

**OMEPRAZOLE DR- omeprazole dr capsule, delayed release**  
**Northwind Pharmaceuticals, LLC**

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**Omeprazole DR**

**INDICATIONS & USAGE**

**1.1 Duodenal Ulcer (adults)**

Omeprazole delayed-release capsules, USP are 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.

Omeprazole delayed-release capsules, USP, in combination with clarithromycin and amoxicillin, are 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.

Omeprazole delayed-release capsules, USP, in combination with clarithromycin are 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 [see Clinical Studies (14.1) and Dosage and Administration (2)].

Among patients who fail therapy, omeprazole delayed-release capsules with clarithromycin are more likely to be associated with the development of clarithromycin resistance as compared with triple therapy. 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 [see Microbiology section (12.4)], and the clarithromycin package insert, Microbiology section.)

**1.2 Gastric Ulcer (adults)**

Omeprazole delayed-release capsules, USP are indicated for short-term treatment (4 to 8 weeks) of active benign gastric ulcer in adults [see Clinical Studies (14.2)].

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

**Symptomatic GERD**

Omeprazole delayed-release capsules, USP are indicated for the treatment of heartburn and other symptoms associated with GERD in pediatric patients and adults.

**Erosive Esophagitis**

Omeprazole delayed-release capsules, USP are indicated for the short-term treatment (4 to 8 weeks) of erosive esophagitis that has been diagnosed by endoscopy in pediatric patients and adults [see Clinical Studies (14.4)].

The efficacy of omeprazole delayed-release capsules, USP used for longer than 8 weeks in these patients has not been established. 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 to 8 week courses of omeprazole may be considered.

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

Omeprazole delayed-release capsules, USP are indicated to maintain healing of erosive esophagitis in pediatric patients and adults.

Controlled studies do not extend beyond 12 months [see Clinical Studies (14.4)].

**1.5 Pathological Hypersecretory Conditions (adults)**

Omeprazole delayed-release capsules, USP are indicated for the long-term treatment of pathological hypersecretory conditions (eg, Zollinger-Ellison syndrome, multiple endocrine adenomas and systemic mastocytosis) in adults.

## **DOSAGE & ADMINISTRATION**

Omeprazole delayed-release capsules should be taken before eating. In the clinical trials, antacids were used concomitantly with omeprazole.

Patients should be informed that the omeprazole delayed-release capsule should be swallowed whole.

For patients unable to swallow an intact capsule, alternative administration options are available [see Dosage and Administration (2.8)].

### **2.1 Short-Term Treatment of Active Duodenal Ulcer**

The recommended adult oral dose of omeprazole delayed-release capsules is 20 mg once daily. Most patients heal within four weeks. Some patients may require an additional four weeks of therapy.

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

#### **Triple Therapy (omeprazole/clarithromycin/amoxicillin)**

The recommended adult oral regimen is omeprazole delayed-release capsules 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 omeprazole delayed-release capsules 20 mg once daily is recommended for ulcer healing and symptom relief.

#### **Dual Therapy (omeprazole/clarithromycin)**

The recommended adult oral regimen is omeprazole delayed-release capsules 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 omeprazole delayed-release capsules 20 mg once daily is recommended for ulcer healing and symptom relief.

### **2.3 Gastric Ulcer**

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

### **2.4 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.

### **2.5 Maintenance of Healing of Erosive Esophagitis**

The recommended adult oral dose is 20 mg daily [see Clinical Studies (14.4)].

### **2.6 Pathological Hypersecretory Conditions**

The dosage of omeprazole delayed-release capsules 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-Ellison syndrome have been treated continuously with omeprazole delayed-release capsules for more than 5 years.

### **2.7 Pediatric Patients**

For the treatment of GERD and maintenance of healing of erosive esophagitis, the recommended daily dose for pediatric patients 2 to 16 years of age is as follows:

Patient Weight	Omeprazole Daily Dose
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 [see Dosage and Administration (2.8)].

## 2.8 Alternative Administration Options

Omeprazole is available as a delayed-release capsule.

For patients who have difficulty swallowing capsules, the contents of an omeprazole delayed-release 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.

## DOSAGE FORMS & STRENGTHS

Omeprazole delayed-release capsules, USP 10 mg are hard gelatin capsules with a pink opaque body and a reddish brown opaque cap. “APO 010” is imprinted on each capsule in black ink.

Omeprazole delayed-release capsules, USP 20 mg are hard gelatin capsules with a pink opaque body and a reddish brown opaque cap. “APO 020” is imprinted on each capsule in black ink.

Omeprazole delayed-release capsules, USP 40 mg are hard gelatin capsules with a pink opaque body and a reddish brown opaque cap. “APO 040” is imprinted on each capsule in black ink.

## CONTRAINDICATIONS

Omeprazole delayed-release capsules are contraindicated in patients with known hypersensitivity to substituted benzimidazoles or to any component of the formulation. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, bronchospasm, interstitial nephritis, and urticaria [see Adverse Reactions (6)].

For information about contraindications of antibacterial agents (clarithromycin and amoxicillin) indicated in combination with omeprazole, refer to the CONTRAINDICATIONS section of their package inserts.

## WARNINGS AND PRECAUTIONS

### 5.1 Concomitant Gastric Malignancy

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

### 5.2 Atrophic Gastritis

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

### 5.3 Clostridium difficile associated diarrhea

Published observational studies suggest that PPI therapy like omeprazole 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 [see Adverse Reactions (6.2)].

Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

*Clostridium difficile* associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents. For more information specific to antibacterial agents (clarithromycin and amoxicillin) indicated for use in combination with omeprazole, refer to WARNINGS and PRECAUTIONS sections of those package inserts.

#### 5.4 Interaction with Clopidogrel

Avoid concomitant use of omeprazole with clopidogrel. Clopidogrel is a prodrug. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. The metabolism of clopidogrel to its active metabolite can be impaired by use with concomitant medications, such as omeprazole, that inhibit CYP2C19 activity. Concomitant use of clopidogrel with 80 mg omeprazole reduces the pharmacological activity of clopidogrel, even when administered 12 hours apart. When using omeprazole, consider alternative anti-platelet therapy [see Drug Interactions (7.3) and Pharmacokinetics (12.3)].

