PROFESSIONAL INFORMATION

SCHEDULING STATUS S4

1. NAME OF THE MEDICINE

RABEMED 10 (tablets)

RABEMED 20 (tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Rabemed 10: Each Rabemed 10 gastro-resistant tablet contains 10 mg rabeprazole sodium, equivalent to 9,42 mg rabeprazole.

Rabemed 20: Each Rabemed 20 gastro-resistant tablet contains 20 mg rabeprazole sodium, equivalent to 18,85 mg rabeprazole.

Each Rabemed 10 tablet contains mannitol (46,00 mg).

Each Rabemed 20 tablet contains mannitol (92,00 mg).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

Rabemed 10: Pink, round, biconvex coated tablets.

Rabemed 20: Yellow, round, biconvex coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

RABEMED is indicated for the treatment of

- Active duodenal ulcer.

- Active benign gastric ulcer.
- Symptomatic erosive or ulcerative gastro-oesophageal reflux disease (GORD).
- Maintenance treatment of healed erosive or ulcerative GORD. Efficacy has not been demonstrated for periods exceeding 12 months.
- Symptomatic treatment of gastro-oesophageal reflux disease (GORD).
- Zollinger-Ellison Syndrome and other pathological hypersecretory conditions.
- *H. Pylori*-positive duodenal ulcers, as part of the eradication programme with appropriate antibiotics.

4.2 Posology and method of administration

Posology:

Adults/elderly:

Active duodenal ulcer and active benign gastric ulcer:

The recommended oral dose for both active duodenal ulcer and active benign gastric ulcer is 20 mg to be taken once daily in the morning. Most patients with either active duodenal ulcer or active benign gastric ulcer heal within 4 or 6 weeks. However, a few patients may require an additional 4 or 6 weeks of therapy to achieve healing.

Erosive or ulcerative gastro-oesophageal reflux disease (GORD):

The recommended oral dose for this condition is 20 mg to be taken once daily for four to eight weeks.

Gastro-oesophageal reflux disease long-term management (GORD maintenance):

For long-term management of up to 12 months, a maintenance dose of RABEMED 20 mg or 10 mg once daily can be used depending upon patient response.

Symptomatic treatment gastro-oesophageal reflux disease (symptomatic GORD):

10 mg once daily in patients without oesophagitis. If symptom control has not been achieved after four weeks of treatment with the prescribed daily dose, further investigation is recommended. Once symptoms have resolved, subsequent symptom control can be achieved using an on-demand regimen taking 10 mg once daily when needed.

Zollinger-Ellison Syndrome and other pathological hypersecretory conditions:

The recommended adult starting dose is 60 mg once a day. The dose may be titrated upwards to 120 mg/day based on individual patient needs. Single daily doses up to 100 mg/day may be given. 120 mg dose may require divided doses, 60 mg twice daily. Treatment should continue for as long as clinically indicated.

Eradication of H. pylori:

Patients with *H. pylori* infection should be treated with eradication therapy. The following combination given for 7 days is recommended: RABEMED 20 mg twice daily plus clarithromycin 500 mg twice daily and amoxicillin 1 g twice daily.

Renal and hepatic impairment:

No dosage adjustment is necessary for patients with renal or hepatic impairment. See section 4.4 for the use of RABEMED in the treatment of patients with severe hepatic impairment.

Paediatric population:

RABEMED is not recommended for use in children, as there is no experience of its use in this group.

Method of administration:

For indications, requiring once daily treatment RABEMED tablets should be taken in the morning, before eating; and although neither the time of day nor food intake was shown to

have any effect on rabeprazole sodium activity, this regimen will facilitate treatment compliance.

Patients should be cautioned that the RABEMED tablets should not be chewed or crushed, but should be swallowed whole.

4.3 Contraindications

RABEMED is contraindicated in patients with known hypersensitivity to rabeprazole sodium, substituted benzimidazoles or to any of the excipients.

RABEMED is contraindicated in pregnancy and during breastfeeding.

