CONPANZOLE®
ENTERIC COATED TABLET

Ingredient(s):
Conpanzole® Enteric Coated Tablet 20mg:
Each tablet contains:
Pantoprazole Sodium Sesquihydrate 22.56mg
(eq. to Pantoprazole 20mg)
Conpanzole® Enteric Coated Tablet 40mg:
Each tablet contains:
Pantoprazole Sodium Sesquihydrate 45.12mg
(eq. to Pantoprazole 40mg)

Pharmacology (Summary of Pharmacodynamic and Pharmacokinetic):
Pharmacodynamic:
During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also Chromogranin (CgA) increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours.
Available published evidence suggests that proton pump inhibitors 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.
Pantoprazole is a substituted benzimidazole which inhibits the secretion of hydrochloric acid in the stomach by specific action on the proton pumps of the parietal cells. Pantoprazole is converted to its active form in the acidic canaliculi of the parietal cells where it inhibits the H^+, K^+ ATPase enzyme that is 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.
Treatment with pantoprazole causes a reduced acidity in the stomach and thereby an increase in 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, the substance can affect hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin).

Pharmacokinetic:
Pantoprazole is rapidly absorbed and the maximal plasma concentration is achieved even after one single oral dose. The absolute bioavailability from tablet was found to be about 77%. On average at about 2.5h p.a. the maximum serum concentrations of about 1-1.5µg/ml (20mg pantoprazole) and 2-3µg/ml (40mg pantoprazole) are achieved and these values remain constant after multiple administration. Volume of distribution is about 0.15L/kg. Terminal half-life is about 1 hour.
Pharmacokinetics does not vary after single or repeated administration. In the dose range of 10 to 80mg, the plasma kinetics of pantoprazole is virtually linear after both oral and intravenous administration.
Pantoprazole's serum protein binding is about 98%. The substance is almost exclusively metabolized in the liver. Renal elimination represents the major route of excretion (about 80%) for the metabolites of pantoprazole, the rest are excreted with the faeces. The main metabolite in both serum and urine is desmethylpantoprazole which is conjugated with sulphate. The half-life of the main metabolite (about 1.5h) is not much longer than that of pantoprazole.

Indication(s):
1. In combination with two appropriate antibiotics for the eradication of *Helicobacter pylori* in patients with peptic ulcers with the objective of reducing the recurrence of duodenal and gastric ulcers caused by this microorganism
2. Duodenal ulcer
3. Gastric ulcer
4. Moderate and severe cases of inflammation of the esophagus (reflux esophagitis)
5. Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions

Dosage and Administration:
Adults and adolescents ≥ 12 years
Reflux disease and associated symptoms:
Mild:
Recommended dose: one 20mg tablet daily
Symptom relief is generally accomplished within 2-4 weeks and a 4-week treatment period is usually required for healing associated esophagitis. When symptom relief has been achieved, recurring symptoms can be controlled using an on demand regimen of one 20mg tablet daily, when required.
Moderate and severe:
One 40mg tablet daily. In individual cases, the dose may be doubled (increased to two 40mg tablet daily) especially when there has been no response to other medicines.
Reflux esophagitis usually require 4 weeks course of treatment, if this should be inadequate, healing will be achieved within further 4 weeks. Treatment should not exceed 8 weeks as experience with long-term use is limited.
Long-term management and prevention:
Maintenance dose: one 20mg tablet daily is recommended, increasing to 40mg tablet daily. If a relapse occurs, use 40mg tablet. After healing of the relapse, the dosage can be reduced back to 20mg tablet per day.

