OMETAC 20 CAPSULES

DESCRIPTION:
Opaque pink/ reddish brown size 2 hard gelatin capsule with OMETAC 20 printed on both cap and body.

COMPOSITION:
Each capsule contains Omeprazole (as enteric-coated pellets) 20 mg

PHARMACODYNAMICS:
Omeprazole inhibits secretion of gastric acid and is considered to do so by irreversibly blocking the enzyme system of hydrogen / potassium adenosine triphosphatase, the so-called proton pump of the gastric parietal cell. It thereby inhibits the final transport of hydrogen ions (via exchange with potassium ions) into the gastric lumen. Omeprazole inhibits both basal and stimulated acid secretion irrespective of the stimulus. Omeprazole also inhibits hepatic cytochrome P-450 mixed-function oxidase system.
Risk of GI Ulceration medicinal products, serum gastrin increases in response to the decreased acid secretion. Also 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.

PHARMACOKINETICS:
Omeprazole is acid-labile and absorption from the gastrointestinal tract appears to be formulation-dependent and dose dependent. Following absorption, it is distributed in tissues, particularly gastric parietal cells. Approximately 95% of the drug is bound to plasma proteins. Omeprazole is almost completely metabolised in the liver and rapidly eliminated mostly in the urine (about 80%) and faeces (about 20%). Although the elimination half-life from plasma is short (0.5 to 1.5 hour), it's duration of action can last up to 72 hours. The inhibition of acid secretion is directly related to the area under the plasma concentration time curve but not to the plasma concentration at any given time.

INDICATIONS:
Duodenal ulcer
Gastric ulcer
NSAID associated gastric and duodenal ulcers or erosions
Helicobacter pylori eradication in peptic ulcer disease
Reflux oesophagitis
Symptomatic gastro-oesophageal reflux disease
Acid related dyspepsia
Zollinger-Ellison syndrome

CONTRAINDICATIONS:
Hypersensitivity to the active substance, substituted benzimidazoles or to any of the excipients. Omeprazole like other proton pump inhibitors (PPIs) must not be used concomitantly with nelfinavir.

SIDE EFFECTS:
Omeprazole is generally well-tolerated and adverse reactions are mostly mild and reversible. Adverse effects which have been reported and which may occur rarely in isolated cases include

haematological disorders (anaemia, eosinopenia, leukocytosis, neutropenia, thrombocytopenia, haematuria), gastrointestinal disturbances (diarrhoea, constipation, nausea, vomiting, flatulence, abdominal pain, heartburn), endocrinological disturbances (gynaecomastia), hepatic abnormalities (hepatitis with or without jaundice, hepatic failure, elevated liver enzymes), dermatological disorders (skin rashes, pruritus, photosensitivity, erythema multiforme), urinary tract infection, dizziness, headache, muscle pain, malaise, fever.

The following table lists the adverse reactions have been identified or suspected by the clinical trials programme for omeprazole and post-marketing. None was found to be dose-related. Adverse reactions listed below are classified according to frequency and System Organ Class (SOC).

SOC/frequency	**Adverse reaction**
Blood and lymphatic system disorders	
Rare:	Leukopenia, thrombocytopenia
Very rare:	Agranulocytosis, pancytopenia
Immune system disorders	
Rare:	Hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock
Metabolism and nutrition disorders	
Rare:	Hyponatraemia
Not known:	Hypomagnesaemia. Severe hypomagnesaemia may result in hypocalcaemia. Fracture may also be associated with hypokalaemia.
Psychiatric disorders	
Uncommon:	Insomnia
Rare:	Agitation, confusion, depression
Very rare:	Aggression, hallucinations
Nervous system disorders	
Common:	Headache
Uncommon:	Dizziness, paraesthesia, somnolence
Rare:	Taste disturbance
Eye disorders	
Rare:	Blurred vision
Ear and labyrinth disorders	
Uncommon:	Vertigo
Respiratory, thoracic and mediastinal disorders	
Rare:	Bronchospasm
Gastrointestinal disorders	
Common:	Abdominal pain, constipation, diarrhoea, flatulence, nausea/vomiting, fundic gland polyps (benign)
Rare:	Dry mouth, stomatitis, gastrointestinal candidiasis
Not known:	Microscopic colitis

