HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use lansoprazole delayed-release capsules safely and effectively. See full prescribing information for:
LANSOPRAZOLE delayed-release capsules USP
For oral administration
Initial U.S. Approval: 1995

RECENT MAJOR CHANGES
Dosage and Administration:
• Important Administration Information (2.3) June 2009
Warnings and Precautions:
• Bone Fracture (5.2) August 2010

INDICATIONS AND USAGE
Lansoprazole delayed-release capsule is a proton pump inhibitor (PPI). Refer to DOSAGE and ADMINISTRATION table (below) for indications and usage.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal Ulcers (1.1, 1.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-Term Treatment</td>
<td>15 mg</td>
<td>Once daily for 4 wks</td>
</tr>
<tr>
<td>Maintenance of Healed</td>
<td>15 mg</td>
<td>Once daily</td>
</tr>
<tr>
<td>H. pylori Eradication to Reduce Recurrence of Duodenal Ulcer (1.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triple Therapy: Lansoprazole delayed-release capsules Amoxicillin Clarithromycin</td>
<td>30 mg</td>
<td>Twice daily for 10 or 14 days</td>
</tr>
<tr>
<td>200 mg</td>
<td>1 gram</td>
<td></td>
</tr>
<tr>
<td>500 mg</td>
<td>500 mg</td>
<td></td>
</tr>
<tr>
<td>Dual Therapy: Lansoprazole delayed-release capsules Amoxicillin</td>
<td>30 mg</td>
<td>Three times daily for 14 days</td>
</tr>
<tr>
<td></td>
<td>1 gram</td>
<td></td>
</tr>
<tr>
<td>Benign Gastric Ulcer (1.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-Term Treatment</td>
<td>30 mg</td>
<td>Once daily up to 8 wks</td>
</tr>
<tr>
<td>NSAID-associated Gastric Ulcer (1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healing Risk Reduction</td>
<td>30 mg</td>
<td>Once daily for 8 wks</td>
</tr>
<tr>
<td></td>
<td>15 mg</td>
<td>Once daily up to 12 wks</td>
</tr>
<tr>
<td>GERD (1.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-Term Treatment of Symptomatic GERD</td>
<td>15 mg</td>
<td>Once daily up to 8 wks</td>
</tr>
<tr>
<td>Short-Term Treatment of EE</td>
<td>30 mg</td>
<td>Once daily up to 8 wks</td>
</tr>
<tr>
<td>Pediatric (8.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1 to 11 years of age) Short-Term Treatment of Symptomatic GERD and Short-Term Treatment of EE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 30 kg</td>
<td>15 mg</td>
<td>Once daily up to 12 wks</td>
</tr>
<tr>
<td>&gt; 30 kg</td>
<td>30 mg</td>
<td>Once daily up to 12 wks</td>
</tr>
<tr>
<td>(12 to 17 years of age) Short-Term Treatment of Symptomatic GERD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonerosive GERD</td>
<td>15 mg</td>
<td>Once daily up to 8 wks</td>
</tr>
<tr>
<td>EE</td>
<td>30 mg</td>
<td>Once daily up to 8 wks</td>
</tr>
<tr>
<td>Maintenance of Healing of EE (1.8)</td>
<td>15 mg</td>
<td>Once daily</td>
</tr>
<tr>
<td>Pathological Hypersecretory Conditions (i.e., ZES) (1.9)</td>
<td>60 mg</td>
<td>Once daily</td>
</tr>
</tbody>
</table>

DOSAGE FORMS AND STRENGTHS
Capsules: 15 mg and 30 mg. (3)

CONTRAINDICATIONS
Contraindicated in patients with known severe hypersensitivity to any component of the lansoprazole delayed-release capsules formulation. (4)

WARNINGS AND PRECAUTIONS
• Symptomatic response with lansoprazole delayed-release capsules does not preclude the presence of gastric malignancy. (5)
• Bone Fracture: Long-term and multiple daily dose PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine. (5.2)
ADVERSE REACTIONS

Most commonly reported adverse reactions (≥1%): diarrhea, abdominal pain, nausea and constipation. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Dr. Reddy’s Laboratories, Inc., at 1-888-375-3784 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

• Do not co-administer with atazanavir. (7)
• May interfere with the absorption of drugs where gastric pH is important for bioavailability (7)

• Concomitant warfarin use may require monitoring for increases in INR and prothrombin time. (7)
• Concomitant tacrolimus use may increase tacrolimus whole blood concentrations. (7)
• Titration of theophylline dosage may be required when concomitant lansoprazole delayed-release capsules use is started or stopped. (7)

USE IN SPECIFIC POPULATIONS

Consider dose adjustment in patients with severe liver impairment (8.7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 10/2010
FULL PRESCRIBING INFORMATION: CONTENTS *

1 INDICATIONS AND USAGE
1.1 Short-Term Treatment of Active Duodenal Ulcer
Lansoprazole delayed-release capsules are indicated for short-term treatment (for 4 weeks) for healing and symptom relief of active duodenal ulcer. [See Clinical Studies (14)]

1.2 H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence
Triple Therapy: Lansoprazole delayed-release capsules/amoxicillin/clarithromycin
Lansoprazole delayed-release capsules in combination with amoxicillin plus clarithromycin as triple therapy is indicated for the treatment of patients with H. pylori infection and duodenal ulcer disease (active or one-year history of a duodenal ulcer) to eradicate H. pylori. Eradication of H. pylori has been shown to reduce the risk of duodenal ulcer recurrence. [See Clinical Studies (14)]
Please refer to the full prescribing information for amoxicillin and clarithromycin.
Dual Therapy: Lansoprazole delayed-release capsules/amoxicillin
Lansoprazole delayed-release capsules in combination with amoxicillin as dual therapy is indicated for the treatment of patients with H. pylori infection and duodenal ulcer disease (active or one-year history of a duodenal ulcer) who are either allergic or intolerant to clarithromycin or in whom resistance to clarithromycin is known or suspected. Eradication of H. pylori has been shown to reduce the risk of duodenal ulcer recurrence. [See Clinical Studies (14)]
Please refer to the full prescribing information for amoxicillin.

1.3 Maintenance of Healed Duodenal Ulcers
Lansoprazole delayed-release capsules are indicated to maintain healing of duodenal ulcers. Controlled studies do not extend beyond 12 months. [See Clinical Studies (14)]

1.4 Short-Term Treatment of Active Benign Gastric Ulcer
Lansoprazole delayed-release capsules are indicated for short-term treatment (up to 8 weeks) for healing and symptom relief of active benign gastric ulcer. [See Clinical Studies (14)]

1.5 Healing of NSAID-Associated Gastric Ulcer
Lansoprazole delayed-release capsules are indicated for the treatment of NSAID-associated gastric ulcer in patients who continue NSAID use. Controlled studies did not extend beyond 8 weeks. [See Clinical Studies (14)]
1.6 Risk Reduction of NSAID-Associated Gastric Ulcer
Lansoprazole delayed-release capsules are indicated for reducing the risk of NSAID-associated gastric ulcers in patients with a history of a documented gastric ulcer who require the use of an NSAID. Controlled studies did not extend beyond 12 weeks. [See Clinical Studies (14)]

1.7 Gastroesophageal Reflux Disease (GERD)
Short-Term Treatment of Symptomatic GERD

Lansoprazole delayed-release capsules is indicated for the treatment of heartburn and other symptoms associated with GERD. [See Clinical Studies (14)]

Short-Term Treatment of Erosive Esophagitis

Lansoprazole delayed-release capsules is indicated for short-term treatment (up to 8 weeks) for healing and symptom relief of all grades of erosive esophagitis.

