For Medical Professional only

Zentro Tablets
(Pantoprazole)

زینٹرو ٹیبلیٹس
(پینٹوپرازول)

DESCRIPTION:
Zentro (pantoprazole sodium) Delayed-Release Tablets, a PPI, is a substituted benzimidazole, sodium 5-(difluoromethoxy)-2- [[(3,4-dimethoxy-2-pyridinyl)methyl] sulfinyl]-1H-benzimidazole sesquihydrate, a compound that inhibits gastric acid secretion. Its empirical formula is $C_{16}H_{14}F_2N_3NaO_4S$ x 1.5 H_2O, with a molecular weight of 432.4.

Composition
Zentro 20mg Tablets:
Each delayed release tablet contains:
Pantoprazole.....20mg as
Pantoprazole Sodium Sesquihydrate U.S.P.
(Product Specs.: U.S.P.)

Zentro 40mg Tablets:
Each delayed release tablet contains:
Pantoprazole.....40mg as
Pantoprazole Sodium Sesquihydrate U.S.P.
(Product Specs.: U.S.P.)

CLINICAL PHARMACOLOGY:
Pharmacodynamic Properties:
Pharmacotherapeutic group: Proton pump inhibitors, ATC code: A02BC02.

Mechanism of Action:
Pantoprazole is a substituted benzimidazole which inhibits the secretion of hydrochloric acid in the stomach by specific blockade of the proton pumps of the parietal cells.
Pantoprazole is converted to its active form in the acidic environment in the parietal cells where it inhibits the H+, K+-ATPase enzyme, i.e. the final stage in the production of hydrochloric acid in the stomach. The inhibition is dose-dependent and affects both basal and stimulated acid secretion. In most patients, freedom from symptoms is achieved in 2 weeks. As with other proton pump inhibitors and H2 receptor inhibitors, treatment with pantoprazole causes a reduced acidity in the stomach and thereby increases gastrin in proportion to the reduction in acidity. The increase in gastrin is reversible. Since pantoprazole binds to the enzyme distal to the cell receptor level, it can inhibit hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin). The effect is the same whether the product is given orally or intravenously.

THERAPEUTIC INDICATIONS:
Pantoprazole is indicated for use in adults and adolescents 12 years of age and above for:
• Symptomatic gastro-oesophageal reflux disease.
• Long-term management and prevention of relapse in reflux oesophagitis.

Pantoprazole is indicated for use in adults for:
• Prevention of gastroduodenal ulcers induced by non-selective non-steroidal anti-inflammatory drugs (NSAIDs) in patients at risk with a need for continuous NSAID treatment.

DOSAGE AND ADMINISTRATION:
Adults and adolescents 12 years of age and above:
Symptomatic gastro-oesophageal reflux disease
The recommended oral dose is one pantoprazole 20 mg gastro-resistant tablet per day. Symptom relief is generally accomplished within 2-4 weeks. If this is not sufficient, symptom relief will normally be achieved within a further 4 weeks. When symptom relief has been achieved, reoccurring symptoms can be controlled using an on-demand regimen of 20 mg once daily, taking one tablet when required. A switch to continuous therapy may be considered in case satisfactory symptom control cannot be maintained with on-demand treatment.

Long-term management and prevention of relapse in reflux oesophagitis
For long-term management, a maintenance dose of one pantoprazole 20 mg gastro-resistant tablet per day is recommended, increasing to 40 mg pantoprazole per day if a relapse occurs. Pantoprazole 40 mg tablet is available for this case. After healing of the relapse the dose can be reduced again to 20 mg pantoprazole.

Adults:
Prevention of gastroduodenal ulcers induced by non-selective non-steroidal anti-inflammatory drugs (NSAIDs) in patients at risk with a need for continuous NSAID treatment.
The recommended oral dose is one pantoprazole 20 mg tablet per day.

Paediatric population:
Pantoprazole is not recommended for use in children below 12 years of age due to limited data on safety and efficacy in this age group.

Elderly:
No dose adjustment is necessary in elderly patients

Patients with Renal Impairment:
A daily dose of 20 mg pantoprazole should not be exceeded in patients with severe liver impairment.

Method of Administration:
The tablets should not be chewed or crushed, and should be swallowed whole 1 hour before a meal with some water.

CONTRAINDICATIONS:
Hypersensitivity to the active substance, substituted benzimidazoles or to any of the excipients listed.

WARNINGS AND PRECAUTIONS:
Hepatic Impairment
In patients with severe liver impairment the liver enzymes should be monitored regularly during treatment with pantoprazole, particularly on long-term use. In the case of a rise of the liver enzymes the treatment should be discontinued.

Co-administration with NSAIDs
The use of Pantoprazole 20mg as a preventive of gastroduodenal ulcers induced by non-selective non-steroidal anti-inflammatory drugs (NSAIDs) should be restricted to patients who require continued NSAID treatment and have an increased risk to develop gastrointestinal complications.
The increased risk should be assessed according to individual risk factors, e.g. high age (>65 years), history of gastric or duodenal ulcer or upper gastrointestinal bleeding.

Gastric Malignancy
Symptomatic response to pantoprazole may mask the symptoms of gastric malignancy and may delay diagnosis. In the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis, anaemia or melaena) and when gastric ulcer is suspected or present, malignancy should be excluded.

Influence on Vitamin B12 Absorption
Pantoprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B12 (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy or if respective clinical symptoms are observed.

Long term treatment
In long term treatment, especially when exceeding a treatment period of 1 year, patients should be kept under regular surveillance.

