Antacid Antigas Chewable Tablets/Liquid

GELUSIL® MPS Tablets/Liquid

(Original-Mint/Xtracool-Mint Flavour)

1. GENERIC NAME

Antacid Antigas Chewable Tablets/ Liquid

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated chewable tablet contains:	
Activated Dimethicone I.P.	50 mg
Magnesium Hydroxide I.P.	250 mg
Dried Aluminium Hydroxide I.P.	250 mg
Magnesium Aluminium Silicate Hydrate	50 mg

Each 5 ml (teaspoonful) contains:	
Activated Dimethicone I.P.	50 mg
Magnesium Hydroxide I.P. (added as Magnesium Hydroxide paste)	250 mg
Dried Aluminium Hydroxide I.P. (added as Aluminium Hydroxide paste)	250 mg
Sorbitol solution (70%) I.P. (Non-Crystallising)	1.25 gm

List of excipients:

Original Mint Flavour -

Liquid:
Glycerin, Saccharin Sodium, Sodium Hypochlorite 5% solution, Erythrosine, Peppermint Oil, Menthol, Guar Gum, Citric Acid Monohydrate, Sodium Benzoate, Benzoic Acid, Butylparaben, Propylparaben, Bronopol, Purified Water.

Tablets:
Sucrose, Mannitol, Saccharin Sodium, Erythrosine, Ponceau 4R, Peppermint Oil, Trusil Peppermint PD Powder, Talc, Purified Water.

Xtra Cool Mint Flavour -

Liquid White:

Glycerin, Saccharin Sodium, Sodium Hypochlorite 5% solution, Peppermint Oil, Menthol, Guar Gum, Citric Acid Monohydrate, Sodium Benzoate, Benzoic Acid, Butylparaben, Propylparaben, Bronopol , Purified Water.

All strengths/presentations mentioned in this document might not be available in the market.

3. DOSAGE FORM AND STRENGTH

Dosage Form - Chewable tablets and Oral Liquid
Strength - Refer Section 2

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

Gelusil is indicated for relief of symptoms of hyperacidity (e.g., heartburn, epigastric discomfort, or their equivalents) that are often associated with dyspepsia, peptic ulcer, gastritis, peptic esophagitis, and hiatus hernia. It is also indicated for relief of flatulence (gas).

4.2 Posology and method of administration

The dose of antacid needed to neutralize gastric acid varies among patients, depending on the amount of acid secreted and the buffering capacity of the particular preparation. The liquid dosage form of antacids is considered to be more effective than the solid or powder dosage form. In most cases, tablets must be thoroughly chewed before being swallowed to ensure that they dissolve completely in the stomach before entering the small intestine.

Gelusil tablets
1-2 tablets to be chewed 30-60 min after meals or whenever symptoms are pronounced.

Gelusil liquid
1-2 teaspoonfuls (approximately 5-10 ml) 30-60 min after meals or whenever symptoms are pronounced.

To achieve adequate antacid effect in the stomach at the optimum time, most antacids are administered 1 and 3 hours after meals for prolonged acid-neutralizing effect and at bedtime.

Gelusil should not be taken in excess of the label specified dosage (10 teaspoonful or 12 tablets) in a 24-hour period. This product should not be employed for more than 2 weeks, except under the strict supervision of a physician.

Use in the Elderly

Metabolic bone disease commonly seen in the elderly may be aggravated by the phosphorus depletion, hypercalciuria, and inhibition of absorption of intestinal fluoride caused by the chronic use of aluminium-containing antacids. Elderly patients are more likely to have age-related renal function impairment, which may lead to aluminium retention. Dosing needs to be adjusted to suit individual patient requirements and characteristics.

Use in Patients with Renal Impairment

Gelusil should be used with caution in patients with renal impairment. In patients with severe renal failure, plasma aluminium and magnesium levels may be elevated, resulting in possible toxicity. Patients should have their aluminium and magnesium levels monitored during prolonged or high-dose therapy. While there are no specific dosing recommendations for use in patients with renal impairment, dosing may need to be adjusted to suit individual patient requirements and characteristics.

Use in Children

Dose requirements for young children have not been extensively evaluated. Antacids should not be given to young children (up to 6 years of age) unless prescribed by a physician. Since children are usually not able to describe their symptoms precisely, proper diagnosis should precede the use of an antacid. This will avoid the complication of an existing condition (e.g., appendicitis) or the appearance of severe adverse effects.

