SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Mecolzine 500 mg gastro-resistant tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet of Mecolzine contains 500 mg of mesalazine.

Excipients with known effect
Each gastro-resistant tablet contains 2.13 mmol of Na (49 mg)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant tablet.

Mecolzine is supplied in oblong orange gastro-resistant tablets.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Mecolzine tablets is indicated in:

- 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 of mesalazine/day, once a day or in divided doses. The 4 g dose is recommended for patients who do not respond to lower doses of mesalazine. The effect of treatment must be assessed 8 weeks after starting it.
- Ulcerative colitis (maintenance): 1.5-3.0 g of mesalazine/day, once a day or in divided doses. The 3 g dose is recommended for patients who do not respond to

lower doses if mesalazine and for patients who required higher doses during the acute phase.

Elderly
No studies have been performed. Administration of Mecolzine 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 under 18 years of age has not been established. Do not administer to children under 5 years of age.

Method of administration

For oral administration.
The tablets must be administered before meals and must be taken whole with some fluid.

4.3. Contraindications

- Hypersensitivity to the active substance or to any of its excipients listed in section 6.1.
- History of hypersensitivity to salicylic acid and its derivatives.
- Severely impaired hepatic and renal function.
- Haemorrhagic diathesis.

4.4. Special warnings and precautions for use

Administration of Mecolzine must be performed with caution in the following cases:

- Patients with severe hepatic or renal impairment. As 5-ASA is cleared 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 Mecolzine should be discontinued immediately if there is evidence of renal deterioration. In patients who develop renal failure during treatment, mesalazine-induced nephrotoxicity may be suspected.

- Cases of nephrolithiasis have been reported with the use of mesalazine, including the occurrence of calculi with a 100% mesalazine content. It is recommended to ensure sufficient fluid intake during treatment.

- There have been reports of increased liver enzyme levels in patients taking medicines containing mesalazine. Liver function should be assessed before and during treatment according to medical criteria. Caution is advised if Mecolzine is administered 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 the event of acute intolerance reactions, such as abdominal cramps, acute abdominal pain, fever, severe headache and rash, treatment should be discontinued immediately.

- Patients with lung disease, particularly asthma, should be monitored carefully during treatment.

- Rarely, mesalazine-induced cardiac hypersensitivity reactions (myocarditis and pericarditis) have been reported. Caution should be exercised when treating patients who have conditions that predispose them to myocarditis or pericarditis with mesalazine. If a cardiac hypersensitivity reaction is suspected, products containing mesalazine should not be administered again.

- Rarely, serious blood dyscrasias have been reported after treatment with mesalazine. Haematological investigations should be performed if the patient suffers from unexplained bleeding, bruising, purpura, anaemia, fever or pharyngolaryngeal pain. Treatment with Mecolzine should be discontinued if blood dyscrasia is suspected (see sections 4.3 and 4.5).

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

- Mecolzine gastro-resistant tablets should not be administered concomitantly with laxatives such as lactulose or similar as this reduces the pH of faeces and can impede release of the drug substance.

- Blood tests (blood differential; liver function tests such as ALT and serum creatinine) should be determined before and during treatment, according to the decision of the treating doctor.

- Severe cutaneous adverse reactions, including drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been observed with mesalazine treatment. Administration of mesalazine should be discontinued at the first signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions or any other signs 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 (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.

Warnings about excipients

This medicinal product contains 49 mg of Na per gastro-resistant tablet, equivalent to 2.5% of the maximum daily intake of 2 g of sodium recommended by the WHO for adults.

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

This medicine has a high sodium content, which should be taken into account in patients with low-sodium diets.

4.5. Interaction with other medicinal products and other forms of interaction

As with other salicylates, mesalazine can:

- Reduce the anticoagulant activity of coumarin-derivative anticoagulants such as warfarin.
- Increase the hypoglycaemic effects of sulphonylureas.
- Antagonise the uricosuric effects of probenecid and sulphinpyrazone.
- Express toxicity of salicylates at doses lower than usual when administered concomitantly with furosemide due to the competition for renal excretion sites.
- Increase the risk of renal adverse reactions with concomitant use of known nephrotoxic agents, including non-steroidal 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 as it may increase the possibility of blood dyscrasias. The patient's haematological parameters (especially leukocytes and thrombocytes) should be monitored regularly, especially at the beginning of this therapeutic combination.
- Reduce the natriuretic effect of spironolactone.
- Mesalazine can delay methotrexate excretion.
- Laxatives such as lactulose or similar can prevent mesalazine release from the tablet thereby reducing 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 breast-feeding, except when the doctor considers that the potential benefits of treatment outweigh the possible risks. The underlying condition itself (Inflammatory Bowel Disease (IBD)) may increase the risks to 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 acetylmesalazine is found in similar concentrations in the umbilical cord and in maternal plasma. Animal studies with oral mesalazine do not indicate any direct or indirect adverse effects with respect to pregnancy, embryo-foetal development, delivery or postnatal development.

