SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Mesalazine Dr Falk Pharma 2 g enema

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each enema contains 2g mesalazine in 59 ml of suspension.

Excipients with known effect:
One Mesalazine Dr Falk Pharma 2 g enema contains 280.8 mg potassium metabisulphite (E 224) and 60 mg sodium benzoate (E211).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Enema.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Therapy and prophylaxis of acute attacks of mild ulcerative colitis, especially in the rectum and sigmoid colon and also in the descending colon.

4.2 Posology and method of administration

Adults and the Elderly: 1 enema once a day at bedtime. The action of Mesalazine Dr Falk Pharma enema is enhanced if the patient lies on the left side when introducing the enema. The dosage should be adjusted to suit the progress of the condition. Do not discontinue treatment suddenly.

The treatment of acute episodes of ulcerative colitis usually last 8 weeks.

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

Method of administration

Rectal

The best results are achieved if the bowels are emptied before administration of the enema.

The patient should be advised to:

- Shake the bottle for 30 seconds.
- Remove the protective cap.
- Hold the bottle at the top and bottom and keep it upright to avoid spillage.
- Lie down comfortably on the left side with the left leg stretched out and the right leg bent. If more convenient, lie on the right side with the right leg stretched out and with the left leg bent. In this case, turn to the left side after application of the enema.
- Insert the applicator deep into the rectum keeping the bottle tipped downwards slightly.
- Slowly squeeze the bottle until empty.
- Slowly withdraw the applicator from the rectum.
- Lie on the left side for at least 30 minutes to allow the contents of the enema to spread.
- If possible, retain the enema all night.

4.3 Contraindications

Mesalazine Dr Falk Pharma enema is contraindicated in cases of:

- Hypersensitivity to the active substance, salicylates or any of the excipients listed in section 6.1.
- Severe impairment of renal or hepatic 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, 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, Mesalazine Dr Falk Pharma enema 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 Dr Falk Pharma enema 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 Dr Falk Pharma enema 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 the enema cause acute intolerance reactions such as abdominal cramps, acute abdominal pain, fever, severe headache and rash, therapy should be discontinued immediately.

Mesalazine Dr Falk Pharma enemas contain potassium metabisulphite, which may rarely cause severe hypersensitivity reactions and bronchospasm.

This medicinal product contains 60 mg sodium benzoate in each Mesalazine Dr Falk Pharma enema. Sodium benzoate may cause local irritation.

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 the 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/fetal development, parturition or postnatal development.

Mesalazine Dr Falk Pharma enema 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 with mesalazine during lactation in women is available to date. Hypersensitivity reactions such as diarrhoea in the infant cannot be excluded. Therefore, Mesalazine Dr Falk Pharma enema 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

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

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 disorders			Impairment of renal function including acute and chronic interstitial nephritis and renal insufficiency	Nephrolithiasis*
Skin and subcutaneous tissue disorders	Rash, pruritus	Photo-sensitivity	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 cholestasis parameters), 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:

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

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: Aminosalicylic acid and similar agents
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 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.

5.3 Preclinical safety data

With the exception of a local tolerance study in dogs, which demonstrated good rectal tolerance, no preclinical studies have been performed with Mesalazine Dr Falk Pharma rectal preparations.

Preclinical data on mesalazine 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

Mesalazine Dr Falk Pharma enema contains the following excipients: Carbomer 35 000, disodium edetate, potassium acetate (E261), potassium metabisulphite (E224), purified water, sodium benzoate (E211), xanthan gum (E415).

6.2. Incompatibilities

None known.

6.3. Shelf Life

24 months.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from light.

6.5. Nature and Contents of Container

Low density concertina shaped polythene bottle with a low density polythene application nozzle packed in cartons containing seven individually blister packed bottles.

6.6 Special precautions for disposal

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Dr Falk Pharma UK Ltd
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SL8 5AS
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8. MARKETING AUTHORISATION NUMBER

PL 10341/0008

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

31st December 2004

10 DATE OF REVISION OF THE TEXT

12/05/2025