Hepatobiliary disorders	
Uncommon:	Increased liver enzymes
Rare:	Hepatitis with or without jaundice
Very rare:	Hepatic failure, encephalopathy in patients with pre-existing liver disease
Skin and subcutaneous tissue disorders	
Uncommon:	Dermatitis, pruritus, rash, urticaria
Rare:	Alopecia, photosensitivity
Very rare:	Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis(TEN)
Not known:	Subacute Cutaneous Lupus Erythematosus (SCLE)
Musculoskeletal and connective tissue disorders	
Uncommon:	Fracture of the hip, wrist or spine
Rare:	Arthralgia, myalgia
Very rare:	Muscular weakness
Renal and urinary disorders	
Rare:	Interstitial nephritis
Reproductive system and breast disorders	
Very rare:	Gynaecomastia
General disorders and administration site conditions	
Uncommon:	Malaise, peripheral oedema
Rare:	Increased sweating

Clostridium Difficile Diarrhea
Infections & infestations: Clostridium difficile associated diarrhea.

Vitamin B12 Deficiency
Metabolic/Nutritional: Vitamin B12 deficiency

WARNING AND PRECAUTIONS:
When gastric ulcer is suspected, the possibility of malignancy should be excluded before treatment with omeprazole is instituted, as treatment may alleviate symptoms and delay diagnosis. Caution should be exercised in patients with chronic hepatic disease or a history of liver disease as this condition may cause the drug to accumulate in the body.

In the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment may alleviate symptoms and delay diagnosis.

Co-administration of atazanavir with proton pump inhibitors is not recommended (see section Interaction with other medicinal products and other forms of interaction). If the combination of atazanavir with a proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g virus load) is recommended in combination with an increase in the dose of atazanavir to 400 mg with 100 mg of ritonavir; omeprazole 20 mg should not be exceeded.

Omeprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B_{12} (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B_{12} absorption on long-term therapy.

Omeprazole is a CYP2C19 inhibitor. When starting or ending treatment with omeprazole, the potential for interactions with drugs metabolised through CYP2C19 should be considered. An interaction is observed between clopidogrel and omeprazole (see section Interaction with other medicinal products and other forms of interaction). The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of omeprazole and clopidogrel should be discouraged.

Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter and, in hospitalised patients, possibly also Clostridium difficile (see section Pharmacodynamic properties).

Some published observational studies suggest that proton pump inhibitor (PPI) therapy may be associated with a small increased risk for osteoporosis related fractures. However, in other similar observational studies no such increased risk was found.
In randomized, double-blind and controlled clinical studies on omeprazole and esomeprazole (including two open long-term studies of up to more than 12 years) there are no indications that PPIs are associated with osteoporotic fractures.

As in all long-term treatments, especially when exceeding a treatment period of 1 year, patients should be kept under regular surveillance

Regular Surveillance
Patients on proton pump inhibitor treatment (particularly those treated for long term) should be kept under regular surveillance.

Subacute Cutaneous Lupus Erythematosus (SCLE)
Proton pump inhibitors are associated with very infrequent cases of subacute cutaneous lupus erythematosus (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 Ometac 20 Capsules. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Hypomagnesaemia
Severe hypomagnesaemia has been reported in patients treated with PPI like Ometac 20 Capsules 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.

Fracture
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 the elderly 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.

Clostridium Difficile Diarrhea
Published observational studies suggest that PPI therapy may be associated with an increased risk of Clostridium difficile associated diarrhea, 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 appropriate to the condition being treated.

Vitamin B12 Deficiency
Daily treatment with any acid-suppressing 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.
Increased Chromogranin A.

Interference with laboratory tests
Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. If the patient(s) are due to have a test on Chromogranin A level, Ometac 20 Capsules 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.

PREGNANCY AND LACTATION:
Pregnancy

No adverse events of omeprazole on pregnancy or on the health of the foetus/newborn child. Omeprazole can be used during pregnancy.

Breast-feeding

Omeprazole is excreted in breast milk but is not likely to influence the child when therapeutic doses are used.

Use in children:
There is no previous experience of the use of omeprazole in children.

DRUG INTERACTIONS:
Active substances with pH dependent absorption

The decreased intragastric acidity during treatment with omeprazole might increase or decrease the absorption of active substances with a gastric pH dependent absorption.