There are no adequate, well-controlled studies on the use of mesalazine in pregnant women. The limited published human data on mesalazine do not show an increase in the overall rate of congenital malformations.

Some data show an increase in the 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 newborns of mothers treated with mesalazine.

In a single case, after prolonged use of a high dose of mesalazine (2-4 g, orally) during pregnancy, renal impairment in the neonate was reported.

Breast-feeding

Mesalazine is excreted in breast milk. The concentration of mesalazine in breast milk is lower than in maternal blood, while the metabolite acetylmesalazine appears in a higher or similar concentration. No controlled studies have been performed with mesalazine during breast-feeding.

To date, there is only limited experience during breast-feeding in women after oral application.

Hypersensitivity reactions such as diarrhoea cannot be ruled out. If the infant experiences diarrhoea, breast-feeding should be discontinued.

Fertility
Animal studies have not shown effects of mesalazine on male or 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 have been performed on effects on the ability to drive and use machines. Mecolzine is considered to have no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

The adverse reactions are listed in the following table by system organ class and frequency. The frequencies are defined as follows: Very frequent (≥1/10); frequent (≥1/100, <1/10); low frequency (≥1/1,000, <1/100); rare (≥1/10,000 and <1/1,000); very rare (<1/10,000) and 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)	
Immune system disorders		Hypersensitivity reactions such as allergic rash, 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		Pulmonary allergic reactions (dyspnoea, cough, allergic alveolitis, eosinophilic pneumonia, pulmonary infiltration, pneumonitis, etc.)	
Gastrointestinal disorders	General malaise, nausea, abdominal pain, diarrhoea, flatulence, vomiting	Acute pancreatitis. Worsening of colitis symptoms	
Hepatobiliary disorders		Changes in liver function parameters (increased 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) and toxic epidermal necrolysis (TEN)**
Musculoskeletal and connective tissue disorders		Myalgia, arthralgia	
Renal and urinary disorders		Interstitial nephritis, Renal impairment, Nephrotic syndrome	Nephrolithiasis
Reproductive system and breast disorders		Oligospermia (reversible)	

*Photosensitivity

Severe reactions have been notified 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 observed in association with the administration of mesalazine (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 National Pharmacovigilance System for Medicinal Products for Human Use.

4.9. Overdose

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

There is no specific antidote for mesalazine overdose and treatment consists of symptom and support measures. Conventional treatment for salicylate toxicity may be beneficial in case of acute overdose.

Hypoglycaemia and fluid and electrolyte imbalance should be corrected by administration of appropriate therapy. Adequate renal function should be maintained.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: 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 (lipoxygenase inhibition pathway), therefore reducing inflammation.
- Inhibition of chemotaxis of macrophages and neutrophils in the inflamed 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 the administration of oral doses of 500 mg of mesalazine three times a day to patients with ulcerative colitis, the steady-state mean plasma concentrations of 5-ASA and Ac-5-ASA (major metabolite) are 0.7 µg/ml and 1.2 µg/ml, respectively. The peak plasma levels with the delayed release forms are obtained at 5 hours post-administration. Recovery (at the highest dose) in urine (44%) and faeces (35%) shows that 5-ASA is available for its local and systemic action. In fasting healthy subjects, the peak plasma concentration of 1.3 µg/ml and 2.3 µg/ml of 5-ASA and Ac-5-ASA, respectively, was obtained at 6 hours post-administration.

Metabolism or 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

The results of preclinical experimentation, based on conventional drug safety, genotoxicity, carcinogenicity or reproductive toxicity studies, did not reveal any special risks for humans.

Renal toxicity has been observed in repeated-dose toxicity studies with the administration of high doses of mesalazine. The clinical relevance of this finding is not known.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Core:
Anhydrous sodium carbonate
Glycine
Povidone
Microcrystalline cellulose
Croscarmellose sodium
Anhydrous colloidal silica
Calcium stearate

Coating:
Methacrylic acid and ethyl acrylate copolymer (1:1) 30% dispersion
Methacrylic acid and methyl methacrylate copolymer (1:1)
Methacrylic acid and methyl methacrylate copolymer (1:2)
Dibutyl sebacate
Povidone
Talc
Titanium dioxide (E-171)
Macrogol
Yellow iron oxide (E-172)
Red iron oxide (E-172)
Isopropyl alcohol.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

4 years.

6.4. Special precautions for storage

Store below 30ºC.

6.5. Nature and contents of container

Mecolzine 500 mg is supplied in OPA/Al/PVC/Al blisters in packs containing 100 gastro-resistant tablets.

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

Eurodrug Laboratories (M) Sdn. Bhd.
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Jalan USJ 25/1C, 47650 Subang Jaya, Selangor, Malaysia.

8. DATE OF REVISION OF THE TEXT

May 2026