

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Antepsin 1g/5ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml dose contains 1 gram sucralfate.

Each 5ml dose also contains sodium propyl hydroxybenzoate (E217) 2.0mg and sodium methyl hydroxybenzoate (E219) 3.75mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension

White to off-white viscous suspension with an odour of aniseed/caramel.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Antepsin is indicated in adults and adolescents over 14 years old for the treatment of duodenal ulcer, gastric ulcer, chronic gastritis, and the prophylaxis of gastrointestinal haemorrhage from stress ulceration in seriously ill patients.

4.2 Posology and method of administration

For oral administration.

Antepsin must not be administered intravenously.

Duodenal ulcer, gastric ulcer, chronic gastritis:

Adults: The usual dose is 2 grams twice daily to be taken on rising and at bedtime, or 1 gram 4 times a day to be taken 1 hour before meals and at bedtime. Maximum daily dose: 8 grams.

Four to six weeks treatment is usually needed for ulcer healing, but up to twelve weeks may be necessary in resistant cases.

Antacids may be used as required for relief of pain, but should not be taken half an hour before or after Antepsin.

Paediatric population: The safety and efficacy of Antepsin in children under 14 years of age has not been established. Currently available data are described in section 5.1 but no recommendation on posology can be made.

Elderly: see below

Prophylaxis of gastrointestinal haemorrhage from stress ulceration:

Adults: The usual dose is 1 gram six times a day. A maximum dose of 8 grams daily should not be exceeded. Antacids may be used as required for relief of pain, but should not be taken half an hour before or after Antepsin.

Paediatric population

The safety and efficacy of Antepsin in children under 14 years of age has not been established. Currently available data are described in section 5.1

Elderly: There are no special dosage requirements for elderly patients but as with all medicines, the lowest effective dose should be used.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Antepsin must not be administered intravenously. Inadvertent intravenous administration of insoluble sucralfate and its insoluble excipients may induce fatal complications, including pulmonary and cerebral emboli. Other severe complications including aluminium intoxication are reported after intravenous administration.

The product should only be used with caution in patients with renal dysfunction, due to the possibility of increased aluminium absorption.

Sucralfate is not recommended for use in individuals on dialysis.

In patients with severe or chronic renal impairment, Antepsin should be used with extreme caution and only for short-term treatment. Small amounts of aluminium are absorbed through the gastrointestinal tract and aluminium may accumulate. Aluminium osteodystrophy, osteomalacia, encephalopathy, and anaemia have been reported in patients with chronic renal impairment. For patients with impairment of renal function, laboratory testing such as aluminium, phosphate, calcium, and alkaline phosphatase is recommended to be periodically performed due to excretion impairment.

The concomitant use of other aluminium containing medications is not recommended in view of the enhanced potential for aluminium absorption and toxicity.

Contains sodium methyl parahydroxybenzoate (E219) and sodium propyl parahydroxybenzoate (E217) which may cause allergic reactions (possibly delayed).

Bezoars have been reported after administration of sucralfate mainly to severely ill patients in intensive care units. The majority of these patients (including neonates in whom sucralfate is not recommended) had underlying conditions that may predispose to bezoar formation (such as delayed gastric emptying due to surgery, drug therapy or diseases that reduce motility), or were receiving concomitant enteral tube feeding.

Paediatric Population

Antepsin is not recommended for use in children under 14 years of age due to insufficient data on safety and efficacy.

4.5 Interaction with other medicinal products and other forms of interactions

Concomitant administration of Antepsin may reduce the bioavailability of certain drugs including fluoroquinolones such as ciprofloxacin and norfloxacin, tetracycline, ketoconazole, sulpiride, digoxin, warfarin, phenytoin, theophylline, levothyroxine, quinidine and H₂ antagonists. The bioavailability of these agents may be restored by separating the administration of these agents from Antepsin by two hours. This interaction appears to be non systemic in origin presumably resulting from these agents being bound by Antepsin in the gastrointestinal tract. Because of the potential of Antepsin to alter the absorption of some drugs from the gastrointestinal tract, the separate administration of Antepsin from that of other agents should be considered when alterations in bioavailability are felt to be critical for concomitantly administered drugs.

Sucralfate should not be co-administered with citrate preparations. Co-administration of citrate preparations with sucralfate may increase the blood concentrations of aluminium. The mechanism may be due to chelation of aluminium, which is assumed to increase its absorption.

The administration of Antepsin Suspension and enteral feeds by nasogastric tube should be separated by one hour in patients receiving Antepsin Suspension for the prophylaxis of stress ulceration. In rare cases bezoar formation has been reported when Antepsin and enteral feeds have been given too closely together.

4.6 Fertility, pregnancy and lactation

Preganacy: Teratogenicity studies in mice, rats and rabbits at dose up to 50 times the human dose have revealed no evidence of harm to the foetus.

