1. NAME OF THE MEDICINAL PRODUCT

INGLIN SUSPENSION (Sucralfate and Oxetacaine)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10ml contains Sucralfate1g and Oxetacaine 20mg

{For a full list of excipients, see section 6.1}

3. PHARMACEUTICAL FORM

Liquid – Oral Suspension (sunset yellow FCF)

4. Clinical particulars

4.1 Therapeutic indications

INGLIN Suspension (Sucralfate and Oxetacaine) is indicated for:

- the treatment of duodenal ulcer,
- fast relief from gastritis,
- fast relief from heartburn,
- lasting relief from pains associated esophagitis and peptic ulcer disease.

4.2 Posology and method of administration

Posology

Adult: 10ml every 6 hours

Pediatric population

Children: 6-12 years 5mls every 6 hours

Method of administration

Oral route of administration

4.3 Contraindications

Hypersensitivity to the active substance 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

INGLIN SUSPENSION 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 aluminum 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 aluminum absorption.

Sucralfate is not recommended for use in individuals on dialysis. In patients with severe or chronic renal impairment, INGLIN Suspension 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.

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.

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.

The product contains Oxetacaine which may lead to allergy.

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, H2 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, immune-suppressants, antipsychotics, benzodiazepine 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.

Oxetacaine in INGLIN increases serum concentration of Acenocoumarol and decreases the metabolism of the following drugs: Alfuzosin, Alprazolam, Aripiprazole, Atorvastatin, Cilostazol, Colchicine, Eliglustat, Eszopiclone.

4.6 Pregnancy and Lactation

Pregnancy: There is insufficient data on the use of sucralfate in pregnant women, 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 INGLIN Suspension 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 INGLIN Suspension is administered to breast-feeding women.

4.7 Effects on ability to drive and use machines

INGLIN Suspension has no or negligible influence on the ability to drive and use machines, however, do not drive if you feel dizzy or drowsy.

4.8 Undesirable effects

Adverse effects occurring after the use of INGLIN Suspension are mild and rarely lead to withdrawal of treatment.

The following table shows the adverse effect in order of decreasing frequency:

Common	Constipation
Uncommon	Diarrhoea, vomiting, nausea, headache, increase in aluminium and ionised calcium levels and decrease in serum organic phosphorus level.
Rare	Dizziness, insomnia, excessive drowsiness, indigestion, flatulence, dry mouth, laryngitis, rhinitis, osteoporosis, osteopaenia facial oedema, pruritus, rash hepatotoxicity toxic nephropathy.

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

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. In the presence of gastric juice, polymers of the drug particles form a viscous paste coating the stomach walls. Three hours after administration, approximately 3% of the administered dose remains in the stomach. The substance does not affect gastric emptying time and digestion. No effects of sucralfate on the cardiovascular and central nervous systems were demonstrated.

Oxetacaine improves common gastrointestinal symptoms. Oxetacaine is part of the anesthetic antacids which increase the gastric pH while providing relief from pain for a longer period of duration at a lower dosage. This property has been reported to relieve the symptoms of hyperacidity. Oxetacaine is reported to produce a reversible loss of sensation and to provide a prompt and prolonged relief of pain. In vitro, oxetacaine was showed to produce an antispasmodic action on the smooth muscle and block the action of serotonin.

Its anesthetic action produces the loss of sensation which can be explained by its inhibitory activity against the nerve impulses and de decrease in permeability of the cell membrane.

Oxetacaine inhibits gastric acid secretion by suppressing gastrin secretion.

Moreover, oxetacaine exerts a local anesthetic effect on the gastric mucosa. This potent local anesthetic effect of oxetacaine may be explained by its unique chemical characteristics in which, as a weak base, it is relatively non-ionized in acidic solutions whereas its hydrochloride salt is soluble in organic solvents and it can penetrate cell membranes. Oxetacaine diminishes the conduction of sensory nerve impulses near the application site which in order reduces the permeability of the cell membrane to sodium ions. This activity is performed by the incorporation of the unionized form into the cell membrane.

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 in feces unchanged 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.

Oxetacaine has a peak plasma concentration of approximately 20 ng/ml about one hour after oral administration. Less than 1/3 of the administered dose is absorbed as it undergoes extensive metabolism. Due to the low half-life, it is thought that oxetacaine, when absorbed, presents a very low protein plasma binding. Oxetacaine is rapidly and extensively metabolized hepatically. After metabolism, there is a formation of primary metabolites such as beta-hydroxy-mephentermine and beta-hydroxy-phentermine. The major metabolites are found in the plasma in insignificant amounts. Less than 0.1% of the amdinistered dose is recovered in urine within 24 hours in the form of unchanged oxetacaine or its metabolites.

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

6.2 Incompatibilities

Not applicable

6.3 Shelf life

6.4 Special precautions for storage

Shake well before use.

Store below 30^{o}c, protect from light.

Keep the medicine out of the reach of children.

6.5 Nature and contents of container

Amber bottles (pack size: 200ml).

6.6 Special precautions for disposal

No special requirements.

7. APPLICANT/MANUFACTURER

Devon Pharmaceuticals Co. LTD.

15 Oke-Afa Road, llupeju, Magboro,

Ogun state, Nigeria.

Manufactured by:

Antila Lifesciences Pvt. Ltd.