4.4 Special warnings and precautions for use

Symptomatic response to therapy with rabeprazole sodium does not preclude the presence of gastric or oesophageal malignancy, therefore the possibility of malignancy should be excluded prior to commencing treatment with RABEMED.

Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance.

A risk of cross-hypersensitivity reactions with other proton pump inhibitor or substituted benzimidazoles cannot be excluded.

Patients should be cautioned that RABEMED tablets should not be chewed or crushed, but should be swallowed whole.

There have been post-marketing reports of blood dyscrasias (thrombocytopenia and neutropenia). In the majority of cases where an alternative aetiology cannot be identified, the

events were uncomplicated and resolved on discontinuation of RABEMED.

Hepatic enzyme abnormalities have been seen in clinical trials and have also been reported since market authorisation. In the majority of cases where an alternative aetiology cannot be identified, the events were uncomplicated and resolved on discontinuation of rabeprazole.

Less frequent reports of hepatic encephalopathy have been received in patients with underlying cirrhosis.

No evidence of significant substance related safety problems was seen in a study of patients with mild to moderate hepatic impairment versus normal age and sex matched controls. However, because there are no clinical data on the use of rabeprazole in the treatment of patients with severe hepatic dysfunction, the prescriber is advised to exercise caution when treatment with RABEMED is first initiated in such patients.

Co-administration of atazanavir with RABEMED is not recommended (see section 4.5).

Treatment with proton pump inhibitors, including RABEMED, may possibly increase the risk of gastrointestinal infections such as *Salmonella, Campylobacter* and *Clostridium difficile* (see section 5.1).

Proton pump inhibitors, especially if used in high doses and over long durations (> 1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly in elderly people or in presence of other recognised risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10 – 40 %. Some of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

Hypomagnesaemia:

Severe hypomagnesaemia has been reported in patients treated with PPIs like RABEMED for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with digoxin or medicinal products that may cause hypomagnesaemia (e.g. diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Concomitant use of RABEMED with methotrexate:

Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of RABEMED may be considered in some patients.

Influence on vitamin B_{12} absorption:

RABEMED, as all acid-blocking medicines, may reduce the absorption of vitamin B_{12} (cyanocobalamin) due to hypo- or a- chlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B_{12} absorption on long-term therapy or if respective clinical symptoms are observed.

Subacute cutaneous lupus erythematosus (SCLE):

Proton pump inhibitors are associated with very infrequent cases of SCLE. If lesions occur,

especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the health care professional should consider stopping RABEMED. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Paediatric population:

RABEMED is not recommended for use in children, as there is no experience of its use in this group.

Interference with laboratory tests:

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, RABEMED treatment should be stopped for at least 5 days before CgA measurements (see section 5.1). If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

Acute Tubulointerstitial Nephritis:

Acute tubulointerstitial nephritis (TIN) has been observed in patients taking rabeprazole and may occur at any point during rabeprazole therapy. Acute tubulointerstitial nephritis can progress to renal failure.

TIN is characterised by an inflammatory reaction within the tubulointerstitial space of the kidney. Acute interstitial inflammatory reactions are associated with damage to the tubulointerstitium, leading to acute kidney injury. TIN may be drug-related, infectious, systemic, autoimmune, genetic, and idiopathic with the most common cause being related to a medication or drug exposure.

Patients may present with varying signs and symptoms from symptomatic hypersensitivity reactions to non-specific symptoms of decreased renal function (e.g., malaise, nausea, anorexia). In reported case series, some patients were diagnosed on biopsy and in the absence of extrarenal manifestations (e.g., fever rash or arthralgia).

Discontinue RABEMED and evaluate patients with suspected acute TIN.

4.5 Interaction with other medicines and other forms of interaction

RABEMED produces a profound and long lasting inhibition of gastric acid secretion. An interaction with compounds whose absorption is pH dependent may occur. Co-administration of rabeprazole sodium with ketoconazole or itraconazole may result in a significant decrease in antifungal plasma levels. Therefore, individual patients may need to be monitored to determine if a dosage adjustment is necessary when ketoconazole or itraconazole are taken concomitantly with RABEMED.

