PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

PRAZOLOC OTC (20 mg enteric-coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each enteric-coated tablet contains pantoprazole sodium sesquihydrate equivalent to 20 mg pantoprazole.

Contains: Mannitol 49,145 mg

For the full list of excipients, see **section 6.1.**

3. PHARMACEUTICAL FORM

Enteric coated tablets

Yellow coloured, capsule shaped, biconvex tablet plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PRAZOLOC OTC is indicated when intended for the temporary short-term relief of heartburn and hyperacidity for a maximum of 14 days.

4.2 Posology and method of administration

Posology

PRAZOLOC OTC should be taken preferably in the morning. PRAZOLOC OTC may be taken with food or on an empty stomach.

PRAZOLOC OTC should be swallowed whole with a little water either before or during breakfast. Do not crush, break, or chew the tablet.

The maximum daily dose is 20 mg per day and the treatment is for a maximum period of 14 days.

Special populations

Elderly patients

No dosage adjustment is necessary in the elderly.

Impaired renal function

No dosage adjustment is required in the presence of impaired renal function.

Impaired liver function

A daily dose of PRAZOLOC OTC should not be exceeded in patients with mild to moderate liver impairment (see **section 4.4** and **5.2**).

Method of administration

For oral use only.

4.3 Contraindications

PRAZOLOC OTC is contraindicated in the following:

- Hypersensitivity to pantoprazole or to any of the other ingredients of PRAZOLOC OTC (see **section 6.1**).

- Severe impairment of liver function.
- Safety and efficacy in children have not been established.
- Co-administration with atazanavir and nelfinavir (see **section 4.5**).

4.4 Special warnings and precautions for use

PRAZOLOC OTC is not indicated for mild gastro-intestinal complaints such as nervous dyspepsia.

Prior to treatment the possibility of malignancy of gastric ulcer or a malignant disease of the oesophagus should be excluded, as the treatment with PRAZOLOC OTC may alleviate the symptoms of malignant ulcers and can thus delay diagnosis.

Daily treatment with any acid-blocking medicines over a long period of time (e.g. longer than 3 years) may lead to malabsorption of cyanocobalamin caused by hypo- or achlorhydria. Rare cases of cyanocobalamin deficiency under acid-blocking therapy have been reported in the literature. This should be considered when respective clinical symptoms are observed.
In the case of a rise of the liver enzymes, PRAZOLOC OTC should be discontinued.

Diagnosis of reflux oesophagitis should be confirmed by endoscopy.

The risk of tubulointerstitial nephritis leading to chronic renal inflammation and reduced renal function is associated with the use of PPI's. Tubulointerstitial nephritis may progress to renal failure as is it not necessarily reversed when treatment is discontinued.

Use of PRAZOLOC OTC as preventative of gastroduodenal ulcers, induced by non-selectivenon-steroidal anti-inflammatory drugs (NSAIDs) should be restricted to patients who require continued NSAID treatment and have an increased risk to develop gastro-intestinal complications.

4.5 Interaction with other medicinal products and other forms of interaction

Pantoprazole decreases the concentrations of atazanavir and nelfinavir. Co-administration of PRAZOLOC OTC and atazanavir or nelfinavir is contraindicated (see **section 4.3**).

PRAZOLOC OTC is metabolised by the cytochrome P450 system, primarily by isoenzyme CYP2C19, and may alter the metabolism of some medicines metabolised by these enzymes.

No clinically significant interactions were, however, observed in specific tests with a number of such medicines or compounds, namely antipyrine, caffeine, carbamazepine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, naproxen, nifedipine, phenytoin, piroxicam, theophylline, warfarin and oral contraceptives. However, the response to anticoagulants such as warfarin, may be affected by PRAZOLOC OTC. It is therefore good practice to monitor the patient with additional PT (prothrombin time) / INR (international normalised ratio) determinations when PRAZOLOC OTC is initiated, discontinued or taken irregularly.

Changes in absorption should be observed when medicines whose absorption is pH-dependent, e.g. ketoconazole, are taken concomitantly.

There are no interactions with concomitantly administered antacids.

Concomitant intake of food has no influence on the bioavailability of PRAZOLOC OTC.

4.6 Fertility, pregnancy and lactation

The use of PRAZOLOC OTC in pregnancy and lactation is not recommended as safety and efficacy have not been established.

