Product Name : NEUTRAFLUX TABLETS

Application Number: 20682

GENERAL AND ADMINISTRATIVE INFORMATION

Section1.17; Provide SmPC for the product Neutraflux Tablets.

Appended below

Summary of Product Characteristics (SPC)

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TABLE OF CONTENTS

1. NAME OF THE MEDICINAL PRODUCT

NEUTAFLUX Tablets (Alginic Acid, Magnesium Hydroxide, Aluminium Hydroxide, Magnesium Trisilicate & Simeticone Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

Alginic Acid	BP	200 mg
Magnesium Hydroxide	BP	250 mg
Dried Aluminium Hydroxide	BP	250 mg
Magnesium Trisilicate	BP	250 mg
Simeticone	BP	125 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Tablets

Pale pink coloured, circular, chewable tablets with mint flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NEUTRAFLUX Tablets are indicated for the treatment of ulcer and non-ulcer dyspepsia, hyperacidity, reflux oesophagitis heartburn and flatulence.

4.2 Posology and method of administration

1 tablet twice daily after meals or as directed by the Physician. The tablets are to be chewed thoroughly and not to be swallowed.

Paediatric use: Antacids should not be given to young children (under 6 years of age) unless prescribed by the Doctor

Elderly patients: There is no need for dosage reduction in the elderly. But patients with bone problems or with Alzheimer's disease should not use aluminium-containing antacids. The Aluminium may cause their condition to get worse.

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4.3 Contraindication

Young children - Antacids should not be given to young children (under 6 years of age) unless prescribed by the Doctor. Aluminium or Magnesium containing medicines should not be given to premature or very young children because they may cause serious side effects, especially when given to children who have kidney disease or who are dehydrated.

Older adults - Elderly persons with bone problems or with Alzheimer's disease should not use Aluminium containing antacids. The Aluminium may cause their condition to get worse.

4.4 Special warnings and precautions for use

NEUTRAFLUX should not be used if patient is allergic to any ingredients of drug. Patients taking any Citrate salts should not use this drug. Aluminium containing antacids should not be used in infants. Patients with kidney disease, Appendicitis or symptoms of Appendicitis (e.g., stomach/abdominal pain, nausea/vomiting), patients with Magnesium restricted diet, patients with sudden change in bowel habits that last for longer than 2 weeks should use the product with caution. During pregnancy, this medication should be used only when clearly needed. Aluminium salts may cause Phosphate depletion, which is generally negligible. On prolonged treatment with large doses hypophosphataemia may occur, especially in patients with restricted Phosphate intake. Serum Phosphate levels should be monitored regularly (bimonthly) in patients on maintenance haemodialysis who are receiving long term Aluminium Hydroxide therapy. Aluminium compounds can cause delayed or decrease the absorption of certain drugs used in combination. To be used with caution in chronic dialysed patients because of risk of encephalopathy due to Aluminium.

Caution: NEUTRAFLUX Tablets contain Aspartame which is a source of Phenylalanine.

4.5 Interaction with other medicinal products and other forms of interaction

Antacids may interfere with drugs by a) Increasing the gastric pH altering disintegration, dissolution, solubility, ionization and gastric emptying time, b) Absorbing or binding drugs to their surface resulting in decreased bioavailability, c)

Increasing urinary pH affecting the rate of drug elimination. Most of the drug interactions can be avoided by taking antacid 2 hrs before or after ingestion of other drugs.

Antacids may interfere with and cause delayed or decreased absorption of certain drugs, e.g. Acetylsalicylic acid, Indometacin, anti tuberculosis drugs (Ethambutol, Isoniazide), Tetracyclines, Quinolones (Ciprofloxacin), Penicillamine, Chloroquine, Ketoconazole, Antihistaminics, Diflunisal, Digoxin, Bisphosphonates, Glucocorticoids, Phenothiazinic Neuroleptics, Sulpiride, Iron salts, Thyroid hormones.

Aluminium Hydroxide may interfere with the absorption of Tetracyclines, Chloroquine, Penicillamine, Phenothiazines and Quinolone Antibacterials, when these are given concomitantly. Magnesium Hydroxide may interfere with the absorption of Cimetidine, Diflunisal, Digoxin, Indomethacin, Iron salts and Tetracyclines. Absorption of buffered or enteric coated Aspirin is increased by simultaneous administration of antacids. Blood concentration of Salicylates will be reduced by antacid-induced changes in urinary pH, increasing urinary excretion.

