

NEW ZEALAND DATA SHEET

1 ASAMAX® 500

Mesalazine (5-aminosalicylic acid) 500 mg suppositories

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Asamax 500 suppository 500 mg: a yellow white to orange grey torpedo shaped suppository with smooth surface of fatty consistency, containing 500 mg mesalazine (5-aminosalicylic acid). Length approx. 3 cm, average weight: 2400 mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suppository

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of ulcerative proctitis.

4.2 Dose and method of administration

The dosage should be adapted to the severity of the disorder. For adults and older children it is generally recommended to take 1 g to 2 g daily in divided doses.

A visit to the toilet is recommended before administration of suppositories.

The suppository is to be inserted into the rectum via the anus. This is easiest when the patient is lying down relaxed on one side with knees pulled up slightly.

4.3 Contraindications

Hypersensitivity to mesalazine, any other component of the product, or salicylates.

Severe liver and/or renal impairment.

Increased tendency to bleeding.

Active ulcers of the stomach and/or duodenum.

4.4 Special warnings and precautions for use

Most patients who are intolerant or hypersensitive to sulfasalazine are able to take Asamax without risk of similar reactions. However, caution is recommended when treating patients allergic to sulfasalazine (risk of allergy to salicylates).

Caution is recommended in patients with impaired liver function. Liver function parameters like alanine aminotransferase (ALT) or aspartate transaminase (AST) should be assessed prior to and during treatment, at the discretion of the treating physician. The medicine is not recommended for use in patients with renal impairment. Mesalazine-induced nephrotoxicity should be suspected in patients developing renal dysfunction during treatment. The renal function should be regularly monitored (e.g. serum creatinine), especially during the initial phase of treatment. The concurrent use of other known nephrotoxic agents, such as non-steroidal anti-inflammatory drugs (NSAIDs) and azathioprine, may increase the risk of renal reactions.

Mesalazine-induced cardiac hypersensitivity reactions (pleuropericarditis) and serious blood dyscrasias have rarely been reported with mesalazine. Concomitant treatment with mesalazine can increase the risk of dyscrasia in patients receiving azathioprine or 6-mercaptopurine. Treatment should be discontinued on suspicion or evidence of these adverse reactions.

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Asamax is not recommended for use in infants and toddlers under 2 years of age due to a lack of data on safety and/or efficacy.

As with all salicylic acid derivatives, special caution is recommended in patients with Chronic Non Specific Lung Disease (CNSLD) due to the potential for hypersensitivity reactions.

4.5 Interaction with other medicines and other forms of interaction

Mesalazine may increase the effect of sulfonylurea-derivatives in lowering levels of blood sugar; coumarin-induced gastrointestinal bleeding; and the toxicity of methotrexate.

The uricosurical effect of probenecid and sulfipyrazone and the diuretic effect of furosemide and spironolactone may be decreased by mesalazine. The anti-tuberculosis effect of rifampicin may be weakened. Theoretically, caution should be practiced in the case of concomitantly administered anti-coagulants.

4.6 Fertility, pregnancy and lactation

Mesalazine is a Pregnancy Category C medication (drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful but reversible effects on the human fetus or neonate without causing malformations).

Asamax should be used with caution during pregnancy and lactation and only if the in lowering levels of blood sugar; potential benefits outweigh the possible hazards.

Mesalazine is known to cross the placental barrier, but the limited data available on the use of this compound in pregnant women do not allow the assessment of possible noxious effects. No teratogenic effects have been observed in animal studies.

Mesalazine is excreted in breastmilk. The concentration is much lower than in maternal blood, whereas the metabolite - acetyl-mesalazine - appears in similar concentrations. There is limited experience of the use of oral mesalazine in lactating women.

4.7 Effects on ability to drive and use machines

Treatment with Asamax is unlikely to affect the ability to drive and/or use machines. When driving or operating machinery, the potential occurrence of dizziness or headache should be borne in mind.

4.8 Undesirable effects

The most frequent adverse reactions seen in clinical trials are diarrhoea (3%), nausea (3%), abdominal pain (3%), headache (3%), vomiting (1%) and rash (1%). Hypersensitivity reactions and drug fever may occasionally occur.

Following rectal administration local reactions such as pruritus, rectal discomfort and urge may occur.

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System Organ Class	Common >1/100, <1/10	Uncommon >1/1000, 1/100	Rare >1/10,000, <1/1000	Very rare <1/10,000
Blood and the lymphatic system disorders				Eosinophilia (as part of an allergic reaction), leucopenia (including granulocytopenia and neutropenia), thrombocytopenia, agranulocytosis, bone marrow depression, increased methaemoglobin levels
Immune system disorders				Pancolitis, hypersensitivity reaction
Nervous system disorders	Dizziness			Peripheral neuropathy
Cardiac disorders				Pleuropericarditis*
Respiratory, thoracic and mediastinal disorders				Allergic and fibrotic lung reactions (including dyspnoea, coughing, bronchospasm, allergic alveolitis, eosinophilic pneumonia, interstitial lung disease, pulmonary infiltration, pneumonitis, pleuritis)
Gastrointestinal disorders	Nausea, diarrhoea, vomiting abdominal pain			Pancreatitis*
Hepato-biliary disorders				Hepatitis*, cholestatic hepatitis, cirrhosis, hepatic failure
Skin and subcutaneous tissue disorders			Allergic dermatitis	
Musculoskeletal and connective tissue disorders				Myalgia, arthralgia, lupus-like syndrome
Reproductive system disorders				Oligospermia (reversible)
Psychiatric disorders	Mood swings			

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System Organ Class	Common >1/100, <1/10	Uncommon >1/1000, 1/100	Rare >1/10,000, <1/1000	Very rare <1/10,000
Renal and urinary disorders				Nephritis interstitial*, nephrotic syndrome, renal failure
General disorders and administration site conditions	Headache		Fever	
Investigations				Blood methaemoglobin present

(*) The mechanism of pleuropericarditis, pancreatitis, hepatitis, or interstitial nephritis caused by Asamax is unknown, but it could be of an allergic origin.