For patients who do not heal with lansoprazole delayed-release capsules for 8 weeks (5 to 10%), it may be helpful to give an additional 8 weeks of treatment. If there is a recurrence of erosive esophagitis an additional 8-week course of lansoprazole delayed-release capsules may be considered. [See Clinical Studies (14)]

1.8 Maintenance of Healing of Erosive Esophagitis (EE)
Lansoprazole delayed-release capsules are indicated to maintain healing of erosive esophagitis. Controlled studies did not extend beyond 12 months. [See Clinical Studies (14)]

1.9 Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome
Lansoprazole delayed-release capsules are indicated for the long-term treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome. [See Clinical Studies (14)]

2 DOSAGE AND ADMINISTRATION
Lansoprazole is available as a capsule, and is available in 15 mg and 30 mg strengths. Directions for use specific to the route and available methods of administration is presented below. Lansoprazole delayed-release capsules should be taken before eating. Lansoprazole delayed-release capsule products SHOULD NOT BE CRUSHED OR CHEWED. In the clinical trials, antacids were used concomitantly with lansoprazole delayed-release capsules.

2.1 Recommended Dose

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
†Controlled studies did not extend beyond indicated duration.
‡For patients who do not heal with lansoprazole delayed-release capsules for 8 weeks (5 to 10%), it may be helpful to give an additional 8 weeks of treatment. If there is a recurrence of erosive esophagitis, an additional 8 week course of lansoprazole delayed-release capsules may be considered.
§The lansoprazole delayed-release capsules dose was increased (up to 30 mg twice daily) in some pediatric patients after 2 or more weeks of treatment if they remained symptomatic. For pediatric patients unable to swallow an intact capsule please see Administration Options.
¶Varies with individual patient.
Recommended adult starting dose is 60 mg once daily. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Dosages up to 90 mg twice daily have been administered. Daily dose of greater than 120 mg should be administered in divided doses. Some patients with Zollinger-Ellison Syndrome have been treated continuously with lansoprazole delayed-release capsules for more than 4 years.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal Ulcers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-Term Treatment</td>
<td>15 mg</td>
<td>Once daily for 4 weeks</td>
</tr>
<tr>
<td>Maintenance of Healed</td>
<td>15 mg</td>
<td>Once daily</td>
</tr>
<tr>
<td><strong>H. pylori Eradication to Reduce the Risk of</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duodenal Ulcer Recurrence‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triple Therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lansoprazole delayed-release capsules</td>
<td>30 mg</td>
<td>Twice daily (q12h) for 10 or 14 days</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>1 gram</td>
<td>Twice daily (q12h) for 10 or 14 days</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500 mg</td>
<td>Twice daily (q12h) for 10 or 14 days</td>
</tr>
<tr>
<td>Dual Therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lansoprazole delayed-release capsules</td>
<td>30 mg</td>
<td>Three times daily (q8h) for 14 days</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>1 gram</td>
<td>Three times daily (q8h) for 14 days</td>
</tr>
<tr>
<td>Benign Gastric Ulcer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-Term Treatment</td>
<td>30 mg</td>
<td>Once daily for up to 8 weeks</td>
</tr>
<tr>
<td>NSAID-associated Gastric Ulcer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healing</td>
<td>30 mg</td>
<td>Once daily for 8 weeks†</td>
</tr>
<tr>
<td>Risk Reduction</td>
<td>15 mg</td>
<td>Once daily for up to 12 weeks†</td>
</tr>
<tr>
<td>Gastroesophageal Reflux Disease (GERD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-Term Treatment of Symptomatic GERD</td>
<td>15 mg</td>
<td>Once daily for up to 8 weeks</td>
</tr>
<tr>
<td>Short-Term Treatment of Erosive Esophagitis</td>
<td>30 mg</td>
<td>Once daily for up to 8 weeks†</td>
</tr>
<tr>
<td>Pediatric (1 to 11 years of age)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Short-Term Treatment of Symptomatic GERD and Short-Term Treatment of Erosive Esophagitis**

<table>
<thead>
<tr>
<th>Weight Range</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 30 kg</td>
<td>15 mg</td>
<td>Once daily for up to 8 weeks</td>
</tr>
<tr>
<td>&gt; 30 kg</td>
<td>30 mg</td>
<td>Once daily for up to 12 weeks</td>
</tr>
</tbody>
</table>

(12 to 17 years of age)

**Short-Term Treatment of Symptomatic GERD**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonerosive GERD</td>
<td>15 mg</td>
<td>Once daily for up to 8 weeks</td>
</tr>
<tr>
<td>Erosive Esophagitis</td>
<td>30 mg</td>
<td>Once daily for up to 8 weeks</td>
</tr>
</tbody>
</table>

**Maintenance of Healing of Erosive Esophagitis**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome</td>
<td>15 mg</td>
<td>Once daily</td>
</tr>
<tr>
<td></td>
<td>60 mg</td>
<td>Once daily%</td>
</tr>
</tbody>
</table>

*Controlled studies did not extend beyond indicated duration.

†For patients who do not heal with lansoprazole delayed-release capsules for 8 weeks (5 to 10%), it may be helpful to give an additional 8 weeks of treatment. If there is a recurrence of erosive esophagitis, an additional 8 week course of lansoprazole delayed-release capsules may be considered.

‡The lansoprazole delayed-release capsules dose was increased (up to 30 mg twice daily) in some pediatric patients after 2 or more weeks of treatment if they remained symptomatic. For pediatric patients unable to swallow an intact capsule please see Administration Options.

¶Varies with individual patient. Recommended adult starting dose is 60 mg once daily. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Dosages up to 90 mg twice daily have been administered. Daily dose of greater than 120 mg should be administered in divided doses. Some patients with Zollinger-Ellison Syndrome have been treated continuously with lansoprazole delayed-release capsules for more than 4 years.

2.2 Special Populations

Renal impairment patients and geriatric patients do not require dosage adjustment. However, consider dose adjustment in patients with severe liver impairment. [See Use in Specific Populations (8.5, 8.6 and 8.7)]

2.3 Important Administration Information

**Administration Options**

**Lansoprazole Delayed-Release Capsules - Oral Administration**

- Lansoprazole delayed-release capsules should be swallowed whole.
- Alternatively, for patients who have difficulty swallowing capsules, lansoprazole delayed-release capsules can be opened and administered as follows:
  - Open capsule.
  - Sprinkle intact granules on one tablespoon of either applesauce, ENSURE® pudding, cottage cheese, yogurt or strained pears.
  - Swallow immediately.
• Lansoprazole Delayed-Release Capsules may also be emptied into a small volume of either apple juice, orange juice or tomato juice and administered as follows:
• Open capsule.
• Sprinkle intact granules into a small volume of either apple juice, orange juice or tomato juice (60 mL – approximately 2 ounces).
• Mix briefly.
• Swallow immediately.
• To ensure complete delivery of the dose, the glass should be rinsed with two or more volumes of juice and the contents swallowed immediately.

Lansoprazole Delayed-Release Capsules - Nasogastric Tube (≥ 16 French) Administration
• For patients who have a nasogastric tube in place, lansoprazole delayed-release capsules can be administered as follows:
• Open capsule.
• Mix intact granules into 40 mL of apple juice. DO NOT USE OTHER LIQUIDS.
• Inject through the nasogastric tube into the stomach.
• Flush with additional apple juice to clear the tube.

USE IN OTHER FOODS AND LIQUIDS HAS NOT BEEN STUDIED CLINICALLY AND IS THEREFORE NOT RECOMMENDED.

3 DOSAGE FORMS AND STRENGTHS
• Lansoprazole delayed release capsules USP, 15 mg are white to pale yellow colored enteric coated pellets filled in size ‘3’ hard gelatin capsules with opaque pink colored cap and opaque green colored body, imprinted ‘RDY’ on cap and ‘398’ on body with white ink.

• Lansoprazole delayed release capsules USP, 30 mg are white to pale yellow colored enteric coated pellets filled in size ‘1’ hard gelatin capsules with opaque pink colored cap and opaque black colored body, imprinted ‘RDY’ on cap and ‘399’ on body with white ink.

4 CONTRAINDICATIONS
Lansoprazole delayed-release capsules are contraindicated in patients with known severe hypersensitivity to any component of the formulation of lansoprazole delayed-release capsules.

5 WARNINGS AND PRECAUTIONS
5.1 Gastric Malignancy
Symptomatic response to therapy with lansoprazole does not preclude the presence of gastric malignancy.

5.2 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 (6.2)].
For information on warnings and precautions for amoxicillin or clarithromycin, refer to their full prescribing information, WARNINGS and PRECAUTIONS sections.

