# ZUNE

## COMPOSITION:

Tablets: ZUNE is available for oral administration as:

1. ZUNE tablets 20mg
Each enteric coated tablet contains:
Esomeprazole Magnesium Trihydrate (U.S.P.) equivalent to
Esomeprazole..... 20mg
Product conforms to the Manufacturer's Specifications.

2. ZUNE tablets 40mg
Each enteric coated tablet contains:
Esomeprazole Magnesium Trihydrate (U.S.P.) equivalent to
Esomeprazole..... 40mg
Product conforms to the Manufacturer's Specifications.

3. ZUNE IV injection 40mg
Each vial contains:
Esomeprazole Sodium equivalent to
Esomeprazole (M.S.)..... 40mg
Product conforms to the Manufacturer's Specifications.

## DESCRIPTION:

Mechanism of action:
Esomeprazole works by binding irreversibly to the H+/K+ ATPase in the proton pump. Because the proton pump is the final pathway for secretion of hydrochloric acid by the parietal cells in the stomach, its inhibition dramatically decreases the secretion of hydrochloric acid into the stomach and alters gastric pH.

## PHARMACOKINETICS:

Absorption:
After oral administration peak plasma levels (Cmax) occur at approximately 1.5 hours (Tmax). The Cmax increases proportionally when the dose is increased and there is a three fold increase in the area under the plasma concentration time curve (AUC) from 20 to 40mg.
At repeated once daily dosing with 40mg, the systemic bioavailability is approximately 90% compared to 64% after a single dose of 40mg.
Effect of Food: The AUC after administration of a single 40mg dose of Esomeprazole is decreased by 43-53% after food intake compared to fasting conditions. Esomeprazole should be taken at least one hour before meals. Food delays and decreases the absorption of Esomeprazole but this does not significantly change its effect on the intragastric acidity.
Distribution:
Esomeprazole is 97% bounded to plasma proteins. Plasma protein binding is constant over the concentration range of 2-20 mol/L. The apparent volume of distribution at steady state in healthy volunteers is approximately 16L.

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Metabolism:
Esomeprazole is extensively metabolized in the liver by the cytochrome P450 (CYP) enzyme system. The metabolites of Esomeprazole lack antisecretory activity. The major part of Esomeprazole's metabolism is dependent upon the CYP2C19 isoenzyme, which forms the hydroxy and desmethyl metabolites. The remaining part is dependent on CYP3A4 which forms the sulphone metabolite.

Excretion:
Total plasma clearence is about 17L/h after a single dose and about 9L/h after repeated administration. The plasma elimination half life of Esomeprazole is approximately 1-1.5 hours. Less than 1% of the parent drug is excreted in the urine. Approximately 80% of an oral dose of Esomeprazole is excreted as inactive metabolites in the urine and the remainder is found as inactive metabolites in the feces.

## THERAPEUTIC INDICATIONS:

Esomeprazole (ZUNE) is indicated for:
1. Gastroesophageal Reflux Disease (GERD)
- Treatment of erosive reflux esophagitis
- Long term management of patients with healed esophagitis to prevent relapse.
- Symptomatic treatment of gastroesophageal reflux disease (GERD) without esophagitis.

2. As a triple therapy (Esomeprazole (ZUNE) plus Amoxicillin and Clarithromycin) for the eradication of helicobacter pylori
- Healing of duodenal ulcer associated with helicobacter pylori infection.
- Prevention of relapse of peptic ulcers in patients with helicobacter pylori associated ulcers.

Note: In patients who failed the therapy, susceptibility testing should be done. If resistance to Clarithromycin is demonstrated or susceptibility testing is not possibe, alternative antimicrobial therapy should be instituted.

## DOSAGE AND ADMINISTRATION: INJECTION

GERD - with Erosive Esophagitis
Adults: Dose is either 20mg or 40mg Esomeprazole (ZUNE) given once daily by intravenous injection (no less than 3 minutes) or intravenous infusion (10 minutes to 30 minutes).
Pediatric: Give the following doses once daily as an intravenous infusion over 10 minutes to 30 minutes
1 year to 17 year:
Body weight less than 55kg: 10mg
Body weight 55kg or greater: 20mg
1 month to less than 1 year of age: 0.5 mg/kg
The intravenous line should always be flushed with either 0.9% NaCl injection, Lactated Ringer's injection or 5% Dextrose injection both prior to or after administration of Esomeprazole (ZUNE) I.V. injection.