It is important to note that several of these disorders also can be attributed to the inflammatory bowel disease itself.

4.9 Overdose

Acute experience in animals

Single oral doses of mesalazine up to 5 g/kg in pigs or a single intravenous dose of mesalazine at 920 mg/kg in rats were not lethal.

Human experience

No cases of overdose have been reported.

Management of overdose in humans

Symptomatic treatment at hospital. Close monitoring of renal function.

Contact the National Poisons Centre on 0800 POISON or 0800 764 766 for advice on management of an overdose.

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Intestinal anti-inflammatory agents (A07 EC02).

5.1 Pharmacodynamic properties

It has been established that mesalazine is the active component of sulfasalazine, which is used for the treatment of ulcerative colitis and Crohn's disease.

Based on clinical results, the therapeutic value of mesalazine after oral or rectal administration appears to be due to local effect on the inflamed intestinal tissue, rather than to systemic effect.

Increased leucocyte migration, abnormal cytokine production, increased production of arachidonic acid metabolites, particularly leukotriene B₄, and increased free radical formation in the inflamed intestinal tissue are all present in patients with inflammatory bowel disease. Mesalazine has *in vitro* and *in vivo* pharmacological effects that inhibit leucocyte chemotaxis, decrease cytokine and leukotriene production, and scavenge for free radicals. It is currently unknown which, if any, of these mechanisms play a predominant role in the clinical efficacy of mesalazine.

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5.2 Pharmacokinetic properties

General characteristics of the active substance

Disposition and local availability

The therapeutic activity of mesalazine most likely depends on local contact of the medicine with the diseased area of the intestinal mucosa.

Asamax suppositories provide the distal part of the intestinal tract with high concentrations of mesalazine. Suppositories exert their local effect on the intestinal border of the rectum.

Absorption

The absorption following rectal administration is low, but depends on the dose, the formulation and the extent of spreading. Based on urine recoveries in healthy volunteers under steady-state conditions given a daily dose of 2 g (1 g x 2), approximately 10% of the dose is absorbed after administration of suppositories.

Distribution

Mesalazine and acetyl-mesalazine do not cross the blood-brain barrier. Protein binding of mesalazine is approximately 50% and of acetyl-mesalazine about 80%.

After a gradual decrease, mesalazine will no longer be detectable 12 hours post-dose. The plasma concentration curve for acetyl-mesalazine follows the same pattern, but the concentrations are generally higher and the elimination is slower.

Biotransformation

Mesalazine is metabolised both pre-systemically by the intestinal mucosa and systemically in the liver to *N*-acetyl-mesalazine (acetyl-mesalazine). Some acetylation also occurs through the action of colonic bacteria. The acetylation seems to be independent of the acetylator phenotype of the patient.

Acetyl-mesalazine is thought to be clinically as well as toxicologically inactive, but this still needs final confirmation.

Elimination

The plasma half-life of pure mesalazine is approximately 1 hour and for acetyl-mesalazine several hours. Both substances are excreted with the urine and faeces. The urinary excretion consists mainly of acetyl-mesalazine.

Characteristics in patients

For use in patients with impaired liver and kidney functions, the resultant decrease in the rate of elimination and increased systemic concentration of mesalazine may constitute an increased risk of nephrotoxic adverse reactions.

5.3 Preclinical safety data

Definitive toxic effect on the kidney was demonstrated in all species. In general, the toxic doses exceed those used in humans by a factor of 5-10.

No significant toxicity associated with the gastrointestinal tract, liver, or haematopoietic system in animals has been observed.

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In vitro test systems and *in vivo* studies showed no evidence of mutagenic effects. Studies of the tumourigenic potential carried out in rats showed no evidence of any substance-related increase in the incidence of tumours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hard fat, cetyl alcohol and docusate sodium.

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years in original packaging

6.4 Special precautions for storage

Store in a dry place at room temperature (at or below 25°C) in original packaging. Keep out of reach of children.

6.5 Nature and contents of container

Asamax 500 suppositories 500 mg – Strip-packaging (PVC/LDPE) in cardboard boxes containing 30 suppositories.

6.6 Special precautions for disposal

None

7 MEDICINE SCHEDULE

Prescription Only Medicine.

8 SPONSOR

New Zealand distributor:

Seqirus (NZ) Ltd

PO Box 62 590

Greenlane

Auckland 1546

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Telephone: 0800 502 757

9 DATE OF FIRST APPROVAL

2 October 2008

10 DATE OF REVISION OF THE TEXT

22 February 2019

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Asamax® is a registered trademark of Astellas Pharma Europe B.V.

SUMMARY TABLE OF CHANGES

Section affected	Summary of new information
Sections 4.2, 4.4, 4.5, 4.6, 4.9, 5.1, 5.3	Reworded for improved readability
All sections	Revised in line with new Data Sheet format as per Medsafe Guideline
Section 8	Update to New Zealand distributor address