1.5.3 Patient information leaflet (PIL).*Refer to attached*

Rabepride capsules

(Rabeprazole Sodium EC and Itropride Hydrochloride SR capsules)

Composition

Each hard gelatin capsules contains: Rabeprazole Sodium 20mg (as enteric coated pellets) and Itopride Hydrochloride 150mg (as sustained release pellets)

Pharmacology

Itopride activates gastrointestinal propulsion motility by antagonizing dopamine D2 receptors and acetyl cholinesterase inhibitory effect. Itopride activates acetylcholine release and inhibits its degradation. Itopride also has an antiemetic effect based on interaction with dopamine D2 receptors entering the chemoreceptor zone.

Itopride has a highly specific effect on the upper gastrointestinal tract. Itopride does not affect plasma gastrin concentrations.

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 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.

Pharmacokinetics

For Itopride absorption is rapidly and almost completely absorbed from the gastrointestinal tract. Relative bioavailability and 60% is given by first-pass metabolism. Food does not affect the biological availability of the product. Maximum plasma concentrations are reached 30 to 50 minutes after administration of itopride. After repeated oral dosing in the itopride and its metabolites have linear pharmacokinetics with minimal accumulation. Distribution 5/6 approximately 96% of itopride binds to Plasma proteins, predominantly albumin. The α-1-acid glycoprotein binds less than 15% of the bound itopride. High concentrations are achieved in kidney, small intestine, liver, adrenal gland and stomach. The elimination half-life of itopride was approximately 6 hours.

Absorption: Rabeprazole 20mg is an enteric-coated (gastro-resistant) formulation of rabeprazole sodium. This presentation is necessary because rabeprazole is acid-labile. Absorption of rabeprazole therefore begins only after the pellets 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.

Rabeprazole is approximately 97 % bound to human plasma proteins. 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 drug metabolising system. Approximately 90 % of the dose was 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 was recovered in faeces

Indications:

Rabepride Capsules is used for the treatment of Stomach acid, Gastroesophageal reflux disease, Duodenal ulcers, Functional dyspepsia, Gastrointestinal conditions.

Dosage and directions for use

Oral administration

Adult: 1 capsule once daily

Swallow the medication whole. Do not chew, divide or crush the capsules.

Contra-indications:

- Hypersensitivity to the active substances or to any of the excipients.
- lactation and pregnancy.

Warning and precautions

Itopride should be used with caution because it enhances the action of acetylcholine Rabeprazole should be used with caution in patients with severe hepatic impairment and Pregnancy.

Adverse reactions

Headache, diarrhea, dizziness, rash

Potentially Fatal: Anaphylaxis, agranulocytosis.

Interaction with other medicinal products and other forms of interaction.

Rabeprazole increase elimination T1/2 of digoxin, decreases effects with amino glutethimide, carbamazepine, phenytoin and rifampin and reduces absorption of ketoconazole and itraconazole.

Anticholinergic agents reduces the action of itopride.

Food Interaction

Avoid alcohol (may irritate gastric mucosa). Rabeprazole has delayed absorption but unaltered Cmax and AUC with high-fat meals.

Fertility, pregnancy and lactation

Pregnancy: Little information is available time regarding the safe use of Rabepride capsules during pregnancy therefore it's contraindicated.

***Lactation*:** Little information is available time regarding the safe use of Rabepride capsules during lactation therefore it's contraindicated.

***Fertility*:** There is no information on the effects of Rabeprazole and Itropride on human fertility.

Effects on driving and use of machine:
Do not drive or operate machinery as Rabepride capsules because alertness is impaired due to somnolence.
Overdose:
There is no experience with overdose in humans. Overdose is the usual measure of gastric lavage a Symptomatic therapy.
Presentation:
Tablet: Blister pack of 3x10's in a unit box.
Storage
Store in a dry place, below 30^0C, Protect from light.
Keep all medicines out of reach of children.
Manufactured by:

DAWA	**DAWA Limited,** **Plot No. 7879/8, Baba Dogo Road, Ruaraka** **P. O. Box 16633 – 00620, Nairobi, Kenya.**

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1.5.4. Mock-ups and specimens. *Not applicable.*