#### 5.5 Bone Fracture

Several published observational studies suggest that proton pump inhibitor (PPI) therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines [see Dosage and Administration (2) and Adverse Reactions (6.3)].

#### 5.6 Hypomagnesemia

Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically [see Adverse Reactions (6.3)].

#### 5.7 Concomitant Use of Omeprazole with St. John's Wort or Rifampin

Drugs which induce CYP2C19 or CYP3A4 (such as St. John's Wort or rifampin) can substantially decrease omeprazole concentrations [see Drug Interactions (7.3)]. Avoid concomitant use of omeprazole with St. John's Wort or rifampin.

#### 5.8 Interactions with Diagnostic Investigations for Neuroendocrine Tumors

Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors. Healthcare providers should temporarily stop omeprazole treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g. for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.

#### 5.9 Concomitant use of Omeprazole with Methotrexate

Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see

methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration a temporary withdrawal of the PPI may be considered in some patients [see Drug Interactions (7.7)].

## **ADVERSE REACTIONS**

### **6.1 Clinical Trials Experience with Omeprazole Monotherapy**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described below reflects exposure to omeprazole delayed-release capsules in 3096 patients from worldwide clinical trials (465 patients from US studies and 2,631 patients from international studies). Indications clinically studied in US trials included duodenal ulcer, resistant ulcer, and Zollinger-Ellison syndrome. The international clinical trials were double blind and open-label in design. The most common adverse reactions reported (i.e., with an incidence rate  $\geq 2\%$ ) from omeprazole-treated patients enrolled in these 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 omeprazole delayed-release 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 the 2 to 16 year age group (18.5%). Similarly, accidental injuries were reported frequently in the 2 to 16 year age group (3.8%) [see Use in Specific Populations (8.4)].

### **6.2 Clinical Trials Experience with Omeprazole in Combination Therapy for H. pylori Eradication**

In clinical trials using either dual therapy with omeprazole and clarithromycin, or triple therapy with omeprazole, 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 (omeprazole/clarithromycin)**

Adverse reactions observed in controlled clinical trials using combination therapy with omeprazole and clarithromycin (n = 346) that differed from those previously described for omeprazole alone were taste perversion (15%), tongue discoloration (2%), rhinitis (2%), pharyngitis (1%) and flu-syndrome (1%). (For more information on clarithromycin, refer to the clarithromycin prescribing information, Adverse Reactions section).

#### **Triple Therapy (omeprazole/clarithromycin/amoxicillin)**

The most frequent adverse reactions observed in clinical trials using combination therapy with omeprazole, clarithromycin, and amoxicillin (n = 274) 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. (For more information on clarithromycin or amoxicillin, refer to the respective prescribing information, Adverse Reactions sections).

### **6.3 Post-marketing Experience**

The following adverse reactions have been identified during post-approval use of omeprazole delayed-release capsules. Because these reactions are voluntarily reported from a population of uncertain size, it is not always possible to reliably estimate their actual frequency or establish a causal relationship to drug exposure.

## Body As a Whole

Hypersensitivity reactions including anaphylaxis, anaphylactic shock, angioedema, bronchospasm, interstitial nephritis, urticaria, (see also Skin below); fever; pain; fatigue; malaise;

## Cardiovascular

Chest pain or angina, tachycardia, bradycardia, palpitations, elevated blood pressure, peripheral edema

## Endocrine

### Gynecomastia

## Gastrointestinal

Pancreatitis (some fatal), anorexia, irritable colon, fecal discoloration, esophageal candidiasis, mucosal atrophy of the tongue, stomatitis, abdominal swelling, dry mouth, microscopic colitis. During treatment with omeprazole, gastric fundic gland polyps have been noted rarely. These polyps are benign and appear to be reversible when treatment is discontinued. Gastroduodenal carcinoids have been reported in patients with ZE syndrome on long-term treatment with omeprazole. This finding is believed to be a manifestation of the underlying condition, which is known to be associated with such tumors.

## Hepatic

Liver disease including hepatic failure (some fatal), liver necrosis (some fatal), hepatic encephalopathy hepatocellular disease, cholestatic disease, mixed hepatitis, jaundice, and elevations of liver function tests [ALT, AST, GGT, alkaline phosphatase, and bilirubin]

## Infections and Infestations

Clostridium difficile associated diarrhea

## Metabolism and Nutritional disorders

Hypoglycemia, hypomagnesemia, with or without hypocalcemia and/or hypokalemia, hyponatremia, weight gain

## Musculoskeletal

Muscle weakness, myalgia, muscle cramps, joint pain, leg pain, bone fracture

## Nervous System/Psychiatric

Psychiatric and sleep disturbances including depression, agitation, aggression, hallucinations, confusion, insomnia, nervousness, apathy, somnolence, anxiety, and dream abnormalities; tremors, paresthesia; vertigo

## Respiratory

Epistaxis, pharyngeal pain

## Skin

Severe generalized skin reactions including toxic epidermal necrolysis (some fatal), Stevens-Johnson syndrome, and erythema multiforme; photosensitivity; urticaria; rash; skin inflammation; pruritus; petechiae; purpura; alopecia; dry skin; hyperhidrosis

## Special Senses

Tinnitus, taste perversion

## Ocular

Optic atrophy, anterior ischemic optic neuropathy, optic neuritis, dry eye syndrome, ocular irritation, blurred vision, double vision

## Urogenital

Interstitial nephritis, hematuria, proteinuria, elevated serum creatinine, microscopic pyuria, urinary tract infection, glycosuria, urinary frequency, testicular pain

#### Hematologic

Agranulocytosis (some fatal), hemolytic anemia, pancytopenia, neutropenia, anemia, thrombocytopenia, leukopenia, leucocytosis

## **DRUG INTERACTIONS**

### 7.1 Interference with Antiretroviral Therapy

Concomitant use of atazanavir and nelfinavir with proton pump inhibitors is not recommended. Co-administration of atazanavir with proton pump inhibitors is expected to substantially decrease atazanavir plasma concentrations and may result in a loss of therapeutic effect and the development of drug resistance. Co-administration of saquinavir with proton pump inhibitors is expected to increase saquinavir concentrations, which may increase toxicity and require dose reduction.