6 ADVERSE REACTIONS
6.1 Clinical
Worldwide, over 10,000 patients have been treated with lansoprazole delayed-release capsules in Phase 2 or Phase 3 clinical trials involving various dosages and durations of treatment. In general, lansoprazole delayed-release capsules treatment has been well-tolerated in both short-term and long-term trials.
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 clinical practice. The following adverse reactions were reported by the treating physician to have a possible or probable relationship to drug in 1% or more of lansoprazole delayed-release capsules-treated patients and occurred at a greater rate in lansoprazole delayed-release capsules-treated patients than placebo-treated patients in Table 1.
Table 1: Incidence of Possibly or Probably Treatment-Related Adverse Reactions in Short-Term, Placebo-Controlled lansoprazole delayed-release capsules Studies

<table>
<thead>
<tr>
<th>Body System/Adverse Event</th>
<th>lansoprazole delayed-release capsules (N= 2768) %</th>
<th>Placebo (N= 1023) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a Whole</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>2.1</td>
<td>1.2</td>
</tr>
<tr>
<td>Digestive System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>1.0</td>
<td>0.4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Nausea</td>
<td>1.3</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Headache was also seen at greater than 1% incidence but was more common on placebo. The incidence of diarrhea was similar between patients who received placebo and patients who received 15 mg and 30 mg of lansoprazole delayed-release capsules, but higher in the patients who received 60 mg of lansoprazole delayed-release capsules (2.9%, 1.4%, 4.2%, and 7.4%, respectively). The most commonly reported possibly or probably treatment-related adverse event during maintenance therapy was diarrhea.

In the risk reduction study of lansoprazole delayed-release capsules for NSAID-associated gastric ulcers, the incidence of diarrhea for patients treated with lansoprazole delayed-release capsules, misoprostol, and placebo was 5%, 22%, and 3%, respectively.

Another study for the same indication, where patients took either a COX-2 inhibitor or lansoprazole and naproxen, demonstrated that the safety profile was similar to the prior study. Additional reactions from this study not previously observed in other clinical trials with lansoprazole delayed-release capsules included contusion, duodenitis, epigastric discomfort, esophageal disorder, fatigue, hunger, hiatal hernia, hoarseness, impaired gastric emptying, metaplasia, and renal impairment.

Additional adverse experiences occurring in less than 1% of patients or subjects who received lansoprazole delayed-release capsules in domestic trials are shown below:

- **Body as a Whole** – abdomen enlarged, allergic reaction, asthenia, back pain, candidiasis, carcinoma, chest pain (not otherwise specified), chills, edema, fever, flu syndrome, halitosis, infection (not otherwise specified), malaise, neck pain, neck rigidity, pain, pelvic pain
- **Cardiovascular System** – angina, arrhythmia, bradycardia, cerebrovascular accident/cerebral infarction, hypertension/hypotension, migraine, myocardial infarction, palpitations, shock (circulatory failure), syncope, tachycardia, vasodilation
- **Digestive System** – abnormal stools, anorexia, bezoar, cardiopasm, cholelithiasis, colitis, dry mouth, dyspepsia, dysphagia, enteritis, eructation, esophageal stenosis, esophageal ulcer, esophagitis, fecal discoloration, flatulence, gastric nodules/fundic gland polyps, gastritis, gastroenteritis, gastrointestinal anomaly, gastrointestinal disorder, gastrointestinal hemorrhage, glossitis, gum hemorrhage, hematemesis, increased appetite, increased salivation, melena, mouth ulceration, nausea and vomiting, nausea and vomiting and diarrhea, gastrointestinal moniliasis, rectal disorder, rectal hemorrhage, stomatitis, tenesmus, thirst, tongue disorder, ulcerative colitis, ulcerative stomatitis
- **Endocrine System** – diabetes mellitus, goiter, hypothyroidism
- **Hemic and Lymphatic System** – anemia, hemolysis, lymphadenopathy
- **Metabolic and Nutritional Disorders** – avitaminosis, gout, dehydration, hyperglycemia/hypoglycemia, peripheral edema, weight gain/loss
- **Musculoskeletal System** – arthralgia, arthritis, bone disorder, joint disorder, leg cramps, musculoskeletal pain, myalgia, myasthenia, ptosis, synovitis
- **Nervous System** – abnormal dreams, agitation, amnesia, anxiety, apathy, confusion, convulsion, dementia, depersonalization, depression, diplopia, dizziness, emotional lability, hallucinations, hemiplegia, hostility aggravated, hypertonia, hypesthesia, insomnia, libido decreased/increased, nervousness, neurosis, paresthesia, sleep disorder, somnolence, thinking abnormality, tremor, vertigo
- **Respiratory System** – asthma, bronchitis, cough increased, dyspnea, epistaxis, hemoptysis, hiccup, laryngeal neoplasia, lung fibrosis, pharyngitis, pleural disorder, pneumonia, respiratory disorder, upper respiratory inflammation/infection, rhinitis, sinusitis, stridor
- **Skin and Appendages** – acne, alopecia, contact dermatitis, dry skin, fixed eruption, hair disorder, maculopapular rash, nail disorder, pruritus, rash, skin carcinoma, skin disorder, sweating, urticaria
- **Special Senses** – abnormal vision, amblyopia, blepharitis, blurred vision, cataract, conjunctivitis, deafness, dry eyes, ear.eye disorder, eye pain, glaucoma, otitis media, parosmia, photophobia, retinal degeneration/disorder, taste loss, taste perversion, tinnitus, visual field defect
- **Urogenital System** – abnormal menses, breast enlargement, breast pain, breast tenderness, dysmenorrhea, dysuria, gynecomastia, impotence, kidney calculus, kidney pain, leukorrhea, menorrhagia, menstrual disorder, penis disorder, polyuria, testis disorder, urethral pain, urinary frequency, urinary retention, urinary tract infection, urinary urgency, urination impaired, vaginitis.
6.2 Postmarketing Experience
Additional adverse experiences have been reported since lansoprazole delayed-release capsules has been marketed. The majority of these cases are foreign-sourced and a relationship to lansoprazole delayed-release capsules has not been established. Because these reactions were reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events are listed below by COSTART body system.

Body as a Whole – anaphylactic/anaphylactoid reactions; Digestive System - hepatotoxicity, pancreatitis, vomiting; Hemic and Lymphatic System - agranulocytosis, aplastic anemia, hemolytic anemia, leukopenia, neutropenia, pancytopenia, thrombocytopenia, and thrombotic thrombocytopenic purpura; Musculoskeletal System - bone fracture, myositis; Skin and Appendages – severe dermatologic reactions including erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (some fatal); Special Senses - speech disorder; Urogenital System – interstitial nephritis, urinary retention.

6.3 Combination Therapy with Amoxicillin and Clarithromycin
In clinical trials using combination therapy with lansoprazole delayed-release capsules plus amoxicillin and clarithromycin, and lansoprazole delayed-release capsules plus amoxicillin, no adverse reactions peculiar to these drug combinations were observed. Adverse reactions that have occurred have been limited to those that had been previously reported with lansoprazole delayed-release capsules, amoxicillin, or clarithromycin.

Triple Therapy: Lansoprazole delayed-release capsules /amoxicillin/clarithromycin
The most frequently reported adverse reactions for patients who received triple therapy for 14 days were diarrhea (7%), headache (6%), and taste perversion (5%). There were no statistically significant differences in the frequency of reported adverse reactions between the 10 and 14 day triple therapy regimens. No treatment-emergent adverse reactions were observed at significantly higher rates with triple therapy than with any dual therapy regimen.

Dual Therapy: Lansoprazole delayed-release capsules /amoxicillin
The most frequently reported adverse reactions for patients who received lansoprazole delayed-release capsules three times daily plus amoxicillin three times daily dual therapy were diarrhea (8%) and headache (7%). No treatment-emergent adverse reactions were observed at significantly higher rates with lansoprazole delayed-release capsules three times daily plus amoxicillin three times daily dual therapy than with lansoprazole delayed-release capsules alone.

