Summary Product Characteristics

1. Name of the medicinal product:

Brand Name :--
Generic Name : Rabeprazole sodium for injection20mg

Route of Administration: Intravenous

2. Qualitative and Quantitative composition:

Sr. No	Ingredients	Specification	Label claim	Quantity / Batch (kg)	% Over ages	Resion of inclusion
Active						
1.	Rabeprazole sodium	USP	20.00	1.0 kg / Filled weight	Nil	proton-pump inhibitors
2.	Water For Injection	BP	QS	QS	-	Vehicle

BP: British Pharmacopoeia

***Calculated on actual assay and water contain basis .**

3. Pharmaceutical Form: Powder for Solution for Injection

4. Clinical Particulars:

4.1 Therapeutic Indications:
For the short-term treatment of gastric and duodenal ulcers, gastro-oesophageal reflux disease (GERD), and as an alternative to oral therapy in patients who are unable to take oral proton-pump inhibitor (PPI).

4.2 Posology and method of administration:
I.V. administration is recommended only in cases where oral administration is not indicated. As soon as an oral therapy is possible, the I.V. therapy should be discontinued.

Recommended dose is I.V. administration of the content of one vial (20 mg rabeprazole) once daily. Parenteral routes of administration other than I.V. are not recommended.

Injection: The content of the vial needs to be reconstituted with 5 ml Sterile Water for Injection and should be given slowly over 5–15 minutes.

Infusion: For I.V. infusion, the reconstituted solution should be further diluted and administered as a short-term infusion over 15–30 minutes.

Compatibility with Various I.V. Fluids

Rabeprazole I.V. is compatible with Sterile Water for Injection, IP, and 0.9% Sodium Chloride Injection, IP. No other solvent or infusion fluid must be used for the administration of rabeprazole I.V. injection.

Reconstitution

To reconstitute, add 5 ml of Sterile Water for Injection to make a solution. After preparation, the reconstituted solution must be used within 4 hours and the unused portion discarded. As with all parenteral admixtures, the reconstituted or further diluted solution should be examined for change in colour, precipitation, haziness or leakage. The unused portion should be discarded.

4.3 Contraindications
Rabeprazole sodium for injection is contraindicated in patients with a known hypersensitivity to rabeprazole, substituted benzimidazoles or to any component of the formulation. Children and elderly or debilitated patients require smaller doses, commensurate with age and physical status

4.4 Special warnings and precautions for use
Presence of Gastric Malignancy

Symptomatic response to therapy with rabeprazole does not preclude the presence of gastric malignancy.

Patients with healed GERD were treated for up to 40 months with rabeprazole and monitored with serial gastric biopsies. Patients without Helicobacter pylori infection (221 of 326 patients) had no clinically important pathologic changes in the gastric mucosa. Patients with H. pylori infection at baseline (105 of 326 patients) had mild or moderate inflammation in the gastric body or mild inflammation in the gastric antrum. Patients with mild grades of infection or inflammation in the gastric body tended to change to moderate, whereas those graded moderate at baseline tended to remain stable. Patients with mild grades of infection or inflammation in the gastric antrum tended to remain stable. At baseline, 8% of patients had atrophy of glands in the gastric body and 15% had atrophy in the gastric antrum. At endpoint, 15% of patients had atrophy of glands in the gastric body and 11% had atrophy in the gastric antrum. Approximately 4% of patients had intestinal metaplasia at some point during follow-up, but no consistent changes were seen.

Interaction with Warfarin

Steady-state interactions of rabeprazole and warfarin have not been adequately evaluated in patients. There have been reports of increased International Normalised Ratio (INR) and prothrombin time in patients receiving a PPI and warfarin concomitantly. Increases in the INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with a proton-pump inhibitor (PPI) and warfarin concomitantly may need to be monitored for increases in the INR and prothrombin time.

Acute Interstitial Nephritis

Acute interstitial nephritis has been observed in patients taking PPIs, including rabeprazole sodium. Acute interstitial nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue rabeprazole sodium if acute interstitial nephritis develops.

