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Nexium advertisement.

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New from AstraZeneca , the maker of Prilosec



We captured
the **ESSENCE** of Prilosec[®] (omeprazole)...

...and created a **NEW** PPI

Introducing **NEXIUM**TM
(esomeprazole magnesium)



The **POWERFUL**
new **PPI** from the maker of
Prilosec® (omeprazole)

*In erosive esophagitis studies
compared with Prilosec*

Proven efficacy in short-term
healing (4-8 weeks)¹

Proven symptom control

Safety and tolerability similar
to Prilosec

The most frequently reported adverse
events with NEXIUM and Prilosec
are headache, diarrhea, and abdominal
pain. Symptomatic response to therapy
does not preclude the presence of
gastric malignancy.

Reference: 1. Prescribing Information for NEXIUM.

NEXIUM and Prilosec should be used only
for the conditions, dosages, and durations
specified in the Prescribing Information.
Before prescribing NEXIUM or Prilosec,
please see brief summary of full Prescribing
Information on next page.

NEW


Nexium™
(esomeprazole magnesium)

FROM THE MAKER OF PRILOSEC



BRIEF SUMMARY: Before prescribing NEXIUM, please see full Prescribing Information.

INDICATIONS AND USAGE: NEXIUM is indicated for the short-term treatment (4 to 8 weeks) in the healing and symptomatic resolution of diagnostically confirmed erosive esophagitis.

CONTRAINDICATIONS: NEXIUM is contraindicated in patients with known hypersensitivity to any component of the formulation or to substituted benzimidazoles.

PRECAUTIONS: Symptomatic response to therapy with NEXIUM does not preclude the presence of gastric malignancy. Atrophic gastritis has been noted occasionally in gastric cancer biopsies from patients treated long-term with omeprazole, of which NEXIUM is an enantiomer. **Information for Patients:** NEXIUM Delayed-Release Capsules should be taken at least one hour before meals. For patients who have difficulty swallowing capsules, one tablespoon of applesauce can be added to an empty bowl and the capsule opened, and the pellets carefully emptied onto the applesauce. The pellets should be mixed with the applesauce and then swallowed immediately. 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 pellet/applesauce mixture should not be stored for future use. Antacids may be used while taking NEXIUM.

