REGISTRATION DOSSIER		
Name of the Product	Alumina, Magnesia and Simethicone Oral Suspension USP	**Module-1 – Administrative Information**
Brand Name	CENTACID Suspension	

1.6 Product information

1.6.1 Prescribing information (Summary of Product Characteristics)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT:

Alumina, Magnesia & Simethicone Oral Suspension USP - **(CENTACID SUSPENSION).**

1.1 Strength:

Each 5 ml contains:

Aluminium Hydroxide Paste

equivalent to Dried Aluminium Hydroxide Gel USP.....250 mg

Magnesium Hydroxide Paste

equivalent to Magnesium Hydroxide BP.....200 mg

Simethicone USP.....40 mg

Colour: Erythrosine

1.2 Pharmaceutical form:

Suspension. Pink coloured suspension with sweet taste and peppermint flavour.

REGISTRATION DOSSIER		
Name of the Product	Alumina, Magnesia and Simethicone Oral Suspension USP	**Module-1 – Administrative Information**
Brand Name	CENTACID Suspension	

2 QUALITATIVE AND QUANTITATIVE COMPOSITION:

2.1 Qualitative Declaration

Sr. No.	Name of Raw Materials	Specification
1	Aluminium Hydroxide Paste–A004 equivalent to Dried Aluminium Hydroxide Gel	USP
2	Magnesium Hydroxide Paste–M013 equivalent to Magnesium Hydroxide	BP
3	Simethicone (Activated Dimethicone)	USP
4	Sugar S018	IHS
5	Hydrogen Peroxide 50% w/v – H006	IHS
6	Methyl paraben	BP
7	Propyl paraben	BP
8	Saccharin Sodium	BP
9	Disodium Edetate	BP
10	Guar Gum (Delca P-225)	BP
11	Sorbitol Solution 70% (Non crystallizing)	BP
12	Chloroform	BP
13	Propylene Glycol	BP
14	Essence Chocolate liquid -E007	IHS
15	Colour Erythrosine - C034	IHS
16	Peppermint Oil	BP
17	Essence Coconut flavour -E014	IHS
18	Bronopol (Bronidiol)	BP
19	Purified Water	BP

2.2 Quantitative Declaration

Batch Size: 2000L

Sr. No.	Name of Raw Materials	Overages	Qty./5ml in mg	Standard batch quantity in Kg
1	Aluminium Hydroxide Paste -A004 equivalent to Dried Aluminium Hydroxide Gel USP	-	250.00	100.000
2	Magnesium Hydroxide Paste–M013 equivalent to Magnesium Hydroxide BP	-	200.00	80.000
3	Simethicone (Activated Dimethicone) USP	5%	40.00	16.800
4	Sugar IHS	-	250.00	100.000
5	Hydrogen Peroxide 50% w/v IHS	-	5.00	2.000
6	Methyl paraben BP	-	8.75	3.500
7	Propyl paraben BP	-	1.75	0.700
8	Saccharin Sodium BP	-	3.95	1.580
9	Disodium Edetate BP	-	0.50	0.200
10	Guar Gum BP	-	21.25	8.500
11	Sorbitol Solution 70% (Non crystallizing) BP	-	325.00	130.000
12	Chloroform BP	-	1.25	0.500
13	Propylene Glycol BP	-	50.00	20.000
14	Essence Chocolate liquid IHS	-	2.5	1.000
15	Colour Erythrosine IHS	-	0.2	0.080
16	Peppermint Oil BP	-	1.00	0.400
17	Essence Coconut flavour HIS	-	2.5	1.000
18	Bronopol (Bronidiol) BP	-	0.50	0.200
19	Purified Water BP	-	5 ml	2000.000

3. PHARMACEUTICAL FORM:

Suspension

Pink coloured suspension with sweet taste and peppermint flavour.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

Centacid suspension is indicated for treatment of acid dyspepsia, Hyperacidity, Reflux Oesophagitis, Gastritis, Duodenitis, Pregnancy heartburn, Hiatus hernia, NSAID gastropathy, Adjunct to H_2 antagonists & proton pump inhibitors in Peptic ulcers.

