1. NAME OF THE MEDICINAL PRODUCT

Rennie Orange

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains 680 mg calcium carbonate, equivalent to 272.3 mg calcium and 80 mg magnesium carbonate, equivalent to 23.1 mg magnesium.
Excipients: each chewable tablet contains 475 mg sucrose.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablets.

Rennie is a cream-coloured, square tablet with rounded edges inscribed with “RENNIE” on both sides; the tablet has an orange flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Relief of hyperacidity and heartburn.

4.2 Posology and method of administration

For adults and children over the age of 12 years: 1 -2 tablets are to be sucked or chewed, as needed, preferably circa 1 hour after food and before going to bed.
For the treatment of heartburn, an additional 1 -2 tablets may be taken between those times.
Do not take more than 10 tablets per day. This medicine is not to be taken by children under the age of 12 years.
It is advisable to wait roughly 1 -2 hours between taking other medicines and taking Rennie.

For oral use. To be chewed or sucked. The tablets can be taken without water.

As with all antacids, in the event of persistent symptoms, diagnostic measures are recommended to exclude serious diseases.

For special warnings and precautions during use: see section 4.4.

4.3 Contraindications

- Severe renal insufficiency, hypercalcaemia and/or conditions resulting in hypercalcaemia.
- Pre-existing hypophosphataemia.
- Nephrolithiasis due to calcium-containing stones.
- Hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings and precautions for use

Prolonged use should be avoided.
If symptoms do not (fully) disappear, further medical testing is required.
As with other antacids, Rennie may mask a malignancy in the stomach.
Rennie should not be used in the following cases:

- Hypercalciuria.
- Caution should generally be exercised in patients with renal impairment.

If Rennie is used in these patients, plasma calcium, phosphate and magnesium levels should be regularly monitored.

Calcium-containing antacids should generally be used with caution in patients with constipation, haemorrhoids and sarcoidosis.
Prolonged use of high dosages may lead to adverse effects, such as hypercalcaemia, hypermagnesaemia and milk-alkali syndrome, especially in patients with renal insufficiency. The product should not be taken with large amounts of milk or dairy products.
Prolonged use increases the risk of development of kidney stones.
There are reports in the literature of a few cases where there was a potential relationship between calcium carbonate and appendicitis, gastrointestinal haemmorrhage, intestinal blockage or oedema.
Patients with rare hereditary forms of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency must not use this medicinal product.
Consult your doctor if the symptoms persist for longer than 14 days.

4.5 Interaction with other medicinal products and other forms of interaction

Changes in gastric acidity, as caused by the ingestion of antacids, may impact the extent and rate of absorption of concomitantly administered medicinal products.
It has been demonstrated that calcium and magnesium-containing antacids may hinder absorption of some antibiotics (such as tetracyclines and quinolones); cardiac glycosides (including digoxin); levothyroxine and eltrombopag through formation of complexes.
Calcium salts reduce the absorption of fluoride and iron-containing products, and calcium and magnesium salts may hinder the absorption of phosphates.
Thiazide diuretics reduce urinary excretion of calcium. Due to an increased risk of hypercalcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics.
Concurrent administration of antacids with these medicinal products is not recommended; antacids should be taken 1-2 hours afterwards.

<u>Effects on laboratory parameters:</u>
The use of antacids may interfere with physiological values: urine pH may increase and serum phosphate and potassium levels may decrease as a result of excessive and prolonged use.

4.6 Pregnancy and lactation

No increased risk of congenital defects has been observed after the use of calcium carbonate and magnesium carbonate during pregnancy. An elevated risk of hypercalcaemia and/or hypermagnesaemia cannot be fully excluded with excessive or prolonged use or renal insufficiency. Rennie can be used as prescribed during pregnancy, but prolonged ingestion of high doses must be avoided. Rennie can be used as prescribed during lactation.
During pregnancy and lactation, it should be taken into consideration that Rennie contains a substantial amount of calcium. Pregnant women must therefore not exceed the recommended dosage and also avoid excessive consumption of milk and dairy products. This warning is intended to prevent excessive calcium ingestion (which may lead to milk-alkali syndrome).

