SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Salcrozine 500 mg suppositories

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains 500 mg of mesalazine.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suppository

Torpedo-shaped suppository with greyish-white to slightly violet-reddish colour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Salcrozine is indicated in adults in distal Ulcerative Colitis (proctitis) for the:

- Treatment of mild or moderate acute exacerbations.
- Maintenance of remission.

4.2 Posology and method of administration

Posology

Individual dose adjustments should be done according to the physician's criteria, depending on the patient's characteristics and intensity of symptoms.

The recommended dose in adults in distal Ulcerative Colitis (proctitis) is:

- Treatment of mild or moderate acute exacerbations: one suppository twice or thrice daily (corresponding to a daily dose of 1000-1500 mg of mesalazine).

- Maintenance of remission: one suppository once or twice daily (corresponding to a daily dose of 500-1000 mg of mesalazine).

Elderly

No studies have been carried out. Administration of this medicine in the elderly must be performed with caution and always limited to patients with normal renal function.

Paediatric population

The safety and efficacy of Mesalazine in children and adolescents has not been established. Salcrozine is not recommended to be given to children and adolescents. Do not administer to children 5 years or less.

Method of administration:

Salcrozine should be used regularly and consistently, either during the acute phase or during the long-term therapy of the maintenance phase, to achieve the intended effect.

It is recommended to empty the bowel before administration of the suppository.

Suppositories should be introduced with the patient lying on the left side, and it is advisable to remain in this position for about 1 hour.

Suppositories should be introduced deeply into the anus and should be retained in the rectum for 1-3 hours to increase the efficacy.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Pre-existing hypersensitivity to salicylic acid and its derivatives.
- Severe renal impairment and severe liver impairment.

4.4 Special warnings and precautions for use

Therapy with Salcrozine should be performed under medical supervision.

- Blood tests (complete blood count, liver function parameters such as transaminases, creatinine) and urine tests, should be performed two weeks after starting therapy and at intervals every 4 weeks for 3 months. If the findings are normal, follow up tests should be carried out every 3 months. If additional symptoms appear the tests should be performed immediately.

- As 5-ASA is eliminated mainly by acetylation and subsequent urinary excretion, patients with impaired liver function or renal failure should be closely monitored, so it is advisable to perform liver and renal function tests before instituting treatment and regularly during it. Treatment with Salcrozine should be stopped immediately if there is evidence of renal deterioration. In patients who develop renal impairment during treatment, mesalazine-induced nephrotoxicity should be suspected.

- 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.

- There have been reports of increases in liver enzyme levels in patients taking preparations with mesalazine. Liver function should be evaluated before and during treatment according to medical criteria. Caution is advised if Salcrozine is given to patients with hepatic impairment. (see 4.3 Contraindications).

- In patients with a history of hypersensitivity to sulfasalazine, Salcrozine therapy should also be performed under close medical supervision. If acute signs of intolerance, such as spasms, acute abdominal pain, fever, headache and severe skin rash occur, therapy should be discontinued immediately.

- In patients with respiratory disease, in particular asthma, strict medical monitoring is recommended during mesalazine therapy.

- Cardiac hypersensitivity reactions (myocarditis, and pericarditis) induced by mesalazine have been rarely reported. They are generally rapidly reversible on discontinuation of treatment, but uncertainty about the mechanism (direct toxicity or hypersensitivity) formally contraindicates any reintroduction.

- Serious blood dyscrasias have been reported very rarely with mesalazine. Concomitant treatment with mesalazine may increase the risk of blood dyscrasia in patients receiving azathioprine or 6-mercaptopurine. Treatment should be discontinued if there is suspicion or certainty of occurrence of these adverse reactions.

- In rare occasions, serious blood dyscrasias have been reported after treatment with mesalazine. Haematological investigations should be performed if patient suffering unexplained haemorrhages, bruises, purpura, anaemia, fever or pharyngolaryngeal pain. Treatment with this medicine should be discontinued in case of suspected blood dyscrasia (see sections 4.3 and 4.5).

- Caution is recommended when treating patients with active gastric or duodenal ulcer.

- 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.

- 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).

- 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.

4.5 Interaction with other medicinal products and other forms of interaction

In common with other salicylates, mesalazine can:

- Reduce the anticoagulant activity of anticoagulants derived from coumarin, such as warfarin.
- Enhance the glucose-lowering effects of sulfonylureas.
- Antagonize the uricosuric effects of probenecid and sulfinpyrazone.
- Express the toxicity of salicylates at lower doses than usual when administered with furosemide due to competition for renal excretion sites.
- Increase the risk of adverse renal reactions with the concomitant use of known nephrotoxic agents, including nonsteroidal anti-inflammatory drugs (NSAIDs) and azathioprine.
- Increase the myelosuppressive effects of azathioprine, 6-mercaptopurine or thioguanine. Caution is advised in patients treated with azathioprine, 6-mercaptopurine or thioguanine and mesalazine since it may increase the possibility of blood dyscrasias. The haematological parameters (especially leukocytes and thrombocytes) should be monitored regularly, especially at the beginning of such a therapeutic combination.
- Decrease the natriuretic effect of spironolactone.
- Mesalazine may delay the excretion of methotrexate.

