Salofalk 500mg/1000mg/1.5g/3g Granu-Stix Gebrauchsinformation (Outsert) für Malaysia

Mat.-Nr.: 12XXXXX (Losan Pharma)
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Laetuscode: 83
Machart: Outsert

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PACKAGE INSERT

1 NAME OF THE MEDICINAL PRODUCT

Salofalk® 500mg gastro-resistant prolonged-release granules
Salofalk® 1000mg gastro-resistant prolonged-release granules
Salofalk® 1.5g gastro-resistant prolonged-release granules
Salofalk® 3g gastro-resistant prolonged-release granules

Mesalazine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet of Salofalk 500mg granules contains 500 mg mesalazine.
Each sachet of Salofalk 1000mg granules contains 1000 mg mesalazine.
Each sachet of Salofalk 1.5g granules contains 1.5 g mesalazine.
Each sachet of Salofalk 3g granules contains 3 g mesalazine.

Excipients with known effect:
Each sachet of Salofalk 500mg granules contains 1.0 mg aspartame and 0.04 mg sucrose.
Each sachet of Salofalk 1000mg granules contains 2.0 mg aspartame and 0.08 mg sucrose.
Each sachet of Salofalk 1.5g granules contains 3.0 mg aspartame and 0.12 mg sucrose.
Each sachet of Salofalk 3g granules contains 6.0 mg aspartame and 0.24 mg sucrose.

WARNING
Unsuitable for phenylketonurics

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gastro-resistant prolonged-release granules
Description: stick-formed or round, greyish white granules

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of acute episodes and the maintenance of remission of mild to moderate ulcerative colitis.

4.2 Posology and method of administration

Posology

Adults and the elderly

For the treatment of acute episodes of ulcerative colitis
Once daily, 1 sachet of Salofalk 3g granules, 1-2 sachets of Salofalk 1.5g granules, 3 sachets of Salofalk 1000mg granules or 3 sachets of Salofalk 500mg granules (equivalent to 1.5-3.0 g mesalazine daily) preferably to be taken in the morning according to the individual clinical requirement.

It is also possible to take the prescribed daily dose in three divided doses (1 sachet of Salofalk 500mg granules 3 times daily or 1 sachet of Salofalk 1000mg granules 3 times daily), if this is more convenient to the patient.

For the maintenance of remission of ulcerative colitis
The standard treatment is 0.5 g mesalazine 3 times daily (in the morning, at midday and in the evening) corresponding to a total dose of 1.5 g mesalazine per day. For patients known to be at increased risk for relapse for medical reasons or due to difficulties to adhere to application of three daily doses, the dosing schedule can be adapted to 3.0 g mesalazine given as a single daily dose, preferably in the morning.

Paediatric population
There is only limited documentation for an effect in children (age 6-18 years).

Children 6 years of age and older
Active disease: To be determined individually, starting with 30-50 mg/kg bw/day once daily preferably in the morning or in divided doses. Maximum dose: 75 mg/kg bw/day. The total dose should not exceed the maximum adult dose.
Maintenance treatment: To be determined individually, starting with 15-30 mg/kg bw/day in divided doses. The total dose should not exceed the recommended adult dose.
It is generally recommended that half the adult dose may be given to children up to a body weight of 40 kg and the normal adult dose to those above 40 kg.

Method of administration
The contents of the sachets of Salofalk granules should not be chewed.
The granules should be taken on the tongue and swallowed, without chewing, with plenty of liquid.

Both in the treatment of acute inflammatory episodes and during long term treatment, Salofalk granules should be used on a regular basis and consistently in order to achieve the desired therapeutic effects.

The treatment of acute episodes of ulcerative colitis usually lasts 8 weeks. The duration of use is determined by the physician.

This product is not interchangeable with other brand or dosage form of products containing mesalazine.

4.3 Contraindications

Salofalk granules are contra-indicated in patients with
– hypersensitivity to the active substance, to 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 tests such as ALT or AST; serum creatinine) and dip stick urinalysis should be determined prior to and during treatment, at the discretion of the treating physician. As a guideline, further testing is recommended 14 days after commencement of treatment, then a further two to three times at intervals of 4 weeks.

If the findings are normal, control examinations should be carried out every three months. If additional symptoms occur, control examinations 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 granules 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 granules 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 granules must 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 granules cause acute intolerability reactions, such as abdominal cramps, acute abdominal pain, fever, severe headache and rash, therapy should be discontinued immediately.

This medicine contains 1 mg/2 mg/3 mg/6 mg aspartame in each sachet of Salofalk 500mg/1000mg/1.5g/3g granules. Aspartame is a source of phenylalanine. It may be harmful in patients with phenylketonuria (PKU).

Salofalk granules contain sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take these medicines.

This medicine contains less than 1 mmol sodium (23 mg) per sachet, that is to say essentially 'sodium-free'.

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

4.5 Interaction with other medicinal products and other forms of interaction

Specific interaction studies have not been performed.

Lactulose or similar preparations which lower stool pH: possible reduction of mesalazine release from granules due to decreased pH caused by bacterial metabolism of lactulose.

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 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 of mesalazine (2-4 g, 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, embryonal/foetal development, parturition or postnatal development.

Salofalk granules 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 granules should only be used during breastfeeding if the potential benefit outweighs the possible risk. If the suckling neonate develops diarrhoea, the breastfeeding should be discontinued.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

See table at the end of this package leaflet.

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 antiinflammatory 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
Mesalazine, orally administered, acts predominantly locally at the gut mucosa and in the submucosal tissue from the luminal side of the intestine. It is important, therefore, that mesalazine is available at the regions of inflammation.

