SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
ULGASTRAN 1 g/5 mL, oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5 mL of suspension contains 1 g of sucralfate (Sucralfatum)
Excipients: methyl para-hydroxybenzoate (0.1 g/100 g), propyl para-hydroxybenzoate (0.05 g/100 g), sorbitol (1.5 g/100 g).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Oral suspension
White, lemon-vanilla flavoured suspension. Minor sedimentation of the suspension may occur; shaking the bottle helps regain a homogeneous dispersion of the product.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
Peptic ulcer disease (PUD).

4.2 Posology and method of administration
Indicated for oral use.
Adults: 1 g (1 teaspoon) 4 times a day (every 6 hours), 0.5–1 hour before each meal and directly before bedtime. Consume with adequate water. Treatment should be continued for 4–6 weeks. The maximum daily drug dose is 8 g (8 teaspoons).
Shake before use.

Posology in renal insufficiency patients
Ulgastran should be used with caution in renal insufficiency patients (see sections 4.3 and 4.4).

Posology in elderly patients
Posology adjustments are not necessary.

Posology in children and adolescents under 18 years of age
There is no relevant use of Ulgastran in children.

4.3 Contraindications
Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
Avoid chronic use in patients with severe renal insufficiency, chronic kidney disease or hypophosphataemia, and in dialysis patients.
4.4 Special warnings and precautions for use

Exercise particular caution when using sucralfate in renal insufficiency patients. In those patients, excretion of aluminium by the kidneys is decreased. Aluminium crosses dialysis membranes poorly due to binding to serum albumins. Use the drug in dialysis patients only when absolutely necessary and for a short period of time. Serum aluminium and phosphorus levels should be monitored in those patients, and upon the end of treatment the presence of aluminium accumulation symptoms (osteodystrophy, osteomalacia, and encephalopathy) should be assessed.

Antacids should be taken 30 minutes before or after sucralfate administration. Concomitant use of other aluminium containing preparations is contraindicated due to increased potential for aluminium absorption and toxicity.

Biologically active excipients

Ulgastran contains sorbitol. Do not use in patients with rare hereditary fructose intolerance. Ulgastran contains para-hydroxybenzoates. The product can cause allergic reactions (which could be delayed).

4.5 Interaction with other medicinal products and other forms of interaction

Upon absorption, sucralfate may interact with food. Due to the possible binding of sucralfate with dietary proteins and increased bioavailability induced by food intake, it is recommended to administer sucralfate an hour before or 2 hours after a meal.

Numerous studies have determined that sucralfate administered concomitantly with other oral drugs can delay or decrease the absorption thereof (pharmacokinetic interaction, bioavailability stage) by creating a physical barrier within the GI tract or by chelating the drugs. This applies to the following drug classes:
- chemotherapeutics belonging to quinolones;
- tetracyclines;
- antifungals;
- H<sub>2</sub> blockers;
- anticoagulants (coumarin derivatives);
- nonsteroidal anti-inflammatory drugs;
- phosphates;
- cardiac glycosides;
- phenytoin;
- theophylline.

By increasing the pH of the gastric juice, antacids decrease the efficacy of sucralfate. In the acidic environment of the gastric acid, sucralfate releases aluminium ions, therefore attention should be paid to possible interactions between ionised aluminium and drugs of other classes:
- antivirals, e.g. protease inhibitors;
- ACE inhibitors;
- beta-blockers;
- antidiabetic drugs;
- immunosuppressants;
- antipsychotics;
- benzodiazipine derivatives;
- oral corticosteroids;
- iron salts.

It is recommended to maintain a time interval between administration of sucralfate and other drugs. Administration of other drugs 2 hours before sucralfate administration eliminates many interactions.

4.6 Fertility, pregnancy and lactation
There is insufficient data on the use of sucralfate in pregnant women. Studies in animals on the course of pregnancy, embryonic and foetal development, course of delivery and/or postpartum development are not comprehensive (see section 5.3). Potential risks in humans are not known. Ulgastran should not be used during pregnancy unless absolutely necessary. Lactating women should not use Ulgastran.

4.7 Effects on ability to drive and use machines

Ulgastran has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse effects occurring after the use of sucralfate are mild and rarely lead to withdrawal of treatment. Each effect has been described according to incidence. The incidence of the adverse effects has been described in line with the following frequency grouping:

- Common (≥1/100 to <1/10);
- Uncommon (≥1/1,000 to <1/100);
- Rare (≥1/10,000 to <1/1,000).

Within each frequency group, adverse effects are listed in order of decreasing severity.