4.3 Contraindications

Gelusil tablets/liquid should not be used in patients with known sensitivity to any of the ingredients.

4.4 Special warnings and precautions for use

COMBINATION: ALUMINUM HYDROXIDE + MAGNESIUM HYDROXIDE + SIMETICONE

Patients over 50 who are experiencing heartburn for the first time, and patients who have noticed unintentional weight loss should consult a physician before using the product

- Patients should stop use and consult a physician if symptoms persist or worsen, new symptoms develop or if they experience dysphagia, (difficulty swallowing), odynophagia (pain on swallowing), severe vomiting, melaena (black stools), choking or chest pain

- Patients with renal impairment should consult a physician before using the product. Both magnesium and aluminum are principally eliminated from the kidney, and the risk of developing hypermagnesaemia / aluminum toxicity is increased with impaired renal function

- Patients with pre-existing hypermagnesaemia should consult a physician before using the product. Magnesium is systemically absorbed following use of oral magnesium-containing antacids, which could result in an increase in already raised magnesium levels

- Gastrointestinal uptake of aluminum is higher in children than in adults and therefore the use of the medicinal product is not recommended in children below 12 years of age

4.5 Drugs interactions

Antacids have potentially important interactions with Beta-blocking agents, Cimetidine, Chloroquine, Digoxin, NSAIDs, Phenytoin, Tetracyclines, Iron preparations, Fluoroquinolones and Quinidine.

Concomitant use of these drugs with antacids should be avoided. When co-prescription of such drugs with Gelusil is indicated, sufficient temporal spacing should be maintained between the administration of these drugs and Gelusil.

Absorption of captopril, dasatinib, itraconazole, rosuvastatin, some tetracyclines including doxycycline, some quinolone antibiotics including ciprofloxacin, levofloxacin, norfloxacin, and ofloxacin, may be impaired in the presence of aluminum hydroxide.

Because of the ability of antacids to change gastric or urinary pH and adsorb or form complexes with other drugs, the rate and/or extent of absorption of other medications may be increased or reduced when such medications are used concurrently with antacids.

In general, patients should be advised not to take any other oral medication within 1 to 2 hours of consuming antacids.

Patients taking aluminium hydroxide should be advised to avoid acid-containing drinks such as fruit juice, wine, etc. Concomitant use of aluminium-containing antacids with acid containing drinks can increase the intestinal absorption of aluminium.

Patients should consult a physician before using this product together with Raltegravir, Dolutegravir, and Elvitegravir. Bio-availability of antiretroviral medications (e.g., integrase inhibitors such as Raltegravir, Dolutegravir, Elvitegravir is significantly reduced by metal-cation containing antacids and dietary supplements.

4.6 Use in special populations

Ask a physician before use if you are pregnant or breastfeeding

Use During Pregnancy

Gelusil tablets/liquid contains activated dimeticone, which is a category C drug. There are no well-controlled studies to show safety in pregnant women, and use in pregnancy should be based on assessment of the risk/benefit ratio.

Use During Lactation

The following have been established for the ingredients used individually:

Although small amounts of aluminium are excreted in human breast milk, aluminium hydroxide has limited maternal absorption and is not concentrated in human milk.

Magnesium-containing emulsions administered orally to mothers did not affect the stools of breast-feeding infants.

Dimeticone
Use in lactation should be based on assessment of the risk/benefit ratio.

4.7 Effects on ability to drive and use machines

There is no reason to expect that Gelusil may impair a patient's ability to drive or use machinery.

4.8 Undesirable effects

Gelusil is generally well tolerated. Hydroxides of magnesium and aluminium are minimally absorbed and there is a low risk of systemic side-effects or alkalosis (except in patients with renal failure where hypermagnesemia or increased aluminium levels may occur).

Magnesium-containing antacids may cause diarrhea and potentially lead to dehydration. Constipation occurs frequently following continued antacid therapy with aluminium-containing products. These effects are minimized with products such as Gelusil that are a combination of aluminium and magnesium hydroxides; one opposing the effect of the other on gastrointestinal motility. Excessive aluminium antacid therapy has been reported to result in obstruction of the intestinal tract.

Musculoskeletal effects including rickets and osteomalacia, have been reported with prolonged or high-dose use of aluminium-containing antacids.

Central nervous system effects including confusion, myoclonus and seizures have been associated with prolonged use of aluminium-containing antacids in patients on dialysis.