Gastrointestinal Infections Caused by Bacteria
Treatment with Pantoprazole may lead to a slightly increased risk of gastrointestinal infections caused by bacteria such as Salmonella and Campylobacter or C. difficile.

Hypomagnesaemia
Severe hypomagnesaemia has been reported in patients treated with PPIs like pantoprazole for at least three

months, and in most cases for a year. 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.

Bone fractures
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 older 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.

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 Pantoprazole. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Interference with laboratory tests
Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, Pantoprazole treatment should be stopped for at least 5 days before CgA measurements. 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.

Pantoprazole tablets contain sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

DRUG INTERACTIONS:
Medicinal products with pH-Dependent Absorption Pharmacokinetics
Because of profound and long lasting inhibition of gastric acid secretion, pantoprazole may interfere with the absorption of other medicinal products where gastric pH is an important determinant of oral availability, e.g some azole antifungals such as ketoconazole, itraconazole, posaconazole and other medicines such as erlotinib.

HIV protease inhibitors
Co-administration of pantoprazole is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH such as atazanavir due to significant reduction in their bioavailability. If the combination of HIV protease inhibitors with a proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g. virus load) is recommended. A pantoprazole dose of 20mg per day should not be exceeded. Dosage of the HIV protease inhibitor may need to be adjusted.

Coumarin anticoagulants (phenprocoumon or warfarin)
There have been reports of increased INR and prothrombin time in patients receiving PPIs and warfarin or phenprocoumon concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding, and even death. Patients treated with pantoprazole and warfarin or phenprocoumon may need to be monitored for increase in INR and prothrombin time.

Methotrexate
Concomitant use of high dose methotrexate (e.g. 300 mg) and proton-pump inhibitors has been reported to increase methotrexate levels in some patients. Therefore in settings where high-dose methotrexate is used, for example cancer and psoriasis, a temporary withdrawal of pantoprazole may need to be considered.

Medicinal products that inhibit or induce CYP2C19
Inhibitors of CYP2C19 such as fluvoxamine could increase the systemic exposure of pantoprazole. A dose reduction may be considered for patients treated long-term with high doses of pantoprazole, or those with hepatic impairment. Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin and St. John's wort (Hypericum perforatum) may reduce the plasma concentrations of PPIs that are metabolised through these enzyme systems.

ADVERSE EFFECTS:
Common:
Fundic gland polyps (benign).

Uncommon:
Sleep disorders, Headache; Dizziness, Diarrhoea; Nausea /vomiting; Abdominal distension and bloating; Constipation; Dry mouth; Abdominal pain and discomfort, Liver enzymes increased (transaminases, γ-GT), Rash / exanthema / eruption; Pruritus, Fracture of the hip, wrist or spine, Asthenia, fatigue and malaise.

Rare:
Agranulocytosis, Hypersensitivity (including anaphylactic reactions and anaphylactic shock), Hyperlipidaemias and lipid increases (triglycerides, cholesterol); Weight changes, Depression (and all aggravations), Taste disorders, Disturbances in vision/ blurred vision, Bilirubin increased, Urticaria; Angioedema, Arthralgia; Myalgia, Gynaecomastia, Body temperature increased; Oedema peripheral.

Very Rare:
Thrombocytopenia, Leukopenia; Pancytopenia, Disorientation (and all aggravations).

Not Known:
Hyponatraemia, Hypomagnesaemia, Hypocalcaemia, Hypokalaemia, Hallucination; Confusion (especially in pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existence), Paraesthesia, Microscopic colitis, Hepatocellular injury; Jaundice; Hepatocellular failure, Stevens-Johnson syndrome; Lyell syndrome; Erythema multiforme; Photosensitivity, Subacute cutaneous lupus erythematosus, Muscle spasm, Interstitial nephritis (with possible progression to renal failure).

USE IN PREGNANCY AND LACTATION:
Pregnancy:
It is preferable to avoid the use of Pantoprazole during pregnancy. Although, a moderate amount of data on pregnant women indicates no malformative or feto/ neonatal toxicity.

Lactation:
There is insufficient information on the excretion of pantoprazole in human milk but excretion into human milk has been reported. A risk to the newborns/ infants cannot be excluded. Therefore, a decision on whether to discontinue breast-feeding or to discontinue/ abstain from Pantoprazole therapy should take into account the benefit of breast-feeding for the child, and the benefit of Pantoprazole therapy for the woman.
OVERDOSE:
There are no known symptoms of overdose in man. As pantoprazole is extensively protein bound, it is not readily dialysable. In the case of overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

SHELF LIFE
3 years

STORAGE AND INSTRUCTIONS:
Protect from heat, sunlight & moisture, store below 30°C.
The expiration date refer to the product correctly stored at the required condition.
Tablet must not be split, chewed or crush before administration.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
Keep out of the reach of children.
To be sold on prescription of a registered medical practitioner only.
Meets USP Dissolution Test 2

PRESENTATION:
Zentro 20mg Tablets: Cold Form & Cold Seal Pack of 14's Tablets.
Zentro 40mg Tablets: Cold Form & Cold Seal Pack of 14's Tablets.

ہدایات :

دھوپ، گرمی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
ٹیبلٹ کو توڑے یا چبائے بغیر پانی سے نگل لیں۔ بچوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

Manufactured by:
Bosch Pharmaceuticals (Pvt) Ltd.
221-223, Sector 23, Korangi Industrial Area,
Karachi - Pakistan