Clostridium difficile-associated Diarrhoea

Published observational studies suggest that PPI therapy such as rabeprazole sodium may be associated with an increased risk of C. difficile-associated diarrhoea (CDAD), especially in hospitalised patients. This diagnosis should be considered for diarrhoea that does not improve.

Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

CDAD has been reported with the use of nearly all antibacterial agents.

Bone Fracture

Several published observational studies in adults suggest that PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for

osteoporosis-related fractures should be managed according to established treatment guidelines.

Cutaneous and Systemic Lupus Erythematosus

Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in patients taking PPIs, including rabeprazole. These events have occurred as both new onset and an exacerbation of existing autoimmune disease. The majority of PPI-induced lupus erythematosus cases were CLE.
The most common form of CLE reported in patients treated with PPIs was subacute CLE (SCLE) and occurred within weeks to years after continuous drug therapy in patients ranging from infants to the elderly. Generally, histological findings were observed without organ involvement.
Systemic lupus erythematosus (SLE) is less commonly reported than CLE in patients receiving PPIs. PPI associated SLE is usually milder than non-drug induced SLE. Onset of SLE typically occurred within days to years after initiating treatment primarily in patients ranging from young adults to the elderly. The majority of patients presented with rash; however, arthralgia and cytopaenia were also reported.
Avoid administration of PPIs for longer than medically indicated. If signs or symptoms consistent with CLE or SLE are noted in patients receiving rabeprazole sodium, discontinue the drug and refer the patient to the appropriate specialist for evaluation. Most patients improve with discontinuation of the PPI alone in 4 to 12 weeks. Serological testing (e.g. ANA) may be positive and elevated serological test results may take longer to resolve than clinical manifestations.

Cyanocobalamin (Vitamin B12) Deficiency

Daily treatment with any acid-suppressing medications over a long period of time (e.g. longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B12) caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency are observed in patients treated with rabeprazole sodium.

Hypomagnesaemia
Hypomagnesaemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least 3 months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesaemia required magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics), healthcare professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.

Interaction with Methotrexate
Literature suggests that concomitant use of PPIs with methotrexate (primarily at a 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 the PPI may be considered in some patients.

Fundic Gland Polyps

PPI use is associated with an increased risk of fundic gland polyps that increases with long-term use, especially beyond one year. Most PPI users who developed fundic gland polyps were asymptomatic and fundic gland polyps were identified incidentally on endoscopy. Use the shortest duration of PPI therapy appropriate to the condition being treated.

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

Drugs Metabolised by CYP450

Rabeprazole is metabolised by the CYP450 drug-metabolising enzyme system. Studies in healthy subjects have shown that rabeprazole does not have clinically significant interactions with other drugs metabolised by the CYP450 system, such as warfarin and theophylline given as single oral doses, diazepam as a single I.V. dose, and phenytoin given as a single I.V. dose (with supplemental oral dosing). Steady-state interactions of rabeprazole and other drugs metabolised by this enzyme system have not been studied in patients.

Warfarin

There have been reports of increased INR and prothrombin time in patients receiving PPIs, including rabeprazole, and warfarin concomitantly. Increases in the INR and prothrombin time may lead to abnormal bleeding and even death.

Cyclosporine

In vitro incubations employing human liver microsomes indicated that rabeprazole inhibited cyclosporine metabolism with an IC50 of 62 micromolar, a concentration that is over 50 times higher than the Cmax in healthy volunteers following 14 days of dosing with 20 mg of rabeprazole. This degree of inhibition is similar to that by omeprazole at equivalent concentrations.

Compounds Dependent on Gastric pH for Absorption

Rabeprazole produces sustained inhibition of gastric acid secretion. An interaction with compounds that are dependent on gastric pH for absorption may occur due to the magnitude of acid suppression observed with rabeprazole. For example, in normal subjects, co-administration of rabeprazole 20 mg q.d. resulted in an approximately 30% decrease in the bioavailability of ketoconazole and increases in the AUC and Cmax for digoxin of 19% and 29%, respectively. Therefore, patients may need to be monitored when such drugs are taken concomitantly with rabeprazole. Co-administration of rabeprazole and antacids produced no clinically relevant changes in plasma rabeprazole concentrations.

The table below includes drugs with clinically important drug interactions and interactions with diagnostics when administered concomitantly with rabeprazole sodium and instructions for preventing or managing them.