Magnesium Hydroxide can affect the drugs like Amphetamines, Quinidine as these drugs can be affected by the amount of Acid in the urine. Magnesium Hydroxide can decrease the absorption of other drugs such as Dasatinib, Delavirdine, Amprenavir, Atazanavir, Gabapentin, Digoxin, Mycophenolate, Phosphate supplements (e.g., Potassium Phosphate), Tetracycline antibiotics (e.g., Doxycycline, Minocycline), certain Azole antifungals (Ketoconazole, Itraconazole), and Quinolone antibiotics (e.g., Ciprofloxacin, Levofloxacin).

4.6 Pregnancy and lactation

Usage in Pregnancy

There are no controlled data on the ingredients of the preparation for use in human pregnancy. Magnesium salts have been used extensively during pregnancy in large doses with no reports of congenital defects. Aluminium salts may cause constipation in large doses and may also interfere with absorption of vital nutrients like Iron and Calcium. Hence the product should be used in pregnancy in moderation and only when benefit outweighs risk. There are no data on the excretion of Alginic Acid, Aluminium Hydroxide, Magnesium Hydroxide and Magnesium Trisilicate into human

Milk. It is not known whether these drugs are excreted into the breast milk. Therefore usage should be considered only when benefit outweighs risk.

4.7 Effects on ability to drive and use machines

Intake of NEUTRAFLUX Tablets was not found to have any effect on the ability to drive and use machines.

4.8 Undesirable effects

Effects due to Aluminium containing antacids: Aluminium Hydroxide may cause constipation. Large doses can cause intestinal obstruction. Excessive doses, or even normal doses in patients with low-Phosphate diets, may lead to Phosphate depletion accompanied by increased bone resorption and hyper-calciuria with the risk of osteomalacia. Aluminium salts are not, in general, well absorbed from the gastrointestinal tract, and systemic effects are therefore rare in patients with normal renal function. However, care is necessary in patients with chronic renal impairment. Osteomalacia or adynamic bone disease, encephalopathy, dementia, and microcytic hypochromic anaemia have been associated with Aluminium accumulation in such patients given large doses of Aluminium Hydroxide as a Phosphate binding agent.

Effects due to Magnesium containing antacids: Laxative effect as saline cathartic may cause diarrhoea, hypomagnesaemia in renal failure patients. In the presence of renal insufficiency Magnesium salts may cause central nervous depression. Magnesium Hydroxide can cause diarrhoea, symptoms of high Magnesium levels (e.g., muscle weakness, slow/irregular heartbeat, slow/shallow breathing, flatulence, mental/mood changes such as confusion), symptoms of dehydration (e.g., decreased urination, dizziness, extreme thirst, very dry mouth). A very serious allergic reaction to this drug is rare.

Other effects: Dose dependant rebound hyperacidity may occur due to Antacids. Other effects reported occasionally were severe allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue); loss of appetite; muscle weakness; nausea; slow reflexes and vomiting.

4.9 Overdose

For Aluminum-containing antacids:

Bone pain; constipation (severe and continuing); feeling of discomfort (continuing); loss of appetite (continuing); mood or mental changes; muscle weakness; swelling of wrists or ankles; weight loss (unusual).

Symptoms and treatment: A single massive dose of Aluminium Hydroxide is unlikely to have harmful sequelae, as Aluminium is not absorbed systemically to any great extent. Gastric lavage should be administered, followed by a mild aperient if required.

Excessive long-term dosage may cause phosphate depletion, manifested in muscle weakness, anorexia and malaise. If left unchecked this condition may give rise to osteomalacia, osteoporosis and urinary calculi.

For Magnesium-containing antacids:

Difficult or painful urination (with Magnesium Trisilicate); dizziness or lightheadedness; feeling of discomfort (continuing); irregular heartbeat; loss of appetite (continuing); mood or mental changes; muscle weakness; unusual tiredness or weakness; weight loss (unusual)

Symptoms and treatment: It includes gastrointestinal irritation and watery diarrhoea. Severe poisoning may produce hypomagnesaemia, symptoms of which include nausea, vomiting, flushing, thirst, dizziness, hypotension, drowsiness, confusion, loss of tendon reflexes, muscle weakness, respiratory depression, flatulence, gastric bloating, GI irritation, cardiac arrhythmias, coma and cardiac arrest. Treatment consists of intravenous administration of calcium gluconate injection 10% in a dose of 10 – 20ml to counteract respiratory depression or heart block. If renal function is normal, adequate fluids should be given to assist removal of Magnesium from the body. Dialysis may be necessary in patients with renal impairment or severe hypomagnesaemia.