Omeprazole has been reported to interact with some antiretroviral drugs. 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 drug. Other possible interaction mechanisms are via CYP2C19.

#### Reduced concentrations of atazanavir and nelfinavir

For some antiretroviral drugs, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole. Following multiple doses of nelfinavir (1250 mg, twice daily) and omeprazole (40 mg daily), AUC was decreased by 36% and 92%, C<sub>max</sub> by 37% and 89% and C<sub>min</sub> by 39% and 75% respectively for nelfinavir and M8. Following multiple doses of atazanavir (400 mg, daily) and omeprazole (40 mg, daily, 2 hr before atazanavir), AUC was decreased by 94%, C<sub>max</sub> by 96%, and C<sub>min</sub> by 95%. Concomitant administration with omeprazole and drugs such as atazanavir and nelfinavir is therefore not recommended.

#### Increased concentrations of saquinavir

For other antiretroviral drugs, such as saquinavir, elevated serum levels have been reported, with an increase in AUC by 82%, in C<sub>max</sub> by 75%, and in C<sub>min</sub> by 106%, following multiple dosing of saquinavir/ritonavir (1000/100 mg) twice daily for 15 days with omeprazole 40 mg daily co-administered days 11 to 15. Therefore, clinical and laboratory monitoring for saquinavir toxicity is recommended during concurrent use with omeprazole. Dose reduction of saquinavir should be considered from the safety perspective for individual patients.

There are also some antiretroviral drugs of which unchanged serum levels have been reported when given with omeprazole.

### 7.2 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. Like with other drugs that decrease the intragastric acidity, the absorption of drugs such as ketoconazole, ampicillin esters, iron salts and erlotinib can decrease, while the absorption of drugs such as digoxin can increase during treatment with omeprazole. Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10% (30% in two subjects). Therefore, patients may need to be monitored when digoxin is taken concomitantly with omeprazole. In the clinical trials, antacids were used concomitantly with the administration of omeprazole.

### 7.3 Effects on Hepatic Metabolism/Cytochrome P-450 Pathways

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. Increases 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 omeprazole.

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. When voriconazole (400 mg Q12h x 1 day, then 200 mg x 6 days) was given with omeprazole (40 mg once daily x 7 days) to healthy subjects, it significantly increased the steady-state C<sub>max</sub> and AUC<sub>0-24</sub> of omeprazole, an average of 2 times (90% CI: 1.8, 2.6) and 4 times (90% CI: 3.3, 4.4) respectively as compared to when omeprazole was given without voriconazole.

Omeprazole acts as an inhibitor of CYP2C19. Omeprazole, given in doses of 40 mg daily for one week to 20 healthy subjects in cross-over study, increased C<sub>max</sub> and AUC of cilostazol by 18% and 26% respectively. C<sub>max</sub> and AUC of one of its active metabolites, 3,4-dihydro-cilostazol, which has 4 to 7 times the activity of cilostazol, were increased by 29% and 69% respectively. Co-administration of cilostazol with omeprazole is expected to increase concentrations of cilostazol and its above mentioned active metabolite. Therefore a dose reduction of cilostazol from 100 mg twice daily to 50 mg twice daily should be considered.

Drugs known to induce CYP2C19 or CYP3A4 (such as rifampin) may lead to decreased omeprazole serum levels. In a cross-over study in 12 healthy male subjects, St. John's Wort (300 mg three times daily for 14 days), an inducer of CYP3A4, decreased the systemic exposure of omeprazole in CYP2C19 poor metabolisers (C<sub>max</sub> and AUC decreased by 37.5% and 37.9%, respectively) and extensive metabolisers (C<sub>max</sub> and AUC decreased by 49.6% and 43.9%, respectively). Avoid concomitant use of St. John's Wort or rifampin with omeprazole.

#### Clonidogrel

Omeprazole is an inhibitor of CYP2C19 enzyme. Clonidogrel is metabolized to its active metabolite in part by CYP2C19. Concomitant use of omeprazole 80 mg results in reduced plasma concentrations of the active metabolite of clonidogrel and a reduction in platelet inhibition. Avoid concomitant administration of omeprazole with clonidogrel. When using omeprazole, consider use of alternative anti-platelet therapy [see Pharmacokinetics (12.3)].

There are no adequate combination studies of a lower dose of omeprazole or a higher dose of clonidogrel in comparison with the approved dose of clonidogrel.

#### 7.4 Tacrolimus

Concomitant administration of omeprazole and tacrolimus may increase the serum levels of tacrolimus.

#### 7.5 Interactions with Investigations of Neuroendocrine Tumors

Drug-induced decrease in gastric acidity results in enterochromaffin-like cell hyperplasia and increased Chromogranin A levels which may interfere with investigations for neuroendocrine tumors [see Warnings and Precautions (5.8) and Clinical Pharmacology (12)].

#### 7.6 Combination Therapy with Clarithromycin

Concomitant administration of clarithromycin with other drugs can lead to serious adverse reactions due to drug interactions [see Warnings and Precautions in prescribing information for clarithromycin]. Because of these drug interactions, clarithromycin is contraindicated for co-administration with certain

drugs [see Contraindications in prescribing information for clarithromycin].

## 7.7 Methotrexate

Case reports, published population pharmacokinetic studies, and retrospective analyses suggest that concomitant administration of PPIs and methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate. However, no formal drug interaction studies of methotrexate with PPIs have been conducted [see Warnings and Precautions (5.9)].

## USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Pregnancy Category C

#### Risk Summary

There are no adequate and well-controlled studies with omeprazole in pregnant women. Available epidemiologic data fail to demonstrate an increased risk of major congenital malformations or other adverse pregnancy outcomes with first trimester omeprazole use.

Animal reproduction studies with omeprazole in rats and rabbits resulted in dose-dependent embryolethality at doses that were approximately 2.8 to 28 times the daily human dose of 40 mg.