Safety in pregnant women has not been established and Antepsin should be used during pregnancy only if clearly needed.

Lactation:

It is not known whether this drug is excreted in human milk. Caution should be exercised when Antepsin is administered to breast-feeding women.

4.7 Effects on ability to drive and use machines

Do not drive if you feel dizzy or drowsy.

4.8 Undesirable effects

Tabulated list of adverse reactions

Immune system disorders
Nervous system disorders
Ear and labyrinth disorders
Gastrointestinal disorders

Skin and subcutaneous tissue disorders
Musculoskeletal and connective tissue disorders
Injury, poisoning and procedural complications

Not known (cannot be estimated from the available data)	Anaphylactic reaction including pruritus, urticaria, oedema, dyspnoea
Not known (cannot be estimated from the available data)	Dizziness, headache, drowsiness
Not known (cannot be estimated from the available data)	Vertigo
Common ($\geq 1\%$ and $<10\%$);	Constipation
Uncommon ($\geq 0.1\%$ and $<1\%$)	Dry mouth, nausea,
Rare ($\geq 0.01\%$ and $<0.1\%$)	Bezoar formation ¹
Not known (cannot be estimated from the available data)	Diarrhoea, vomiting, gastric discomfort, indigestion, flatulence
Rare ($\geq 0.01\%$ and $<0.1\%$)	Rash
Not known (cannot be estimated from the available data)	Back pain
Not known (cannot be estimated from the available data)	Osteodystrophy ² , osteomalacia ² , encephalopathy ² , anaemia ²

¹Reported in patients with impaired gastric emptying, patients with enteral tube feeding or low birth weight infants

²Reported in patients with chronic renal impairment

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.

Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

In a clinical trial on healthy men of overdose with sucralfate, most cases remained asymptomatic, but symptoms of abdominal pain, nausea, and vomiting were reported in a few cases.

Acute oral toxicity studies in animals, using doses up to 12 g/kg body weight, could not find a lethal dose. Risks associated with overdose, should, therefore, be minimal.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Alimentary tract and metabolism, ATC code: A02B X02

Mechanism of action

The action of Antepsin is non-systemic as the drug is only minimally absorbed from the gastro-intestinal tract. The small amounts that are absorbed are excreted primarily in the urine. Antepsin exerts a generalised cytoprotective effect by preventing gastro-intestinal mucosal injury.

Studies in humans and animal models show that Antepsin forms an ulcer adherent complex with the proteinaceous exudate of the ulcer site. This property enables Antepsin to form a protective barrier over the ulcer lesion giving sustained protection against the penetration and action of gastric acid, pepsin and bile. Studies both in humans and animals demonstrate that Antepsin protects the gastric mucosa against various irritants such as alcohol, acetylsalicylic acid and sodium taurocholate. Antepsin also directly inhibits pepsin activity and absorbs bile salts. It has only weak antacid activity. It does not alter gastric emptying time, nor normal digestive function. Antepsin has no demonstrated pharmacological effect on the cardiovascular or central nervous systems.

Paediatric population

In the literature, there are limited clinical data on the use of sucralfate in children, mainly for stress ulcer prophylaxis, reflux oesophagitis and mucositis. The dose used in these studies was 0.5-1g four times a day, depending on the children's age and the severity of the underlying disease, and was applied without major safety concerns. In view of the limited data, use of sucralfate in children under 14 years of age is currently not recommended.

5.2 Pharmacokinetic propertiesAbsorption

Sucralfate is only minimally absorbed from the gastro-intestinal tract. The small amounts that are absorbed are excreted primarily in the urine. Absorption of aluminium from sucralfate may be increased in patients on dialysis or with renal dysfunction (see also "other special warnings and precautions").

5.3 Preclinical safety data

There was no evidence of carcinogenesis in mice and rats receiving oral sucralfate in dosages of up to 1g/kg daily (12 times the usual human dosage) for 2 years. In animal studies there was no effect evidence of impaired fertility. The effect of sucralfate on human fertility is not known.

6 PHARMACEUTICAL PARTICULARS**6.1 List of excipients**

Saccharin sodium
Sodium dihydrogen phosphate dihydrate Ph. Eur.
Purified water
Glycerol
Sodium propyl hydroxybenzoate (E217)
Sodium methyl hydroxybenzoate (E219)
Xanthan gum
Aniseed flavour
Caramel flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.
After first opening: 28 days.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Glass bottle (pack size 250 ml).

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Chugai Pharma France
100-101 Quartier Boieldieu Tour Franklin
Arche Sud
92042 Paris la Défense CEDEX
France

8 MARKETING AUTHORISATION NUMBER

PA22641/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31 March 2000
Date of last renewal: 31 March 2010

10 DATE OF REVISION OF THE TEXT

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