6.4 Laboratory Values
The following changes in laboratory parameters in patients who received lansoprazole delayed-release capsules were reported as adverse reactions:
Abnormal liver function tests, increased SGOT (AST), increased SGPT (ALT), increased creatinine, increased alkaline phosphatase, increased globulins, increased GGTP, increased/decreased/abnormal WBC, abnormal AG ratio, abnormal RBC, bilirubinemia, blood potassium increased, blood urea increased, crystal urine present, eosinophilia, hemoglobin decreased, hyperlipemia, increased/decreased electrolytes, increased/decreased cholesterol, increased glucocorticoids, increased LDH, increased/decreased/abnormal platelets, increased gastrin levels and positive fecal occult blood. Urine abnormalities such as albuminuria, glycosuria, and hematuria were also reported. Additional isolated laboratory abnormalities were reported.
In the placebo controlled studies, when SGOT (AST) and SGPT (ALT) were evaluated, 0.4% (4/978) and 0.4% (11/2677) patients, who received placebo and lansoprazole delayed-release capsules, respectively, had enzyme elevations greater than three times the upper limit of normal range at the final treatment visit. None of these patients who received lansoprazole delayed-release capsules reported jaundice at any time during the study.
In clinical trials using combination therapy with lansoprazole delayed-release capsules plus amoxicillin and clarithromycin, and lansoprazole delayed-release capsules plus amoxicillin, no increased laboratory abnormalities particular to these drug combinations were observed.
For information on laboratory value changes with amoxicillin or clarithromycin, refer to their full prescribing information, ADVERSE REACTIONS sections.

7 DRUG INTERACTIONS
Drugs with pH-Dependent Absorption Kinetics
Lansoprazole delayed-release capsules causes long-lasting inhibition of gastric acid secretion. Lansoprazole delayed-release capsules and other PPIs are likely to substantially decrease the systemic concentrations of the HIV protease inhibitor atazanavir, which is dependent upon the presence of gastric acid for absorption, and may result in a loss of therapeutic effect of atazanavir and the development of HIV resistance. Therefore, lansoprazole delayed-release capsules and other PPIs should not be co-administered with atazanavir. [See Clinical Pharmacology (12.5)]

It is theoretically possible that lansoprazole delayed-release capsules and other PPIs may interfere with the absorption of other drugs where gastric pH is an important determinant of oral bioavailability (e.g., ampicillin esters, digoxin, iron salts, ketoconazole). [See Clinical Pharmacology (12.5)]

Warfarin
In a study of healthy subjects, co-administration of single or multiple 60 mg doses of lansoprazole delayed-release capsules and warfarin did not affect the pharmacokinetics of warfarin nor prothrombin time (see Clinical Pharmacology (12.5). However, there have been reports of increased INR and prothrombin time in patients receiving PPIs and warfarin concomitantly. Increases in INR and
prothrombin time may lead to abnormal bleeding and even death. Patients treated with PPIs and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time. [See Clinical Pharmacology (12.5)]

**Tacrolimus**
Concomitant administration of lansoprazole and tacrolimus may increase whole blood levels of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19.

**Theophylline**
A minor increase (10%) in the clearance of theophylline was observed following the administration of lansoprazole delayed-release capsules concomitantly with theophylline. Although the magnitude of the effect on theophylline clearance is small, individual patients may require additional titration of their theophylline dosage when lansoprazole delayed-release capsules is started or stopped to ensure clinically effective blood levels. [See Clinical Pharmacology (12.5)]

For information on drug interactions for amoxicillin or clarithromycin, refer to their full prescribing information, DRUG INTERACTIONS sections.

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

**Teratogenic effects**

Pregnancy Category B. Reproduction studies have been performed in pregnant rats at oral doses up to 40 times the recommended human dose and in pregnant rabbits at oral doses up to 16 times the recommended human dose and have revealed no evidence of impaired fertility or harm to the fetus due to lansoprazole. There are, however, no adequate or 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 [See Nonclinical Toxicology (13.2)].

See full prescribing information for clarithromycin before using in pregnant women.

#### 8.3 Nursing Mothers

Lansoprazole or its metabolites are excreted in the milk of rats. It is not known whether lansoprazole is excreted in human milk. Because many drugs are excreted in human milk, because of the potential for serious adverse reactions in nursing infants from lansoprazole, and because of the potential for tumorigenicity shown for lansoprazole in rat carcinogenicity studies, a decision should be made whether to discontinue nursing or to discontinue lansoprazole, taking into account the importance of lansoprazole to the mother.

#### 8.4 Pediatric Use

The safety and effectiveness of lansoprazole delayed-release capsules have been established in pediatric patients 1 to 17 years of age for short-term treatment of symptomatic GERD and erosive esophagitis.

**One to 11 years of age**

In an uncontrolled, open-label, U.S. multicenter study, 66 pediatric patients (1 to 11 years of age) with GERD were assigned, based on body weight, to receive an initial dose of either lansoprazole delayed-release capsules 15 mg daily if ≤ 30 kg or lansoprazole delayed-release capsules 30 mg daily if greater than 30 kg administered for 8 to 12 weeks. The lansoprazole delayed-release capsules dose was increased (up to 30 mg twice daily) in 24 of 66 pediatric patients after 2 or more weeks of treatment if they remained symptomatic. At baseline 85% of patients had mild to moderate overall GERD symptoms (assessed by investigator interview), 58% had non-erosive GERD and 42% had erosive esophagitis (assessed by endoscopy).

After 8 to 12 weeks of lansoprazole delayed-release capsules treatment, the intent-to-treat analysis demonstrated an approximate 50% reduction in frequency and severity of GERD symptoms.

Twenty-one of 27 erosive esophagitis patients were healed at 8 weeks and 100% of patients were healed at 12 weeks by endoscopy (Table 2).

**Table 2: GERD symptom improvement and Erosive Esophagitis healing rates in pediatric patients age 1 to 11**

<table>
<thead>
<tr>
<th>GERD</th>
<th>Final Visit † % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic GERD</td>
<td>76% (47/62 ‡)</td>
</tr>
<tr>
<td>Improvement in Overall GERD Symptoms †</td>
<td></td>
</tr>
<tr>
<td>Erosive Esophagitis</td>
<td>81% (22/27)</td>
</tr>
<tr>
<td>Improvement in Overall GERD Symptoms †</td>
<td>100% (27/27)</td>
</tr>
<tr>
<td>Healing Rate</td>
<td></td>
</tr>
</tbody>
</table>
In a study of 66 pediatric patients in the age group 1 year to 11 years old after treatment with lansoprazole delayed-release capsules given orally in doses of 15 mg daily to 30 mg twice daily, increases in serum gastrin levels were similar to those observed in adult studies. Median fasting serum gastrin levels increased 89% from 51 pg/mL at baseline to 97 pg/mL [interquartile range (25th–75th percentile) of 71-130 pg/mL] at the final visit.

The pediatric safety of lansoprazole delayed-release capsules has been assessed in 66 pediatric patients aged 1 to 11 years of age. Of the 66 patients with GERD 85% (56/66) took lansoprazole delayed-release capsules for 8 weeks and 15% (10/66) took it for 12 weeks.

The most frequently reported (2 or more patients) treatment-related adverse reactions in patients 1 to 11 years of age (N=66) were constipation (5%) and headache (3%).

**Twelve to 17 years of age**

In an uncontrolled, open-label, U.S. multicenter study, 87 adolescent patients (12 to 17 years of age) with symptomatic GERD were treated with lansoprazole delayed-release capsules for 8 to 12 weeks. Baseline upper endoscopies classified these patients into two groups: 64 (74%) nonerosive GERD and 23 (26%) erosive esophagitis (EE). The nonerosive GERD patients received lansoprazole delayed-release capsules 15 mg daily for 8 weeks and the EE patients received lansoprazole delayed-release capsules 30 mg daily for 8 to 12 weeks. At baseline, 89% of these patients had mild to moderate overall GERD symptoms (assessed by investigator interviews). During 8 weeks of lansoprazole delayed-release capsules treatment, adolescent patients experienced a 63% reduction in frequency and a 69% reduction in severity of GERD symptoms based on diary results.

Twenty-one of 22 (95.5%) adolescent erosive esophagitis patients were healed after 8 weeks of lansoprazole delayed-release capsules treatment. One patient remained unhealed after 12 weeks of treatment (Table 3).