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>constipation</td>
<td>diarrhoea, vomiting, nausea, headache,</td>
<td>dizziness, insomnia, excessive drowsiness,</td>
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<tr>
<td></td>
<td></td>
<td>increase in aluminium and ionised calcium levels and decrease in serum</td>
<td>indigestion, flatulence, dry mouth,</td>
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<tr>
<td></td>
<td></td>
<td>organic phosphorus level</td>
<td>laryngitis, rhinitis,</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>osteoporosis, osteopaenia</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>facial oedema, pruritus, rash</td>
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<td></td>
<td></td>
<td></td>
<td>hepatotoxicity</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>toxic nephropathy</td>
</tr>
</tbody>
</table>

4.9 Overdose

The specific symptoms of sucralfate overdose are not known. Studies in animals on acute toxicity have shown no toxic effects for doses of 12 g/kg of body mass. Sucralfate is minimally absorbed into the bloodstream. Should significant amounts of the drug be taken, a gastric lavage may be considered within two hours of ingestion.
5. **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

Pharmacotherapeutic group: Other drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD), ATC code: A02BX02

Sucralfate is a sucrose sulphate-aluminium hydroxide complex (basic aluminium salt of sucrose octasulphate). This compound belongs to the group of protective drugs with no antacid or gastric secretion inhibitory effects, and is used in the treatment of PUD. In an acidic environment, sucralfate becomes strongly polar and binds to ulcer floor tissues for approximately 12 hours, with a relatively weak bonding to the normal lining of the stomach and the duodenum. In the presence of muriatic acid, sucralfate binds to positively charged glycoprotein groups. It can form a gel-like complex with mucous particles, which can prevent the later from being broken down by pepsin. It is assumed that its adherence to the granulation tissue inhibits the diffusion of protons to the ulcer floor. Moreover, it binds bile acid salts and pepsin, thus reducing their destructive effects. Sucralfate increases the tissue concentration of endogenous prostaglandins and binds to the epidermal growth factor and other growth factors, engaging them in local mucosal protection. Its efficacy in healing ulcers and preventing PUD is similar to the efficacy of other antacids (alkalifying agents) and H₂ antagonists.

5.2 **Pharmacokinetic properties**

After oral administration, sucralfate is poorly absorbed (2–5%) from the GI tract. In the stomach, sucralfate partially dissociates (approximately 10%) into Al(OH)₃ and sucrose octasulphate. Released aluminium ions bind to phosphates and other anions in the stomach and intestines, forming dissoluble and poorly absorbable compounds or soluble compounds of minor availability. The absorption of aluminium ions amounts to 0.1–10%. In patients using chronic sucralfate treatment, the determined aluminium concentration was 8.41 mg of Al ions/L. No statistically significant deviation between a placebo arm was observed.

Upon absorption, sucralfate may interact with food. Due to the possible binding of sucralfate with dietary proteins and increased bioavailability induced by food intake, it is recommended to administer sucralfate an hour before or 2 hours after a meal.

The aim of sucralfate treatment is to achieve a therapeutic effect within the mucosa of the stomach and duodenum. Due to their minor absorption, the highest concentration of aluminium ions occurs in the stomach and duodenum. With normal renal functioning, the main compartment for sucralfate is the lumen of the GI tract.

In the presence of muriatic acid in the stomach, sucralfate releases aluminium ions, which bind to positively charged protein groups of the mucosa. Sucrose sulphate formed in the presence of muriatic acid is not metabolised and is excreted with the stool in an unchanged form within 48 hours (more than 90% of the dose ingested). Sucralfate is primarily excreted via the GI tract, and only 0.5–22% is excreted by the kidneys with urine.

5.3 **Preclinical safety data**

Non-clinical data obtained in conventional pharmacology studies on the safety, repeated dose toxicity, genotoxic effects, potential carcinogenicity, and reproductive toxicity have not revealed any particular risks for humans.

6. **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**

Hypromellose
30% simethicone emulsion
Methyl para-hydroxybenzoate
Propyl para-hydroxybenzoate
Glycerol
Sorbitol
Sodium saccharin
Citric acid
Vanillin
Lemon oil
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Orange glass bottle, in a cardboard box.

250 ml in bottle.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORIZATION HOLDER

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ul. ks. J. Poniatowskiego 5
05-825 Grodzisk Mazowiecki
tel.: (22) 755 50 81

8. MARKETING AUTHORIZATION NUMBER(S)

Registration certificate of the Health and Welfare Ministry No. 3892,
Authorisation No. R/1646
9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29 December 1992
24 May 1999
11 March 2004
06 September 2004
14 June 2005
13 August 2008

10. DATE OF REVISION OF THE TEXT

13 August 2008
24 May 2010