Consult the labelling of concomitantly used drugs to obtain further information about interactions with PPIs.

Clinically Relevant Interactions Affecting Drugs Co-Administered with Rabeprazole Sodium and Interactions with Diagnostics

Antiretrovirals	
Clinical Impact	The effect of PPI on antiretroviral drugs is variable. The clinical importance and the mechanisms behind these interactions are not always known. • Decreased exposure of some antiretroviral drugs (e.g. rilpivirine, atazanavir and nelfinavir) when used concomitantly with rabeprazole may reduce the antiviral effect and promote the development of drug resistance. • Increased exposure of other antiretroviral drugs (e.g. saquinavir) when used concomitantly with rabeprazole may increase toxicity. • There are other antiretroviral drugs that do not result in clinically relevant interactions with rabeprazole.
Intervention	Rilpivirine-containing products: Concomitant use with rabeprazole sodium is contraindicated. See the prescribing information. Atazanavir: See the prescribing information for atazanavir for dosing information. Nelfinavir: Avoid concomitant use with rabeprazole sodium. See prescribing information for nelfinavir. Saquinavir: See the prescribing information for saquinavir and monitor for potential saquinavir toxicities. Other antiretrovirals: See the prescribing information.
Warfarin	
Clinical Impact	Increased INR and prothrombin time in patients receiving PPIs, including rabeprazole and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death.
Intervention	Monitor INR and prothrombin time. Dose adjustment of warfarin may be needed to maintain target INR range. See prescribing information for warfarin.
Methotrexate	
Clinical Impact	Concomitant use of rabeprazole with methotrexate (primarily at high doses) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate, possibly leading to methotrexate toxicities. No formal drug interaction studies of methotrexate with PPIs have been conducted.
Intervention:	A temporary withdrawal of rabeprazole sodium may be considered in some patients receiving high-dose methotrexate administration.
Digoxin	

Clinical Impact	Potential for increased exposure of digoxin.
Intervention	Monitor digoxin concentrations. Dose adjustment of digoxin may be needed to maintain therapeutic drug concentrations.

Drugs Dependent on Gastric pH for Absorption (e.g. iron salts, erlotinib, dasatinib, nilotinib, mycophenolate mofetil, ketoconazole, itraconazole)

Clinical Impact	Rabeprazole can reduce the absorption of other drugs due to its effect on reducing intragastric acidity.
Intervention	Mycophenolate mofetil (MMF): Co-administration of PPIs in healthy subjects and in transplant patients receiving MMF has been reported to reduce the exposure to the active metabolite, mycophenolic acid (MPA), possibly due to a decrease in MMF solubility at an increased gastric pH. The clinical relevance of reduced MPA exposure on organ rejection has not been established in transplant patients receiving rabeprazole sodium and MMF. Use rabeprazole sodium with caution in transplant patients receiving MMF.

Combination Therapy with Clarithromycin and Amoxicillin

Clinical Impact	Concomitant administration of clarithromycin with other drugs can lead to serious adverse reactions, including potentially fatal arrhythmias, and are contraindicated. Amoxicillin also has drug interactions.
Intervention	See Contraindications and Warnings and Precautions in the prescribing information for clarithromycin.

Tacrolimus

Clinical Impact	Potentially increased exposure of tacrolimus, especially in transplant patients who are intermediate or poor metabolisers of CYP2C19.
Intervention	Monitor tacrolimus whole blood trough concentrations. Dose adjustment of tacrolimus may be needed to maintain therapeutic drug concentrations. See prescribing information for tacrolimus.

Interactions with Investigations of Neuroendocrine Tumours

Clinical Impact	Serum chromogranin A (CgA) levels increase secondary to PPI-induced decreases in gastric acidity. The increased CgA level may cause false-positive results in diagnostic investigations for neuroendocrine tumours.

Intervention	Temporarily stop rabeprazole sodium treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g. for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.
Interaction with Secretin Stimulation Test	
Clinical Impact	Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma.
Intervention	Temporarily stop treatment with rabeprazole sodium at least 14 days before assessing to allow gastrin levels to return to baseline.
False-Positive Urine Tests for THC	
Clinical Impact	There have been reports of false-positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving PPIs.
Intervention	An alternative confirmatory method should be considered to verify positive results.