4.2 Posology and

5 – 10 ml between meals & bed time.

4.3 Method of administration: as directed by the physician.

4.4 Contraindications:

Known hypersensitivity to Hypophosphataemia.

4.5 Special warnings and precautions for use:

Should be used with caution in patients having congestive heart failure, renal failure or cirrhosis and hypophosphatemia.

4.6 Pediatric population

None.

4.7 Interaction with other medicinal products and other forms of interaction:

Centacid suspension may interfere with the absorption of certain drugs including tetracyclines, vitamins, ciprofloxacin, ketoconazole, hydroxychloroquine, chloroquine, chlorpromazine and rifampicin**.**

4.8 Additional information on special populations

4.9 Pediatric population

None.

4.10 Fertility, Pregnancy and lactation:

4.10.1 General principles

4.10.2 Woman of childbearing potential / Contraception in males and females.

4.10.3 Pregnancy

4.10.4 Breastfeeding

4.10.5 Fertility

No clinical data on exposed pregnancies are available. Use of antacids should be avoided in the first trimester of pregnancy. Caution should be exercised when prescribing to pregnant and lactating women.

4.11 Effects on ability to drive and use machines:

None stated.

4.12 Undesirable effects:

Aluminium Antacids:

The most frequent adverse effect of aluminium antacids is constipation. Decreased bowel motility, dehydration, or fluid restriction may predispose patients to intestinal obstruction. Hemorrhoids and fissures, or faecal impaction may occur. In patients with chronic renal failure, hyperaluminemia may occur and aluminium may accumulate in bones, lungs, and nerve tissue. Aluminium accumulation in the CNS may be the cause of dialysis dementia, which sometimes occurs in chronic renal failure patients receiving long-term aluminium antacid therapy for hyper-phosphatemia. Aluminium intoxication with severe osteomalacia and extensive aluminium deposition at the junction between calcified and noncalcified bone has been reported in several young children who were receiving large

dosages of aluminium hydroxide for the management of hyperphoshatemia associated with azotemia; the children were not undergoing hemodialysis during aluminium hydroxide therapy.

Aluminium salts may cause phosphorus depletion which is generally neligible. However, with prolonged administration or large doses, hypophosphatemia may occur, especially in patients with inadequate dietary intake of phosphorus; hypercalciuria secondary to bone resorption and increased intestinal absorption of calcium results. This phosphorus depletion syndrome is characterized by anorexia, malaise, and muscle weakness, and prolonged aluminium antacid therapy may cause urinary calculi, osteomalacia, and osteoporosis. A low phosphorus diet, diarrhoea excessive phosphorus losses from malabsorption, and restoration of renal function after a kidney transplant increase the likelihood of the syndrome. Serum phosphate concentrations should be monitored at monthly or bimonthly intervals in patients on maintenance hemodialysis who are receiving chronic aluminium antacid therapy.

Magnesium Antacids:

Magnesium-containing antacids commonly cause a laxative effect and frequent administration of these antacids alone often cannot be tolerated; repeated doses cause diarrhoea which may cause fluid and electrolyte imbalances. Chronic administration of magnesium trisilicate infrequently produces silica renal stones.

In patients with severe renal impairment, hypermagnesemia characterized by hypotension, nausea, vomiting, ECG changes, respiratory or mental depression, and coma has occurred after administration of magnesium-containing antacids. Magnesium-containing antacids should not be administered in patients with renal failure, and antacid products containing more than 50 mEq of magnesium in the recommended daily dosage should be used cautiously and only under the supervision of a physician who should monitor electrolytes in patients with renal disease

4.13 Overdose:

Serious symptoms are unlikely following overdose. Discontinue medication and correct fluid deficiency if necessary.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

