Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Galtasa 1000 mg gastro-resistant tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet of Galtasa contains 1000 mg of mesalazine.

Excipient with known effect
Each gastro-resistant tablet contains 4.26 mmols of sodium (98 mg).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gastro-resistant tablet.

Oblong tablets of 22 mm of length and 11 mm of diameter, with homogeneous gastro-resistant orange coloured coating.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Galtasa is indicated for:

- Treatment of the acute phase of mild or moderate ulcerative colitis.
- Maintenance treatment of remission in ulcerative colitis.

4.2 Posology and method of administration

Posology
During the acute inflammatory phase and in long-term maintenance therapy, the patient must accurately follow the treatment established by the doctor to ensure the intended therapeutic effect.

Adults
The dosage should be adjusted according to patient response. The following dosage is recommended:

- Ulcerative colitis (acute phase): 1.5 - 4 g mesalazine daily, once daily or in divided doses. The dose of 4 g is recommended for patients who do not respond to lower doses of mesalazine. The effect of the treatment should be evaluated 8 weeks after initiation.
- Ulcerative colitis (maintenance): 1.5 – 3 g mesalazine daily, once daily or in divided doses. The dose of 3 g is recommended for patients who do not respond to lower doses of mesalazine and for those who required higher doses during acute phase.

Galtasa 500 mg gastro-resistant tablets may be used to adjust the dose.

Elderly
No studies have been carried out. Administration of Galtasa 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 aged younger than 18 years of age has not been established. Do not administer to children under 5 years.

Method of administration

Oral use.
The tablets must be administered before meals and must be taken whole with some fluid.
Galtasa gastro-resistant tablets consist of a mesalazine-containing core and an inert coating. Modified release of mesalazine is dependent on an intact coating. For this reason, the tablets should not be divided, chewed or crushed.

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 impairment of hepatic and renal function
- Haemorrhagic diathesis.

4.4 Special warnings and precautions for use

- Patients with severe liver or renal insufficiency. As mesalazine, also known as 5-aminosalicylic acid (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 Galtasa 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 Galtasa is given to patients with hepatic impairment (see 4.3 Contraindications).

- Patients with a history of hypersensitivity to sulfasalazine should be kept under close medical surveillance. In case of acute intolerance reactions, such as abdominal cramps, acute abdominal pain, fever, severe headache and rashes, treatment should be discontinued immediately.

- Patients with pulmonary diseases, particularly asthma, should be carefully monitored during treatment.

- Cardiac hypersensitivity reactions induced by mesalazine (myo- and pericarditis) have been rarely reported. Caution should beexercised when treating patients with conditions that predispose them tomyocarditis or pericarditis, with mesalazine. If there is a suspicion of acardiac hypersensitivity reaction, products containing mesalazine should not bere-administered.

- In rare occasions, serious blood dyscrasias have been reported after treatment with mesalazine. Hematological investigations should be performed if patient suffering unexplained haemorrhages, bruises, purpura, anaemia, fever or pharyngolaryngeal pain. Treatment with Galtasa 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.

- Galtasa gastro-resistant tablets should not be administered concomitantly with lactulose-type laxatives or the like, since it lowers the pH of the faeces and may prevent the release of the active ingredient.

- Blood tests (differential blood count; liver function tests such as ALT and serum creatinine) should be determined prior to and during treatment, at the discretion of the treating physician.

- 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).

This medicinal product contains 98 mg sodium per gastro-resistant tablet, equivalent to 5 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

The maximum daily dose of this product (4 g) is equivalent to 20 % of the WHO recommended maximum daily intake for sodium.

Galtasa is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

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.
- Lactulose-type laxatives or similar can prevent the release of mesalazine from the gastro-resistant tablet, which would reduce its effect (see section 4.4 Special warnings and special precautions for use).

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 mesalazine 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 (2-4 g, 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 mesalazine during breast-feeding have been carried out. There is limited data available on the use of oral mesalazine in breast-feeding women.Hypersensitivity reactions like diarrhoea can not 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. Galtasa 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) and not known (cannot be estimated from the available data).

Organ Class System	***Frequency According to MedDRA 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).	
Immune system disorders		Hypersensitivity reactions such as allergic exanthema, drug fever, lupus erythematosus syndrome, pancolitis.	
Nervous system disorders	Headache, dizziness.	Peripheral neuropathy.	
Cardiac disorders	Myocarditis, pericarditis.		
Respiratory, thoracic and mediastinal disorders		Allergic lung reactions (dyspnoea, cough, allergic alveolitis, eosinophilic pneumonia, lung infiltration, pneumonitis).	
Gastrointestinal disorders	Discomfort, nausea, abdominal pain, diarrhoea, flatulence, 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 have been reported in patients with pre-existing skin conditions, such as atopic dermatitis and atopic eczema.

** 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).

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 HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Mesalazine is an aminosalicylate, and signs of salicylate toxicity include tinnitus, vertigo, headache, confusion, drowsiness, pulmonary oedema, dehydration as a result of sweating, diarrhoea and vomiting, hypoglycaemia, hyperventilation, disruption of electrolyte balance and blood-pH and hyperthermia.

There is no specific antidote for mesalazine overdose and treatment is symptomatic and supportive. Conventional therapy for salicylate toxicity may be beneficial in the event of acute overdosage. Hypoglycaemia, fluid and electrolyte imbalance should be corrected by the administration of appropriate therapy. Adequate renal function should be maintained.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Aminosalicylic acid and similar, code ATC: 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
In healthy fasting subjects, maximum plasma levels with delayed release forms are obtained at 6 hours after intake, with a peak plasma concentration of 1.98 µg/mL of 5-ASA.

Biotransformation
Acetylation of 5-ASA occurs in the liver and the colon wall, regardless of the 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 curve of plasma concentration vs. time for 5-ASA evidenced any deviation from linearity of the dose in the steady state.

Elimination
After oral administration, 5-ASA is cleared at a high percentage as Ac-5-ASA both in urine and in faeces. In fact, over 90 % of the drug identified in urine is in metabolite form.

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

Core:
Sodium carbonate, anhydrous
Glycine
Povidone
Cellulose, microcrystalline
Croscarmellose sodium
Silica, colloidal anhydrous
Calcium stearate

Coating:
Methacrylic acid Ethyl acrylate copolymer (1:1) dispersion 30 per cent
Methacrylic acid Methyl methacrylate copolymer (1:1)
Methacrylic acid Methyl methacrylate copolymer (1:2)
Dibutyl sebacate
Talc
Titanium dioxide (E-171)
Macrogol
Yellow iron oxide (E-172)
Red iron oxide (E-172)
Povidone

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PVDC-Aluminium blister packed in cartons containing 60 or 100 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Faes Farma S.A.
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8 MARKETING AUTHORISATION NUMBER

PA0864/001/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 18th August 2024

10 DATE OF REVISION OF THE TEXT

January 2024