Aluminium-containing antacids inhibit the intestinal absorption of phosphorus as evidenced by a marked increase in fecal phosphorus and a distinct decrease of phosphorus in the urine. Patients with poor dietary intake, such as alcoholics, who might receive high dose antacid therapy for gastrointestinal bleeding, are at the greatest risk for this syndrome, which may appear as early as 4 to 7 days after the start of therapy. Daily supplementation with 20 to 30 mmol of phosphate may be necessary in these patients.

Post Marketing Data

Adverse drug reactions (ADRs) identified during post-marketing experience with aluminium hydroxide + magnesium hydroxide + activated dimeticone are included in Table 1 and Table 2.

The frequencies are provided according to the following convention:

Very common ≥1/10
Common ≥1/100 and < 1/10
Uncommon ≥1/1,000 and <1/100
Rare ≥1/10,000 and <1/1,000
Very rare <1/10,000
Not known (cannot be estimated from the available data)

In Table 1, ADRs identified are presented by frequency category based on 1) incidence in adequately designed clinical trials or epidemiology studies, if available or 2) when incidence is unavailable, frequency category is listed as Not known.

In Table 2, the same ADRs are presented with ADR frequency categories estimated from spontaneous reporting rates where the numerator represents total number of reported Company AEs under given PT or medical concept and denominator represents exposure data calculated from sales data.

Table 1. Adverse Drug Reactions Identified During Post-Marketing Experience with Aluminium Hydroxide/Magnesium Hydroxide/activated Dimeticone by Frequency Category Estimated from Clinical Trials or Epidemiology Studies

SOC Frequency Category	Adverse Event Preferred Term
Immune System Disorders	
Not known	*Angioedema*
Not known	*Hypersensitivity*
Nervous System Disorders	
Not known	*Burning sensation*
Not known	*Dysgeusia*
Gastrointestinal Disorders	
Not known	*Constipation*
Not known	*Diarrhoea*
Not known	*Nausea*[a]
Not known	*Vomiting*[a]
Skin and Subcutaneous Tissue Disorders	
Not known	*Rash*
Not known	*Urticaria*
For Aluminium hydroxide, no ADRs have been identified from post marketing safety review.	
[a]: As nausea and vomiting are often part of the underlying condition, it is difficult to conclude that this relationship is causal.	

Table 2. Adverse Drug Reactions Identified During Post-Marketing Experience with Aluminium Hydroxide/Magnesium Hydroxide/activated Dimeticone by Frequency Category Estimated from Spontaneous Reporting Rates

SOC Frequency Category	Adverse Event Preferred Term
Immune System Disorders	
Very rare	*Angioedema*
Very rare	*Hypersensitivity*
Nervous System Disorders	
Very rare	*Burning sensation*
Very rare	*Dysgeusia*

Gastrointestinal Disorder	
Very rare	*Constipation*
Very rare	*Diarrhoea*
Very rare	*Nausea*[a]
Very rare	*Vomiting*[a]
Skin and Subcutaneous Tissue Disorders	
Very rare	*Rash*
Very rare	*Urticaria*
For Aluminium hydroxide, no ADRs have been identified from post marketing safety review.	
[a]: As nausea and vomiting are often part of the underlying condition, it is difficult to conclude that this relationship is causal.	

4.9 Overdose

There are no reports of overdosage with Gelusil. Potential effects, based on the pharmacology of ingredients, include major electrolyte imbalances such as elevated serum magnesium and aluminium levels, hypophosphatemia, metabolic alkalosis, hyperosmolarity and dehydration.

In the event of overdosage, symptomatic treatment, with supportive measures and gastric lavage, if necessary, is recommended.

The following symptoms of overdosage were identified from a review of the literature:

Aluminium hydroxide
Aluminium toxicity occurs almost exclusively in patients who are unable to excrete aluminium due to impaired renal function. Signs and symptoms include hypercalcemia, reversible microcytic anemia unresponsive to iron replacement therapy, vitamin D refractory osteodystrophy, progressive encephalopathy and phosphorus depletion syndrome, characterized by anorexia, malaise, and muscle weakness.

Magnesium hydroxide
The oral ingestion of magnesium rarely results in toxicity in patients with normal renal function. Signs of hypermagnesemia typically begin to develop with plasma levels around 4 mEq/L (4.8 mg/dL). Symptoms generally correlate to magnesium blood levels, however there is variability among literature reports in patients with similar blood levels. Symptoms associated with blood levels between 4 and 10 mEq/L (4.8 to 12 mg/dL) include nausea, vomiting, flushing, somnolence, and hypotension. Symptoms that appear at or above plasma levels of 10 mEq/L (12 mg/dL) include ECG changes, loss of deep tendon reflex, paralysis of voluntary muscle, and respiratory depression. Around 15 mEq/L (18 mg/dL) heart block and cardiac arrest may occur.