4.7 Effects on ability to drive and use machines

Rennie is not expected to influence these functions.

4.8 Undesirable effects

Immune system disorders:
Hypersensitivity reactions have been reported very rarely. The clinical symptoms were rash, urticaria, angioedema and anaphylaxis.

Metabolism and nutrition disorders:
Prolonged use of high doses may lead to hypermagnesaemia or hypercalcaemia and alkalosis (gastrointestinal symptoms include nausea and vomiting, fatigue, confusion, polyuria, polydipsia and dehydration), especially in patients with impaired kidney function. Prolonged use of high doses of calcium carbonate with milk may lead to Burnett's syndrome (milk-alkali syndrome).

Gastrointestinal disorders:
Nausea, vomiting, gastric symptoms and diarrhoea may occur.

Musculoskeletal and connective tissue disorders
Muscle weakness may occur.

4.8.1 Undesirable effects occurring only with milk-alkali syndrome (see 4.9):

Gastrointestinal disorders:
Ageusia may occur with milk-alkali syndrome.

General disorders and administration site conditions:
Calcinosis and asthenia may occur with milk-alkali syndrome.

Nervous system disorders:
Headaches may occur with milk-alkali syndrome.

Renal and urinary disorders:
Azotaemia may occur with milk-alkali syndrome.

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
Especially in patients with impaired renal function, prolonged use of high doses of calcium carbonate and magnesium carbonate may result in renal insufficiency, hypermagnesaemia, hypercalcaemia and alkalosis which may result in digestive symptoms (nausea, vomiting, constipation) and muscle weakness. Stop the administration and ingest plenty of fluids if this occurs. In severe cases of overdose (e.g. milk-alkali syndrome), a doctor must be consulted, because other measures of rehydration (including infusion) may be needed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: antacids, other combinations ATC code: A02 AX.

Rennie is a combination of two antacids, calcium carbonate and magnesium carbonate. Calcium carbonate and magnesium carbonate have a localised mechanism of action based on neutralisation of gastric acid and is independent of systemic absorption. Calcium carbonate has a rapid, prolonged and powerful neutralising effect. This effect is increased by the addition of magnesium carbonate which also has a strong neutralising effect. In healthy volunteers, a significant increase in gastric pH was

reached within 2 minutes. The total neutralising capacity of 2 tablets is 29 mEq/H+ (titration to endpoint pH 2.5).

5.2 Pharmacokinetic properties

Calcium and magnesium:
Calcium and magnesium carbonates react with gastric acid in the stomach to produce water and soluble mineral salts.
$CaCO_3 + 2\ HCl \rightarrow CaCl_2 + H_2O + CO_2$
$MgCO_3 + 2\ HCl \rightarrow MgCl_2 + H_2O + CO_2$

Calcium and magnesium are absorbed from these soluble salts. However, the extent of absorption is patient and dose dependent. Less than 10% calcium and 15-20% magnesium are absorbed.

In healthy people, the small amounts of absorbed calcium and magnesium are generally rapidly excreted via the kidneys. Serum calcium and magnesium levels may be increased in patients with impaired kidney function.
Various digestive juices outside the stomach result in conversion of soluble salts in the gastrointestinal tract to insoluble salts which are excreted in the faeces.

5.3 Preclinical safety data

No special data.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each Rennie Orange chewable tablet contains the following excipients: sucrose, orange flavour, talc, pregelatinised maize starch, potato starch, magnesium stearate, light liquid paraffin, saccharin sodium, water.

6.2 Incompatibilities

None.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25 °C. Store in the original packaging.

6.5 Nature and contents of container

Boxes of 36 chewable tablets in PVC/aluminium blister strips.

6.6 Special precautions for disposal and other handling

None.

7. MARKETING AUTHORISATION HOLDER

Bayer Israel Ltd., 36 Hacharash Street, Hod Hasharon 45240.

Revised on 09/2020.