Oltrix

Omeprazole

اولٹرکس

(اومیپرازول)

۴۰ ملی گرام آئی وی انجکشن

40mg I.V. For Injection

1. PRODUCT NAME

OLTRIX Injection 40 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Vial Contains:

Omeprazole Sodium equivalent to Omeprazole 40mg
(BP Specification)

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Omeprazole Injection 40 mg is indicated primarily for the treatment of Zollinger-Ellison syndrome, and may also be used for the treatment of gastric ulcer, duodenal ulcer, and reflux oesophagitis.

4.2 Dose and Method of Administration

In patients with duodenal ulcer, gastric ulcer or reflux oesophagitis where oral medication is inappropriate, Omeprazole Injection 40 mg once daily is recommended.

In patients with Zollinger-Ellison syndrome the recommended initial dose of omeprazole given intravenously is 60 mg daily. Higher daily doses may be required and the dose should be adjusted individually. When doses exceed 60 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 plasma half-life of omeprazole is 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

There is limited experience with omeprazole I.V. in children.

Method of Administration

Omeprazole Injection 40 mg should be given as a slow intravenous injection. The solution for IV injection is obtained by adding to the vial of the solvent provided. (No other solvent should be used). Discoloration may occur if incorrect reconstitution technique is used. After reconstitution the injection should be given slowly over a period of at least 2.5 minutes at a maximum rate of 4 ml per minute. The solution should be used within 4 hours of reconstitution.

4.3 Contraindications
Known hypersensitivity to omeprazole.

4.4 Special Warnings and Precautions for Use
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, the possibility of malignancy should be excluded, as treatment may alleviate symptoms and delay diagnosis

4.5 Interaction with Other Medicines and Other Forms of Interaction
Effects of omeprazole on the pharmacokinetics of other medicines Nelfinavir, Atazanavir: Omeprazole has been reported to interact with some antiretroviral medicines. The clinical importance and the mechanisms behind these interactions are not always known. Increased gastric pH during omeprazole treatment may change the absorption of the antiretroviral medicine. Other possible interaction mechanisms are via CYP 2C19. For some antiretroviral medicines, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole. Concomitant administration with omeprazole and medicines such as atazanavir and nelfinavir is therefore not recommended.

Citalopram / Escitalopram
Co-administration of omeprazole (20 mg) with citalopram (20 mg single dose) doubles the AUC of the S-isomer of citalopram, but the R-isomer of citalopram is not affected. A reduction in the dose of citalopram may be necessary based on clinical judgement. For patients taking omeprazole, the citalopram dose should not exceed the maximum dose of 20 mg/day.

Co-administration of omeprazole (30 mg) with escitalopram (20 mg single dose) increased the plasma levels (approximately 50%) and terminal half-life (31%) of escitalopram. A reduction in the dose of escitalopram may be necessary based on clinical judgement.

Digoxin
Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10% (up to 30% in two out of ten subjects).

Clopidogrel
Results from studies in healthy subjects have shown a pharmacokinetic/pharmacodynamic interaction between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and omeprazole (80 mg p.o. daily, i.e. four times the recommended dose) resulting in decreased exposure to the active metabolite of clopidogrel by an average of 46%, and resulting in decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 16%.

It is, however, uncertain to what extent this interaction is clinically important. One prospective, randomised (but incomplete) study (in over 3760 patients comparing placebo with omeprazole 20 mg in patients treated with clopidogrel and ASA) and non-randomised, post-hoc analyses of data from large, prospective, randomised clinical outcome studies (in over 47000 patients) did not show any evidence of an increased risk for adverse cardiovascular outcome when clopidogrel and PPIs, including omeprazole, were given concomitantly.

Results from a number of observational studies are inconsistent with regard to increased risk or no increased risk for CV thromboembolic events when clopidogrel is given together with a PPI.
When clopidogrel was given together with a fixed dose combination of esomeprazole 20 mg + ASA 81 mg compared to clopidogrel alone in a study in healthy subjects there was a decreased exposure by almost 40% of the active metabolite of clopidogrel. However, the maximum levels of inhibition of (ADP induced) platelet aggregation in these subjects were the same in the clopidogrel and the clopidogrel + the combined (esomeprazole + ASA) product groups, likely due to the concomitant administration of low dose ASA.

Other active substances
The absorption of 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 inhibits CYP2C19, the major omeprazole metabolising enzyme. Thus, the metabolism of concomitant medicines also metabolised by CYP2C19, such as diazepam, phenytoin, warfarin (R-warfarin) or other vitamin K antagonists and cilostazol, may be delayed.