A 22 % increase in trough digoxin levels has been observed in normal subjects.

In clinical trials, antacids were used concomitantly with the administration of rabeprazole and, in a specific medicine-medicine interaction study, no interaction with liquid antacids was observed.

Co-administration of atazanavir 300 mg/ritonavir 100 mg with omeprazole (40 mg once daily) or atazanavir 400 mg with lansoprazole (60 mg once daily) to healthy volunteers resulted in a substantial reduction in atazanavir exposure. The absorption of atazanavir is pH dependent. Although not studied, similar results are expected with other proton pump inhibitors. Therefore, PPIs, including RABEMED, should not be co-administered with atazanavir (see section 4.4).

Methotrexate:

Case reports, published population pharmacokinetic studies, and retrospective analyses suggest that concomitant administration of PPIs and methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate. However, no formal interaction studies of methotrexate with PPIs have been conducted.

Studies in healthy subjects have shown that rabeprazole sodium does not have clinically significant interactions with amoxicillin. Rabeprazole does not adversely influence plasma concentrations of amoxicillin or clarithromycin when co-administered for the purpose of eradicating upper gastrointestinal *H. pylori* infection.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Safety in pregnancy and lactation has not been established (see section 4.3).

There are no data on the safety of RABEMED in human pregnancy. Reproduction studies performed in rats and rabbits have revealed no evidence of impaired fertility or harm to the foetus due to rabeprazole sodium, although low foeto-placental transfer occurs in rats.

RABEMED is contraindicated during pregnancy.

Lactation:

It is not known whether rabeprazole sodium is excreted in human breast milk. No studies in lactating women have been performed. Rabeprazole sodium is however, excreted in rat mammary secretions. Therefore, RABEMED should not be used during breastfeeding.

4.7 Effects on ability to drive and use machines

Based on the pharmacodynamic properties and the adverse events profile, it is unlikely that RABEMED would cause an impairment of driving performance or compromise the ability to use machinery. If, however, alertness may be impaired due to somnolence, it is recommended that driving and operating complex machinery be avoided.

4.8 Undesirable effects

The most commonly reported undesirable effects; during controlled clinical trials with rabeprazole were headache, diarrhoea, abdominal pain, asthenia, flatulence, rash and dry mouth. The majority of undesirable effects experienced during clinical studies were mild or moderate in severity, and transient in nature.

Infections and infestations:

***Frequent*:** Infection

Blood and the lymphatic system disorders:

***Less frequent*:** Neutropenia, leucopenia, thrombocytopenia, leukocytosis, agranulocytosis

Immune system disorders:

Less frequent: Hypersensitivity[1,2]

Metabolism and nutrition disorders:

***Less frequent*:** Anorexia

Not known: Hyponatraemia, hypomagnesaemia (see section 4.4)

Psychiatric disorders:

Frequent: Insomnia

Less frequent: Nervousness, agitation, hallucinations, anxiety with panic attacks, episodic night terrors, attention deficit, depression

Not known: Confusion

Nervous system disorders:

***Frequent*:** Headache, dizziness

***Less frequent*:** Paraesthesia, somnolence

Eye disorders:

Less frequent: Visual disturbance, anterior ischaemic optic neuropathy

Vascular disorders:

***Not known*:** Peripheral oedema

Respiratory, thoracic and mediastinal disorders:

Frequent: Cough, pharyngitis, rhinitis

Less frequent: Bronchitis, sinusitis

Gastrointestinal disorders:

Frequent: Diarrhoea, vomiting, nausea, abdominal pain, constipation, flatulence, fundic gland polyps (benign)

Less frequent: Dyspepsia, dry mouth, eructation, gastritis, stomatitis, taste disturbance

Not known: Microscopic colitis

Hepatobiliary disorders:

Less frequent: Hepatitis, jaundice, hepatic encephalopathy[3]

Skin and subcutaneous tissue disorders:

Less frequent: Rash, erythema[2], alopecia, urticaria, bullous reactions[2], pruritus, sweating, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), erythema multiforme

Not known: Subacute cutaneous lupus erythematosus (see section 4.4)