Simeticone:

No treatment is necessary for the Simeticone ingestion as overdose.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: A02 AF - Antacids with antiflatulents

5.1 Pharmacodynamic properties

Pharmacological effects

Alginic Acid acts as mucosal protectant and forms protective foam that sits on top of the stomach contents. This foam helps to prevent acid irritation to the oesophagus. Alginate antacid products form an alginate foam raft on top of the gastric contents. The antacid components remain entrained in the alginate raft and exert little or no effect on gastric pH.

The presence of the foam raft helps to impede gastro-oesophageal reflux. If reflux is forced the alginate antacid foam enters the oesophagus first coating it with a protective demulcent and antacid layer. This coating process is repeated as the reflux subsides. Any refluxed gastric acid is thus rapidly neutralised, the oesophageal mucosa is protected and any pre-existing oesophagitis or ulceration can heal normally.

Antacids like Aluminium and Magnesium compounds neutralize or reduce stomach acid, thereby resulting in an increase in the pH of the stomach and duodenal bulb. It helps relieve symptoms of excessive stomach acidity in patients with indigestion, heartburn, or Gastro oesophageal Reflux Disorder (GERD).

Aluminium Hydroxide is a slow-acting antacid. It is used to provide symptomatic relief in gastric hyperacidity. In addition, the antipeptic and demulcent activity of Aluminium Hydroxide helps to protect inflamed gastric mucosa against further irritation by gastric secretions.

Magnesium Hydroxide is a fast acting antacid. The combination of Aluminium Hydroxide and Magnesium Hydroxide produces a fast onset of action and an increase in total buffering time. Aluminium Hydroxide on its own is an astringent and may cause constipation. This effect may be balanced by the cathartic effect of the Magnesium salts.

Simeticone is an antiflatulent. It is a silicon polymer that lowers surface tension. It works by helping the formation of larger gas bubbles, which frees gas and makes it easier to eliminate by belching or passing rectally. It relieves flatulence by dispersing and preventing formation of mucus surrounded gas pockets in GI tract. It is also used as an adjunct in treatment of many conditions in which gas retention may be problem.

5.2 Pharmacokinetic properties

Pharmacokinetics of Alginic Acid: After oral ingestion, Alginic Acid is not converted in the gastro-intestinal tract; 80-100% of the quantity ingested is excreted. Absorption of Alginic salts is negligible.

Pharmacokinetics of Aluminium salts: Aluminium Hydroxide, given orally, slowly reacts with the Hydrochloric Acid in the stomach to form soluble Aluminium Chloride, some of which is absorbed. About 100 to 500 micrograms of the cation is reported to be absorbed from standard daily doses of an Aluminium-containing antacid, leading to about a doubling of usual Aluminium concentrations in the plasma of patients with normal renal function. Absorbed Aluminium is eliminated in the urine, and patients with renal failure are therefore at particular risk of accumulation (especially in bone and the CNS) and Aluminium toxicity. The Aluminium compounds remaining in the gastrointestinal tract, which account for most of a dose, form insoluble, poorly absorbed Aluminium salts in the intestines including Hydroxides, Carbonates, Phosphates and fatty acid derivatives, which are excreted in the faeces.

Pharmacokinetics of Magnesium salts: Magnesium Hydroxide reacts rapidly with gastric Acid to form Magnesium Chloride. Approximately 15-30% of the Magnesium Chloride formed is absorbed from the small intestine and is rapidly excreted by the kidneys in patients with normal renal function.

Magnesium Trisilicate is converted to Magnesium Chloride and Silicon Dioxide during neutralisation of gastric acid. Some Magnesium is absorbed and traces of the Silicon Dioxide may be absorbed and excreted in the urine.

5.3 Preclinical safety data

Alginic Acid:

Animal Toxicity data:

Lethal dose	Route	Animal	Dose
LD50	oral	Rodent-rat	>5 gm/kg
LD	Intraperitoneal	Rodent-rat	>1 gm/kg
LD50	Intravenous	Rodent-rat	1 gm/kg
LDLo	Intraperitoneal	Rodent-mouse	500 mg/kg
LD50	Intraperitoneal	Mammal-cat	250 mg/kg
LD50	Intravenous	Rodent-rabbit	100 mg/kg

Potential Health Effects

Eye: May cause eye irritation.

Skin: May cause skin irritation.

Ingestion: May cause gastrointestinal irritation with nausea, vomiting and diarrhoea.

Inhalation: May cause respiratory tract irritation.