DRUG INTERACTIONS: Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. *In vitro* and *in vivo* studies have shown that esomeprazole is not likely to inhibit CYPs 2A6, 2C9, 2D6, 2E1 and 3A4. No clinically relevant interactions with drugs metabolized by these CYP enzymes would be expected. Drug interaction studies have shown that esomeprazole does not have any clinically significant interactions with phenytoin, warfarin, quinidine, clarithromycin or amoxicillin. Esomeprazole may potentially interfere with CYP2C19, the major esomeprazole-metabolizing enzyme. Coadministration of esomeprazole 30 mg and diazepam, a CYP2C19 substrate, resulted in a 45% decrease in clearance of diazepam. Increased plasma levels of diazepam were observed 12 hours after dosing and onwards. However, at that time, the plasma levels of diazepam were below the therapeutic interval, and thus this interaction is unlikely to be of clinical relevance. Coadministration of oral contraceptives, diazepam, phenytoin, or quinidine did not seem to change the pharmacokinetic profile of esomeprazole. Esomeprazole inhibits gastric acid secretion, therefore, it is theoretically possible that esomeprazole and omeprazole may interfere with absorption of drugs where gastric pH is an important determinant of their bioavailability (e.g., ketoconazole and ampicillin esters, digoxin, and iron salts). **Carcinogenesis, Mutagenesis, Impairment of Fertility:** The carcinogenic potential of esomeprazole was assessed using omeprazole studies. 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 0.7 to 57 times the human dose of 20 mg/kg/day expressed on a body surface area basis) produced gastric ECL cell carcinomas 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 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 0.56 times the human dose on a body surface area basis) for 1 year, 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 year 1 (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 2 years. For this strain of rat no similar tumor has been noted historically, but a finding involving only one tumor is difficult to interpret. A 78-week mouse carcinogenicity study of omeprazole did not show increased tumor occurrence, but the study was not conclusive. Esomeprazole was negative in the Ames mutation test, in the *in vivo* rat bone marrow cell chromosome aberration test, and the *in vivo* mouse micronucleus test. Esomeprazole, however, was positive in the *in vitro* human lymphocyte chromosome aberration test. Omeprazole was positive in the *in vitro* human lymphocyte chromosome aberration test, the *in vivo* mouse bone marrow cell chromosome aberration test, and the *in vivo* mouse micronucleus test. The potential effects of esomeprazole on fertility and reproductive performance were assessed using omeprazole studies. Omeprazole at oral doses up to 138 mg/kg/day in rats (about 56 times the human dose on a body surface area basis) was found to have no effect on reproductive performance of parental animals. **Pregnancy: Teratogenic Effects, Pregnancy Category B -** Teratology studies have been performed in rats at oral doses up to 280 mg/kg/day (about 57 times the human dose on a body surface area basis) and in rabbits at oral doses up to 86 mg/kg/day (about 35 times the human dose on a body surface area basis) and have revealed no evidence of impaired fertility or harm to the fetus due to esomeprazole. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Teratology studies conducted with omeprazole in rats at oral doses up to 138 mg/kg/day (about 56 times the human dose on a body surface area basis) and in rabbits at oral doses up to 69 mg/kg/day (about 56 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 5.5 to 56 times the human dose on a body surface area basis) produced dose-related increases in embryo-letality, 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 5.6 to 56 times the human dose on a body surface area basis). There are no adequate and well-controlled studies in pregnant women. Sporadic reports have been received of congenital abnormalities occurring in infants born to women who have received omeprazole during pregnancy. **Nursing Mothers:** The excretion of esomeprazole in milk has not been studied. However, omeprazole concentrations have been measured in breast milk of a woman following oral administration of 20 mg. Because esomeprazole and omeprazole are likely to be excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from esomeprazole and because of the potential for tumorigenicity shown for omeprazole in rat carcinogenicity studies, a decision should be made to discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use:** Safety and effectiveness in pediatric patients have not been established. **Geriatric Use:** Of the total number of patients who received NEXIUM in clinical trials, 778 were 65 to 74 years of age and 124 patients were ≥ 75 years of age. No overall differences in safety and efficacy were observed between the elderly and younger individuals, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS: The safety of NEXIUM was evaluated in over 10,000 patients (aged 18-84 years) in clinical trials worldwide including over 7,400 patients in the United States and over 2,600 patients in Europe and Canada. Over 2,900 patients were treated in long-term studies for up to 6-12 months. In general, NEXIUM was well tolerated in both short- and long-term clinical trials. The safety in the treatment of healing of erosive esophagitis was assessed in four randomized comparative clinical trials, which included 1,240 patients on NEXIUM 20 mg, 4,234 patients on NEXIUM 40 mg, and 3,008 patients on omeprazole 20 mg daily. The most frequently occurring adverse events (≥1% in all three groups) were headache (5.5, 5.0, and 3.8, respectively) and diarrhea (no difference among the three groups). Nausea, flatulence, abdominal pain, constipation, and dry mouth occurred at similar rates among patients taking NEXIUM or omeprazole. Additional adverse events that were reported as possibly or probably related to NEXIUM with an incidence < 1% are listed below by body system: **Body as a Whole:** abdomen enlarged, allergic reaction, asthenia, back pain, chest pain, chest pain substernal, facial edema, leg edema, peripheral edema, hot flashes, fatigue, fever, flu-like disorder, generalized edema, leg edema, malaise, pain, rigors; **Cardiovascular:** flushing, hypertension, tachycardia; **Endocrine:** goiter; **Gastrointestinal:** bowel irregularity, constipation aggravated, dyspepsia, dysphagia, dysplasia GI, epigastric pain, eructation, esophageal disorder, frequent stools, gastroenteritis, GI hemorrhage, GI symptoms NOS, hiccup, melena, mouth disorder, pharynx disorder, rectal disorder, serum gastrin increased, tongue disorder, tongue edema, ulcerative stomatitis, vomiting; **Hearing:** earache, tinnitus; **Hematology:** anemia, anemia hypochromic, cervical lymphadenopathy, epistaxis, leucocytosis, leukopenia, thrombocytopenia; **Hepatic:** bilirubinemia, hepatic function abnormal, SGOT increased, SGPT increased; **Metabolic/Nutritional:** glycosuria, hyperuricemia, hyponatremia, increased alkaline phosphatase, thiamin B12 deficiency, weight increase, weight decrease; **Musculoskeletal:** arthralgia, arthritis aggravated, arthralgia, cramps, fibromyalgia syndrome, hernia, polymyalgia rheumatica; **Nervous System/Psychiatric:** anorexia, apathy, appetite decreased, depression, dizziness, headache, insomnia, hypotension, hypoesthesia, impotence, insomnia, migraine, migraine aggravated, paresthesia, sleep disorder, somnolence, syncope, vertigo; **Reproductive:** dysmenorrhea, menstrual disorder, vaginitis; **Respiratory:** asthma aggravated, coughing, dyspnea, larynx edema, pharyngitis, rhinitis, sinusitis; **Skin and Appendages:** acne, angioedema, dermatitis, pruritus, pruritus ani, rash, rash erythematous, rash maculo-papular, skin inflammation, sweating increased, urticaria; **Special Senses:** otitis media, parosmia, taste loss, taste perversion; **Urogenital:** abnormal urine, albuminuria, cystitis, dysuria, fungal infection, hematuria, micturition frequency, moniliasis, genital moniliasis, polyuria; **Visual:** conjunctivitis, vision abnormal. Endoscopic findings that were reported as adverse events include: duodenitis, esophagitis, esophageal stricture, esophageal ulceration, esophageal varices, gastric ulcer, gastritis, hernia, benign polyps or nodules, Barrett's esophagus, and mucosal discoloration. Other adverse events not observed with NEXIUM, but occurring with omeprazole can be found in the omeprazole package insert.