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Salofalk® gastro-resistant prolonged-release granules

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Systemic bioavailability/plasma concentrations of mesalazine therefore are of no relevance for therapeutic efficacy, but rather a factor for safety. In order to realise this, Salofalk granules are gastric juice resistant and release mesalazine in a pH dependent manner due to an Eudragit L coating, and prolonged manner due to the matrix granule structure.

5.2 Pharmacokinetic properties

General considerations of mesalazine

Absorption

Mesalazine absorption is highest in proximal 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 %, depending on the 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 granules specific

Distribution

Owing to the granule size of approx. 1 mm, transit from the stomach to the small intestine is fast. A combined pharmacoscintigraphic/pharmacokinetic study showed that the compound reaches the ileocaecal region within approx. 3 hours and the ascending colon within approx. 4 hours. The total transit time in the colon amounts to about 20 hours. Approximately 80 % of an administered oral dose is estimated to be available in the colon, sigmoid colon and rectum.

Absorption

Mesalazine release from Salofalk granules starts after a lag phase of about 2-3 hours. Peak plasma concentrations are reached at about 4-5 hours. The systemic bioavailability of mesalazine after oral administration is estimated to be approximately 15-25 %. Food intake delays absorption by 1 to 2 hours but does not change the rate and extent of absorption.

Elimination

From a 3 x 500 mg daily mesalazine dose in long-term therapy, a total renal elimination of mesalazine and N-Ac-5-ASA under steady state conditions was calculated to be about 25 %. The unmetabolised excreted mesalazine part was less than 1 % of the oral dose. The terminal elimination half-life observed after single dose administration of 3 * 500 mg or 3 * 1000 mg Salofalk granules was 10.5 hours.

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 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

1. Aspartame (E 951)
2. Carmellose sodium
3. Citric acid
4. Silica, colloidal anhydrous
5. Hypromellose
6. Magnesium stearate
7. Methacrylic acid-methyl methacrylate copolymer (1:1) ((MW approx. 135000)) (Eudragit L 100),
8. Methylcellulose
9. Cellulose, microcrystalline
10. Polyacrylate dispersion 40 % (Eudragit NE 40 D containing 2 % Nonoxynol 100)
11. Povidone K 25
12. Simeticone
13. Sorbic acid
14. Talc
15. Titanium dioxide (E 171)
16. Triethyl citrate
17. Vanilla custard flavouring (containing sucrose)
18. Ethanol (only present as residue in the final product, up to 1.25 %)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store below 30 °C.

6.5 Nature and contents of container

Sachet of polyester (PETP)/aluminium/polyethylene (LDPE) foil.

Each sachet of Salofalk 500mg granules contains 0.93 g granules.
Each sachet of Salofalk 1000mg granules contains 1.86 g granules.
Each sachet of Salofalk 1.5g granules contains 2.79 g granules.
Each sachet of Salofalk 3g granules contains 5.58 g granules.

Pack sizes
50 sachets, 100 sachets and 300 sachets Salofalk 500mg granules.
50 sachets, 100 sachets and 150 sachets Salofalk 1000mg granules.
35 sachets and 100 sachets Salofalk 1.5g granules.
20 sachets, 50 sachets and 100 sachets Salofalk 3g granules.
Not all package sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MANUFACTURER

Contract manufactured by:
Losan Pharma GmbH
Otto-Hahn-Straße 13
79395 Neuenburg
Germany

For:

DR. FALK PHARMA GmbH
Leinenweberstr. 5
79108 Freiburg im Breisgau
Germany

8 PRODUCT REGISTRATION HOLDER

DCH Auriga (Malaysia) Sdn Bhd (719-V)
Lot 6, Persiaran Perusahaan, Seksyen 23,
40300 Shah Alam, Selangor Darul Ehsan, Malaysia.

9 PRODUCT REGISTRATION NUMBER

MAL18081002ACRZ: Salofalk 500mg gastro-resistant prolonged-release granules
MAL18081004ACRZ: Salofalk 1000mg gastro-resistant prolonged-release granules
MAL18081003ACRZ: Salofalk 1.5g gastro-resistant prolonged-release granules
MAL18081005ACRZ: Salofalk 3g gastro-resistant prolonged-release granules

10 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10.08.2018
Date of last renewal of the authorisation: 10.08.2023

11 DATE OF REVISION

May 2025

Undesirable effects

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

System organ class	*Frequency according to MedDRA convention*				
	Common	*Uncommon*	*Rare*	*Very rare*	*Not known*
Blood and lymphatic system disorders				Altered blood counts (aplastic anaemia, agranulocytosis, pancytopenia, neutropenia, leukopenia, thrombocytopenia)	
Immune system disorders				Hypersensitivity reactions such as allergic exanthema, drug fever, lupus erythematosus syndrome, pancolitis	
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, dyspepsia, flatulence, nausea, vomiting, acute pancreatitis			
Hepatobiliary disorders			Cholestatic hepatitis	Hepatitis	
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			Arthralgia	Myalgia	
Renal and urinary disorders				Impairment of renal function including acute and chronic interstitial nephritis and renal insufficiency	Nephrolithiasis*
Reproductive system and breast disorders				Oligospermia (reversible)	
General disorders			Asthenia, fatigue		
Investigations		Changes in liver function parameters (increase in transaminases and parameters of cholestasis), changes in pancreatic enzymes (lipase and amylase increased), eosinophil count increased			

* 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).

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