Aluminium and its salts, which are extensively used in the household and in industry, do not constitute a carcinogenic, mutagenic or teratogenic hazard, except, perhaps, in cases of extremely high exposure. The large majority of the experiments performed to assess the carcinogenicity of Aluminium in laboratory animals gave negative results or even suggested some antitumor activity. Moreover, epidemiological studies have not provided clear evidence of a carcinogenic hazard of Aluminium to man, and short-term tests made in vitro and in vivo to demonstrate mutagenic activity of Al were negative except for some experiments in plants. The embryotoxic properties suggested by the studies on birds and mammals could result from the influence of Al on Phosphate and Calcium metabolism or from interference with the polymerization of microtubules.

References to Aluminium toxicity in dialysis patients and the possible association between Aluminium ingestion and Alzheimer's disease are included under Aluminium.

Aluminium accumulation does not generally appear to be significant in patients with normal renal function taking therapeutic doses of Aluminium-containing antacids, and there is little evidence that such antacids are a risk factor for Alzheimer's disease. Elevated plasma-aluminium concentrations have been reported in infants with normal renal function given Aluminium-containing antacids but there were no obvious signs of toxicity. There have, however, been reports of phosphate depletion and rickets in a few infants caused by the use of antacids containing Magnesium and Aluminium Hydroxides. In these cases the antacid had been started within a few months of birth and continued for up to 8 months. In reports that described a total of 3 infants, the authors suggested that the use of soya-based infant feeding formulas, the phytates of which can interfere with mineral absorption, may have exacerbated the phosphate-binding effect of the antacid. In another case a dosing error resulted in the infant receiving an excessive dose of antacid for 6 months. The BNFC advises against the use of any Aluminium-containing antacid in neonates and infants.

Aluminium accumulation resulting in osteomalacia or encephalopathy with seizures and dementia has been reported in children with renal failure (but not on dialysis) treated with Aluminium-containing phosphate binders. In an adult male patient with severe chronic renal failure who was not on dialysis, self-medication with antacids for at least 3 years resulted in Aluminium toxicity associated with encephalopathy, bone disease, and microcytic anaemia. Aluminium-containing antacids should therefore be used with caution in patients with chronic renal failure, especially in children.

Oral citrate salts increase the absorption of Aluminium from the gastrointestinal tract and patients with renal failure taking Aluminium compounds should avoid citrate-containing preparations, which include many effervescent or dispersible tablets. Ascorbic Acid has also been reported to enhance Aluminium absorption.

Magnesium Trisilicate toxicity:

Acute toxicity:

Primary irritant effect:

On the skin: Irritant to skin and mucous membranes.

On the eye: Irritating effect.

Sensitization: No sensitizing effects known.

Sub acute to chronic toxicity: Inhalation of Magnesium compounds may cause metal fume fever. Metallic Magnesium which perforates the skin may cause local lesions. Some Magnesium salts have produced muscle weakness, cardiac arrhythmias, respiratory effects and changes in blood chemistry following ingestion.

Magnesium Hydroxide: Hazardous effects:

Potential Health Effects:

Eye: May cause eye irritation.

Skin: May cause skin irritation.

Ingestion: May cause gastrointestinal irritation with nausea, vomiting and diarrhoea.

Inhalation: Dust is irritating to the respiratory tract.

Chronic: Repeated exposure may cause kidney damage and digestive tract abnormalities.

Animal Toxicity data:

Oral, mouse: LD50 = 8500 mg/kg;

Oral, rat: LD50 = 8500 mg/kg;

IP, rat: LD50=2780mg/kg;

IP, mouse: LD50=815mg/kg.

No carcinogenicity data.

Simeticone: General: proper use provided, no adverse health effects have been observed. Eye contact may produce oil film causing harmless, revesible, shortlasting dimness of eyes. Acute oral LD50: no data available.

Simeticone and Carbamazepine, when taken together, may be a cause of carbamazepine toxicity. The risk of Carbamazepine overdose should be considered when prescribing Simeticone to a patient who is using Carbamazepine.

There are no known human/animal data on long-term potential for mutagenicity or carcinogenicity.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Sucrose, Maize Starch, Microcrystalline Cellulose, Lactose, Mannitol, Sodium Methylparaben, Sodium Propylparaben, Colloidal Anhydrous Silica, Magnesium Stearate, Aspartame, Peppermint Flavour, Erythrosine & Ponceau-4R.

6.2 Incompatibilities:

Not applicable

6.3 Shelf life:

24 Months

6.4 Special precaution for storage:

No special precautions for storage.

General storage instructions:

Do not store above 30°C. Protect from light.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container:

10 blister strips of 10 tablets in an outer carton with pack insert.

3 blister strips of 10 tablets in an outer carton with pack insert.

1 blister strip of 10 tablets in an outer carton with pack insert.

6.6 Special precautions for disposal:

No special instructions needed.

7. REGISTRANT:

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