OVERDOSAGE: A single oral dose of esomeprazole at 510 mg/kg (about 103 times the human dose on a body surface area basis), was lethal to rats. The major signs of acute toxicity were reduced motor activity, changes in respiratory frequency, tremor, ataxia, and intermittent clonic convulsions. There have been no reports of overdose with esomeprazole. Reports have been received of overdose with omeprazole in humans. Doses ranged up to 2,400 mg (120 times the usual recommended clinical dose). Manifestations were variable, but included confusion, drowsiness, blurred vision, tachycardia, nausea, diaphoresis, flushing, headache, dry mouth, and other adverse reactions similar to those seen in normal clinical experience (see omeprazole package insert-ADVERSE REACTIONS). No specific antidote for esomeprazole is known. Since esomeprazole is extensively protein bound, it is not expected to be removed by dialysis. In the event of overdose, 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, a certified Regional Poison Control Center should be contacted. Telephone numbers are listed in the Physicians' Desk Reference (PDR) or local telephone book.

BRIEF SUMMARY: Before prescribing PRIOLOSEC, please see full Prescribing Information.

INDICATIONS AND USAGE: Erosive Esophagitis; PRIOLOSEC Delayed-Release Capsules are indicated for the short-term treatment (4-8 weeks) in the healing of erosive esophagitis, which has been diagnosed by endoscopy.

CONTRAINDICATIONS, Omeprazole: PRIOLOSEC Delayed-Release Capsules are contraindicated in patients with known hypersensitivity to any component of the formulation.