Teratogenicity was not observed in animal reproduction studies with administration of oral esomeprazole magnesium in rats and rabbits with doses about 57 times and 35 times, respectively, an oral human dose of 40 mg. However, changes in bone morphology were observed in offspring of rats dosed through most of pregnancy and lactation at doses equal to or greater than approximately 33.6 times an oral human dose of 40 mg (see Animal Data). Because of the observed effect at high doses of esomeprazole magnesium on developing bone in rat studies, omeprazole should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

#### Human Data

Four published epidemiological studies compared the frequency of congenital abnormalities among infants born to women who used omeprazole during pregnancy with the frequency of abnormalities among infants of women exposed to H<sub>2</sub>-receptor antagonists or other controls.

A population-based retrospective cohort epidemiological study from the Swedish Medical Birth Registry, covering approximately 99% of pregnancies, from 1995 to 99, reported on 955 infants (824 exposed during the first trimester with 39 of these exposed beyond first trimester, and 131 exposed after the first trimester) whose mothers used omeprazole during pregnancy. The number of infants exposed in utero to omeprazole that had any malformation, low birth weight, low Apgar score, or hospitalization was similar to the number observed in this population. The number of infants born with ventricular septal defects and the number of stillborn infants was slightly higher in the omeprazole-exposed infants than the expected number in this population.

A population-based retrospective cohort study covering all live births in Denmark from 1996 to 2009, reported on 1,800 live births whose mothers used omeprazole during the first trimester of pregnancy and 837, 317 live births whose mothers did not use any proton pump inhibitor. The overall rate of birth defects in infants born to mothers with first trimester exposure to omeprazole was 2.9% and 2.6% in infants born to mothers not exposed to any proton pump inhibitor during the first trimester.

A retrospective cohort study reported on 689 pregnant women exposed to either H<sub>2</sub>-blockers or omeprazole in the first trimester (134 exposed to omeprazole) and 1,572 pregnant women unexposed to either during the first trimester. The overall malformation rate in offspring born to mothers with first trimester exposure to omeprazole, an H<sub>2</sub>-blocker, or were unexposed was 3.6%, 5.5%, and 4.1% respectively.

A small prospective observational cohort study followed 113 women exposed to omeprazole during pregnancy (89% first trimester exposures). The reported rate of major congenital malformations was 4% in the omeprazole group, 2% in controls exposed to non-teratogens, and 2.8% in disease-paired controls. Rates of spontaneous and elective abortions, preterm deliveries, gestational age at delivery, and mean birth weight were similar among the groups.

Several studies have reported no apparent adverse short-term effects on the infant when single dose oral or intravenous omeprazole was administered to over 200 pregnant women as premedication for cesarean section under general anesthesia.

#### Animal Data

Reproductive studies conducted with omeprazole in rats at oral doses up to 138 mg/kg/day (about 28 times an oral human dose of 40 mg on a body surface area basis) and in rabbits at doses up to 69 mg/kg/day (about 28 times an oral human dose of 40 mg on a body surface area basis) did not disclose any evidence for a teratogenic potential of omeprazole. In rabbits, omeprazole in a dose range of 6.9 to 69.1 mg/kg/day (about 2.8 to 28 times an oral human dose of 40 mg on a body surface area basis) produced dose-related increases in embryo-lethality, fetal resorptions, and pregnancy disruptions. In rats, dose-related embryo/fetal toxicity and postnatal developmental toxicity were observed in offspring resulting from parents treated with omeprazole at 13.8 to 138.0 mg/kg/day (about 2.8 to 28 times an oral human doses of 40 mg on a body surface area basis).

Reproduction studies have been performed with esomeprazole magnesium in rats at oral doses up to 280 mg/kg/day (about 57 times an oral human dose of 40 mg on a body surface area basis) and in rabbits at oral doses up to 86 mg/kg/day (about 35 times an oral human dose of 40 mg on a body surface area basis) and have revealed no evidence of impaired fertility or harm to the fetus due to esomeprazole magnesium.

A pre- and postnatal developmental toxicity study in rats with additional endpoints to evaluate bone development was performed with esomeprazole magnesium at oral doses of 14 to 280 mg/kg/day (about 3.4 to 57 times an oral human dose of 40 mg on a body surface area basis). Neonatal/early postnatal (birth to weaning) survival was decreased at doses equal to or greater than 138 mg/kg/day (about 33 times an oral human dose of 40 mg on a body surface area basis). Body weight and body weight gain were reduced and neurobehavioral or general developmental delays in the immediate post-weaning timeframe were evident at doses equal to or greater than 69 mg/kg/day (about 16.8 times an oral human dose of 40 mg on a body surface area basis). In addition, decreased femur length, width and thickness of cortical bone, decreased thickness of the tibial growth plate and minimal to mild bone marrow hypocellularity were noted at doses equal to or greater than 14 mg/kg/day (about 3.4 times an oral human dose of 40 mg on a body surface area basis). Physeal dysplasia in the femur was observed in offspring of rats treated with oral doses of esomeprazole magnesium at doses equal to or greater than 138 mg/kg/day (about 33.6 times an oral human dose of 40 mg on a body surface area basis).

Effects on maternal bone were observed in pregnant and lactating rats in the pre- and postnatal toxicity study when esomeprazole magnesium was administered at oral doses of 14 to 280 mg /kg/day (about 3.4 to 57 times an oral human dose of 40 mg on a body surface area basis). When rats were dosed from gestational day 7 through weaning on postnatal day 21, a statistically significant decrease in maternal femur weight of up to 14% (as compared to placebo treatment) was observed at doses equal to or greater than 138 mg/kg/day (about 33.6 times an oral human dose of 40 mg on a body surface area basis).

A pre- and postnatal development study in rats with esomeprazole strontium (using equimolar doses compared to esomeprazole magnesium study) produced similar results in dams and pups as described above.

