Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Sabezole® DSR

2. Qualitative and Quantitative composition:

Each hard gelatin capsule contains:
Rabeprazole Sodium USP 20mg
(As enteric coated pellets)
Domperidone BP 30mg
(As sustained release pellets)
Excipients ..... q.s.
(For the full list of excipients, see section 6.1)

3. Pharmaceutical form:

Hard gelatin Capsules
Pink colour cap & transparent body, hard gelatin capsules size "2" filled with Spherical multi colour pellets.

4. Clinical particulars

4.1 Therapeutic indications

Used in the management of

- Gastroesophageal reflux disease (GERD) and dyspepsia
- Chronic gastritis and diabetic gastroparesis
- Control of nausea and vomiting
- Reduced GI motility and hyperacidity
- Duodenal and gastric ulcer
- Daytime and nocturnal heartburn

4.2 Posology and method of administration

The recommended dose is 1 capsule to be administered once daily for 4 to 8 weeks, or as prescribed by the physician.

Method of administration

SABEZOLE® DSR Capsules may be administered with or without food. The capsules should be swallowed whole with water and not to be opened, chewed or crushed.

4.3 Contraindications

SABEZOLE® DSR Capsules are contraindicated in the following:

- Patients with known hypersensitivity to rabeprazole or to any substituted benzimidazole derivative or to domperidone or to any component of the formulation.
- In patients receiving rilpivirine-containing products.
- Prolactin-releasing pituitary tumour (prolactinoma).
- In patients with gastrointestinal haemorrhage, mechanical obstruction or perforation (i.e., when stimulation of the gastric motility could be harmful).
- In patients with moderate or severe hepatic impairment.

- In patients who have known existing prolongation of cardiac conduction intervals, particularly QTc.
- Patients with significant electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesemia) or underlying cardiac disease such as congestive heart failure (CHF).
- Co-administration with QT-prolonging drugs.
- Co-administration with potent CYP3A4 inhibitors.

4.4 Special warnings and precautions for use

Rabeprazole:

Gastric Malignancy: In adults, symptomatic response to rabeprazole therapy does not preclude the presence of gastric malignancy; therefore, the possibility of malignancy should be excluded prior to commencing treatment with rabeprazole.

Acute Interstitial Nephritis: Acute interstitial nephritis has been observed in patients taking PPIs, including rabeprazole. Discontinue rabeprazole if acute interstitial nephritis develops.

Cyanocobalamin (Vitamin B12) Deficiency: Daily treatment with acid-suppressing drugs over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature

Hypomagnesemia: Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs.

Risk of Bone Fractures: The risk of fracture was found to increase in patients who received high-dose and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy. Patients at risk of osteoporosis should have an adequate intake of vitamin D and calcium.

Domperidone:

Cardiovascular Effects: Domperidone is contraindicated in patients with known existing prolongation of cardiac conduction intervals, particularly QTc, in patients with significant electrolyte disturbances (hypokalaemia, hyperkalaemia, hypomagnesaemia), or bradycardia, or in patients with underlying cardiac diseases such as congestive heart failure (CHF) due to increased risk of ventricular arrhythmia

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

Rabeprazole:

Antiretroviral Drugs: Decreased exposure of some antiretroviral drugs (e.g., rilpivirine, atazanavir, and nelfinavir) when used concomitantly with rabeprazole may reduce antiviral effect and promote the development of drug resistance.

Ketoconazole/Itraconazole: Co-administration of rabeprazole with ketoconazole or itraconazole may result in a significant decrease in antifungal plasma levels.

Mycophenolate Mofetil: Co-administration of PPIs with mycophenolate mofetil in healthy and transplant patients has been reported to reduce exposure to the active metabolite, mycophenolic acid.

Antacids: Antacids were used concomitantly with the administration of rabeprazole and, in a specific drug-drug interaction study, no interaction with liquid antacids was observed.

Methotrexate: Literature suggests that concomitant use of PPIs with methotrexate may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicity. A temporary withdrawal of rabeprazole therapy may be considered in some patients receiving high dose of methotrexate.

Domperidone:

The main metabolic pathway of domperidone is through CYP3A4. In vitro data suggest that the concomitant use of drugs that significantly inhibit this enzyme may result in increased plasma levels of domperidone.

There is increased risk of occurrence of QT-interval prolongation, due to pharmacodynamic and/or pharmacokinetic interactions.

4.6 Fertility, pregnancy and lactation

Pregnancy: Not recommended in pregnancy (Category C).

Lactation: SABEZOLE® DSR Capsules should not be used during breast feeding as domperidone is excreted in breast milk.

4.7 Effects on ability to drive and use machines

Based on the pharmacodynamic properties and the adverse events profile, it is unlikely that Rabeprazole sodium would cause an impairment of driving performance or compromise the ability to use machinery. If however, alertness is impaired due to somnolence, care should be taken before driving or using machinery until the patient's individual reaction on the medicine has been established.

4.8 Undesirable effects

Rabeprazole: adverse reactions include headache, diarrhea, skin rash, pruritus and dizziness

Domperidone: Serum prolactin level may rise resulting in galactorrhea in females and less frequently gynecomastia in males. Dry mouth, thirst, headache, nervousness, drowsiness, diarrhea, skin rashes and itching may follow on treatment with domperidone.

