

Zolbi

(Omeprazole)



COMPOSITION

Each **ZOLBI** 20mg capsule contains 20 mg of omeprazole in the form of enteric-coated pellets.  
Each **ZOLBI** 40mg capsule contains 40 mg of omeprazole in the form of enteric-coated pellets.

CLINICAL PHARMACOLOGY

Mechanism of Action

Omeprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that suppress gastric acid secretion by specific inhibition of the H<sup>+</sup>/K<sup>+</sup> ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the gastric mucosa, omeprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus.

Pharmacokinetics

Absorption

**ZOLBI** capsules contain an enteric-coated pellet formulation of omeprazole (because omeprazole is acid-labile), so that absorption of omeprazole begins only after the pellets leave the stomach. Absorption is rapid, with peak plasma levels of omeprazole occurring within 0.5 to 3.5 hours. The systemic bioavailability of omeprazole from a single oral dose of **ZOLBI** is approximately 35%. After repeated once-daily administration, the bioavailability increases to about 60%. In healthy subjects the plasma half-life is 0.5 to 1 hour. Concomitant intake of food has no influence on the bioavailability.

Distribution

Protein binding is approximately 95%.

Metabolism

Omeprazole is extensively metabolized by the cytochrome P450 (CYP) enzyme system.

Elimination

About 80% of the metabolites are excreted in the urine and the rest in the faeces. The two main urinary metabolites are hydroxy-omeprazole and the corresponding carboxylic acid.

Special Populations

Geriatric Population

The elimination rate of omeprazole was somewhat decreased in the elderly, and bioavailability was increased.

Pediatric Use

The pharmacokinetics of omeprazole have been investigated in pediatric patients 2 to 16 years of age.

Hepatic Impairment

Dose reduction, particularly where maintenance of healing of erosive esophagitis is indicated, for the hepatically impaired should be considered.

Renal Impairment

Because urinary excretion is a primary route of excretion of omeprazole metabolites, their elimination slowed in proportion to the decreased creatinine clearance. No dose reduction is necessary in patients with renal impairment.

Asian Population

Dose reduction, particularly where maintenance of healing of erosive esophagitis is indicated, for Asian subjects should be considered.

INDICATIONS

Duodenal Ulcer (adults)

- **ZOLBI** is indicated for short-term treatment of active duodenal ulcer in adults. Most patients heal within four weeks. Some patients may require an additional four weeks of therapy.
- **ZOLBI** in combination with clarithromycin and amoxicillin, is indicated for treatment of patients with H. pylori infection and duodenal ulcer disease (active or up to 1-year history) to eradicate H. pylori in adults.
- **ZOLBI** in combination with clarithromycin is indicated for treatment of patients with H. pylori infection and duodenal ulcer disease to eradicate H. pylori in adults.

Eradication of H. pylori has been shown to reduce the risk of duodenal ulcer recurrence. In patients who fail therapy, susceptibility testing should be done. If resistance to clarithromycin is demonstrated or susceptibility testing is not possible, alternative antimicrobial therapy should be instituted.

Gastric Ulcer (adults)

**ZOLBI** is indicated for short-term treatment (4-8 weeks) of active benign gastric ulcer in adults.

Treatment of Gastroesophageal Reflux Disease (GERD) (adults and pediatric patients)

Symptomatic GERD

**ZOLBI** is indicated for the treatment of heartburn and other symptoms associated with GERD in pediatric patients and adults.

Erosive Esophagitis

**ZOLBI** is indicated for the short-term treatment (4-8 weeks) of erosive esophagitis that has been diagnosed by endoscopy in pediatric patients and adults. If a patient does not respond to 8 weeks of treatment, an additional 4 weeks of treatment may be given. If there is recurrence of erosive esophagitis or GERD symptoms (eg, heartburn), additional 4-8 week courses of omeprazole may be considered.

Maintenance of Healing of Erosive Esophagitis (adults and pediatric patients)

**ZOLBI** is indicated to maintain healing of erosive esophagitis in pediatric patients and adults. Controlled studies do not extend beyond 12 months.

Pathological Hypersecretory Conditions (adults)

**ZOLBI** is indicated for the long-term treatment of pathological hypersecretory conditions (eg, Zollinger-Elison syndrome, multiple endocrine adenomas and systemic mastocytosis) in adults.

DOSAGE AND ADMINISTRATION

**ZOLBI capsules** should be taken before eating. In the clinical trials, antacids were used concomitantly with **ZOLBI**. Patients should be informed that the **ZOLBI** capsule should be swallowed whole.

Short-Term Treatment of Active Duodenal Ulcer

The recommended adult oral dose of **ZOLBI** is 20 mg once daily. Most patients heal within four weeks. Some patients may require an additional four weeks of therapy.