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NOTE:
Intravenous injection (20mg or 40mg) should be administered over no less than 3 minutes.
The freeze dried powder should be reconstituted with 5ml of 0.9% Sodium Chloride Injection.
Withdraw 5ml of the reconstituted solution and administer an intravenous injection over no less than 3 minutes.
Intravenous Infusion (40mg) over 10 minutes to 30 minutes
A solution for intravenous infusion is prepared by first reconstituting the contents of one vial with 5ml of 0.9% Sodium Chloride Injection or Lactated Ringer's Injection or 5% Dextrose Injection and further diluting the resulting solution to a final volume of 50ml. The solution (admixture) should be administered as an intravenous infusion over a period of 10 minutes to 30 minutes.
The reconstituted solution should be stored at room temperature up to 30OC (86OF) and administered within 12 hours after reconstitution. No refrigeration is required.
Pediatric Population
Intravenous infusion over 10 minutes to 30 minutes (0.5 mg/kg) for Patients age 1 month to less than 1 year of age:
A solution for intravenous infusion is prepared by first reconstituting the contents of one vial with 5ml of 0.9% Sodium Chloride Injection and further diluting the resulting solution to a final volume of 50ml.
The resultant concentration after diluting to a final volume of 50ml is as follows:
40mg vial: 0.8 mg/mL
Withdraw appropriate amount of volume for desired dose (0.5mg/kg) and administer as an intravenous infusion over 10 minutes to 30 minutes.
Intravenous Infusion (10mg and 20mg) over 10 minutes to 30 minutes for Patients age 1 year to 17 years of age:
40mg vial
A solution for intravenous infusion is prepared by first reconstituting the contents of one vial with 5ml of 0.9% Sodium Chloride Injection and further diluting the resulting solution to a final volume of 50ml.
The resultant concentration after diluting to a final volume of 50ml is 0.8 mg/mL.
20mg dose: Withdraw 25ml of the final solution and administer as an intravenous infusion over 10 minutes to 30 minutes.
10mg dose: Withdraw 12.5ml of the final solution and administer as an intravenous infusion over 10 minutes to 30 minutes.
Caution
No other solvents / drug for I.V. injection should be used simultaneously in same infusion.

## DOSAGE AND ADMINISTRATION: TABLET

The recommended adult dosages are outlined in the table below. Esomeprazole (ZUNE) tablets should be swallowed whole and taken at least one hour before meals.

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| Recommended Adult Dosage Schedule | | |
|---|---|---|
| **Indication** | **Dose** | **Frequency** |
| **1. Gastroesophageal Reflux Disease**<br>Healing of erosive esophagitis | 40mg<br>or<br>20mg | Once daily 4 to 8 weeks (an additional 4-8 weeks treatment may be considered if symptoms persist or esophagitis does not heal) |
| Maintenance of healing erosive esophagitis. | 20mg | Once daily |
| Symptomatic gastroesophageal reflux disease without esophagitis. | 40mg<br>or<br>20mg | Once daily for 4 weeks (an additional 4-8 weeks treatment may be considered if symptoms does not resolve completely) |
| **2. H. Pylori eradiaction to reduce the risk of duodenal ulcer recurrence**<br>Esomeprazole (ZUNE)<br>Amoxicillin<br>Clarithromycin | <br>40mg<br>1000mg<br>500mg | <br>Once daily for 10 days<br>Twice daily for 10 days<br>Twice daily for 10 days |

For patients with severe liver impairment (Child Pugh Class C), a dose of 20mg of Esomeprazole (ZUNE) should not be exceeded.

## CONTRAINDICATIONS:

Esomeprazole (ZUNE) is contraindicated in patients with known hypersensitivity to drug or any component of the formulation or to substituted benzimidazoles.

## ADVERSE REACTIONS:

Esomeprazole (ZUNE) is contraindicated in patients with known hypersensitivity to drug or any component of the formulation or to substituted benzimidazoles.

## DRUG-DRUG INTERACTIONS:

Esomeprazole (ZUNE) inhibits gastric acid secretion and may interfere with the absorption of drugs where gastric pH is important determinant of bioavailability (e.g Ketoconazole, Iron salts and Digoxin). Patients treated with Esomeprazole (ZUNE) and Digoxin may need to be monitored for Digoxin toxicity.
Patients treated with Proton Pump Inhibitors and Warfarin concomitantly may need to be monitored for increases in INR and prothrombin time.
Esomeprazole (ZUNE) may reduce the plasma levels of Atazanavir, Nelfinavir and Saquinavir.
Concomitant treatment with a combined inhibitor of CYP2C19 and CYP3A4, such as Voriconazole may result in more than doubling of the Esomeprazole (ZUNE) exposure.
May increase systemic exposure of Cilostazole and an active metabolite. Consider dose reduction.
Tacrolimus: Esomeprazole (ZUNE) may increase serum levels of Tacrolimus.
Methotrexate: Esomeprazole (ZUNE) may increase serum levels of Methotrexate.

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## STORAGE:

Store in a cool & dry place below 25OC.
Protect from light, heat and moisture.
Keep out of reach of children.

## PRESENTATION:

Tablets:
ZUNE 20mg tablets are available in a blister pack of 20's.
ZUNE 40mg tablets are available in a blister pack of 20's.
Injection:
ZUNE 40mg injection is available as one vial of sterile freeze dried powder with one ampoule of 0.9% Sodium Chloride Injection.