Table 3: GERD symptom improvement and Erosive Esophagitis healing rates in pediatric patients age 12 to 17

<table>
<thead>
<tr>
<th>GERD</th>
<th>Final Visit % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic GERD (All Patients)</td>
<td></td>
</tr>
<tr>
<td>Improvement in Overall GERD Symptoms *</td>
<td>73.2% (60/82) †</td>
</tr>
<tr>
<td>Nonerosive GERD</td>
<td></td>
</tr>
<tr>
<td>Improvement in Overall GERD Symptoms *</td>
<td>71.2% (42/59) †</td>
</tr>
<tr>
<td>Erosive Esophagitis</td>
<td></td>
</tr>
<tr>
<td>Improvement in Overall GERD Symptoms *</td>
<td>78.3% (18/23)</td>
</tr>
<tr>
<td>Healing Rate ‡</td>
<td>95.5% (21/22) ‡</td>
</tr>
</tbody>
</table>

*Symptoms assessed by patient diary (parents/caregivers as necessary).
†No data available for 5 patients.
‡Data from one healed patient was excluded from this analysis due to timing of final endoscopy.

In these 87 adolescent patients, increases in serum gastrin levels were similar to those observed in adult studies, median fasting serum gastrin levels increased 42% from 45 pg/mL at baseline to 64 pg/mL [interquartile range (25th – 75th percentile) of 44 – 88 pg/mL] at the final visit. (Normal serum gastrin levels are 25 to 111 pg/mL).

The safety of lansoprazole delayed-release capsules has been assessed in these 87 adolescent patients. Of the 87 adolescent patients with GERD, 6% (5/87) took lansoprazole delayed-release capsules for less than 6 weeks, 93% (81/87) for 6-10 weeks, and 1% (1/87) for greater than 10 weeks.

The most frequently reported (at least 3%) treatment-related adverse reactions in these patients were headache (7%), abdominal pain (5%), nausea (3%) and dizziness (3%). Treatment-related dizziness, reported in this package insert as occurring in less than 1% of adult patients, was reported in this study by 3 adolescent patients with nonerosive GERD, who had dizziness concurrently with other reactions (such as migraine, dyspnea, and vomiting).
8.5 Geriatric Use
No dosage adjustment of lansoprazole delayed-release capsules is necessary in geriatric patients. The incidence rates of lansoprazole delayed-release capsules-associated adverse reactions and laboratory test abnormalities are similar to those seen in younger patients. [See Clinical Pharmacology (12.4)]

8.6 Renal Impairment
No dosage adjustment of lansoprazole delayed-release capsules is necessary in patients with renal impairment. The pharmacokinetics of lansoprazole in patients with various degrees of renal impairment were not substantially different compared to those in subjects with normal renal function. [See Clinical Pharmacology (12.4)]

8.7 Hepatic Impairment
In patients with various degrees of chronic hepatic impairment, an increase in the mean AUC of up to 500% was observed at steady state compared to healthy subjects. Consider dose reduction in patients with severe hepatic impairment. [See Clinical Pharmacology (12.4)]

8.8 Gender
Over 4,000 women were treated with lansoprazole delayed-release capsules. Ulcer healing rates in females were similar to those in males. The incidence rates of adverse reactions in females were similar to those seen in males. [See Clinical Pharmacology (12.4)]

8.9 Race
The pooled mean pharmacokinetic parameters of lansoprazole delayed-release capsules from twelve U.S. Phase 1 studies (N=513) were compared to the mean pharmacokinetic parameters from two Asian studies (N=20). The mean AUCs of lansoprazole delayed-release capsules in Asian subjects were approximately twice those seen in pooled U.S. data; however, the inter-individual variability was high. The C\textsubscript{max} values were comparable.

10 OVERDOSAGE
Lansoprazole delayed-release capsules are not removed from the circulation by hemodialysis. In one reported overdose, a patient consumed 600 mg of lansoprazole delayed-release capsules with no adverse reaction. Oral lansoprazole delayed-release capsules doses up to 5000 mg/kg in rats [approximately 1300 times the 30 mg human dose based on body surface area BSA)] and in mice (about 675.7 times the 30 mg human dose based on (BSA) did not produce deaths or any clinical signs.

11 DESCRIPTION
The active ingredient in lansoprazole delayed-release capsules USP is lansoprazole USP, a substituted benzimidazole, 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl] sulfinyl] benzimidazole, a compound that inhibits gastric acid secretion. Its empirical formula is C\textsubscript{16}H\textsubscript{14}F\textsubscript{3}N\textsubscript{3}O\textsubscript{2}S with a molecular weight of 369.37. Lansoprazole USP has the following structure:

Lansoprazole USP is a white to brownish-white powder which melts with decomposition at approximately 166°C. Lansoprazole USP is freely soluble in dimethylformamide and practically insoluble in water. Lansoprazole USP is stable when exposed to light for up to two months. The rate of degradation of the compound in aqueous solution increases with decreasing pH. The degradation half-life of the drug substance in aqueous solution at 25°C is approximately 0.5 hour at pH 5.0 and approximately 18 hours at pH 7.0. Lansoprazole USP is supplied as delayed-release capsules. The delayed-release capsules are available in two dosage strengths: 15 mg and 30 mg of lansoprazole USP per capsule. Each delayed-release capsule contains enteric-coated granules consisting of 15 mg or 30 mg of lansoprazole USP (active ingredient) and the following inactive ingredients: ammonium hydroxide, hydroxypropyl cellulose, low substituted hydroxypropyl cellulose, magnesium carbonate, methacrylic acid copolymer, polyethylene glycol, polysorbate 80, propylene glycol, shellac, simethicone, starch, sucrose, sugar spheres, talc, and titanium dioxide. Components of the gelatin capsule include gelatin, iron oxide red, iron oxide yellow, FD&C Blue 2, sodium lauryl sulphate and titanium dioxide for 15 mg capsules and gelatin, iron oxide black, iron oxide red, iron oxide yellow, sodium lauryl sulphate and titanium dioxide for 30 mg capsules.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Lansoprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that suppress gastric acid secretion by specific inhibition of the (H\textsuperscript{+}, K\textsuperscript{+})-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 parietal cell, lansoprazole 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 gastric acid secretion irrespective of the stimulus. Lansoprazole does not exhibit anticholinergic or histamine type-2 antagonist activity.

12.2 Pharmacodynamics

*Antisecretory Activity:* After oral administration, lansoprazole was shown to significantly decrease the basal acid output and significantly increase the mean gastric pH and percent of time the gastric pH was greater than 3 and greater than 4. Lansoprazole also significantly reduced meal-stimulated gastric acid output and secretion volume, as well as pentagastrin-stimulated acid output. In patients with hypersecretion of acid, lansoprazole significantly reduced basal and pentagastrin-stimulated gastric acid secretion. Lansoprazole inhibited the normal increases in secretion volume, acidity and acid output induced by insulin.

The intragastric pH results of a five-day, pharmacodynamic, crossover study of 15 mg and 30 mg of once daily lansoprazole are presented in Table 4:

**Table 4: Mean Antisecretory Effects After Single and Multiple Daily Lansoprazole Dosing**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline Value</th>
<th>Lansoprazole</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>15 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Day 1</td>
</tr>
<tr>
<td>Mean 24-Hour pH</td>
<td>2.1</td>
<td>2.7*</td>
</tr>
<tr>
<td>Mean Nighttime pH</td>
<td>1.9</td>
<td>2.4</td>
</tr>
<tr>
<td>% Time Gastric pH &gt; 3</td>
<td>18</td>
<td>33*</td>
</tr>
<tr>
<td>% Time Gastric pH &gt; 4</td>
<td>12</td>
<td>22*</td>
</tr>
</tbody>
</table>

NOTE: An intragastric pH of greater than 4 reflects a reduction in gastric acid by 99%.

*(p<0.05) versus baseline only.
†(p<0.05) versus baseline and lansoprazole 15 mg.

