1. NAME OF THE MEDICINAL PRODUCT

Maalox Plus Chewable Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200 mg of Magnesium Hydroxide, 200mg of Hydrated Aluminium Oxide and 25mg of Dimethicone.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Bi-layered, white/pale yellow circular, bevel-edged, lemon flavoured chewable tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Antacid, antiflatulent, relief of sensation of heartburn

4.2 Posology and method of administration

For oral administration.

Recommended Dosage:

Adults (including elderly persons): 1-2 tablets well chewed, four times a day, taken twenty minutes to one hour after meals and at bedtime, or as required.

Children: Not recommended.

4.3 Contraindications

Should not be used in patients who are Hypersensitivity to the active ingredients or to any of the excipients, are severely debilitated or suffering from kidney failure, or hypophosphataemia or if there is severe abdominal pain and/or the possibility of bowel obstruction.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.4 Special warnings and precautions for use

Aluminium hydroxide may cause constipation and magnesium salts overdose may cause hypomotility of the bowel; large doses of this product may trigger or aggravate intestinal

obstruction and ileus in patients at higher risk such as those with renal impairment, or the elderly.

Aluminium hydroxide is not well absorbed from the gastrointestinal tract, and systemic effects are therefore rare in patients with normal renal function. However, excessive doses or long-term use, or even normal doses in patients with low-phosphorus diets may lead to phosphate depletion (due to aluminium-phosphate binding) accompanied by increased bone resorption and hypercalciuria with the risk of osteomalacia. Medical advice is recommended in case of long-term use or in patients at risk of phosphate depletion.

Magnesium salts may cause central nervous depression in the presence of renal insufficiency and should be used with extreme caution in patients with kidney disease.

In patients with renal impairment, plasma levels of both aluminium and magnesium increase. In these patients, a long-term exposure to high doses of aluminium and magnesium salts may lead to encephalopathy, dementia, microcytic anaemia, or worsen dialysis-induced osteomalacia.

Aluminium hydroxide may be unsafe in patients with porphyria undergoing hemodialysis. The prolonged use of antacids in patients with renal failure should be avoided.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

Care should be observed if used by diabetics because of the sugar content in the tablet.

4.5 Interaction with other medicinal products and other forms of interaction

Maalox Plus should not be taken simultaneously with other medicines as they may interfere with their absorption if taken within 1 hour.

Aluminium-containing antacids may prevent the proper absorption of drugs such as tetracyclines, vitamins, ciprofloxacin, ketoconazole, hydroxychloroquine, chloroquine, chlorpromazine, rifampicin, cefdinir, cefpodoxime, levothyroxine, rosuvastatin, H_2 antagonists, atenolol, cyclines, diflunisal, digoxin, bisphosphonates, ethambutol, fluoroquinolones, sodium fluorure, glucocorticoids, indometacine, isoniazide, lincosamides, metoprolol, neuroleptics phenothiazines, pencillamine, propranolol, iron salts.

Staggering the administration times of the interacting drug and the antacid by at least 2 hours (4 hours of the fluoroquinolones) will often help avoid undesirable drug interactions.

Levothyroxine may also bind to simeticone which may delay or reduce the absorption of levothyroxine.

Polystyrene sulphonate (Kayexalate):
Caution is advised when used concomitantly with polystyrene sulphonate due to the potential risk of reduced effectiveness of the resin in binding potassium, of metabolic alkalosis in patients with renal failure (reported with aluminium hydroxide and magnesium hydroxide), and of intestinal obstruction (reported with aluminium hydroxide).

Quinidine:
Concomitant use with quinidines may increase the serum levels of quinidine and lead to quinidine overdosage.

Tetracycline:
Because of the aluminium content, Maalox Plus should not be concomitantly administered with tetracycline-containing antibiotics or any tetracycline salts.

Citrates:
Aluminium hydroxide and citrates may result in increased aluminium levels, especially in patients with renal impairment.

Urine alkalinisation secondary to administration of magnesium hydroxide may modify excretion of some drugs; thus, increased excretion of salicylates has been seen.

4.6 Fertility, Pregnancy and lactation

The safety of Maalox Plus Tablets in pregnancy has not been established.

Pregnancy:
There are no available data on Maalox Plus use in pregnant women. No conclusions can be drawn regarding whether or not Maalox Plus is safe for use during pregnancy. Maalox Plus should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks, including those to the fetus.
The use of Maalox Plus should be avoided during the first trimester of pregnancy.

Lactation:
Because of the limited maternal absorption when used as recommended, minimal amounts, if any, of aluminium hydroxide and magnesium salt combinations are expected to be excreted into breast milk.

Simeticone is not absorbed from the gastrointestinal tract.

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to aluminium hydroxide, magnesium hydroxide and simeticone is negligible

4.7 Effects on ability to drive and use machines

None stated

4.8 Undesirable Effects

The following CIOMS frequency rating is used, when applicable:
Very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from available data).

<u>Immune system disorders</u>
Frequency not known: hypersensitivity reactions, such as pruritus, urticaria, angioedema and anaphylactic reactions

<u>Gastrointestinal disorders</u>
Gastrointestinal side-effects are uncommon.
Uncommon: diarrhoea or constipation (see section 4.4).
Frequency not known: Abdominal pain

Injury, poisoning and procedural complications:
Frequency not known:

Hyperaluminemia (related to Aluminium component).

Metabolism and nutrition disorders
Very rare: Hypermagnesemia, including observations after prolonged administration of magnesium hydroxide to patients with renal impairment

Frequency not known:
Hyperaluminemia
Hypophosphatemia, in prolonged use or at high doses or even normal doses of the product in patients with low-phosphorus diets which may result in increased bone resorption, hypercalciuria, osteomalacia (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il/

4.9 Overdose

Serious symptoms are unlikely following overdosage.

Reported symptoms of acute overdose with aluminium hydroxide and magnesium salts combination include diarrhoea, abdominal pain, vomiting.
Large doses of this product may trigger or aggravate intestinal obstruction and ileus in patients at risk (see section 4.4).

Aluminium and magnesium are eliminated through urinary route; treatment of acute overdose consists of administration of IV Calcium Gluconate, rehydration and forced diuresis. In case of renal function deficiency, haemodialysis or peritoneal dialysis is necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dried aluminium hydroxide gel	- antacid
Magnesium Hydroxide	- antacid
Simeticone	- antifoaming agent/antiflatulent

The antacids are balanced such that gastrointestinal side effects (constipation and diarrhoea) are minimal.

5.2 Pharmacokinetic properties

None stated

5.3 Preclinical safety data

None stated

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Glucose anhydrous- 500.50 mg/tab , Maize starch, Mannitol- 75 mg/tab, Sucrose- 75mg/tab, Sorbitol liquid non-crystallizing- 32.80mg/ml (corresponding to 22.96 mg of Sorbitol), Sorbitol - 22.04 mg/tab, Talc, Magnesium Stearate, Pregelatinized starch (Maize starch), Lemon Flavour, Citric Acid anhydrous, Saccharin sodium, Swiss Cream flavour, Iron oxide yellow (E-172).

6.2 Incompatibilities

None stated.

6.3 Shelf life

The expiry date is indicated on the packaging materials

6.4 Special precautions for storage

Do not store above 25^{o}C. Do not freeze.
Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

PVC /aluminium strip packs.

Packs of 40 or 50 tablets. Not all pack sizes may be available.

7. MARKETING AUTHORISATION HOLDER AND IMPORTER

Sanofi-aventis Israel ltd.

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MAALPLUS-TAB-16.0