A treatment period of 1 year should be exceeded only after careful consideration of the benefit/risk ratio, as drug safety over several years is not sufficiently established.
Adults
Prevention of gastroduodenal ulcers induced by NSAIDs in patients at risk with a need for continuous NSAIDs treatment:
Recommended dose: One 20mg tablet/day. A daily dose of 20mg/tablet should not be exceeded in patients with severe liver impairment. No dose adjustment is necessary in elderly patients or in those with impaired renal function.
Eradication of *H. pylori* in combination with 2 appropriate antibiotics:
In cases of duodenal or gastric ulcer in which infection with *H. pylori* has been confirmed, the microorganism should be eradicated by combination treatment. Depending upon the resistance pattern the following combinations can be recommended. The combination therapy should be administered twice daily.
A) 40mg tablet pantoprazole + 1000mg amoxicillin + 500mg clarithromycin
B) 40mg tablet pantoprazole + 500mg metronidazole + 500mg clarithromycin
C) 40mg tablet pantoprazole + 1000mg amoxicillin + 500mg metronidazole
Combination therapy for eradication of *H. pylori* infection usually lasts 7 days and can be extended to a maximum of 2 weeks.
Duodenal and gastric ulcers (If combination therapy is not an option, or patient has been tested negative for *H. pylori*.
One 40mg tablet daily in most cases. In individual cases, the dose may be doubled (increased to two 40mg tablet daily) especially when there has been no response to other medicines.
Gastric ulcer: administer for 4 weeks, extend for another 4 weeks if necessary.
Duodenal ulcer: administer for 2 weeks, extend for another 2 weeks if necessary.
Treatment should not exceed 8 weeks as experience with long-term use is limited.
In patients with severe liver impairment, the dose has to be reduced to one 40mg pantoprazole tablet every other day and liver enzymes should be monitored.
The daily dose of 40mg pantoprazole should not be exceeded in elderly patients or in those with impaired renal function. An exception in combination therapy for eradication of *H. pylori* where elderly patients should received the usual pantoprazole dose (40mg twice daily) during first week treatment.
Long-term management of Zollinger-Ellison syndrome and other pathological hypersecretory conditions:
The recommended daily dose at the beginning of treatment is 80mg (two 40mg tab). Thereafter, the dosage can be titrated up or down as needed using measurements of gastric acid secretion to guide. Doses more than 80mg daily should be divided and given twice daily. A temporary increase in dosage to more than 160mg pantoprazole is possible but should not be applied longer than required for acid control.
Treatment duration in Zollinger-Ellison syndrome and other pathological hypersecretory conditions is not limited and should be adapted according to clinical needs.

Route of administration: Oral

Side Effect(s) / Adverse Reaction(s):
Blood and lymphatic system: Thrombocytopenia, leucopenia
Nervous system disorder: Headache, dizziness
Eye disorders: Disturbance in vision/ blurred vision.
Gastrointestinal disorders: Diarrhoea, nausea/ vomiting, abdominal distension, bloating, constipation, dry mouth, abdominal pain, discomfort, microscopic colitis (frequency not known), fundic gland polyps (benign) (frequency common).
Skin and subcutaneous tissue disorders: Rash/exanthema/eruption, pruritus, urticaria, angioedema
Musculoskeletal, connective tissue disorders: Arthralgia, myalgia, fracture of the hip, wrist or spine (frequency uncommon).
Metabolism and nutrition disorders: hyperlipidaemias and lipid increases, weight changes, hypomagnesaemia (frequency not known), vitamin B12 deficiency.
General disorders and administration site conditions: Asthenia, fatigue, malaise, body temperature increases, oedema peripheral.
Immune system disorders: hypersensitivity (including anaphylactic reactions and anaphylactic shock.)
Hepatobiliary disorders: liver enzymes increased (transaminases, γ-GT), bilirubin increased, hepatocellular injury, jaundice, hepatocellular failure.
Phychiatric disorders: sleep disorders, depression (and all aggravations), disorientation (and all aggravations).
Psychiatric disorders: hallucination, confusion (especially in pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existance)
Renal and urinary disorders: Interstitial nephritis
Skin and subcutaneous tissue disorders: Stevens-Johnson syndrome, Lyell syndrome, erythema multiforme, photosensitivity. Subacute Cutaneous Lupus Erythematosus (SCLE): (frequency unknown)
Infections and infestations: *Clostridium difficile*-associated diarrhea.