4.6 Pregnancy and Lactation:

Pregnant Women

There are no data on the safety of rabeprazole 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. Rabeprazole is contraindicated during pregnancy.

Lactating Women

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, rabeprazole must not be used during breast feeding.

Paediatric Patients

Rabeprazole is not recommended for use in children due to a lack of data on safety and efficacy.

Geriatric Patients

Of the total number of subjects (n=2,009) in clinical studies of rabeprazole sodium delayed-release tablets, 19% were 65 years and over, while 4% were 75 years and over. No overall

differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

4.7 Effects on the ability to drive and use machines

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

4.8 Undesirable effects:

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

The following adverse events have been reported from clinical trial and post-marketing experience.

Frequencies are defined as follows: common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1000) very rare (<1/10,000), not known (cannot be estimated from the available data).

System Organ Class	Common	Uncommon	Rare	Very rare	Not Known
Infections and infestations	Infection				
Blood and the lymphatic system disorders			Neutropaenia Leucopaenia Thrombocytopaenia Leucocytosis		
Immune System disorders			Anorexia		Hyponatraemia Hypomagnesaemia
Psychiatric disorders	Insomania	Nervousness	Depression		Confusion
Nervous system disorders	Headache Dizziness	Somnolence			
Eye disorders			Visual disturbance		
Vascular disorders					Peripheral oedema
Respiratory, thoracic and mediastinal disorders	Cough Pharyngitis Rhinitis	Bronchitis Sinusitis			
Gastrointestinal disorders	Diarrhoea Vomiting Nausea Abdominal pain Constipation	Dyspepsia Dry mouth Eructation	Gastritis Stomatitis Taste disturbance		Microscopic colitis

	Flatulence Fundic gland polyps (benign)				
Hepato-biliary disorders			Hepatitis Jaundice Hepatic encephalopathy[3]		
Skin and subcutaneous tissue disorders		Rash Erythema[2]	Pruritus Sweating Bullous reactions[2]	Erythema multiforme, toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS)	Sub-acute cutaneous lupus erythematosus[4]
Musculoskeletal connective tissue and bone disorders	Non- specific painBack pain	Myalgia Leg cramps Arthralgia Fractureof the hip, wrist or spine[4]			
Renal and urinary disorders		Urinary tract infection	Interstitial nephritis		
Reproductive system and breast disorders					Gynaecomastia
General disorders and administration site conditions	Asthenia Influenza- like illness	Chest pain Chills Pyrexia			
Investigations	Increased hepatic enzymes[3]	Weight increased			

[1] Includes facial swelling, hypotension and dyspnea.

[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 the treatment of patients with severe hepatic dysfunction, the prescriber is advisedto exercise caution when treatment with rabeprazole 10 mg gastro-resistant tablets is first initiated in such patients.

[4] See Special Warnings and Precautions for Use.

PPI use was found to be associated with increased risks for acute kidney injury and

chronic kidney disease.

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 reversible without further medical intervention. No specific antidote is known. Rabeprazole sodium is extensively protein bound and is, therefore, not dialysable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.

5. Pharmacological Particulars:

5.1 Mechanism of Action

Rabeprazole sodium belongs to the class of anti-secretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H2 histamine antagonist properties, but suppress 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.

5.2 Pharmacodynamic Properties

Anti-Secretory Activity

After oral administration of a 20 mg dose of rabeprazole sodium, the onset of the anti-secretory effect occurs within 1 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 drug is discontinued, secretory activity normalises over 2 to 3 days.

Decreased gastric acidity due to any means, including PPIs such as rabeprazole, increases counts of bacteria normally present in the gastrointestinal tract. Treatment with PPIs 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.

During treatment with anti-secretory 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 PPIs 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.

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 central nervous system (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 sodium does not adversely influence plasma concentrations of amoxicillin or clarithromycin when co-administered for the purpose of eradicating upper gastrointestinal H. pylori infection.