#### 8.3 Nursing Mothers

Omeprazole is present in human milk. Omeprazole concentrations were measured in breast milk of a woman following oral administration of 20 mg. The peak concentration of omeprazole in breast milk was less than 7% of the peak serum concentration. This concentration would correspond to 0.004 mg of

omeprazole in 200 mL of milk. Caution should be exercised when omeprazole is administered to a nursing woman.

#### 8.4 Pediatric Use

Use of omeprazole in pediatric and adolescent patients 2 to 16 years of age for the treatment of GERD and maintenance of healing of erosive esophagitis is supported by a) extrapolation of results from adequate and well-controlled studies that supported the approval of omeprazole for adults, and b) safety and pharmacokinetic studies performed in pediatric and adolescent patients [see Clinical Pharmacology, Pharmacokinetics, Pediatric for pharmacokinetic information (12.3) and Dosage and Administration (2), Adverse Reactions (6.1) and Clinical Studies, (14.6)]. The safety and effectiveness of omeprazole for the treatment of GERD in patients <1 year of age have not been established. The safety and effectiveness of omeprazole for other pediatric uses have not been established.

#### Juvenile Animal Data

In a juvenile rat toxicity study, esomeprazole was administered with both magnesium and strontium salts at oral doses about 34 to 57 times a daily human dose of 40 mg based on body surface area. Increases in death were seen at the high dose, and at all doses of esomeprazole, there were decreases in body weight, body weight gain, femur weight and femur length, and decreases in overall growth [see Nonclinical Toxicology (13.2)].

#### 8.5 Geriatric Use

Omeprazole was administered to over 2000 elderly individuals ( $\geq 65$  years of age) in clinical trials in the U.S. and Europe. 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.

Pharmacokinetic studies have shown the elimination rate was somewhat decreased in the elderly and bioavailability was increased. The plasma clearance of omeprazole was 250 mL/min (about half that of young volunteers) and its plasma half-life averaged one hour, about twice that of young healthy volunteers. However, no dosage adjustment is necessary in the elderly [see Clinical Pharmacology (12.3)].

#### 8.6 Hepatic Impairment

Consider dose reduction, particularly for maintenance of healing of erosive esophagitis [see Clinical Pharmacology (12.3)].

#### 8.7 Renal Impairment

No dosage reduction is necessary [see Clinical Pharmacology (12.3)].

#### 8.8 Asian Population

Consider dose reduction, particularly for maintenance of healing of erosive esophagitis [see Clinical Pharmacology (12.3)].

### **OVERDOSAGE**

Reports have been received of overdosage with omeprazole in humans. Doses ranged up to 2400 mg (120 times the usual recommended clinical dose). Manifestations were variable, but included confusion, drowsiness, blurred vision, tachycardia, nausea, vomiting, diaphoresis, flushing, headache, dry mouth, and other adverse reactions similar to those seen in normal clinical experience [see Adverse Reactions (6)]. Symptoms were transient, and no serious clinical outcome has been reported when omeprazole was taken alone. No specific antidote for omeprazole overdosage is known. Omeprazole is extensively protein bound and is, therefore, not readily dialyzable. In the event of overdosage, treatment should be symptomatic and supportive.

As with the management of any overdose, the possibility of multiple drug ingestion should be

considered. For current information on treatment of any drug overdose, contact a Poison Control Center at 1-800-222-1222.

Single oral doses of omeprazole at 1350, 1339, and 1200 mg/kg were lethal to mice, rats, and dogs, respectively. Animals given these doses showed sedation, ptosis, tremors, convulsions, and decreased activity, body temperature, and respiratory rate and increased depth of respiration.

## **DESCRIPTION**

The active ingredient in omeprazole delayed-release capsules is a substituted benzimidazole, 5-methoxy-2-[[[4-methoxy-3, 5-dimethyl-2-pyridinyl) methyl] sulfinyl]-1H-benzimidazole, a compound that inhibits gastric acid secretion. Its empirical formula is C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>S, with a molecular weight of 345.42.

Omeprazole is a white to off-white crystalline powder that melts with decomposition at about 155°C. It is a weak base, freely soluble in ethanol and methanol, and slightly soluble in acetone and isopropanol and very slightly soluble in water. The stability of omeprazole is a function of pH; it is rapidly degraded in acid media, but has acceptable stability under alkaline conditions.

Omeprazole Delayed-Release Capsules meet USP Dissolution Test 2.

Omeprazole is supplied as delayed-release capsules for oral administration. Each delayed-release capsule contains either 10 mg, 20 mg or 40 mg of omeprazole in the form of enteric-coated granules with the following inactive ingredients: magnesium hydroxide, mannitol, methacrylic acid copolymer dispersion, povidone and triethyl citrate. The capsule shells have the following inactive ingredients: gelatin, red iron oxide and titanium dioxide. The capsule imprinting ink contains ammonium hydroxide, black iron oxide, ethyl alcohol, isopropyl alcohol, n-butyl alcohol, potassium hydroxide, propylene glycol and shellac.

## **NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

In two 24-month carcinogenicity studies in rats, omeprazole at daily doses of 1.7, 3.4, 13.8, 44.0 and 140.8 mg/kg/day (about 0.35 to 28 times a human dose of 40 mg/day, as expressed on a body surface area basis) produced gastric ECL cell carcinoids in a dose-related manner in both male and female rats; the incidence of this effect was markedly higher in female rats, which had higher blood levels of omeprazole. Gastric carcinoids seldom occur in the untreated rat. In addition, ECL cell hyperplasia was present in all treated groups of both sexes. In one of these studies, female rats were treated with 13.8 mg omeprazole/kg/day (about 2.8 times a human dose of 40 mg/day, based on body surface area) for one year, and then followed for an additional year without the drug. No carcinoids were seen in these rats. An increased incidence of treatment-related ECL cell hyperplasia was observed at the end of one year (94% treated vs 10% controls). By the second year the difference between treated and control rats was much smaller (46% vs 26%) but still showed more hyperplasia in the treated group. Gastric adenocarcinoma was seen in one rat (2%). No similar tumor was seen in male or female rats treated for two years. For this strain of rat no similar tumor has been noted historically, but a finding involving only one tumor is difficult to interpret. In a 52-week toxicity study in Sprague-Dawley rats, brain astrocytomas were found in a small number of males that received omeprazole at dose levels of 0.4, 2, and 16 mg/kg/day (about 0.1 to 3.2 times the human dose of 40 mg/day, based on a body surface area basis). No astrocytomas were observed in female rats in this study. In a 2-year carcinogenicity study in Sprague-Dawley rats, no astrocytomas were found in males or females at the high dose of 140.8 mg/kg/day (about 28 times the human dose of 40 mg/day on a body surface area basis). A 78-week mouse carcinogenicity study of omeprazole did not show increased tumor occurrence, but the study was not conclusive. A 26-week p53 (+/-) transgenic mouse carcinogenicity study was not positive.