The mechanism of action of antacids is complex. A proposed mechanism is the prevention of back-diffusion of hydrogen ions across the gastrointestinal mucosa. It is not clear at what pH this action takes effect. It is readily apparent that one can neutralize 50% of the acid in a given amount of gastric juice with a pH of 1.3 by raising the pH to 1.6,90% by raising the pH to 2.3 and 99% by raising the pH to 3.3. It generally is accepted that raising the gastric pH to approximately 4 prevents stress ulcer, which is thought to be mediated by acid back-diffusion. Another action of antacids is to prevent the conversion of gas-tric pepsinogen, a proenzyme, to pepsin, the active form. This is a proteolytic enzyme thought to mediate tissue injury in ulcer disease. Pepsinogens are inactivated reversibly at pH 5 and inactivated irreversibly at pH 7. It thus may be necessary to raise the pH to 5 to achieve the maximum benefit from antacids. Antacids also may enhance cytoprotection in the stomach. Finally, antacids may confer a therapeutic benefit by inactivating bile salts which are thought to reflux from the duodenum into the stomach and play some role in acid peptide disease.

5.2 Pharmacokinetic properties:

The clinical use of antacids is based on their ability to increase the pH of gastric secretions. With usual doses, antacids generally do not increase and maintain gastric pH above 4-5. Although antacids do not neutralize all gastric acid, increasing gastric pH from 1.3 to 2.3 neutralizes 90% and increasing pH to 3.3 neutralizes 99% of gastric acid. Consequently, the amount of gastric acid back-diffusing through the gastric mucosa and the amount of acid reaching the duodenum is

decreased. It is not known how much or for how long neutralization is required for optimal healing of peptic ulcers, but most clinicians believe that gastric pH should be maintained at about 3-3.5 for as many of the 24 hours as is possible. Antacids, in decreasing order of their ability to neutralize a given amount of acid, are calcium carbonate, sodium bicarbonate, magnesium salts, and aluminum salts. Magnesium hydroxide and aluminum hydroxide are the most potent magnesium and aluminum salts. Magnesium oxide has essentially the same acid neutralizing effect as magnesium hydroxide. Because magnesium trisilicate is slowly solubilized, it is a less effective buffer than magnesium hydroxide, carbonate, or phosphate.

Sodium bicarbonate rapidly reacts with hydrochloric acid to form sodium chloride carbon dioxide, and water; excess bicarbonate that does not neutralize gastric acid rapidly empties into the small intestine and is absorbed. When sodium bicarbonate is given orally, gastric acid is neutralized by exogenous bicarbonate instead of intestinal bicarbonate. The net effect of administering sodium bicarbonate whether it reacts with gastric acid or reaches the small intestine is that all of a dose reaches the extracellular fluid. Mild metabolic alkalosis occurs; in patients with normal renal function, the kidneys excrete the excess sodium and bicarbonate ions and the urine becomes alkaline.

Antacids other than sodium bicarbonate neutralize gastric secretions but generally do not cause metabolic alkalosis, because the cation formed in the stomach is minimally absorbed and regains a basic anion in the small intestine. However, to the extent that the cation is absorbed and does not react with intestinal bicarbonate, the extracellular fluid recieves a bicarbonate load; urinary pH is usually increased.

Aluminum hydroxide or oxide is slowly solubilized in the stomach and reacts with hydrochloric acid to form aluminum chloride and water. In addition to forming aluminum chloride, dihydroxyaluminum sodium carbonate and aluminum carbonate form carbon dioxide, and aluminum phosphate forms phosphoric acid. About 17-30% of the aluminum chloride formed is absorbed and is rapidly excreted by the kidneys in patients with normal renal function. In the

small intestine, aluminum chloride is rapidly converted to insoluble, poorly absorbed basic aluminum salts, which are probably a mixture of hydrated aluminum oxide, oxyaluminum hydroxide, various basic aluminum carbonates, and aluminum soaps. Aluminum-containing antacids (except aluminum phosphate) also combine with dietary phosphate in the intestine forming insoluble, nonabsorbable aluminum phosphate, which is excreted in the feces. If phosphate intake is limited in patients with normal renal function aluminum antacids (except aluminum phosphate) decrease phosphate absorption and hypophosphatemia and hypophosphaturia occur; calcium absorption is increased. In vitro studies indicate that aluminum hydroxide binds bile salts with an affinity and capacity similar to that of cholestyramine; aluminum phosphate binds bile salts, but to a much lesser degree than does aluminum hydroxide.