PRECAUTIONS: Symptomatic response to therapy with omeprazole does not preclude the presence of gastric malignancy. Atrophic gastritis has been noted occasionally in gastric cancer biopsies from patients treated long-term with omeprazole. **Information for Patients:** PRIOLOSEC Delayed-Release Capsules should be taken before eating and should not be opened, chewed or crushed, and should be swallowed whole. **DRUG INTERACTIONS:** Other. Omeprazole can prolong the elimination of diazepam, warfarin and phenytoin, drugs that are metabolized by oxidation in the liver. 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 P-450 system (e.g., cyclosporine, disulfiram, and benzodiazepines). Patients should be monitored to determine if it is necessary to adjust the dosage of these drugs when taken concomitantly with PRIOLOSEC. Omeprazole inhibits gastric acid secretion, therefore, 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, digoxin, and iron salts). In clinical trials, antacids were used concomitantly with the administration of PRIOLOSEC. **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 (approximately 4 to 352 times the human dose, based on a patient weight of 50 kg and a human dose of 20 mg) produced gastric ECL cell carcinomas 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 (approximately 35 times the human dose on a body surface area basis) for 1 year, 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. An unusual primary malignant tumor in the stomach 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. A 78-week mouse carcinogenicity study of omeprazole did not show increased tumor occurrence, but the study was not conclusive. Omeprazole was not mutagenic in an *in vitro* Ames Salmonella typhimurium assay, an *in vitro* mouse lymphoma cell assay and an *in vivo* rat liver DNA damage assay. A mouse micronucleus test at 625 and 6250 times the human dose gave a borderline result, as did an *in vivo* bone marrow chromosome aberration test. A 6250 times mouse micronucleus study at 2000 times the human dose, but with different (suboptimal) sampling times, was negative. In a rat fertility and general reproductive performance test, omeprazole in a dose range of 13.8 to 138.0 mg/kg/day (approximately 35 to 345 times the human dose) was not toxic or deleterious to the reproductive performance of parental animals. **Pregnancy: Category C -** In rabbits, omeprazole in a dose range of up to 69 mg/kg/day (approximately 172 times the human dose) 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 (approximately 17 to 172 times the human dose) produced dose-related increases in embryo-letality, 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 13.8 to 138.0 mg/kg/day (approximately 35 to 345 times the human dose). There are no adequate or well-controlled studies in pregnant women. Sporadic reports have been received of congenital abnormalities occurring in infants born to women who have received omeprazole during pregnancy. **Nursing Mothers:** It is not known whether omeprazole is excreted in human milk. In rats, omeprazole administration during late gestation and lactation at doses of 13.8 to 138 mg/kg/day (35 to 345 times the human dose) resulted in decreased weight gain in pups. Because many drugs are excreted in human milk, because of the potential for serious adverse reactions in nursing infants from omeprazole, and because of the potential for tumorigenicity shown for omeprazole in rat carcinogenicity studies, 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:** Safety and effectiveness in pediatric patients have not been established. **Geriatric Use:** No overall differences in safety and efficacy were observed between the elderly and younger individuals, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS: In the U.S. clinical trial population of 465 patients (including duodenal ulcer, Zollinger-Ellison syndrome and resistant ulcer patients), the following adverse experiences were reported to occur in 1% or more of patients on therapy with PRIOLOSEC. Numbers in parentheses indicate percentages of the adverse experiences considered by investigators as possibly, probably or definitely related to the drug:

	Omeprazole (n=465)	Placebo (n=64)	Ranitidine (n=195)
Headache	6.9 (2.4)	6.3	7.7 (2.6)
Diarrhea	3.0 (1.9)	3.1 (1.6)	2.1 (0.5)
Abdominal Pain	2.4 (0.4)	3.1	2.1
Nausea	2.2 (0.9)	3.1	4.1 (0.5)
URI	1.9	1.6	2.6
Dizziness	1.5 (0.6)	4.0	2.6 (1.0)
Vomiting	1.5 (0.4)	4.7	1.5 (0.5)
Rash	1.5 (1.1)	0.0	0.0
Constipation	1.1 (0.9)	0.0	0.0
Cough	1.1	0.0	1.5
Asthenia	1.1 (0.2)	1.6 (1.6)	1.5 (1.0)
Back Pain	1.1	0.0	0.5