5.3 Pharmacokinetic Properties

After oral administration of 20 mg rabeprazole, peak plasma concentrations (Cmax) of rabeprazole occur over a range of 2.0 to 5.0 hours (Tmax). The rabeprazole Cmax and AUC are linear over an oral dose range of 10 mg to 40 mg. There is no appreciable accumulation when doses of 10–40 mg are administered every 24 hours; the pharmacokinetics of rabeprazole is not altered by multiple dosing. The plasma half-life ranges from 1 to 2 hours.

Absorption and Distribution

Absolute bioavailability rabeprazole I.V. is 100%. Rabeprazole is 96.3% bound to human plasma proteins.

Metabolism

Rabeprazole is extensively metabolized. The thioether and sulphone are the primar metabolites measured in human plasma. These metabolites were not observed to have significant antisecretory activity. In vitro studies have demonstrated that rabeprazole is metabolized in the liver primarily by CYP450 3A (CYP3A) to a sulphone metabolite and CYP450 2C19 (CYP2C19) to desmethylrabeprazole. The thioether metabolite is formed non-enzymatically by reduction of rabeprazole. CYP2C19 exhibits a known genetic polymorphism due to its deficiency in some sub-populations (e.g. 3–5% of Caucasians and 17–20% of Asians). Rabeprazole metabolism is slow in these sub-populations; therefore, they are referred to as poor metabolizers of the drug.

Elimination

Following a single 20 mg oral dose of 14 C-labelled rabeprazole, approximately 90% of the drug was eliminated in the urine, primarily as thioether carboxylic acid; its glucuronide, and mercapturic acid metabolites. The remainder of the dose was recovered in the faeces. Total recovery of radioactivity was 99.8%. No unchanged rabeprazole was recovered in the urine or faeces.

Special Populations

Geriatric: In 20 healthy elderly subjects, after oral administration of rabeprazole 20 mg once daily for 7days, AUC values approximately doubled and the Cmax increased by 60% compared with values in a parallel younger control group. There was no evidence of drug accumulation after once-daily administration.

Paediatric: The pharmacokinetics of rabeprazole in paediatric patients under the age of 18years has not been studied.

Gender and Race: In analyses adjusted for body mass and height, rabeprazole pharmacokinetics showed no clinically significant differences between male and femalesubjects. In studies that used different formulations of rabeprazole, AUC0–infinityvalues forhealthy Japanese men were approximately 50–60% greater than values derived frompooled data from healthy men in the United States.

Renal Impairment: In 10 patients with stable end-stage renal disease requiring maintenance haemodialysis (creatinine clearance: 2), no clinically significant differences were observed in the pharmacokinetics of rabeprazole after a single 20 mg oral dose when compared with10 healthy volunteers.

Hepatic Impairment: In a single-dose study of 10 patients with chronic mild-to-moderate compensated cirrhosis of the liver who were administered a 20 mg dose of rabeprazole, AUC0–24 was approximately doubled, the elimination half-life was 2- to 3-fold higher, and total body clearance was decreased to less than half compared with values in healthy men.

In a multiple-dose study of 12 patients with mild-to-moderate hepatic impairment administered 20 mg rabeprazole once daily for 8 days, AUC0–infinity and Cmax values increased approximately 20% compared with values in healthy age- and gender-matched subjects. These increases were not statistically significant. No information exists on rabeprazole disposition in patients with severe hepatic impairment.

5.3 Pre-clinical Safety:
Not Applicable

6. Pharmaceutical Particulars:

List of Excipients:
No excipients added.

6.2 Incompatibilities:

Not applicable

6.3 Shelf Life: 24 months

6.4 Special Precautions for storage:
Store below 25°C in a dry place, protected from light.
Keep medicines out of reach of children.

6.5 Nature and contents of container:
White crystalline powder filled in a 10 ml amber glass vial, plugged with grey butyl rubber plug with flip-off seal, packed in a carton along with a plastic tray containing 10 ml FFS ampoule of sterile water for injection and Pack insert

6.6 Special precautions for disposal and other handling:
No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder:
Malven Medics Int'l Co.Ltd.
No. 4 Ligali Street Ogudu, Lagos Nigeria.

8. Marketing Authorization Number: ---

9. Date of first Authorization /renewal of the authorization: ---

10. Date of revision of text: Feb 2024