Omeprazole was positive for clastogenic effects in an in vitro human lymphocyte chromosomal

aberration assay, in one of two in vivo mouse micronucleus tests, and in an in vivo bone marrow cell chromosomal aberration assay. Omeprazole was negative in the in vitro Ames test, an in vitro mouse lymphoma cell forward mutation assay, and an in vivo rat liver DNA damage assay.

Omeprazole at oral doses up to 138 mg/kg/day in rats (about 28 times an oral human dose of 40 mg on a body surface area basis) was found to have no effect on fertility and reproductive performance.

In 24-month carcinogenicity studies in rats, a dose-related significant increase in gastric carcinoid tumors and ECL cell hyperplasia was observed in both male and female animals [see Warnings and Precautions (5)]. Carcinoid tumors have also been observed in rats subjected to fundectomy or long-term treatment with other proton pump inhibitors or high doses of H2-receptor antagonists.

## 13.2 Animal Toxicology and/or Pharmacology

### Reproduction Studies

#### Reproductive Toxicology Studies

Reproductive studies conducted with omeprazole in rats at oral doses up to 138 mg/kg/day (about 28 times the human dose of 40 mg/day on a body surface area basis) and in rabbits at doses up to 69 mg/kg/day (about 28 times the human dose on a body surface area basis) did not disclose any evidence for a teratogenic potential of omeprazole. In rabbits, omeprazole in a dose range of 6.9 to 69.1 mg/kg/day (about 2.8 to 28 times the human dose of 40 mg/day on a body surface area basis) produced dose-related increases in embryo-lethality, fetal resorptions, and pregnancy disruptions. In rats, dose-related embryo/fetal toxicity and postnatal developmental toxicity were observed in offspring resulting from parents treated with omeprazole at 13.8 to 138.0 mg/kg/day (about 2.8 to 28 times the human dose of 40 mg/day on a body surface area basis) [see Pregnancy, Animal Data (8.1)].

#### Juvenile Animal Study

A 28-day toxicity study with a 14-day recovery phase was conducted in juvenile rats with esomeprazole magnesium at doses of 70 to 280 mg/kg/day (about 17 to 57 times a daily oral human dose of 40 mg on a body surface area basis). An increase in the number of deaths at the high dose of 280 mg/kg/day was observed when juvenile rats were administered esomeprazole magnesium from postnatal day 7 through postnatal day 35. In addition, doses equal to or greater than 140 mg/kg/day (about 34 times a daily oral human dose of 40 mg on a body surface area basis), produced treatment-related decreases in body weight (approximately 14%) and body weight gain, decreases in femur weight and femur length, and affected overall growth. Comparable findings described above have also been observed in this study with another esomeprazole salt, esomeprazole strontium, at equimolar doses of esomeprazole.

## INFORMATION FOR PATIENTS

“See FDA-Approved Medication Guide”

Omeprazole delayed-release capsule should be taken before eating. Patients should be informed that the omeprazole delayed-release capsule should be swallowed whole.

For patients who have difficulty swallowing capsules, the contents of an omeprazole delayed-release 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.

Advise patients to immediately report and seek care for diarrhea that does not improve. This may be a sign of *Clostridium difficile* associated diarrhea [see Warnings and Precautions (5.3)].

Advise patients to immediately report and seek care for any cardiovascular or neurological symptoms

including palpitations, dizziness, seizures, and tetany as these may be signs of hypomagnesemia [see Warnings and Precautions (5.6)].

## **MEDICATION GUIDE**

### MEDICATION GUIDE

Omeprazole Delayed-Release Capsules, USP

(oh mep' ra zole)

Read this Medication Guide before you start taking omeprazole delayed-release capsules and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is the most important information I should know about omeprazole delayed-release capsules?

Omeprazole delayed-release capsules may help your acid-related symptoms, but you could still have serious stomach problems. Talk with your doctor.

Omeprazole delayed-release capsules can cause serious side effects, including:

**Diarrhea.** Omeprazole may increase your risk of getting severe diarrhea. This diarrhea may be caused by an infection (*Clostridium difficile*) in your intestines.

Call your doctor right away if you have watery stool, stomach pain, and fever that does not go away.

**Bone fractures.** People who take multiple daily doses of proton pump inhibitor medicines for a long period of time (a year or longer) may have an increased risk of fractures of the hip, wrist, or spine. You should take omeprazole delayed-release capsules exactly as prescribed, at the lowest dose possible for your treatment and for the shortest time needed. Talk to your doctor about your risk of bone fracture if you take omeprazole delayed-release capsules.

Omeprazole can have other serious side effects. See “What are the possible side effects of omeprazole delayed-release capsules?”

What are omeprazole delayed-release capsules?

Omeprazole delayed-release capsules is a prescription medicine called a proton pump inhibitor (PPI). Omeprazole delayed-release capsules reduces the amount of acid in your stomach. Omeprazole delayed-release capsules are used in adults:

for up to 8 weeks for the healing of duodenal ulcers. The duodenal area is the area where food passes when it leaves the stomach.

with certain antibiotics to treat an infection caused by bacteria called *H. pylori*. Sometimes *H. pylori* bacteria can cause duodenal ulcers. The infection needs to be treated to prevent the ulcers from coming back.

for up to 8 weeks for healing stomach ulcers.

for up to 4 weeks to treat heartburn and other symptoms that happen with gastroesophageal reflux disease (GERD).