Nelfinavir, atazanavir
The plasma levels of nelfinavir and atazanavir are decreased in case of co-administration with omeprazole.
Concomitant administration of omeprazole with nelfinavir is contraindicated .
Concomitant administration of omeprazole with atazanavir is not recommended .

Digoxin
Caution should be exercised when omeprazole is given at high doses in elderly patients. Therapeutic drug monitoring of digoxin should then be reinforced.

Clopidogrel
Concomitant use of omeprazole and clopidogrel should be discouraged.

Other active substances

The absorption of posaconazole, erlotinib, ketoconazole and itraconazole is significantly reduced and thus clinical efficacy may be impaired. For posaconazole and erlotinib concomitant use should be avoided.

Active substances metabolised by CYP2C19

Omeprazole is a moderate inhibitor of CYP2C19, the major omeprazole metabolising enzyme. Thus, the metabolism of concomitant active substances also metabolised by CYP2C19, may be decreased and the systemic exposure to these substances increased. Examples of such medicinal products are R-warfarin and other vitamin K antagonists, cilostazol, diazepam and phenytoin.

Unknown mechanism

Saquinavir
Concomitant administration of omeprazole with saquinavir/ritonavir resulted in increased plasma levels for saquinavir associated with good tolerability in HIV-infected patients.

Tacrolimus
Concomitant administration of omeprazole has been reported to increase the serum levels of tacrolimus.

Methotrexate
When given together with proton pump inhibitors, methotrexate levels have been reported to increase in some patients. In high-dose methotrexate administration a temporary withdrawal of omeprazole may need to be considered.

Effects of other active substances on the pharmacokinetics of omeprazole
Inhibitors of CYP2C19 and/or CYP3A4
Since omeprazole is metabolised by CYP2C19 and CYP3A4, active substances known to inhibit CYP2C19 or CYP3A4 (such as clarithromycin and voriconazole) may lead to increased omeprazole serum levels by decreasing omeprazole's rate of metabolism. Concomitant voriconazole treatment resulted in more than doubling of the omeprazole exposure. As high doses of omeprazole have been well-tolerated adjustment of the omeprazole dose is not generally required. However, dose adjustment should be considered in patients with severe hepatic impairment and if long-term treatment is indicated.

Inducers of CYP2C19 and/or CYP3A4
Active substances known to induce CYP2C19 or CYP3A4 or both (such as rifampicin and St John's wort) may lead to decreased omeprazole serum levels by increasing omeprazole's rate of metabolism.

DOSAGE & ADMINISTRATION:
Ometac 20 Capsules are recommended to be taken in the morning and swallowed whole with liquid. For patients with swallowing difficulties, the capsules may be opened and the contents swallowed or suspended in a slightly acidic fluid such as juice, soured milk or non-carbonated water. The dispersion should be taken immediately or within 30 minutes. Alternatively, patients can suck the capsule and swallow the pellets with liquid. The pellets must not be chewed or crushed.

Duodenal ulcer:
The recommended dosage in patients with an active duodenal ulcer is 20 mg once daily. Symptom resolution is rapid and in most patients healing occurs within 2 weeks.
For those patients who may not be fully healed after the initial course, healing usually occurs during a further 2 week treatment period.
In patients with poorly responsive duodenal ulcer 40 mg once daily is recommended and healing is usually achieved within 4 weeks.
For the prevention of relapse in patients with duodenal ulcer disease the recommended dose is 10 mg once daily. If needed the dose can be increased to 20-40mg once daily.
For NSAID associated duodenal ulcers see NSAID associated gastroduodenal lesions.
For eradication of Helicobacter pylori see Helicobacter pylori (Hp) eradication regimens in peptic ulcer disease.

Gastric ulcer:
The recommended dosage is 20 mg once daily. Symptom resolution is rapid and in most patients healing occurs within 4 weeks. For those patients who may not be fully healed after the initial course, healing usually occurs during a further 4 weeks' treatment period.

In patients with poorly responsive gastric ulcer 40 mg once daily is recommended and healing is usually achieved within 8 weeks.

For the prevention of relapse in patients with poorly responsive gastric ulcer the recommended dose is 20 mg once daily. If needed the dose can be increased to 40 mg once daily.

For eradication of Helicobacter pylori see Helicobacter pylori (Hp) eradication regimens in peptic ulcer disease.