4.7 Effects on ability to drive and use machines

PRAZOLOC OTC may cause dizziness, disturbances in vision, somnolence or vertigo. Patients should be advised to refrain from operating machinery or driving, until they know how PRAZOLOC OTC affects them.

4.8 Undesirable effects

The following side effects may occur:

Infections and infestations:

Frequent: Gastrointestinal infection.

Blood and lymphatic system disorders:

Less frequent: Thrombocytopenia, leukopenia, agranulocytosis.

Immune system disorders:

Less frequent: Anaphylactic reactions including anaphylactic shock, allergic reactions such as skin rash, pruritus, and angioedema.

Metabolism and nutrition disorders:

Less frequent: Elevated triglycerides and increased body temperature.

Psychiatric disorders:

Frequent: Insomnia.

Less frequent: Depression subsiding after termination of therapy, reversible confusional state, agitation, hallucinations, somnolence. (Ref 1: D7)

Nervous system disorders:

Frequent: Headache.

Less frequent: Dizziness or disturbances in vision (blurred vision), paraesthesia.

Eye disorders:

Less frequent: Disturbances in vision (blurred vision), anterior ischaemic optic neuropathy.

Ear and labyrinth disorders:

Less frequent: Vertigo, tinnitus.

Vascular disorders:

Less frequent: Peripheral oedema.

Respiratory, thoracic and mediastinal disorders:

Less frequent: Dyspnoea, bronchospasm.

Gastrointestinal disorders:

Frequent: Gastro-intestinal complaints such as upper abdominal pain, diarrhoea, nausea, constipation, or flatulence, vomiting and dry mouth have been reported.

Less frequent: Stomatitis, taste disturbances.

Hepatobiliary disorders:

Less frequent: Severe hepatocellular damage leading to jaundice with or without hepatic failure, increased liver enzymes (transaminases, γ-GT), hepatitis, hepatic encephalopathy.

Skin and subcutaneous tissue disorders:

Less frequent: Allergic reactions such as pruritus, and skin rash, urticaria, severe skin reactions, such as Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis (Lyell-syndrome) and photosensitivity.

Musculoskeletal, connective tissue and bone disorders:

Less frequent: Arthralgia, myalgia subsiding after termination of therapy.

Renal and urinary system disorders:

Less frequent: Difficulty in urinating, increased frequency and volume of urination, painful urination, and interstitial nephritis (with possible progression to renal failure as it is not necessarily reversed when treatment is discontinued).

Reproductive system and breast disorders:

Less frequent: Impotence, gynaecomastia.

General disorders and administrative site conditions:

Frequent: Fatigue.

Less frequent: Increased sweating, malaise, Increased body temperature and peripheral oedema, both subsiding after termination of treatment.

Post-marketing exposure:

Frequency unknown: Interstitial nephritis with possible progression to renal failure as it is not necessarily reversed when treatment is discontinued.

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 and to Cipla Medpro (Pty) Ltd at drugsafetysa@cipla.com or telephone 080 222 6662 (toll free).

4.9 Overdose

No specific therapeutic recommendation can be made in cases of overdosage. There are no known symptoms of overdosage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification

A 11.4.3 Medicine acting on the gastro-intestinal tract - Other.

Pharmacotherapeutic group: A02BC02 Proton pump inhibitors

Pantoprazole is a proton pump inhibitor, which inhibits specifically and dose proportionally, gastric H^+,K^+-ATPase, the enzyme which is responsible for gastric acid secretion in the parietal cells of the stomach. Pantoprazole is a substituted benzimidazole which accumulates in the acidic compartment of the parietal cells after absorption.

In the parietal cell it is protonated and chemically rearranged to the active inhibitor, a cyclic sulphenamide, which binds to the H^+,K^+-ATPase, thus inhibiting the proton pump and causing suppression of stimulated and basal gastric acid secretion after single oral pantoprazole dosing. Because pantoprazole acts distal to the receptor level, it can influence gastric acid secretion irrespective of the nature of the stimulus.

Pantoprazole exerts its full effect in a strongly acidic environment (pH < 3) and remains mostly inactive at higher pH values, which explains its selectivity for the acid secreting parietal cells of the stomach. Therefore, the complete pharmacological and therapeutic effect for pantoprazole can only be achieved in the acid secreting parietal cells. By means of a feedback mechanism the effect is diminished at the same rate as acid secretion is inhibited.

