SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Salofalk®4g (Enemas)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One Salofalk 4g/60ml enema (= 60 g rectal suspension) contains 4 g mesalazine.

Excipients with known effects:
One Salofalk®4g (Enemas) contains 280.8 mg potassium metabisulphite and 60 mg sodium benzoate.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Rectal suspension

Appearance: very light tan to brown homogeneous suspension, free from foreign matter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Acute attacks of ulcerative colitis (a chronic inflammatory disease of the large bowel)

4.2 Posology and method of administration

Posology

Adults and elderly

In patients with symptoms of acute inflammation, the content of one enema bottle (60 g rectal suspension) is administered into the intestine as a clyster once daily at bedtime.

Children and adolescents

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

Duration of treatment

The duration of treatment is determined by the physician.

General instructions for use:
Salofalk®4g (Enemas) are used once daily at bedtime.

Treatment with Salofalk®4g (Enemas) must be administered regularly and consistently, because only in this way can healing be successfully achieved.

Method of administration:

Rectal use.
The best results are achieved if the bowel is emptied before administration of the Salofalk® 4g (Enemas) .

Preparation:
- The bottle should be shaken for 30 seconds.
- Then the protective cap of the applicator is removed.
- The bottle should be held at the top and bottom.

The correct position for administration is as follows:
- The patient should lie down on his/her left side with his/her left leg stretched out and right leg bent. This makes it easier for the rectal suspension to be administered and for the enema to be effective.

Administration of the rectal suspension:
- The tip of the applicator should be inserted deep into the rectum.
- The bottle should be tipped downwards slightly and then squeezed slowly.
- Once the bottle is empty, the applicator tip should be slowly withdrawn from the rectum.
- The patient should remain lying down in this position for at least 30 minutes to allow the contents of the enema to spread throughout the rectum.
- If possible, the rectal suspension should be allowed to exert its effects all night.

4.3 Contraindications

Salofalk®4g (Enemas) are contraindicated in patients with

- hypersensitivity to the active substance, salicylates or to 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 like 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®4g (Enemas) 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. Mesalazine should be discontinued in case of suspected or confirmed blood dyscrasia.

Cardiac hypersensitivity reactions (myocarditis, and pericarditis) induced by mesalazine have been rarely reported. Mesalazine 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.

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®4g (Enemas) cause acute intolerance reactions such as abdominal cramps, acute abdominal pain, fever, severe headache and rash, therapy should be discontinued immediately.

Salofalk®4g (Enemas) contain potassium metabisulphite. Potassium metabisulphite may rarely cause severe hypersensitivity reactions and bronchospasms.

This medicinal product contains 60 mg sodium benzoate in each enema. Sodium benzoate may cause local irritation. Sodium benzoate may increase jaundice in newborn babies.

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 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 of mesalazine (2-4 g/day, 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®4g (Enemas) should only be used during pregnancy if the potential benefit outweighs the possible risk.

Breast-feeding
N-acetyl-5-aminosalicylic acid, and to a lesser degree mesalazine, are excreted in breast milk. Only limited experience with mesalazine during lactation in women is available to date. Hypersensitivity reactions such as diarrhoea in the infant cannot be excluded.

Therefore, Salofalk®4g (Enemas) 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 or use machines.

4.8 Undesirable effects

The following undesirable effects have been observed after administration of mesalazine:

System organ class	***Frequency according to MedDRA convention***			
	Common (≥ 1/100 to<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	
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),

System organ class	*Frequency according to MedDRA convention*			
	Common (≥ 1/100 to<1/10)	***Rare (≥ 1/10,000; <1/1,000)***	***Very rare (< 1/10,000)***	***Not known (cannot be estimated from the available data)***
				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.

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 the 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 (5-Aminosalicylic acid / 5-ASA) may also function as a radical scavenger of reactive oxygen compounds.
Pharmacodynamic effects
On reaching the intestinal lumen, rectally administered mesalazine has largely local effects on the intestinal mucosa and submucosal 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 in 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.

Salofalk®4g (Enemas) specific:

Distribution:
An imaging study in patients with mild-to-moderate acute ulcerative colitis showed that the rectal suspension, at the start of treatment and at remission after 12 weeks, is distributed mainly in the rectum and sigmoid colon, and to a lesser extent in the descending colon.

Absorption and elimination:
In a study in ulcerative colitis patients in remission, peak plasma concentrations of 0.92 µg/ml 5-ASA and 1.62 µg/ml N-Ac-5-ASA were achieved after approximately 11-12 hours under steady-state conditions. The elimination rate was approximately 13% (45-hour value), with most (approximately 85%) being eliminated in the form of the metabolite, N-Ac-5-ASA.
The steady-state plasma concentrations of 5-ASA and N-Ac-5-ASA in children with chronic inflammatory bowel disease under treatment with Salofalk®4g (Enemas) were 0.5-2.8 µg/ml and 0.9-4.1 µg/ml respectively.

5.3 Preclinical safety data

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 tubule (pars convoluta) 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

1. Carbomer (e.g. Carbopol 974P)
2. Potassium acetate
3. Potassium metabisulphite (max. 0.28 g, equivalent to max. 0.16 g SO_2)
4. Sodium benzoate
5. Disodium edetate
6. Water, purified
7. Xanthan gum

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Do not use this medicine after the expiry date which is stated on label on the bottom of the bottle and on the carton.

6.4 Special precautions for storage

Store in the original sealed blister packs in order to protect from light.
Do not store at temperature exceeding 30 °C.
Shake well before use.
Store medicines out the reach of children.

6.5 Nature and contents of the container

Container
Round, white, concertina-shaped LDPE bottle with a green protective LDPE cap
Pack sizes
Packs containing 1 bottle per blister and contain 1,2,3,4,5,6,7,8,9,10,15,20,30,40,50,70, 80,100,200,300,400,500,1000,2000,3000,4000,5000 and 10,000 blisters per carton.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Manufactured by Corden Pharma Fribourg AG, Zweigniederlassung Ettingen, Ettingen, Switzerland

Batch released by Dr. Falk Pharma GmbH, Freiburg im Breisgau, Germany

Imported by
A. Menarini (Thailand) Limited, Bangkok

8. MARKETING AUTHORISATION NUMBER

1C 116/49

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 16-Mar-2006

10. DATE OF REVISION OF THE TEXT

Jul 2024