NSAID associated ulcers or gastroduodenal erosions:
NSAID associated gastric ulcers, duodenal ulcers or gastroduodenal erosions in patients with or without continued NSAID treatment the recommended dosage is 20 mg once daily. Symptom resolution is rapid and in most patients healing occurs within 4 weeks.
For those patients who may not be fully healed after the initial course, healing usually occurs during a further 4 weeks treatment period.
For the prevention of NSAID associated gastric ulcers, duodenal ulcers, gastroduodenal erosions and dyspeptic symptoms the recommended dosage is 20 mg once daily.

Helicobacter pylori (Hp) eradication regimens in peptic ulcer disease:
Triple therapy regimens
Omeprazole 20 mg, amoxicillin 1 g and clarithromycin 500 mg, all twice a day for one week
or
Omeprazole 20 mg, metronidazole 400 mg (or tinidazole 500 mg) and clarithromycin 250

mg, all twice a day for one week
or
Omeprazole 40 mg once daily with amoxicillin 500 mg and metronidazole 400 mg both three times a day for one week.

Dual therapy regimens:
Omeprazole 40-80 mg daily with amoxicillin 1.5 g daily in divided doses for two weeks. In clinical studies daily doses of 1.5-3 g of amoxicillin have been used
or
Omeprazole 40 mg once daily and clarithromycin 500 mg three times a day for two weeks.
To ensure healing in patients with active peptic ulcer disease, see further dosage recommendations for Duodenal and Gastric ulcer.
In each regimen if the patient is still Hp positive, therapy may be repeated.

For reflux oesophagitis**:**
The recommended dosage is 20 mg once daily.
Symptoms resolve rapidly and most patients are healed within 4 weeks. For those who are not fully healed after the initial course, healing usually occurs during a further 4 weeks' treatment period.
In patients with severe reflux oesophagitis, 40 mg once daily is recommended and healing is usually achieved within 8 weeks.
For long-term management of patients with healed reflux oesophagitis, the recommended dose is 10 mg once daily. If required, dosage may be increased to 20 – 40 mg once daily.

Symptomatic gastro-oesophageal reflux disease:
The recommended dosage is 20 mg daily. Symptom relief is rapid. Patients may respond adequately to 10 mg daily, and therefore individual dose adjustment should be considered.

If symptom control has not been achieved after 4 weeks treatment with 20 mg daily, further investigation is recommended.

Acid related dyspepsia:
In the relief of symptoms in patients with epigastric pain/discomfort with or without heartburn the recommended dosage is 20 mg once daily.
If symptom control has not been achieved after 4 weeks treatment with 20 mg daily, further investigation is recommended.

Zollinger-Ellison syndrome:
In patients with Zollinger-Ellison syndrome the dosage should be individually adjusted and treatment continued as long as is clinically indicated. The recommended initial dosage is 60 mg daily. All patients with severe disease and inadequate response to other therapies have been effectively controlled and more than 90% of the patients maintained on doses of 20-120 mg daily. When doses exceed 80 mg daily, the dose should be divided and given twice daily.

Impaired renal function:
Dose adjustment is not needed in patients with impaired renal function.

Impaired hepatic function:
As bioavailability and plasma half-life of omeprazole are increased in patients with impaired hepatic function a daily dose of 10-20 mg may be sufficient.

Elderly:
Dose adjustment is not needed in the elderly.

Children:
Ometac 20mg are not approved for use in children

ROUTE OF ADMINISTRATION:
Oral administration

OVERDOSAGE & TREATMENT:
Symptoms include blurred vision, confusion, diaphoresis, drowsiness, dryness of mouth, flushing, headache, nausea, and tachycardia. Since there is no specific antidote, treatment should be symptomatic and supportive.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Omeprazole is not likely to affect the ability to drive or use machines. Adverse reactions such as dizziness and visual disturbances may occur. If affected, patients should not drive or operate machinery.

PRESENTATION: 7 capsules per PVC/Alumunium blister. Boxes of 2 blisters.

STORAGE CONDITION:
Store in a dry place below 30°C.
Keep medicines out of reach of children.

MANUFACTURER & PRODUCT REGISTRATION HOLDER:
Noripharma Sdn. Bhd. 200701034604 (792633-A)
Lot 5030, Jalan Teratai,
5 1/2 Mile off Jalan Meru
41050 Klang, Selangor, Malaysia

DATE OF REVISION:
January 2024