Magnesium hydroxide rapidly reacts with hydrochloric acid to form magnesium chloride and water. In addition, magnesium carbonate forms carbon dioxide. Magnesium trisilicate is slowly solubilized and reacts with hydrochloric acid to form magnesium chloride, silicon dioxide, and water. About 15-30% of the magnesium chloride formed is absorbed and is rapidly excreted by the kidneys in patients with normal renal function. Any magnesium hydroxide that is not converted to magnesium chloride in the stomach is presumably subsequently changed in the small intestine to soluble but poorly absorbed salts. Magnesium hydroxide binds bile salts in vitro, but to a much lesser extent than does aluminum hydroxide. Magnesium-containing antacids have a laxative action. (See Saline Laxatives 56:12.)

Antacid-induced increases in gastric pH inhibit the proteolytic action of pepsin an effect that is particularly important in patients with peptic ulcer disease. The optimum pH for pepsin activity is 1.5-2.5 and progressive inhibition occurs as gastric pH increases; above pH 4, the proteolytic activity of pepsin is minimal. Although some investigators have reported that aluminum-or calcium-containing antacids adsorb pepsin and thus have direct antipepsin effects, one study in which pH was controlled indicates that the antipepsin effects of antacids are due entirely to increased pH. Antacids do not coat the lining of peptic ulcers or the GI mucosa. Although some

antacids, such as aluminum hydroxide, have astr-ingent and demulcent actions. These effects are probably not important in the treatment of peptic ulcers.

In patients with peptic ulcers, antacids increase serum gastrin concentrations probably by increasing gastric pH. Single dose studies indicate that calcium carbonate causes gastric acid hypersecretion and acid rebound probably as a result of a local effect of calcium on gastrin producing cells. Other antacids also increase secretion of gastric acid but do not cause acid rebound after the antacids has left the stomach. Aluminum-containing antacids delay gastric emptying time, an effect that is related to the concentration of aluminum in the stomach.

5.3 Preclinical safety data

No relevant data.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients:

Sr. No.	Name of Raw Materials	Specification
1	Aluminium Hydroxide Paste A004 equivalent to Dried Aluminium Hydroxide Gel	USP
2	Magnesium Hydroxide Paste M013 equivalent to Magnesium Hydroxide	BP
3	Simethicone (Activated Dimethicone)	USP
4	Sugar S018	IHS
5	Hydrogen Peroxide 50% w/v – H006	IHS
6	Methyl paraben	BP
7	Propyl paraben	BP
8	Saccharin Sodium	BP
9	Disodium Edetate	BP
10	Guar Gum (Delca P-225)	BP
11	Sorbitol Solution 70% (Non crystallizing)	BP
12	Chloroform	BP
13	Propylene Glycol	BP
14	Essence Chocolate liquid -E007	IHS
15	Colour Erythrosine - C034	IHS
16	Peppermint Oil	BP
17	Essence Coconut flavour -E014	IHS
18	Bronopol (Bronidiol)	BP
19	Purified Water	BP

6.2 Incompatibilities: None

6.3 Shelf life: 36 months from the date of manufacture.

6.4 Special precautions for storage: Store at temperature between 15°C - 30°C in a dark place.

6.5 Nature and contents of container:

Centacid suspension is packed in a well-labeled 200ml pet bottle.

6.6 Special precautions for disposal and other handling:

Any unused product or waste material should be disposed of in accordance with local requirements**.**

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS:

Marketing Authorization holder:

Centaur Pharmaceuticals Pvt. Ltd.

Manufacturing Site address:

Centaur Pharmaceuticals Pvt. Ltd.

Address: Plant: I, Plot No: 3, Tivim Industrial Estate, Karaswada, Mapusa Goa-403526

8. MARKETING AUTHORISATION NUMBER

Not applicable.

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

10. DATE OF REVISION OF THE TEXT: June 2019

11. DOSIMETRY (IF APPLICABLE): NOT APPLICABLE.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)

NOT APPLICABLE.

1.6.2 Container labeling

Enclosed herewith