GERD happens when acid in your stomach backs up into the tube (esophagus) that connects your mouth to your stomach. This may cause a burning feeling in your chest or throat, sour taste, or burping.

for up to 8 weeks to heal acid-related damage to the lining of the esophagus (called erosive esophagitis or EE). If needed, your doctor may decide to prescribe another 4 weeks of omeprazole delayed-release capsules.

to maintain healing of the esophagus. It is not known if omeprazole delayed-release capsules is safe and effective when used for longer than 12 months (1 year) for this purpose.

for the long-term treatment of conditions where your stomach makes too much acid. This includes a rare condition called Zollinger-Ellison Syndrome.

For children and adolescents 2 to 17 years of age, omeprazole delayed-release capsules are used:

for up to 4 weeks to treat heartburn and other symptoms that happen with gastroesophageal reflux disease (GERD).

for up to 8 weeks to heal acid-related damage to the lining of the esophagus (called erosive esophagitis or EE)

to maintain healing of the esophagus. It is not known if omeprazole delayed-release capsules are safe and effective when used longer than 12 months (1 year) for this purpose.

It is not known if omeprazole delayed-release capsules are safe and effective for the treatment of gastroesophageal reflux disease (GERD) in children under 1 year of age.

Who should not take omeprazole delayed-release capsules?

Do not take omeprazole delayed-release capsules if you:

are allergic to omeprazole delayed-release capsules or any of the ingredients in omeprazole delayed-release capsules. See the end of this Medication Guide for a complete list of ingredients in omeprazole delayed-release capsules.

are allergic to any other Proton Pump Inhibitor (PPI) medicine.

What should I tell my doctor before taking omeprazole delayed-release capsules?

Before you take omeprazole delayed-release capsules, tell your doctor if you:

have been told that you have low magnesium levels in your blood

have liver problems

have any other medical conditions

are pregnant or plan to become pregnant. It is not known if omeprazole will harm your unborn baby.

are breastfeeding or plan to breastfeed. Omeprazole passes into your breast milk. Talk to your doctor about the best way to feed your baby if you take omeprazole delayed-release capsules.

Tell your doctor about all of the medicines you take including prescription and non-prescription drugs, anti-cancer drugs, vitamins and herbal supplements. Omeprazole delayed-release capsules may affect how other medicines work, and other medicines may affect how omeprazole delayed-release capsules works.

Especially tell your doctor if you take:

atazanavir (Reyataz)

nelfinavir (Viracept)

saquinavir (Fortovase)

cilostazol (Pletal)

ketoconazole (Nizoral)

voriconazole (Vfend)

an antibiotic that contains ampicillin, amoxicillin or clarithromycin

products that contain iron

warfarin (Coumadin, Jantoven)

digoxin (Lanoxin)

tacrolimus (Prograf)

diazepam (Valium)

phenytoin (Dilantin)

disulfiram (Antabuse)

clopidogrel (Plavix)

St. John's Wort (*Hypericum perforatum*)

rifampin (Rimactane, Rifater, Rifamate),

erlotinib (Tarceva)

methotrexate

Ask your doctor or pharmacist for a list of these medicines if you are not sure.

Know the medicines that you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I take omeprazole delayed-release capsules?

Take omeprazole delayed-release capsules exactly as prescribed by your doctor.

Do not change your dose or stop omeprazole delayed-release capsules without talking to your doctor.

Take omeprazole delayed-release capsules at least 1 hour before a meal.

Swallow omeprazole delayed-release capsules whole. Do not chew or crush omeprazole delayed-release capsules.

If you have trouble swallowing omeprazole delayed-release capsules, you may take as follows:

Place 1 tablespoon of applesauce into a clean bowl.

Carefully open the capsule and empty the contents (pellets) onto the applesauce. Mix the pellets with the applesauce.

Swallow the applesauce and pellet mixture right away with a glass of cool water. Do not chew or crush the pellets. Do not store the applesauce and pellet mixture for later use.

If you forget to take a dose of omeprazole delayed-release capsules, take it as soon as you remember. If it is almost time for your next dose, do not take the missed dose. Take the next dose on time. Do not take a double dose to make up for a missed dose.

If you take too much omeprazole delayed release capsules, tell your doctor right away.

What are the possible side effects of omeprazole delayed-release capsules?

Omeprazole can cause serious side effects, including:

See “What is the most important information I should know about omeprazole?”

Chronic (lasting a long time) inflammation of the stomach lining (Atrophic Gastritis). Using omeprazole delayed-release capsules for a long period of time may increase the risk of inflammation to your stomach lining. You may or may not have symptoms. Tell your doctor if you have stomach pain, nausea, vomiting, or weight loss.

Low magnesium levels in your body. Low magnesium can happen in some people who take a proton pump inhibitor medicine for at least 3 months. If low magnesium levels happen, it is usually after a year of treatment. You may or may not have symptoms of low magnesium.

Tell your doctor right away if you develop any of these symptoms:

seizures

dizziness

abnormal or fast heart beat

jitteriness

jerking movements or shaking (tremors)

muscle weakness

spasms of the hands and feet

cramps or muscle aches

spasm of the voice box

Your doctor may check the level of magnesium in your body before you start taking omeprazole delayed-release capsules or during treatment if you will be taking omeprazole delayed-release capsules for a long period of time.

The most common side effects with omeprazole delayed-release capsules in adults and children include:

headache

stomach pain

nausea

diarrhea

vomiting  
gas

In addition to the side effects listed above, the most common side effects in children 2 to 16 years of age include:

respiratory system events  
fever

Other side effects:

Serious allergic reactions. Tell your doctor if you get any of the following symptoms with omeprazole:

rash  
face swelling  
throat tightness  
difficulty breathing

Your doctor may stop omeprazole if these symptoms happen.

Tell your doctor if you have any side effect that bothers you or that do not go away. These are not all the possible side effects with omeprazole delayed-release capsules.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store omeprazole delayed-release capsules?

Store omeprazole delayed-release capsules at room temperature between 68°F to 77°F (20°C to 25°C). Keep the container of omeprazole delayed-release capsules closed tightly.