4.9 Overdose

No data are available with regard to overdosage with this product. 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 utilized.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of Action:

Rabeprazole:

Pharmacotherapeutic group: Proton Pump Inhibitors

ATC Code: A02BC04

Rabeprazole belongs to a class of antisecretory compounds (substituted benzimidazole, proton-pump inhibitors - PPIs). As a weak base, rabeprazole is rapidly absorbed following oral dose and is concentrated in the acidic environment of the parietal cells. In gastric parietal cells (at pH 1.2), rabeprazole is converted to the active

'sulphenamide' form through 'protonation' and it subsequently reacts with the available cysteines on the proton pump. Rabeprazole suppress gastric acid (hydrochloric acid – HCl) secretion by inhibiting the gastric H+/K+-ATPase enzyme at the secretory surface of the gastric parietal cell. Because this enzyme is regarded as the acid (proton) pump within the parietal cell, rabeprazole has been characterized as a gastric proton-pump inhibitor.

Rabeprazole blocks the final step of gastric acid secretion. The effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus.

Domperidone:

Pharmacotherapeutic group: Propulsives

ATC Code: A03FA03

Domperidone is a dopamine receptor (D2) antagonist. Domperidone act predominantly on peripheral dopamine receptors and produces anti-emetic and gastrokinetic effects. Domperidone does not readily cross the blood-brain barrier (BBB).

Thus, in domperidone users, especially in adults, extrapyramidal side effects are very rare (unlike metoclopramide). Anti-emetic effect of domperidone is due to a combination of peripheral (gastrokinetic) effects and antagonism of dopamine receptors (D2) in the chemoreceptor trigger zone (CTZ), which lies outside the BBB in the area postrema. Oral domperidone also increases lower oesophageal sphincter (LES) pressure, thus, improve antroduodenal motility and accelerate gastric emptying.

5.2 Pharmacokinetic properties Rabeprazole:

Absorption

After oral administration of rabeprazole 20 mg, peak plasma concentrations (Cmax) occur over a range of 2 to 5 hours (Tmax). Absolute bioavailability for rabeprazole 20 mg (compared to intravenous administration) is

approximately 52% (because of extensive pre- systemic metabolism). Additionally, the bioavailability does not appear to increase with repeat dose administration of rabeprazole. Effect of Food: With rabeprazole, there was no clinically relevant interaction with food. Neither food nor the time of day of administration affects the absorption of rabeprazole. Thus, rabeprazole may be administered without regard to timing of meals.

Distribution

Rabeprazole is 96.3% bound to human plasma proteins.

Metabolism

Rabeprazole is extensively metabolized. Rabeprazole is metabolized in the liver primarily by cytochromes P450 3A (CYP3A) to a sulphone metabolite and cytochrome 12 P450 2C19 (CYP2C19) to desmethyl rabeprazole. The thioether and sulphone are the primary metabolites measured in human plasma. These metabolites were not observed to have significant antisecretory activity. A significant portion of rabeprazole is also metabolized via systemic non-enzymatic reduction to a thioether compound.

Elimination

Following a single 20 mg oral dose of rabeprazole, approximately 90% of the drug was eliminated in the urine, primarily as thioether carboxylic acid, glucuronide, and mercapturic acid metabolites. The remainder of the dose was recovered in the faeces. No unchanged rabeprazole was recovered in the urine or faeces. In healthy subjects, the plasma half-life is approximately one hour (range 0.7 to 1.5 hours), and the total body clearance is estimated to be 283 ± 98 ml/min.

Domperidone:

Absorption:

Domperidone is rapidly absorbed after oral administration, with peak plasma concentrations occurring at approximately 1 hour after dosing. Effect of Food: Domperidone's bioavailability is enhanced in normal subjects when taken after a meal. The time of peak absorption is slightly delayed and the AUC somewhat increased when domperidone is taken after a meal.

Distribution:

Oral domperidone does not appear to accumulate or induce its own metabolism. The peak plasma concentration (Cmax) of 18 ng/ml to 21 ng/ml occurs 1.5 hours (Tmax) after the oral dose. Domperidone is 91 to 93% bound to plasma proteins.

Metabolism:

Domperidone undergoes rapid and extensive hepatic metabolism by hydroxylation and N- dealkylation. In vitro metabolism experiments with diagnostic inhibitors revealed that CYP3A4 is a major form of cytochrome P-450 involved in the N-dealkylation of domperidone, whereas CYP3A4, CYP1A2 and CYP2E1 are involved in domperidone aromatic hydroxylation.

Elimination

After oral dose, domperidone is excreted mainly by renal (31%) and biliary (66%) routes. The proportion of the drug excreted unchanged is small (10% of faecal excretion and approximately 1% of urinary excretion). The plasma half-life after a single oral dose is 7 to 9 hours in healthy subjects but is prolonged in patients with severe renal insufficiency.

5.3 Preclinical safety data
None Available

6. Pharmaceutical particulars
6.1 List of Excipients:
Dummy Pellets (White Pellets)
Hard Gelatin capsule
Shell ”2” Color Pink / White

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 Months.

6.4 Special precautions for storage
Store below 30°C, protect from direct sunlight, heat & moisture.

6.5 Nature and contents of container
Sabezole® -DSR is available in a pack of 1x10’s ALU-ALU blister pack.

6.6 Special precautions for disposal and other
Any unused medicine product or waste material should be disposed of in accordance with the local requirements.

7. Marketing authorization holder and manufacturing site addresses
Manufactured in India by:
MAGBRO HEALTHCARE PVT. LTD.
Village Mehsa Tibba,
P.O. Manjholi, Teh. Nalagarh,
Distt. Solan-174 101 (HP) India

Manufactured For & Marketed by:
KRISHNA CHEMISTS LTD.
P.O. BOX 3328-00506
NAIROBI, KENYA.

8. Marketing authorisation number(s)
CTD4444
9. Date of first Registration/ Renewal of Registration
10. Date of revision of text
06/11/2025