The following adverse reactions which occurred in 1% or more of omeprazole-treated patients have been reported in international double-blind, and open-label, clinical trials in which 2,631 patients and subjects received omeprazole and 120 patients took a placebo. A causal relationship was not assessed. The percentages are given omeprazole then placebo, respectively. **Body as a Whole, site unspecified:** Abdominal Pain 5.2% and 3.3%; Asthenia 1.3% and 0.8%; **Digestive System:** Constipation 1.5 and 0.8; Diarrhea 3.7 and 2.5; Flatulence 2.7 and 5.8; Nausea 4.0 and 6.7; Vomiting 3.2 and 10.0; Acid regurgitation 1.9 and 3.3; **Nervous System/Psychiatric:** Headache 2.9 and 2.5. Additional adverse experiences occurring in < 1% of patients or subjects in domestic and/or international trials, or occurring since the drug was marketed, are shown below within each body system. In many instances, the relationship to PRIOLOSEC was unclear. **Body As a Whole:** Allergic reactions, including, rarely, anaphylaxis (see also Skin below); fever, pain, fatigue, malaise, abdominal swelling. **Cardiovascular:** Chest pain or angina, tachycardia, bradycardia, palpitation, elevated blood pressure, peripheral edema. **Gastrointestinal:** Pancreatitis (some fatal), anorexia, irritable colon, flatulence, fecal discoloration, esophageal candidiasis, mucosal atrophy of the tongue, dry mouth. 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. Gastrointestinal carcinoids have been reported in patients with ZE syndrome on long-term treatment with PRIOLOSEC. This finding is believed to be a manifestation of the underlying condition, which is known to be associated with such tumors. **Hepatic:** Mild and, rarely, marked elevations of liver function tests [ALT (SGPT), AST (SGOT), γ -glutamyl transpeptidase, alkaline phosphatase, and bilirubin (jaundice)]. In rare instances, overt liver disease has occurred, including hepatocellular, cholestatic, or mixed hepatitis (jaundice). In rare instances, overt liver disease has occurred, including hepatocellular, cholestatic, or mixed hepatitis (jaundice). **Nervous System/Psychiatric:** Anxiety, depression, dizziness, headache, insomnia, hypotension, hypoesthesia, impotence, insomnia, migraine, migraine aggravated, paresthesia, sleep disorder, somnolence, syncope, vertigo; **Reproductive:** Dysmenorrhea, menstrual disorder, vaginitis; **Respiratory:** Asthma aggravated, coughing, dyspnea, larynx edema, pharyngitis, rhinitis, sinusitis; **Skin and Appendages:** Acne, angioedema, dermatitis, pruritus, pruritus ani, rash, rash erythematous, rash maculo-papular, skin inflammation, sweating increased, urticaria; **Special Senses:** Otitis media, parosmia, taste loss, taste perversion; **Urogenital:** Abnormal urine, albuminuria, cystitis, dysuria, fungal infection, hematuria, micturition frequency, moniliasis, genital moniliasis, polyuria; **Visual:** Conjunctivitis, vision abnormal. Endoscopic findings that were reported as adverse events include: duodenitis, esophagitis, esophageal stricture, esophageal ulceration, esophageal varices, gastric ulcer, gastritis, hernia, benign polyps or nodules, Barrett's esophagus, and mucosal discoloration. Other adverse events not observed with NEXIUM, but occurring with omeprazole can be found in the omeprazole package insert.

OVERDOSAGE: Rare reports have been received of overdose with omeprazole. Doses ranged from 320 mg to 900 mg (16-45 times the usual recommended clinical dose). Manifestations were variable, but included confusion, drowsiness, blurred vision, tachycardia, nausea, diaphoresis, flushing, headache, and dry mouth. Symptoms were transient, and no serious clinical outcome has been reported. No specific antidote for omeprazole overdose is known. Omeprazole is extensively protein bound and is, therefore, not readily dialyzable. In the event of overdose, treatment should be symptomatic and supportive.

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