Monitoring of patients receiving phenytoin is recommended and a reduction of the phenytoin dose may be necessary. However concomitant treatment with omeprazole capsules 20 mg, daily did not change the blood concentration of phenytoin in patients on continuous treatment with this medicine.

In patients receiving warfarin or other vitamin K antagonists, monitoring of INR is recommended and a reduction of the warfarin (or other vitamin K antagonist) dose may be necessary. Concomitant treatment with omeprazole 20 mg orally, daily did, however, not change coagulation time in patients on continuous treatment with warfarin.

Cilostazol
Omeprazole, given in doses of 40 mg to healthy subjects in a cross-over study, increased Cmax and AUC for cilostazol by 18% and 26% respectively, and one of its active metabolites by 29% and 69% respectively.

Other
Omeprazole is partly metabolised also by CYP3A4, but omeprazole does not inhibit this enzyme. Thus, omeprazole does not affect the metabolism of medicines metabolised by CYP3A4, such as cyclosporin, lidocaine, quinidine, oestradiol, erythromycin, and budesonide. However, omeprazole has been shown to induce CYP1A2-mediated metabolism of clozapine. Close monitoring of plasma clozapine levels is recommended.

Results from a range of interaction studies with omeprazole versus other medicines demonstrate that omeprazole, 20-40 mg daily, has no significant influence on any other CYP enzymes relevant for medicine metabolism, as shown by the lack of metabolic interaction with substrates for CYP1A2 (such as caffeine, theophylline), CYP2C9 (such as S-warfarin, piroxicam, diclofenac, naproxen), CYP2D6 (such as metoprolol, propranolol), CYP2E1 (such as ethanol). However, omeprazole has been shown to induce CYP1A2-mediated metabolism of clozapine. Close monitoring of plasma clozapine levels is recommended.

Unknown mechanism: Tacrolimus
Concomitant administration of omeprazole and tacrolimus may 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.

Saquinavir
For other antiretroviral medicines, such as saquinavir, elevated serum levels have been reported. There are also some antiretroviral medicines of which unchanged serum levels have been reported when given with omeprazole.

Effects of Omeprazole on the Pharmacokinetics of Other Medicines
Inhibitors CYP2C19 and/or CYP3A4
Since omeprazole is metabolised by CYP2C19 and CYP3A4, medicines known to inhibit CYP 2C19 or CYP 3A4 or both (such as clarithromycin and voriconazole) may lead to increased omeprazole serum levels by decreasing the rate of omeprazole's metabolism.

Concomitant voriconazole treatment resulted in more than doubling of the omeprazole exposure. Since high doses of omeprazole have been well-tolerated, adjustment of the omeprazole dose is not required during temporary concomitant use.

Inducers of CYP2C19 and/or CYP3A4
Medicines known to induce CYP 2C19 or CYP 3A4 or both (such as rifampicin) may lead to decreased omeprazole serum levels by increasing omeprazole's rate of metabolism.

4.6 Fertility, pregnancy and lactation
Pregnancy
Results from three prospective epidemiological studies indicate no adverse effects 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.

4.7 Effects on ability to drive and use machines
Omeprazole is not likely to affect the ability to drive or use machines.

4.9 Overdose
Omeprazole I.V. doses of up to 270 mg on a single day and up to 650 mg over a three-day period have been given in clinical trials without any dose-related adverse reactions.

5 PHARMACEUTICAL PARTICULARS

5.1 Shelf life
2 years at a temperature not exceeding 25ºC.

5.2 Storage Condition / Instruction
Any unused product or waste material should be disposed
Store below 25ºC.
Keep out of reach of children
Protect from light and moisture

5.3 How to Supplied
Pack of 1 vial contains Omeprazole lyophilized powder 40mg and one ampoule of sterile water for injection.

5.4 Special precautions for disposal
Of in accordance with local requirements.

CORRECTION REQUIRED "MANUFACTURED BY"

MANUFACTURED FOR:
NAWAN LABORATORIES (PVT.) LTD.
136, Sector 15, Korangi Industrial Area, Karachi-Pakistan.

MANUFACTURER BY:
Bio-Labs (Pvt.) Ltd.
Plot No145, Industrial Triangle,
Kahuta Road, Islamabad-Pakistan.
URL: www.BIO-LABS.net
ISO 9001, 14001 & 18001 CERTIFIED
Mfg. Lic. No.: 000296