Musculoskeletal, connective tissue and bone disorders:

Frequent: Non-specific pain, back pain

Less frequent: Myalgia, leg cramps, arthralgia, myopathy, rhabdomyolysis, fracture of the hip, wrist or spine (see section 4.4)

Renal and urinary disorders:

Less frequent: Urinary tract infection, tubulointerstitial nephritis (with possible progression to renal failure)

Reproductive system and breast disorders:

Less frequent: Impotence

Not known: Gynaecomastia

General disorders and administration site conditions:

Frequent: Asthenia, influenza-like illness

Less frequent: Chest pain, chills, pyrexia, malaise

Ear and labyrinth disorders:

Less frequent: Vertigo, tinnitus

Investigations:

Less frequent: Increased hepatic enzymes[3], weight increased

[1] Includes facial swelling, hypotension and dyspnoea

[2] Erythema, bullous reactions and hypersensitivity reactions have usually resolved after

discontinuation of therapy.

[3] Rare reports of hepatic encephalopathy have been received in patients with underlying cirrhosis. In treatment of patients with severe hepatic dysfunction, the prescriber is advised to exercise caution when treatment with RABEMED is first initiated in such patients (see section 4.4).

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

Suspected adverse reactions can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

4.9 Overdose

Experience to date with deliberate or accidental overdose is limited. The maximum established exposure has not exceeded 60 mg twice daily, or 160 mg once daily. Effects are, generally minimal, representative of the known adverse event profile and may be reversible without further medical intervention.

No specific antidote for rabeprazole is known. Rabeprazole sodium is extensively protein bound and is, therefore, not readily dialysable. Treatment should be symptomatic and general supportive measures should be utilised.

5. PHARMACOLOGICAL PROPERTIES

ATC code: A02BC04, proton pump inhibitors

5.1 Pharmacodynamic properties

Mechanism of action:

Rabeprazole sodium belongs to the class of anti-secretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H_2 histamine antagonist properties, but suppresses gastric acid secretion by the specific inhibition of the H^+/K^+-ATPase enzyme (the acid or proton pump). The effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus. Animal studies indicate that after administration, rabeprazole sodium rapidly disappears from both the plasma and gastric mucosa. As a weak base, rabeprazole is rapidly absorbed following all doses and is concentrated in the acid environment of the parietal cells. Rabeprazole is converted to the active sulphenamide form through protonation and it subsequently reacts with the available cysteines on the proton pump.

Anti-secretory activity:

After oral administration of a 20 mg dose of rabeprazole sodium the onset of the anti-secretory effect occurs within one hour, with the maximum effect occurring within 2 to 4 hours. Inhibition of basal and food stimulated acid secretion 23 hours after the first dose of rabeprazole sodium are 69 % and 82 % respectively and the duration of inhibition lasts up to 48 hours. The inhibitory effect of rabeprazole sodium on acid secretion increases slightly with repeated once-daily dosing, achieving steady state inhibition after 3 days. When the medicine is discontinued, secretory activity normalises over 2 to 3 days.

Decreased gastric acidity due to any means, including proton pump inhibitors such as RABEMED, increases counts of bacteria normally present in the gastrointestinal tract. Treatment with proton pump inhibitors, including RABEMED may possibly increase the risk of gastrointestinal infections such as *Salmonella, Campylobacter* and *Clostridium difficile*.

Serum gastrin effects:

In clinical studies, patients were treated once daily with 10 or 20 mg rabeprazole sodium, for up to 43 months duration. Serum gastrin levels increased during the first 2 to 8 weeks reflecting the inhibitory effects on acid secretion and remained stable while treatment was continued. Gastrin values returned to pre-treatment levels, usually within 1 to 2 weeks after discontinuation of therapy.

Human gastric biopsy specimens from the antrum and the fundus from over 500 patients receiving rabeprazole or comparator treatment for up to 8 weeks have not detected changes in ECL cell histology, degree of gastritis, incidence of atrophic gastritis, intestinal metaplasia or distribution of *H. pylori* infection. In over 250 patients followed for 36 months of continuous therapy, no significant change in findings present at baseline was observed.