Activated dimeticone
No symptoms of overdosage have been identified from the analysis of post-marketing data and a review of literature.

Keep out of reach of children. In the event of overdose, get medical help.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

The antacids that act by neutralizing the acid in the stomach and by inhibiting pepsin, which is a proteolytic enzyme.

5.2 Pharmacodynamic properties

Aluminium hydroxide
Aluminium hydroxide is slowly solubilized in the stomach and reacts with hydrochloric acid to form aluminium chloride and water. Aluminium hydroxide raises the pH of the stomach contents and provides relief from hyperacidity. Aluminium hydroxide has also been shown to enhance the activity of mucosal prostaglandin cyclooxygenase which could mediate a protective effect.

Magnesium hydroxide
Magnesium hydroxide reacts with gastric hydrochloric acid to form magnesium chloride and water. This reaction partially neutralizes stomach acid. By neutralizing stomach acid, magnesium hydroxide raises the pH of the stomach contents.

Gelusil also contains activated dimethicone, which is an antifoaming agent that decreases acid reflux and acts as an antiflatulent. The mechanism of action is based on the spreading of the silicone oil on foam films and local changes of the surface tension in the contact area. Thus, fast liquid drainage takes part and the film can rupture by "pinch off" mechanisms. The free gas can then be absorbed or expelled.

5.3 Pharmacokinetic properties

COMBINATION: ALUMINUM HYDROXIDE + MAGNESIUM HYDROXIDE + SIMETICONE

Absorption

Aluminum absorption is strongly determined by the doses of aluminium administered, as well as physio-chemical environment in the gastrointestinal tract and presence of dietary elements. Bioavailability varies from 0.001-24% in humans depending on the aluminum intake, but is likely to be towards the lower part of the range. After reaction between aluminum hydroxide and gastric acid, about 17- 30% of the aluminum chloride formed in the stomach is absorbed Approximately one-third of the magnesium administered orally is slowly absorbed from the small intestines [35], however in cases of low dietary intake magnesium absorption increases The normal dietary intake of magnesium generally ranges from 140 – 360 mg/day, with a net intestinal absorption of about 100 mg/d. Simeticone is a chemically inert substance, physiologically inactive and not absorbed by the gastrointestinal tract.

Distribution

Most (80-90%) of absorbed aluminum becomes bound to serum proteins (mainly transferrin). The remainder is bound to low molecular mass compounds, mainly citrate. Aluminum may accumulate in bones, lungs, spleen, brain and nerve tissue. Total body magnesium content is about 25 g (1000 mmol), with half of that amount located in bone. The remaining magnesium is almost entirely intracellular, with only 1% located in the extracellular fluid. Normal serum magnesium levels range from 1.5 – 2.5 mEq/L (0.7 – 1 mmol/L). Approximately 30% of magnesium in the blood is bound to protein, 15% complexes with phosphate and other anions, and the remainder exists as free, ionized magnesium.

Metabolism

This section is not applicable.

Elimination

The majority of aluminum is excreted renally; biliary aluminum accounts for approximately 2% of total aluminum elimination. Urinary excretion, and thus serum magnesium concentration, is controlled by renal reabsorption following filtration, and the net excretion is generally equal to net absorption. The majority (60%) of magnesium reabsorption occurs via the paracellular route in the cortical thick ascending limb of the loop of Henle and is increased by parathyroid hormone and decreased by hypercalcemia and hypermagnesemia. Lesser amounts of the total filtered magnesium are reabsorbed in the proximal tubule (20%) and distal convoluted tubule (5 – 10%)

Gelusil is expected to provide rapid relief of symptoms associated with hyperacidity. The duration of action ranges from 1 to 3 hours after a single dose. This can be prolonged by taking Gelusil after meals.

Antacids vary in the extent to which they are absorbed. Gelusil contains aluminium, and magnesium and these are less completely absorbed than those that contain sodium bicarbonate. When the neutralization products enter the small intestine, some (5-10%) of the cations (Al, Mg) are absorbed. Unreacted insoluble antacids pass through the intestines and are eliminated in the feces.

6. NONCLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

Non-clinical studies performed with the combination of actives were not found in the published literature. Thus, non-clinical safety data on the individual active ingredients was reviewed.

Summary:
Preclinical data reveal no special hazard for humans based on conventional studies of single and repeated dose toxicity, genotoxicity, carcinogenicity and toxicity to reproduction and development.

General Toxicology

Aluminium Hydroxide
The acute oral toxicity for aluminium hydroxide was very low. Exposure to doses as high as 1,252 mg Al/kg/day of aluminium hydroxide for 30 or 60 days in rats was well tolerated.

Magnesium Hydroxide
Magnesium hydroxide has acute, oral LD50 value of 8,500 mg/kg in rats and mice. In a 13 weeks repeat dose toxicity study on magnesium salt in mice, the no adverse effect level of magnesium was determined to be 420 mg/kg/day.

Activated Dimethicone
Activated dimeticone has a low level of toxicity by oral route. Repeated oral administration of activated dimethicone in rat studies demonstrated minimal clinical signs of toxicity.

Genetic Toxicology

Aluminium Hydroxide
In various *in vitro* and *in vivo* studies, aluminium and its compounds were reported to be negative for genotoxic potential.

Magnesium Hydroxide
Magnesium hydroxide is considered non-genotoxic based on the negative findings in genotoxicity studies of other magnesium salts.

Activated Dimethicone
In *in vitro* and *in vivo* assays activated dimeticone was non-genotoxic.

Carcinogenicity

Aluminium Hydroxide
Aluminium and its compounds were considered non-carcinogenic.

Magnesium Hydroxide
There are insufficient data to determine carcinogenic potential of magnesium hydroxide through oral route. Given the essential nature of magnesium, oral administration of magnesium hydroxide would not be expected to pose a cancer risk. Supporting this statement is a negative finding in a 2-year study with magnesium chloride in mice.

Activated Dimethicone (Dimethicone + Silicon Dioxide)

Dimethicone
Based on several long term studies, dimethicone does not indicate a carcinogenic potential.

Teratogenicity

Aluminium Hydroxide
Based on various developmental and teratogenicity studies carried out in mammals, Aluminium hydroxide was found to be non-teratogenic.

Magnesium Hydroxide
No relevant experimental data on developmental toxicity is reported on magnesium hydroxide. Oral administration of magnesium chloride and magnesium sulphate solution had no adverse level of 800 mg/kg/d (equivalent to 96 mg Mg^{2+}/kg/d) and 450 mg/kg bw/day respectively for developmental and maternal toxicity.

Activated Dimethicone (Dimethicone + Silicon Dioxide)
Dimethicone

Dimethicone was not teratogenic in rats or rabbits.

7. DESCRIPTION

Tablet: A light pink to pink round, flat bevel edged uncoated chewable, mint flavoured tablet with "GELUSIL MPS" debossed on both sides of the tablet, with some degree of mottling.

Original Mint Flavour Liquid: Viscous pink suspension with mint flavour, free from visible contaminants

Xtracool Mint Flavour White: Viscous white to off-white suspension with mint flavour, free from visible contaminants

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

None

8.2 Shelf-life

24 months from the date of manufacture.

Storage and handling information

Tablets: Store in a dry place away from sunlight.

Liquid: Store away from sunlight. Shake well before use. Keep bottle tightly closed and avoid freezing.

8.3 Packaging Information

Tablet: 15 Tablets per blister in Aluminium foil and transparent PVC film.

Original Mint Flavour Liquid: 50 ml, 200 ml, and 400 ml in clear PET bottles.

Xtracool Mint Flavour White: 50 ml and 200 ml in clear PET bottles.

9. DETAILS OF MANUFACTURER

Pfizer Limited at Plot no. 9/2, IDA, Uppal, Hyderabad - 500039
Pfizer Limited at Plot No. 9/5 & 6, I.D.A., Uppal, Hyderabad - 500039
Pfizer Limited at Khata No. 845/713 and 1108/970/1, 34th K.M., Tumkur Road, T.Begur, Nelamangala, Bangalore Rural - 562123
Pfizer Limited at Plot No. D33, Gokul Shirgaon, MIDC, Kolhapur - 416234

Please refer outer carton for the specific manufacturer of the batch.

10. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

Gelusil Tablet: MF-577/2010 dated 06-Jul-2010
Gelusil Liquid: MF-458/2010 dated 28-May-2010

11. DATE OF REVISION

September 2021