4.6 Fertility, pregnancy and lactation

Mesalazine should not be used during pregnancy and lactation except when the potential benefits of the treatment outweigh the possible hazards in the opinion of the physician. The underlying condition itself (Inflammatory bowel disease (IBD)) may increase risks for the pregnancy outcome.

Pregnancy:

Mesalazine is known to cross the placental barrier and its concentration in umbilical cord plasma is lower than the concentration in maternal plasma. The metabolite acetyl-mesalazine is found at similar concentrations in umbilical cord and maternal plasma. Animal studies on oral mesalazine do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or postnatal development. There are no adequate and well controlled studies of Salcrozine use in pregnant women. Limited published human data on mesalazine show no increase in the overall rate of congenital malformations. Some data show an increased rate of preterm birth, stillbirth, and low birth weight; however, these adverse pregnancy outcomes are also associated with active inflammatory bowel disease.

Blood disorders (leukopenia, thrombocytopenia, anaemia) have been reported in new-borns of mothers being treated with mesalazine.

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.

Breast-feeding:

Mesalazine is excreted in breast milk. The mesalazine concentration in breast milk is lower than in maternal blood, whereas the metabolite acetyl-mesalazine appears in similar or increased concentrations. No controlled studies with Salcrozine during breast-feeding have been carried out. Only limited experience during lactation in women after oral application is available to date. Hypersensitivity reactions like diarrhoea cannot be excluded. If the infant develops diarrhoea, breast-feeding should be discontinued.

Fertility:

Studies in animals have shown no effects of mesalazine on male and female fertility (see section 5.3). There are no or limited data on the effect of mesalazine on fertility in humans.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Salcrozine is considered to have negligible influence on these abilities.

4.8 Undesirable effects

Adverse reactions are listed in the table below by system organ class and frequency. Frequencies are defined as: very common (≥1/10); common (≥ 1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare: (<1/10,000); Not known (cannot be estimated from the available data).

System Organ Class	**MedDRA Frequency Convention**		
	Rare (≥1/10,000 to <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 (agranulocytosis, pancytopenia, leukopenia, neutropenia, thrombocytopenia, aplastic anaemia).	Hypereosinophilia
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 lung reactions (dyspnoea, cough, allergic alveolitis, eosinophilic pneumonia, lung infiltration, pneumonitis).	
Gastrointestinal disorders	Discomfort and abdominal pain, diarrhoea, flatulence, nausea, vomiting.	Acute pancreatitis. Worsening of colitis symptoms.	
Hepatobiliary disorders		Changes in liver function parameters (increase in transaminases and cholestasis parameters), hepatitis, cholestatic hepatitis.	
Skin and subcutaneous tissue disorders	Photosensitivity*	Alopecia. Erythema multiforme	Drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN)**
Musculoskeletal and connective tissue disorders		Myalgia, arthralgia.	

Renal and urinary disorders		Interstitial nephritis, renal insufficiency, nephrotic syndrome.	Nephrolithiasis
Reproductive system and breast disorders		Oligospermia (reversible).	

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

** Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in association with mesalazine treatment (see section 4.4).

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 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

No cases of overdose toxicity have been reported. There are rare data on overdosage (e.g., intended suicide with high oral doses of mesalazine), which do not indicate renal or hepatic toxicity.

Under normal circumstances the absorption of mesalazine by the colon is limited.

Since there is no specific antidote, in case of overdose, treatment should be 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

Although the anti-inflammatory mechanism of action of 5-ASA is unknown, several possibilities are considered:

- Inhibition of prostaglandin synthesis (cyclooxygenase inhibition pathway), reducing inflammatory prostaglandin output.
- Inhibition of chemotactic leukotriene synthesis (lipooxygenase inhibition pathway), therefore reducing inflammation.
- Inhibition of chemotaxis of macrophages and neutrophils in the swollen tissue.

The most recent data suggest that 5-ASA is a biological antioxidant and its activity is based on the uptake of oxygen free radicals.

5.2 Pharmacokinetic properties

Absorption

After administration of suppositories of 500 mg of mesalazine, three times a day to patients with ulcerative colitis, it produces constant plasma concentrations of mesalazine (5-ASA) and N-Acetyl-5-ASA of 0.10 µg/ml and 0.50 µg/ml, respectively. Systemic availability, measured based on urinary recovery, represents 13 %. Systemic availability for patients was only slightly higher than for healthy volunteers (13 % versus 10.8 %).

Biotransformation

Acetylation of 5-ASA occurs in the liver and colon wall, regardless of acetylator status. It appears that the acetylation process is saturable; however, at therapeutic doses (250-500 mg) neither the peak plasma concentration nor the area under the plasma concentration versus time curve for 5-ASA showed any deviation from steady-state dose linearity.

Elimination

After rectal administration, 5-ASA is eliminated unchanged, mainly in the faeces.

5.3 Preclinical safety data

Non clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity, carcinogenic and toxicity to reproduction and development.

Renal toxicity has been seen in repeated-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

4 years.

6.4 Special precautions for storage

Do not store above 30°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

Suppositories are packaged in PVC/LDPE strips.

Each pack contains 12, 24, 30, 60 and 100 suppositories.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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48940 Leioa (Bizkaia)
Spain

8 MARKETING AUTHORISATION NUMBER(S)

PL 18945/0010

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17/01/2023

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03/11/2025