H. pylori Eradication for the Reduction of the Risk of Duodenal Ulcer Recurrence

- Triple Therapy (**ZOLBI**/clarithromycin/amoxicillin) - The recommended adult oral regimen is **ZOLBI** 20 mg plus clarithromycin 500 mg plus amoxicillin 1000 mg each given twice daily for 10 days. In patients with an ulcer present at the time of initiation of therapy, an additional 18 days of **ZOLBI** 20mg once daily is recommended for ulcer healing and symptom relief.
- Dual Therapy (**ZOLBI**/clarithromycin) - The recommended adult oral regimen is **ZOLBI** 40 mg once daily plus clarithromycin 500 mg three times daily for 14 days. In patients with an ulcer present at the time of initiation of therapy, an additional 14 days of **ZOLBI** 20 mg once daily is recommended for ulcer healing and symptom relief.

Gastric Ulcer

The recommended adult oral dose is 40 mg once daily for 4-8 weeks.

Gastroesophageal Reflux Disease (GERD)

The recommended adult oral dose for the treatment of patients with symptomatic GERD and no esophageal lesions is 20 mg daily for up to 4 weeks. The recommended adult oral dose for the treatment of patients with erosive esophagitis and accompanying symptoms due to GERD is 20 mg daily for 4 to 8 weeks.

Maintenance of Healing of Erosive Esophagitis

The recommended adult oral dose is 20 mg daily.

Pathological Hypersecretory Conditions

The dosage of **ZOLBI** in patients with pathological hypersecretory conditions varies with the individual patient. The recommended adult oral starting dose is 60 mg once daily. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Doses up to 120 mg three times daily have been administered. Daily dosages of greater than 80 mg should be administered in divided doses. Some patients with Zollinger-Elison syndrome have been treated continuously with **ZOLBI** for more than 5 years.

Pediatric Patients

For the treatment of GERD and maintenance of healing of erosive esophagitis, the recommended daily dose for pediatric patients 1 to 16 years of age is as follows:

| Patient Weight | Omeprazole Daily Dose |
|----------------|-----------------------|
| 5 <10 kg       | 5 mg                  |
| 10 <20 kg      | 10 mg                 |
| ≥20 kg         | 20 mg                 |

On a per kg basis, the doses of omeprazole required to heal erosive esophagitis in pediatric patients are greater than those for adults. Alternative administrative options can be used for pediatric patients unable to swallow an intact capsule.

Alternative Administration Options

**ZOLBI** is available as a enteric coated pellets capsule. For patients who have difficulty swallowing capsules, the contents of a **ZOLBI** capsule can be added to applesauce. One tablespoon of applesauce should be added to an empty bowl and the capsule should be opened. All of the pellets inside the capsule should be carefully emptied on the applesauce. The pellets should be mixed with the applesauce and then swallowed immediately with a glass of cool water to ensure complete swallowing of the pellets. The applesauce used should not be hot and should be soft enough to be swallowed without chewing. The pellets should not be chewed or crushed. The pellets/applesauce mixture should not be stored for future use.

## SIDE EFFECTS

### Clinical Trials Experience with ZOLBI Monotherapy

The most common adverse reactions reported (i.e., with an incidence rate  $\geq 2\%$ ) from ZOLBI-treated patients enrolled in studies included headache (6.9%), abdominal pain (5.2%), nausea (4.0%), diarrhea (3.7%), vomiting (3.2%), and flatulence (2.7%). Additional adverse reactions that were reported with an incidence  $\geq 1\%$  included acid regurgitation (1.9%), upper respiratory infection

(1.9%), constipation (1.5%), dizziness (1.5%), rash (1.5%), asthenia (1.3%), back pain (1.1%), and cough (1.1%). The clinical trial safety profile in patients greater than 65 years of age was similar to that in patients 65 years of age or less. The clinical trial safety profile in pediatric patients who received ZOLBI capsules was similar to that in adult patients. Unique to the pediatric population, however, adverse reactions of the respiratory system were most frequently reported in both the 1 to <2 and 2 to 16 year age groups (75.0% and 18.5%, respectively). Similarly, fever was frequently reported in the 1 to 2 year age group (33.0%), and accidental injuries were reported frequently in the 2 to 16 year age group (3.8%).

### Clinical Trials Experience with ZOLBI in Combination Therapy for H. pylori Eradication

In clinical trials using either dual therapy with ZOLBI and clarithromycin, or triple therapy with ZOLBI, clarithromycin, and amoxicillin, no adverse reactions unique to these drug combinations were observed. Adverse reactions observed were limited to those previously reported with omeprazole, clarithromycin, or amoxicillin alone.

#### Dual Therapy (ZOLBI/clarithromycin)

Adverse reactions observed in controlled clinical trials using combination therapy with ZOLBI and clarithromycin were taste perversion (15%), tongue discoloration (2%), rhinitis (2%), pharyngitis (1%) and flu-syndrome (1%).

#### Triple Therapy (ZOLBI/clarithromycin/amoxicillin)

The most frequent adverse reactions observed in clinical trials using combination therapy with ZOLBI, clarithromycin, and amoxicillin were diarrhea (14%), taste perversion (10%), and headache (7%). None of these occurred at a higher frequency than that reported by patients taking antimicrobial agents alone.