After the initial dose in this study, increased gastric pH was seen within 1 to 2 hours with 30 mg of lansoprazole and 2 to 3 hours with 15 mg of lansoprazole. After multiple daily dosing, increased gastric pH was seen within the first hour post-dosing with 30 mg of lansoprazole and within 1 to 2 hours post-dosing with 15 mg of lansoprazole.

Acid suppression may enhance the effect of antimicrobials in eradicating Helicobacter pylori (*H. pylori*). The percentage of time gastric pH was elevated above 5 and 6 was evaluated in a crossover study of lansoprazole delayed-release capsules given daily, twice daily and three times daily (Table 5).

**Table 5: Mean Antisecretory Effects After 5 Days of twice daily and three times daily Dosing**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Lansoprazole</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 mg daily</td>
</tr>
<tr>
<td>% Time Gastric pH &gt; 5</td>
<td>43</td>
</tr>
<tr>
<td>% Time Gastric pH &gt; 6</td>
<td>20</td>
</tr>
</tbody>
</table>

*(p<0.05) versus lansoprazole 30 mg daily
†(p<0.05) versus lansoprazole 30 mg daily, 15 mg twice daily and 30 mg twice daily.

The inhibition of gastric acid secretion as measured by intragastric pH gradually returned to normal over two to four days after multiple doses. There was no indication of rebound gastric acidity.

*Enterochromaffin-like (ECL) Cell Effects*

During lifetime exposure of rats with up to 150 mg/kg/day of lansoprazole dosed seven days per week, marked hypergastrinemia was observed followed by ECL cell proliferation and formation of carcinoid tumors, especially in female rats. Gastric biopsy specimens from the body of the stomach from approximately 150 patients treated continuously with lansoprazole for at least one year did not show evidence of ECL cell effects similar to those seen in rat studies. Longer term data are needed to rule out the possibility of an increased risk of the development of gastric tumors in patients receiving long-term therapy with lansoprazole. [See *Nonclinical Toxicology* (13.1)]

*Other Gastric Effects in Humans*

Lansoprazole did not significantly affect mucosal blood flow in the fundus of the stomach. Due to the normal physiologic effect caused by the inhibition of gastric acid secretion, a decrease of about 17% in blood flow in the antrum, pylorus, and duodenal bulb
was seen. Lansoprazole significantly slowed the gastric emptying of digestible solids. Lansoprazole increased serum pepsinogen levels and decreased pepsin activity under basal conditions and in response to meal stimulation or insulin injection. As with other agents that elevate intragastric pH, increases in gastric pH were associated with increases in nitrate-reducing bacteria and elevation of nitrite concentration in gastric juice in patients with gastric ulcer. No significant increase in nitrosamine concentrations was observed.

**Serum Gastrin Effects**

In over 2100 patients, median fasting serum gastrin levels increased 50% to 100% from baseline but remained within normal range after treatment with 15 to 60 mg of oral lansoprazole. These elevations reached a plateau within two months of therapy and returned to pretreatment levels within four weeks after discontinuation of therapy.

**Endocrine Effects**

Human studies for up to one year have not detected any clinically significant effects on the endocrine system. Hormones studied include testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH), sex hormone binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEA-S), prolactin, cortisol, estradiol, insulin, aldosterone, parathormone, glucagon, thyroid stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), and somatotropic hormone (STH). Lansoprazole in oral doses of 15 to 60 mg for up to one year had no clinically significant effect on sexual function. In addition, lansoprazole in oral doses of 15 to 60 mg for two to eight weeks had no clinically significant effect on thyroid function. In 24-month carcinogenicity studies in Sprague-Dawley rats with daily lansoprazole dosages up to 150 mg/kg, proliferative changes in the Leydig cells of the testes, including benign neoplasm, were increased compared to control rats.

**Other Effects**

No systemic effects of lansoprazole on the central nervous system, lymphoid, hematopoietic, renal, hepatic, cardiovascular, or respiratory systems have been found in humans. Among 56 patients who had extensive baseline eye evaluations, no visual toxicity was observed after lansoprazole treatment (up to 180 mg/day) for up to 58 months. After lifetime lansoprazole exposure in rats, focal pancreatic atrophy, diffuse lymphoid hyperplasia in the thymus, and spontaneous retinal atrophy were seen.

**Microbiology**

Lansoprazole, clarithromycin and/or amoxicillin have been shown to be active against most strains of Helicobacter pylori *in vitro* and in clinical infections as described in the INDICATIONS AND USAGE section. [See Indications and Usage (1.2)]

**Helicobacter pylori Pretreatment Resistance**

Clarithromycin pretreatment resistance (≥2.0 mcg/mL) was 9.5% (91/960) by E-test and 11.3% (12/106) by agar dilution in the dual and triple therapy clinical trials (M93-125, M93-130, M93-131, M95-392, and M95-399).

Amoxicillin pretreatment susceptible isolates (≤0.25 mcg/mL) occurred in 97.8% (936/957) and 98% (98/100) of the patients in the dual and triple therapy clinical trials by E-test and agar dilution, respectively. Twenty-one of 957 patients (2.2%) by E-test and 2 of 100 patients (2%) by agar dilution had amoxicillin pretreatment MICs of greater than 0.25 mcg/mL. One patient on the 14-day triple therapy regimen had an unconfirmed pretreatment amoxicillin minimum inhibitory concentration (MIC) of greater than 256 mcg/mL by E-test and the patient was eradicated of *H. pylori* (Table 6).

---

**Table 6: Clarithromycin Susceptibility Test Results and Clinical/Bacteriological Outcomes**

<table>
<thead>
<tr>
<th>Clarithromycin Pretreatment Results</th>
<th>Clarithromycin Post-treatment Results</th>
<th><em>H. pylori</em> negative - eradicated</th>
<th><em>H. pylori</em> positive - note eradicated</th>
<th>Post-treatment susceptibility results</th>
<th>No MIC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H. pylori positive</td>
<td>S†</td>
<td>I†</td>
<td>R†</td>
<td>No MIC</td>
</tr>
<tr>
<td>Triple Therapy 14-day (lansoprazole 30 mg twice daily/amoxicillin 1 g twice daily/clarithromycin 500 mg twice daily) (M95-399, M93-131, M95-392)</td>
<td>Susceptible†</td>
<td>112</td>
<td>105</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Intermediate†</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resistant†</td>
<td>17</td>
<td>6</td>
<td>7</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Triple Therapy 10-Day (lansoprazole 30 mg twice daily/amoxicillin 1 g twice daily/clarithromycin 500 mg twice daily) (M95-399)</td>
<td>Susceptible†</td>
<td>42</td>
<td>40</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Intermediate†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Resistant† 4 1

*Includes only patients with pretreatment clarithromycin susceptibility test results

†Susceptible (S) MIC ≤ 0.25 mcg/mL, Intermediate (I) MIC 0.5 - 1 mcg/mL, Resistant (R) MIC ≥ 2 mcg/mL

Patients not eradicated of H. pylori following lansoprazole/amoxicillin/clarithromycin triple therapy will likely have clarithromycin resistant H. pylori. Therefore, for those patients who fail therapy, clarithromycin susceptibility testing should be done when possible. Patients with clarithromycin resistant H. pylori should not be treated with lansoprazole/amoxicillin/clarithromycin triple therapy or with regimens which include clarithromycin as the sole antimicrobial agent.

Amoxicillin Susceptibility Test Results and Clinical/Bacteriological Outcomes: In the dual and triple therapy clinical trials, 82.6% (195/236) of the patients that had pretreatment amoxicillin susceptible MICs (≤ 0.25 mcg/mL) were eradicated of H. pylori. Of those with pretreatment amoxicillin MICs of greater than 0.25 mcg/mL, three of six had the H. pylori eradicated. A total of 30% (21/70) of the patients failed lansoprazole 30 mg three times daily/amoxicillin 1 gm three times daily dual therapy and a total of 12.8% (22/172) of the patients failed the 10 and 14 day triple therapy regimens. Post-treatment susceptibility results were not obtained on 11 of the patients who failed therapy. Nine of the 11 patients with amoxicillin post-treatment MICs that failed the triple therapy regimen also had clarithromycin resistant H. pylori isolates.