Contraindications:
1. Hypersensitivity to any component of this product or of the combination partners.
2. This product must not be used in combination treatment for eradication of *H. pylori* in patients with moderate to severe hepatic or renal dysfunction.

Warnings and Precautions:
Increased CgA level may interfere with investigations for neuroendocrine tumours. If the patient(s) are due to have a test on Chromogranin A level, Conpanzole Enteric

Coated Tablet treatment should be stopped for at least 5 days before CgA measurements to avoid this interference (see section Pharmacodynamic). 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.

1. Liver enzyme should be monitored during pantoprazole therapy. In case liver enzymes rise, pantoprazole should be discontinued.
2. Pantoprazole is not indicated for mild gastrointestinal complaints eg: nervous dyspepsia.
3. In the case of combination therapy, the summaries of product characteristics of the respective drugs should be observed.
4. Prior to treatment, the possibility of malignancy of gastric ulcer or a malignant disease of the esophagus should be excluded as the treatment with pantoprazole may alleviate the symptoms of malignant ulcers and can thus delay diagnosis.
5. Diagnosis of reflux esophagitis should be confirmed by endoscopy.
6. Effects on ability to drive or operate machinery: There are no known effects on the ability to drive, use machines or working without firm support.
7. Use in children: To date, there has been no experience with treatment in children.
8. Regular Surveillance: Patients on proton pump inhibitor treatment (particularly those treated for long term) should be kept under regular surveillance.
9. 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 Conpanzole Enteric Coated Tablet. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.
10. Hypomagnesaemia: Severe hypomagnesaemia has been reported in patients treated with PPI like Conpanzole Enteric Coated Tablet for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. 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 PPI with digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.
11. Fracture: PPIs 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 the elderly or in presence of other recognised risk factors. Observational studies suggest that PPIs 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.
12. *Clostridium Difficile* Diarrhoea: Published observational studies suggest that PPI therapy may be associated with an increased risk of *Clostridium difficile*-associated Diarrhoea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.
13. Vitamin B12 Deficiency: Daily treatment with any acid-supressing 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.

Interaction with Other Medicaments:

1. Changes in absorption should be observed when drugs whose absorption is pH-dependent e.g. ketoconazole are taken concomitantly. This precaution also applies to drugs taken a short time before this drug.
2. Pantoprazole sodium is metabolized in liver via the cytochrome P450 enzyme system. An interaction of pantoprazole with other drugs or compounds which are metabolized using the same enzyme system cannot be excluded. However, no clinically significant interactions were observed in specific tests with a number of such drugs or compounds eg.carbamazepine, caffeine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, nifedipine, phenprocoumon, warfarin, theophylline, phenytoin and an oral contraceptive.
3. There were also no interactions with concomitantly administered antacids.
4. No clinically relevant interactions with the respective antibiotics (clarithromycin, metronidazole, amoxicillin) were observed.

Pregnancy and Lactation:

Clinical study in human is limited. Studies in animal have shown fetotoxicity. There is no information on the excretion of pantoprazole into human breast milk. Pantoprazole should only be used when the benefit to the mother is considered greater than the potential risk to the foetus/baby.

Symptoms and Treatment for Overdosage, and Antidote(s):

There are no known symptoms of overdose in man. In the case of overdose with clinical signs of intoxication, the usual rules of intoxication therapy apply. If you have taken too little this product or have forgotten to take it, do not take the dose late but continue with the next regular dose on your dosing schedule. Talk to your doctor if you want to interrupt or prematurely discontinue treatment with this product.

Shelf-Life:
3 years from the date of manufacture.

Storage Condition(s):
Store at temperature below 30ºC. Protect from light and moisture.

Product Description and Packing(s):
Conpanzole Enteric Coated Tablet 20mg:
A yellow color oval shape enteric coated tablet "  ".
Blister packing of 14's x 2 and 14's x 30.

Conpanzole Enteric Coated Tablet 40mg:
A yellow color oval shape enteric coated tablet "  ".
Blister packing of 14's x 1, 14's x 2 and 14's x 30.

Y. S. P.®
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