## DRUG INTERACTIONS

### Drugs for which gastric pH can affect bioavailability

Because of its profound and long lasting inhibition of gastric acid secretion, it is theoretically possible that omeprazole may interfere with absorption of drugs where gastric pH is an important determinant of their bioavailability (e.g., ketoconazole, ampicillin esters, and iron salts). In the clinical trials, antacids were used concomitantly with the administration of ZOLBI.

### Drugs metabolized by cytochrome P450 (CYP)

- Omeprazole can prolong the elimination of diazepam, warfarin and phenytoin, drugs that are metabolized by oxidation in the liver. There have been reports of increased INR and prothrombin time in patients receiving proton pump inhibitors, including omeprazole, and warfarin concomitantly. Increase in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with proton pump inhibitors and warfarin may need to be monitored for increases in INR and prothrombin time.
- Although in normal subjects no interaction with theophylline or propranolol was found, there have been clinical reports of interaction with other drugs metabolized via the cytochrome P450 system (e.g., cyclosporine, disulfiram, benzodiazepines). Patients should be monitored to determine if it is necessary to adjust the dosage of these drugs when taken concomitantly with ZOLBI.
- Concomitant administration of omeprazole and voriconazole (a combined inhibitor of CYP2C19 and CYP3A4) resulted in more than doubling of the omeprazole exposure. Dose adjustment of omeprazole is not normally required. However, in patients with Zollinger-Ellison syndrome, who may require higher doses up to 240 mg/day, dose adjustment may be considered.
- Concomitant use of atazanavir and proton pump inhibitors is not recommended. Co-administration of atazanavir with proton pump inhibitors is expected to substantially decrease atazanavir plasma concentrations and thereby reduce its therapeutic effect.
- Concomitant administration of omeprazole and tacrolimus may increase the serum levels of tacrolimus.

## PRECAUTIONS

### Concomitant Gastric Malignancy

Symptomatic response to therapy with omeprazole does not preclude the presence of gastric malignancy.

### Atrophic Gastritis

Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole.

### Combination Use of ZOLBI with Amoxicillin

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Before initiating therapy with amoxicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, amoxicillin should be discontinued and appropriate therapy instituted. Pseudomembranous colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

### Combination Use of ZOLBI with Clarithromycin

Clarithromycin should not be used in pregnant women except in clinical circumstances where no alternative therapy is appropriate. If pregnancy occurs while taking clarithromycin, the patient should be apprised of the potential hazard to the fetus.

Co-administration of omeprazole and clarithromycin has resulted in increases in plasma levels of omeprazole, clarithromycin, and 14-hydroxy-clarithromycin.

Concomitant administration of clarithromycin with cisapride or pimozide, is contraindicated.

### Use in Specific Populations

#### Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies on the use of omeprazole in pregnant women. This drug should be used during pregnancy only if clearly needed.

#### Nursing Mothers

Omeprazole is excreted in human milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

#### Pediatric Use

Use of ZOLBI in pediatric and adolescent patients 1 to 16 years of age for the treatment of GERD is supported by a) extrapolation of results, already included in the currently approved labeling, from adequate and well-controlled studies that supported the approval of ZOLBI for adults, and b) safety and pharmacokinetic studies performed in pediatric and adolescent patients. The safety and effectiveness of ZOLBI for the treatment of GERD in patients <1 year of age have not been established. The safety and effectiveness of ZOLBI for other pediatric uses have not been established.

#### Geriatric Use

There were no differences in safety and effectiveness between the elderly and younger subjects. Other reported clinical experience has not identified differences in response between the elderly and younger subjects, but greater sensitivity of some older individuals cannot be ruled out.

#### Hepatic Impairment

Consider dose reduction, particularly for maintenance of healing of erosive esophagitis.

#### Renal Impairment

No dosage reduction is necessary.

#### Asian Population

Consider dose reduction, particularly for maintenance of healing of erosive esophagitis.

## CONTRAINDICATIONS

### Omeprazole

ZOLBI capsules are contraindicated in patients with known hypersensitivity to any component of the formulation.

### Clarithromycin

Clarithromycin is contraindicated in patients with a known hypersensitivity to any macrolide antibiotic.

Concomitant administration of clarithromycin with cisapride, pimozide, or terfenadine is contraindicated.

### Amoxicillin

Amoxicillin is contraindicated in patients with a history of allergic reaction to any of the penicillins.

## PRESENTATION

ZOLBI capsule 20mg: 2x7's/pack

ZOLBI capsule 40mg: 2x7's/pack

## DOSEAGE:

As directed by the physician.

## INSTRUCTIONS:

Store below 30°C.

Protect from light & moisture.

Keep out of reach of children.

Issued : 11/2011

Detailed prescribing information is available on request.

Manufactured by:  
**AsianContinental (Pvt.) Ltd.**  
D-32, S.I.T.E. II, Super Highway,  
Karachi-Pakistan.



An ISO Certified Company

LFT/012/02

خوراک:  
ڈاکٹر کی ہدایت کے مطابق۔  
ہدایات:  
دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔  
دھوپ اور نمی سے بچائیں۔  
بچوں کی پہنچ سے دور رکھیں۔