Susceptibility Test for Helicobacter pylori: The reference methodology for susceptibility testing of H. pylori is agar dilution MICs. One to three microliters of an inoculum equivalent to a No. 2 McFarland standard (1 x 10⁷ to 1 x 10⁸ CFU/mL for H. pylori) are inoculated directly onto freshly prepared antimicrobial-containing Mueller-Hinton agar plates with 5% aged defibrinated sheep blood (≥ 2 weeks old). The agar dilution plates are incubated at 35°C in a microaerobic environment produced by a gas generating system suitable for campylobacters. After 3 days of incubation, the MICs are recorded as the lowest concentration of antimicrobial agent required to inhibit growth of the organism. The clarithromycin and amoxicillin MIC values should be interpreted according to the following criteria (Table 7):

<table>
<thead>
<tr>
<th>Table 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarithromycin MIC (mcg/mL)*</td>
</tr>
<tr>
<td>≤ 0.25</td>
</tr>
<tr>
<td>0.5-1</td>
</tr>
<tr>
<td>≥ 2</td>
</tr>
<tr>
<td>Amoxicillin MIC (mcg/mL)*</td>
</tr>
<tr>
<td>≤ 0.25</td>
</tr>
</tbody>
</table>

* These are tentative breakpoints for the agar dilution methodology and they should not be used to interpret results obtained using alternative methods.

† There were not enough organisms with MICs greater than 0.25 mcg/mL to determine a resistance breakpoint.

Standardized susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures. Standard clarithromycin and amoxicillin powders should provide the following MIC values (Table 8):

<table>
<thead>
<tr>
<th>Table 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microorganism</td>
</tr>
<tr>
<td>H. pylori ATCC 43504</td>
</tr>
<tr>
<td>H. pylori ATCC 43504</td>
</tr>
</tbody>
</table>

* These are quality control ranges for the agar dilution methodology and they should not be used to control test results obtained using alternative methods.

12.3 Pharmacokinetics
Lansoprazole delayed-release capsules contain an enteric-coated granule formulation of lansoprazole. Absorption of lansoprazole begins only after the granules leave the stomach. Absorption is rapid, with mean peak plasma levels of lansoprazole occurring after
approximately 1.7 hours. After a single-dose administration of 15 mg to 60 mg of oral lansoprazole, the peak plasma concentrations \( (C_{\text{max}}) \) of lansoprazole and the area under the plasma concentration curves (AUCs) of lansoprazole were approximately proportional to the administered dose. Lansoprazole does not accumulate and its pharmacokinetics are unaltered by multiple dosing.

**Absorption:** The absorption of lansoprazole is rapid, with the mean \( C_{\text{max}} \) occurring approximately 1.7 hours after oral dosing, and the absolute bioavailability is over 80%. In healthy subjects, the mean (±SD) plasma half-life was 1.5 (±1.0) hours. Both the \( C_{\text{max}} \) and AUC are diminished by about 50% to 70% if lansoprazole is given 30 minutes after food, compared to the fasting condition. There is no significant food effect if lansoprazole is given before meals.

**Distribution:** Lansoprazole is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 0.05 to 5.0 mcg/mL.

**Metabolism:** Lansoprazole is extensively metabolized in the liver. Two metabolites have been identified in measurable quantities in plasma (the hydroxylated sulfinyl and sulfone derivatives of lansoprazole). These metabolites have very little or no antisecretory activity. Lansoprazole is thought to be transformed into two active species which inhibit acid secretion by blocking the proton pump \([(H^+, K^+)-\text{ATPase} \text{ enzyme system}]\) at the secretory surface of the gastric parietal cell. The two active species are not present in the systemic circulation. The plasma elimination half-life of lansoprazole is less than 2 hours while the acid inhibitory effect lasts more than 24 hours. Therefore, the plasma elimination half-life of lansoprazole does not reflect its duration of suppression of gastric acid secretion.

**Elimination:** Following single-dose oral administration of lansoprazole delayed-release capsules, virtually no unchanged lansoprazole was excreted in the urine. In one study, after a single oral dose of \(^{14}\)C-lansoprazole, approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the feces. This implies a significant biliary excretion of the lansoprazole metabolites.

### 12.4 Specific Populations

#### Pediatric Use:

**One to 17 years of age**

The pharmacokinetics of lansoprazole were studied in pediatric patients with GERD aged 1 to 11 years and 12 to 17 years in two separate clinical studies. In children aged 1 to 11 years, lansoprazole was dosed 15 mg daily for subjects weighing ≤ 30 kg and 30 mg daily for subjects weighing greater than 30 kg. Mean \( C_{\text{max}} \) and AUC values observed on Day 5 of dosing were similar between the two dose groups and were not affected by weight or age within each weight-adjusted dose group used in the study. In adolescent subjects aged 12 to 17 years, subjects were randomized to receive lansoprazole at 15 mg or 30 mg daily. Mean \( C_{\text{max}} \) and AUC values of lansoprazole were not affected by body weight or age; and nearly dose-proportional increases in mean \( C_{\text{max}} \) and AUC values were observed between the two dose groups in the study. Overall, lansoprazole pharmacokinetics in pediatric patients aged 1 to 17 years were similar to those observed in healthy adult subjects.

**Geriatric Use:** The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased approximately 50% to 100%. Because the mean half-life in the elderly remains between 1.9 to 2.9 hours, repeated once daily dosing does not result in accumulation of lansoprazole. Peak plasma levels were not increased in the elderly. No dosage adjustment is necessary in the elderly [See Use in Specific Populations (8.5)].

**Renal Impairment:** In patients with severe renal impairment, plasma protein binding decreased by 1% to 1.5% after administration of 60 mg of lansoprazole. Patients with renal impairment had a shortened elimination half-life and decreased total AUC (free and bound). The AUC for free lansoprazole in plasma, however, was not related to the degree of renal impairment; and the \( C_{\text{max}} \) and \( t_{\text{max}} \) (time to reach the maximum concentration) were not different than the \( C_{\text{max}} \) and \( t_{\text{max}} \) from subjects with normal renal function. No dosage adjustment is necessary in patients with renal impairment [See Use in Specific Populations (8.6)].

**Hepatic Impairment:** In patients with various degrees of chronic hepatic impairment, the mean plasma half-life of lansoprazole was prolonged from 1.5 hours to 3.2 to 7.2 hours. An increase in the mean AUC of up to 500% was observed at steady state in hepatically-impaired patients compared to healthy subjects. Consider dose reduction in patients with severe hepatic impairment [See Use in Specific Populations (8.7)].

**Gender:** In a study comparing 12 male and 6 female human subjects who received lansoprazole, no gender differences were found in pharmacokinetics and intragastric pH results [See Use in Specific Populations (8.5)].

### 12.5 Drug-Drug Interactions

It is theoretically possible that lansoprazole may interfere with the absorption of other drugs where gastric pH is an important determinant of bioavailability (e.g., ketoconazole, ampicillin esters, iron salts, digoxin).
Lansoprazole is metabolized through the cytochrome P₄₅₀ system, specifically through the CYP3A and CYP2C19 isozymes. Studies have shown that lansoprazole does not have clinically significant interactions with other drugs metabolized by the cytochrome P₄₅₀ system, such as warfarin, antipyrine, indomethacin, ibuprofen, phenytoin, propranolol, prednisone, diazepam, or clarithromycin in healthy subjects. These compounds are metabolized through various cytochrome P₄₅₀ isozymes including CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A.

**Atazanavir:** Lansoprazole delayed-release capsules causes long-lasting inhibition of gastric acid secretion. lansoprazole delayed-release capsules substantially decreases the systemic concentrations of the HIV protease inhibitor atazanavir, which is dependent upon the presence of gastric acid for absorption, and may result in a loss of therapeutic effect of atazanavir and the development of HIV resistance. Therefore, lansoprazole delayed-release capsules, or other proton pump inhibitors, should not be co-administered with atazanavir.

**Theophylline:** When lansoprazole delayed-release capsules were administered concomitantly with theophylline (CYP1A2, CYP3A), a minor increase (10%) in the clearance of theophylline was seen. Because of the small magnitude and the direction of the effect on theophylline clearance, this interaction is unlikely to be of clinical concern. Nonetheless, individual patients may require additional titration of their theophylline dosage when lansoprazole delayed-release capsules is started or stopped to ensure clinically effective blood levels.