Other effects:

Systemic effects of rabeprazole sodium in the CNS, cardiovascular and respiratory systems have not been found to date. Rabeprazole sodium, given in oral doses of 20 mg for 2 weeks, had no effect on thyroid function, carbohydrate metabolism, or circulating levels of parathyroid hormone, cortisol, oestrogen, testosterone, prolactin, cholecystokinin, secretin, glucagon, follicle stimulating hormone (FSH), luteinising hormone (LH), renin, aldosterone or somatotrophic hormone.

Studies in healthy subjects have shown that rabeprazole sodium does not have clinically significant interactions with amoxicillin. Rabeprazole does not adversely influence plasma concentrations of amoxicillin or clarithromycin when co-administered for the purpose of eradicating upper gastrointestinal *H. pylori* infection.

During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also CgA increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours.

Available published evidence suggests that proton pump inhibitors should be discontinued between 5 days and 2 weeks prior to CgA measurements. This is to allow CgA levels that might be spuriously elevated following PPI treatment to return to reference range.

5.2 Pharmacokinetic properties

Absorption:

RABEMED is an enteric-coated (gastro-resistant) tablet formulation of rabeprazole sodium. This presentation is necessary because rabeprazole is acid labile. Absorption of rabeprazole therefore begins only after the tablet leaves the stomach. Absorption is rapid, with peak plasma levels of rabeprazole occurring approximately 3,5 hours after a 20 mg dose. Peak plasma concentrations (C_{max}) of rabeprazole and AUC are linear over the dose range of 10 mg to 40 mg. Absolute bioavailability of an oral 20 mg dose (compared to intravenous administration) is about 52 % due in large part to pre-systemic metabolism. Additionally, the bioavailability does not appear to increase with repeat administration. In healthy subjects, the plasma half-life is approximately 1 hour (range 0,7 to 1,5 hours), and the total body clearance is estimated to be 283 ± 98 ml/min. There is no clinically relevant interaction with food. Neither food nor the time of day of administration of the treatment affects the absorption of rabeprazole sodium.

Distribution:

Rabeprazole is approximately 97 % bound to human plasma proteins.

Biotransformation and elimination:

Rabeprazole sodium, as is the case with other members of the proton pump inhibitor (PPI) class of compounds, is metabolised through the cytochrome P450 (CYP450) hepatic metabolising system.

In vitro studies with human liver microsomes indicated that rabeprazole sodium is metabolised by isoenzymes of CYP450 (CYP2C19 and CYP3A4). In these studies, at expected human plasma concentrations rabeprazole neither induces nor inhibits CYP3A4; and although *in vitro* studies may not always be predictive of *in vivo* status these findings indicate that no interaction is expected between rabeprazole and cyclosporine. In humans the thioether (M1) and carboxylic acid (M6) are the main plasma metabolites, with the sulphone (M2), desmethyl-thioether (M4) and mercapturic acid conjugate (M5) minor metabolites observed at lower levels. Only the desmethyl metabolite (M3) has a small amount of anti-secretory activity, but it is not present in plasma.

Following a single 20 mg ^{14}C labelled oral dose of rabeprazole sodium, no unchanged medicinal product was excreted in the urine. Approximately 90 % of the dose is eliminated in urine mainly as the two metabolites: a mercapturic acid conjugate (M5) and a carboxylic acid (M6), plus two unknown metabolites. The remainder of the dose is excreted via the faeces.

Gender:

Adjusted for body mass and height, there are no significant gender differences in pharmacokinetic parameters following a single 20 mg dose of rabeprazole.

Renal dysfunction:

In patients with stable, end-stage, renal failure requiring maintenance haemodialysis (creatinine clearance ≤ 5 ml/min/1,73 m^2), the disposition of rabeprazole is very similar to that in healthy volunteers. The AUC and the C_{max} in these patients are about 35 % lower than the corresponding parameters in healthy volunteers. The mean half-life of rabeprazole is 0,82

hours in healthy volunteers, 0,95 hours in patients during haemodialysis and 3,6 hours post dialysis. The clearance of rabeprazole in patients with renal disease requiring maintenance haemodialysis is approximately twice that in healthy volunteers. Chronic renal failure does not lead to medicine accumulation with a once a day dosing of rabeprazole.

