SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Asacol 1 g Suppositories

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains 1 g mesalazine.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suppository
Light beige coloured, torpedo-shaped suppositories dimension of 33 x 11 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of acute mild to moderate ulcerative colitis limited to the rectum (ulcerative proctitis).

4.2 Posology and method of administration

Posology

Adults and older people
One Mesalazin 1 g Suppository once daily (equivalent to 1 g mesalazine daily) inserted into the rectum.

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

Method of administration
For rectal administration only.
Asacol 1 g Suppositories should be administered preferably at bedtime.
Treatment with Asacol 1 g Suppositories must be administered regularly and consistently, because only in this way can healing be successfully achieved.

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

4.3 Contraindications

Asacol 1 g Suppositories are contraindicated in patients with:
- known hypersensitivity to salicylates or to the excipient 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.

Asacol 1 g Suppositories should not be used in patients with impaired renal function.
Mesalazine-induced renal toxicity should be considered if renal function deteriorates during treatment.

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.

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 pulmonary disease, in particular asthma, should be very carefully monitored during a course of treatment with Asacol 1 g Suppositories.

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 Asacol 1 g Suppositories. Should Asacol 1 g Suppositories cause acute intolerance reactions such as abdominal cramps, acute abdominal pain, fever, severe headache and rash, therapy should be discontinued immediately.

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).

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.

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 Asacol 1 g Suppositories 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, 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.
Asacol 1 g 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, Asacol 1 g Suppositories should only be used during breastfeeding if the potential benefit outweighs the possible risk. If the infant develops diarrhoea, breastfeeding should be discontinued.

4.7 Effects on ability to drive and use machines

Asacol 1 g Suppositories have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

In clinical studies involving 248 participants, approximately 3% experienced adverse reactions while receiving mesalazine 1 g suppositories. The most commonly reported ADRs were headache, in approximately 0.8%, and gastrointestinal side effects (constipation in approximately 0.8%; nausea, vomiting and abdominal pain in 0.4% each).

The following side effects have been reported with the use of mesalazine:

Organ Class System	**Frequency According to MedDRA Convention**		
	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*

Organ Class System	Frequency According to MedDRA Convention		
	Rare (≥ 1/10,000; <1/1,000)	**Very rare (<1/10,000)**	**Not known (cannot be estimated from the available data)**
Skin and subcutaneous tissue disorders	Photosensitivity	Alopecia	Drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), and 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 listed in Appendix V.

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

Clinical efficacy and safety
Clinical efficacy and safety of mesalazine 1 g suppositories was evaluated in a multicentre phase III study, which included 403 patients with endoscopically and histologically confirmed mild to moderately active ulcerative proctitis. The mean disease activity index (DAI) at base line was 6.2 ± 1.5 (range: 3 – 10). Patients were randomised to treatment with one mesalazine 1 g suppository (1 g OD group) or 3 suppositories containing 0.5 g mesalazine (0.5 g TID group) per day for 6 weeks. The primary efficacy variable was clinical remission defined as DAI < 4 at the final visit or withdrawal. At the final per protocol analysis, 87.9% of the patients in the 1 g OD group and 90.7% of the 0.5 g TID group were in clinical remission (Intention-to-treat analysis: 1 g OD group: 84.0%; 0.5 g TID group: 84.7%). The mean change in DAI from baseline was -4.7 in both treatment groups. No drug-related serious AEs occurred.

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.

Mesalazine 1 g suppositories specific
Distribution
Scintigraphic studies with a similar medicinal product, technetium-labelled mesalazine 500 mg suppositories showed peak spread of the suppository that had melted due to body temperature after 2 – 3 hours. The spread was limited primarily to the rectum and rectosigmoid junction. It is assumed that mesalazine 1 g suppositories act very similar and thus are particularly suitable for treating proctitis (ulcerative colitis of the rectum).

Absorption
In healthy subjects and in fasting conditions, mean peak plasma concentrations of 5-ASA after a single rectal dose of 1g mesalazine suppository were 192 ± 125 ng/ml (range 19 –557 ng/ml), those of the main metabolite N-Ac-5-ASA were 402 ± 211 ng/ml (range 57 – 1070 ng/ml). Time to reach the peak plasma concentration of 5-ASA was 7.1 ±4.9 h (range 0.3 – 24 h).

Elimination
In healthy subjects and in fasting conditions, after a single rectal dose of 1 g mesalazine suppository approx. 14 % of the administered 5-ASA dose were recovered in the urine during 48 hours.

5.3 Preclinical safety data

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

Hard fat

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in the original container in order to protect contents from light.
Do not store above 30°C.

6.5 Nature and contents of container

Container (strip): PVC/polyethylene film
Package sizes: 10, 20, 30, 60, 90
Not all pack sizes may be marketed.

6.6 Special precautions for disposal <and other handling>

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

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2025-05-23

Detailed information on this medicinal product is available on the website of {name of MS Agency (link)}