Effect on gastric acid secretion:

Following oral administration, pantoprazole inhibits the pentagastrin stimulated gastric acid secretion. The mean acid inhibition was 85 %, 2½ to 3½ hours after dosing with pantoprazole 40 mg/day for 7 days.

After stopping the administration of pantoprazole, there is no evidence of rebound hypersecretion and 7 days after administering the last dose the acid output is normal.

Pantoprazole maintains the physiological pH-rhythm. The values, however, are shifted to higher levels. During the night, periods with pH values approximating placebo have been found to occur.

Although pantoprazole has a half-life of approximately 1 hour, the antisecretory effect increases during repeated once daily administration, demonstrating that the duration of action markedly exceeds the serum elimination half-life.

5.2 Pharmacokinetic properties

Absorption and distribution:

Pantoprazole is administered orally in the form of an enteric-coated tablet. Pantoprazole is unstable in acid.

Since an acidic pH in the parietal cell acid canaliculi is required for activation, and since food stimulates acid production, pantoprazole should be taken about 30 minutes before meals.

Absorption takes place in the small intestine. Concurrent administration of food may somewhat reduce the rate of absorption of proton pump inhibitors. Concomitant use of other medicines that inhibits acid secretion, such as H_2-receptor antagonists, might be predicted to lessen the effectiveness of the proton pump inhibitors, such as pantoprazole.

On average, the maximum serum/plasma concentrations are approximately 2 to 3 µg/mL about 2½ hours after administration of 40 mg pantoprazole daily, as a single or multiple dose. The absolute systemic bioavailability of pantoprazole from single and multiple oral doses of pantoprazole is approximately 77 %.

The plasma kinetics for pantoprazole after oral administration is linear over the dose range 10 – 80 mg.

Metabolism:

Pantoprazole is almost exclusively metabolised in the liver. The main metabolite is desmethylpantoprazole, which is conjugated with sulphate.

Elimination:

Renal elimination represents the most important route of excretion (approximately 80 %) for the metabolites of pantoprazole. The balance is excreted with the faeces. The half-life of the main metabolite is approximately 1½ hours which is slightly longer than that of pantoprazole.

Pharmacokinetic profile in patients with impaired liver or renal function:

For patients with mild to moderate hepatic cirrhosis the elimination half-life values increase to between 7 to 9 hours. The AUC values increase by a factor of 5 to 8, while the maximum serum concentration only increases by a factor of 1,5 in comparison with healthy subjects.

In patients with renal impairment the half-life of the main metabolite is moderately increased but there is no accumulation at therapeutic doses. The half-life of pantoprazole in patients with renal impairment is comparable to the half-life of pantoprazole in healthy subjects. Pantoprazole is poorly dialysed. A slight increase in AUC and C_{max} occurs in elderly volunteers compared with younger people.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol

Sodium carbonate

Crospovidone (CLM)

Hydroxypropyl cellulose

Calcium stearate

Seal coating

Hypromellose

Titanium dioxide

Ferric oxide (Yellow)

Propylene glycol

Enteric coating

Methacrylic acid-Ethyl Acrylate copolymer (Eudragit L 30 D-55)

Triethyl citrate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light.

Keep the blisters in the outer carton until required for use.

6.5 Nature and contents of container

Plain aluminium foil blister strips of 7, 10 or 14 tablets packed in a carton.

6.6 Special precautions for disposal and other handling

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

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8 REGISTRATION NUMBER(S)

43/11.4.3/1145

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 September 2016

10 DATE OF REVISION OF THE TEXT

03/02/2023

Namibia: NS2 10/11.4.3/0406

References

1. SAHPRA-approved PI, Peptazol 20, by Pharmacrp (Pty) Ltd, dated August 2013, Date PI revised 19 July 2021

2. Current SAHPRA Guideline for Professional Information for Human Medicines (Categories A and D), dated July 2019.
3. Annex to the European Commission guideline on ‘Excipients in the labelling and package leaflet of medicinal products for human use’ (SANTE-2017-11668)
4. Module 3.2.P.1 Description and composition.
5. Module 3.2.P.8.1: Stability summary and conclusion.