Keep omeprazole delayed-release capsules and all medicines out of the reach of children.

General information about omeprazole delayed-release capsules

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use omeprazole delayed-release capsules for a condition for which it was not prescribed. Do not give omeprazole delayed-release capsules to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about omeprazole delayed-release capsules.

For more information, ask your doctor. You can ask your doctor or pharmacist for information that is written for healthcare professionals.

For more information contact Apotex Corp., Drug Safety at 1-800-706-5575.

Instructions for Use

For instructions on taking omeprazole delayed-release capsules, please see “How should I take omeprazole delayed-release capsules?”

What are the ingredients in omeprazole delayed-release capsules?

Active ingredient in omeprazole delayed-release capsules: omeprazole

Inactive ingredients in omeprazole delayed-release capsules: magnesium hydroxide, mannitol, methacrylic acid copolymer dispersion, povidone and triethyl citrate. The capsule shells have the following inactive ingredients: gelatin, red iron oxide and titanium dioxide. The capsule imprinting ink contains ammonium hydroxide, black iron oxide, ethyl alcohol, isopropyl alcohol, n-butyl alcohol, potassium hydroxide, propylene glycol and shellac.

This Medication Guide and Instructions for Use has been approved by the U.S. Food and Drug Administration.

**PACKAGE LABEL.PRINCIPAL DISPLAY PANEL**

NDC: 51655-022-26

MFG: 60505-0065-1

OMEPRAZOLE DR 20 MG

90 Capsules

Rx Only

Lot#

Exp. Date:

Medication guide is found at [www.fda.gov/drugs/drugsafety/ucm085729](http://www.fda.gov/drugs/drugsafety/ucm085729)

Dosage: See prescriber's instructions

Each capsule contains 20 mg omeprazole

Store at 68 to 77 degrees F.

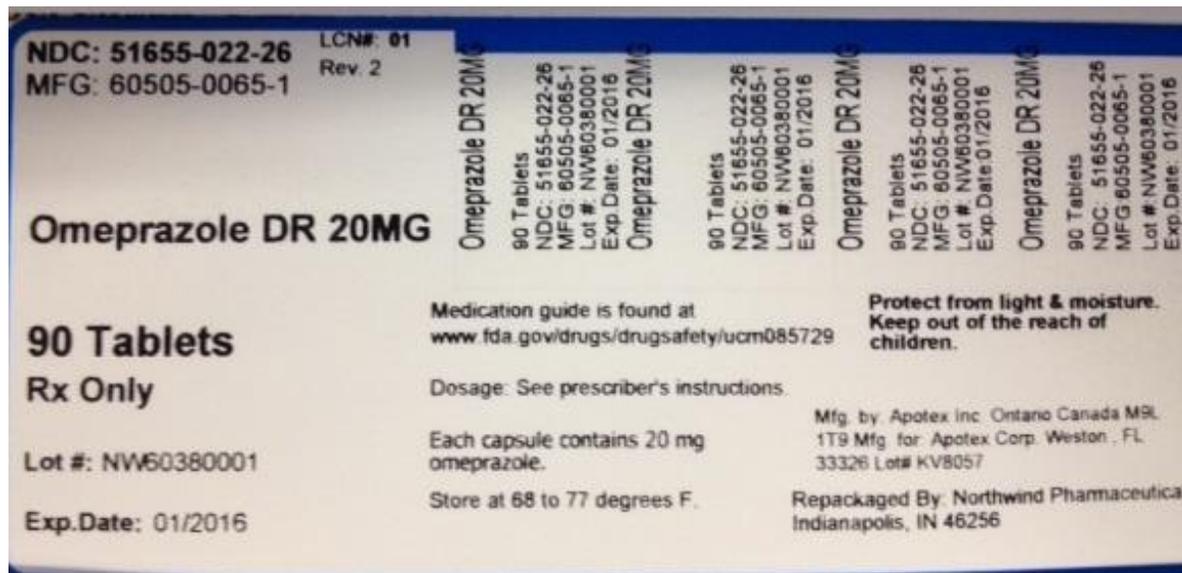
Protect from light and moisture

Keep out of the reach of children.

Mfg. by Apotex Inc. Ontario Canada M9L 1T9

Mfg for Apotex Corp. Weston, FL 33326 Lot#

Repackaged by Northwind Pharmaceuticals, Indianapolis, IN 46256



**Package Label.Principal Display Section**

NDC: 51655-022-25

MFG: 60505-0065-1

Omeprazole DR 20MG

60 Capsules

Rx Only

Lot #:

Exp Date:



METHACRYLIC ACID - ETHYL ACRYLATE COPOLYMER (1:1) TYPE A (UNII: NX76LV5T8J)	
POVIDONE K30 (UNII: U725QWY32X)	
TRIETHYL CITRATE (UNII: 8Z96QXD6UM)	
GELATIN (UNII: 2G86QN327L)	
FERRIC OXIDE RED (UNII: 1K09F3G675)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
AMMONIA (UNII: 5138Q19F1X)	
FERROSFERRIC OXIDE (UNII: XM0M87F357)	
ALCOHOL (UNII: 3K9958V90M)	
ISOPROPYL ALCOHOL (UNII: ND2M416302)	
BUTYL ALCOHOL (UNII: 8PJ61P6TS3)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SHELLAC (UNII: 46N107B71O)	

### Product Characteristics

Color	pink (opaque) , brown (reddish brown)	Score	no score
Shape	capsule	Size	18mm
Flavor		Imprint Code	APO;020
Contains			

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:51655-022-26	90 in 1 BOTTLE, DISPENSING; Type 0: Not a Combination Product		
2	NDC:51655-022-25	60 in 1 BOTTLE, DISPENSING; Type 0: Not a Combination Product		

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA076048	10/27/2014	

**Labeler** - Northwind Pharmaceuticals, LLC (036986393)

**Registrant** - Northwind Pharmaceuticals, LLC (036986393)

### Establishment

Name	Address	ID/FEI	Business Operations
Northwind Pharmaceuticals, LLC		036986393	repack(51655-022)