reactive oxygen compounds. Mesalazine acts predominantly locally at the gut mucosa and in the submucus tissue from the luminal side of the intestine. It is important therefore that mesalazine is available at the regions of inflammation. Systemic bioavailability / plasma concentrations of mesalazine therefore are of no relevance for therapeutic efficacy, but rather a factor for safety.

5.2 Pharmacokinetic properties

General considerations of mesalazine
Absorption
Mesalazine absorption is highest in the 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%, dependant 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.

Salofalk rectal foam specific
Distribution
A combined pharmacoscintigraphic / pharmacokinetic study showed that spreading of Salofalk Foam is homogeneous and fast, and is almost complete within 1 hour. It reaches the gut regions rectum, sigmoid colon, and left-sided colon in dependence of extension of inflammation.

Absorption
Absorption of mesalazine is fast, and peak plasma concentrations for mesalazine and its metabolite N-Ac-5-ASA are reached at about 4 hours. However, plasma concentrations of a 2g mesalazine rectal dose of foam are about comparable with an 250mg oral dose mesalazine, reaching maximum concentrations of about 0.4 µg/ml.

Pre-systemic metabolisation is fast, and N-Ac-5-ASA reaches its maximum plasma concentrations also at about 4 hours, like mesalazine, but plasma concentrations are about 4-5 times higher, about 2 µg/ml

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 rectal foam.

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

Sodium metabisulphite (E223)
cetostearyl alcohol
polysorbate 60
disodium edetate
propylene glycol

Propellants:
propane
n-butane
isobutane

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.
After first actuation: 12 weeks.

6.4 Special precautions for storage

Do not store above 30°C. Do not refrigerate or freeze. This is a pressurised container, containing 3.75% by mass of inflammable propellant. It should be kept away from any flames, sparks or incandescent material including cigarettes. It should be protected from direct sunlight and temperatures over 50°C and must not be pierced or burned even when empty.

6.5 Nature and contents of container

Aluminium pressurised container with metering valve containing 80g (14 actuations, which equals 7 doses) of suspension together with 14 PVC applicators coated with white soft paraffin and liquid paraffin for administration of the foam.

Package sizes:

Package with 1 spray can Salofalk 1g actuation Rectal Foam containing 80 g suspension (14 actuations, which equals 7 doses)

Bundle pack with 4 spray cans Salofalk 1g/actuation Rectal Foam containing 80 g suspension each.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused product waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Dr. Falk Pharma GmbH
Leinenweberstrasse 5
79108 Freiburg
Germany

8 MARKETING AUTHORISATION NUMBER

PA0573/004/005

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 30th October 2013

10 DATE OF REVISION OF THE TEXT

December 2025