Hepatic dysfunction:

Following a single 20 mg dose of rabeprazole to patients with chronic mild to moderate hepatic impairment the AUC doubled and there is a 2-3 fold increase in half-life of rabeprazole compared to the healthy volunteers. However, following a 20 mg dose daily for 7 days the AUC had increased to only 1,5-fold and the C_{max} to only 1,2-fold. The half-life of rabeprazole in patients with hepatic impairment is 12,3 hours compared to 2,1 hours in healthy volunteers. The pharmacodynamic response (gastric pH control) in the two groups was clinically comparable.

Elderly people:

Elimination of rabeprazole is somewhat decreased in the elderly. Following 7 days of daily dosing with 20 mg of rabeprazole sodium, the AUC approximately doubles, the C_{max} increases by 60 % and $t_{½}$ increases by approximately 30 % as compared to young healthy volunteers. However, there is no evidence of rabeprazole accumulation.

CYP2C19 polymorphism:

Following a 20 mg daily dose of rabeprazole for 7 days, CYP2C19 slow metabolisers, the AUC and $t_{½}$ are approximately 1,9 and 1,6 times the corresponding parameters in extensive metabolisers whilst C_{max} increased by 40 %.

5.3 Preclinical safety data

Non-clinical effects were observed only at exposures sufficiently in excess of the maximum human exposure that make concerns for human safety negligible in respect of animal data.

Studies on mutagenicity gave equivocal results. Tests in mouse lymphoma cell line were positive, but *in vivo* micronucleus and *in vivo* and *in vitro* DNA repair tests were negative. Carcinogenicity studies revealed no special hazard for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydroxide, mannitol, low-substituted hydroxypropyl cellulose, sodium stearyl fumarate, hypromellose, talc, hypromellose phthalate, dibutyl sebacate, yellow ferric oxide (E172), red ferric oxide (E172), titanium dioxide (E171).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from moisture and heat.

Keep the blisters in the carton until required for use.

KEEP OUT OF THE REACH OF CHILDREN

6.5 Nature and contents of container

Rabemed 10: Packed in Alcan blisters (Al/Al blister with a desiccant). The Al/Al blister with a desiccant consists of a coldform foil (soft, aluminium foil, matte, with a desiccant) and a lidding foil (hard aluminium foil). The lidding foil is primered and coated with LDPE, acting as the heatseal lacquer which seals to HDPE

coating of the forming foil. 4 blisters are packed into an outer cardboard carton box as 28 tablets.

Rabemed 20: Packed in Alcan blisters (Al/Al blister with a desiccant). The Al/Al blister with a desiccant consists of a coldform foil (soft, aluminium foil, matte, with a desiccant) and a lidding foil (hard aluminium foil). The lidding foil is primered and coated with LDPE, acting as the heatseal lacquer which seals to HDPE coating of the forming foil. 2 or 4 blisters are packed into an outer cardboard carton box as 14 or 28 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Sandoz SA (Pty) Ltd[1]

Magwa Crescent West

Waterfall City

Jukskei View

Midrand

2090

8. REGISTRATION NUMBER(S)

Rabemed 10: 44/11.4.3/0597

Rabemed 20: 44/11.4.3/0598

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14 September 2012

10. DATE OF REVISION OF THE TEXT

To be confirmed

Additional country registration details:

Country	*Product name*	*Scheduling status (or Category of distribution)*	*Registration number*
Namibia	Rabemed 10	NS2	17/11.4.3/0053
	Rabemed 20	NS2	17/11.4.3/0054

ATC Code: A.11.4.3 Medicines acting on gastro-intestinal tract

Name and address of manufacturer:

Lek Pharmaceuticals d.d.
Verovškova 57,
SI-1526 Ljubljana,
Slovenia

[1]Company Reg. No.: 1990/001979/07