**Warfarin:** In a study of healthy subjects neither the pharmacokinetics of warfarin enantiomers nor prothrombin time were affected following single or multiple 60 mg doses of lansoprazole. However, there have been reports of increased International Normalized Ratio (INR) and prothrombin time in patients receiving proton pump inhibitors, including lansoprazole delayed-release capsules, 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 concomitantly may need to be monitored for increases in INR and prothrombin time.

**Methotrexate and 7-hydromethotrexate:** In an open-label, single-arm, eight-day, pharmacokinetic study of 28 adult rheumatoid arthritis patients (who required the chronic use of 7.5 to 15 mg of methotrexate given weekly), administration of 7 days of naproxen 500 mg twice daily and lansoprazole delayed-release capsules 30 mg daily had no effect on the pharmacokinetics of methotrexate and 7-hydmoxymethotrexate. While this study was not designed to assess the safety of this combination of drugs, no major adverse reactions were noted.

**Amoxicillin:** Lansoprazole delayed-release capsules has also been shown to have no clinically significant interaction with amoxicillin.

**Sucralfate:** In a single-dose crossover study examining lansoprazole delayed-release capsules 30 mg and omeprazole 20 mg each administered alone and concomitantly with sucralfate 1 gram, absorption of the proton pump inhibitors was delayed and their bioavailability was reduced by 17% and 16%, respectively, when administered concomitantly with sucralfate. Therefore, proton pump inhibitors should be taken at least 30 minutes prior to sucralfate. In clinical trials, antacids were administered concomitantly with lansoprazole delayed-release capsules and there was no evidence of a change in the efficacy of lansoprazole delayed-release capsules.

### 13 Nonclinical Toxicology

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In two 24-month carcinogenicity studies, Sprague-Dawley rats were treated with oral lansoprazole doses of 5 to 150 mg/kg/day – about 1 to 40 times the exposure on a body surface (mg/m²) basis of a 50 kg person of average height [1.46 m² body surface area (BSA)] given the recommended human dose of 30 mg/day. Lansoprazole produced dose-related gastric enterochromaffin-like (ECL) cell hyperplasia and ECL cell carcinoids in both male and female rats. It also increased the incidence of intestinal metaplasia of the gastric epithelium in both sexes. In male rats, lansoprazole produced a dose-related increase of testicular interstitial cell adenomas. The incidence of these adenomas in rats receiving doses of 15 to 150 mg/kg/day (4 to 40 times the recommended human dose based on BSA) exceeded the low background incidence (range = 1.4 to 10%) for this strain of rat.

In a 24-month carcinogenicity study, CD-1 mice were treated with oral lansoprazole doses of 15 to 600 mg/kg/day, 2 to 80 times the recommended human dose based on BSA. Lansoprazole produced a dose-related increased incidence of gastric ECL cell hyperplasia. It also produced an increased incidence of liver tumors (hepatocellular adenoma plus carcinoma). The tumor incidences in male mice treated with 300 and 600 mg/kg/day (40 to 80 times the recommended human dose based on BSA) and female mice treated with 150 to 600 mg/kg/day (20 to 80 times the recommended human dose based on BSA) exceeded the ranges of background incidences in historical controls for this strain of mice. Lansoprazole treatment produced adenoma of rete testis in male mice receiving 75 to 600 mg/kg/day (10 to 80 times the recommended human dose based on BSA).

A 26-week p53 (+/-) transgenic mouse carcinogenicity study was not positive. Lansoprazole was not genotoxic in the Ames test, the *ex vivo* rat hepatocyte unscheduled DNA synthesis (UDS) test, the *in vivo* mouse micronucleus test, or the rat bone marrow cell chromosomal aberration test. It was positive in *in vitro* human lymphocyte chromosomal aberration assays.

Lansoprazole at oral doses up to 150 mg/kg/day (40 times the recommended human dose based on BSA) was found to have no effect on fertility and reproductive performance of male and female rats.
13.2 Animal Toxicology and/or Pharmacology

Reproductive Toxicology Studies

Reproduction studies have been performed in pregnant rats at oral lansoprazole doses up to 150 mg/kg/day [40 times the recommended human dose (30 mg/day) based on body surface area (BSA)] and pregnant rabbits at oral lansoprazole doses up to 30 mg/kg/day (16 times the recommended human dose based on BSA) and have revealed no evidence of impaired fertility or harm to the fetus due to lansoprazole.

14 CLINICAL STUDIES

Duodenal Ulcer

In a U.S. multicenter, double-blind, placebo-controlled, dose-response (15, 30, and 60 mg of lansoprazole delayed-release capsules once daily) study of 284 patients with endoscopically documented duodenal ulcer, the percentage of patients healed after two and four weeks was significantly higher with all doses of lansoprazole delayed-release capsules than with placebo. There was no evidence of a greater or earlier response with the two higher doses compared with lansoprazole delayed-release capsules 15 mg. Based on this study and the second study described below, the recommended dose of lansoprazole delayed-release capsules in duodenal ulcer is 15 mg per day (Table 9).

Table 9: Duodenal Ulcer Healing Rates

<table>
<thead>
<tr>
<th>Week</th>
<th>Lansoprazole 15 mg daily (N=68)</th>
<th>Lansoprazole 30 mg daily (N=74)</th>
<th>Lansoprazole 60 mg daily (N=70)</th>
<th>Placebo (N=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>42.4%*</td>
<td>35.6%*</td>
<td>39.1%*</td>
<td>11.3%</td>
</tr>
<tr>
<td>4</td>
<td>89.4%*</td>
<td>91.7%*</td>
<td>89.9%*</td>
<td>46.1%</td>
</tr>
</tbody>
</table>

*(p≤0.001) versus placebo.

Lansoprazole delayed-release capsules 15 mg was significantly more effective than placebo in relieving day and nighttime abdominal pain and in decreasing the amount of antacid taken per day.

In a second U.S. multicenter study, also double-blind, placebo-controlled, dose-comparison (15 and 30 mg of lansoprazole delayed-release capsules once daily), and including a comparison with ranitidine, in 280 patients with endoscopically documented duodenal ulcer, the percentage of patients healed after four weeks was significantly higher with both doses of lansoprazole delayed-release capsules than with placebo. There was no evidence of a greater or earlier response with the higher dose of lansoprazole delayed-release capsules. Although the 15 mg dose of lansoprazole delayed-release capsules was superior to ranitidine at 4 weeks, the lack of significant difference at 2 weeks and the absence of a difference between 30 mg of lansoprazole delayed-release capsules and ranitidine leaves the comparative effectiveness of the two agents undetermined (Table 10).

Table 10: Duodenal Ulcer Healing Rates

<table>
<thead>
<tr>
<th>Week</th>
<th>Lansoprazole 15 mg daily (N=80)</th>
<th>Lansoprazole 30 mg daily (N=77)</th>
<th>Ranitidine 300 mg h.s. (N=82)</th>
<th>Placebo (N=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>35.0%</td>
<td>44.2%</td>
<td>30.5%</td>
<td>34.2%</td>
</tr>
<tr>
<td>4</td>
<td>92.3%*</td>
<td>80.3%†</td>
<td>70.5%†</td>
<td>47.5%</td>
</tr>
</tbody>
</table>

*(p≤0.05) versus placebo and ranitidine.
†(p≤0.05) versus placebo.

H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence

Randomized, double-blind clinical studies performed in the U.S. in patients with H. pylori and duodenal ulcer disease (defined as an active ulcer or history of an ulcer within one year) evaluated the efficacy of lansoprazole delayed-release capsules in combination with amoxicillin capsules and clarithromycin tablets as triple 14 day therapy or in combination with amoxicillin capsules as dual 14 day therapy for the eradication of H. pylori. Based on the results of these studies, the safety and efficacy of two different eradication regimens were established:

Triple therapy: Lansoprazole delayed-release capsules 30 mg twice daily / amoxicillin 1 gm twice daily / clarithromycin 500 mg twice daily
Dual therapy: Lansoprazole delayed-release capsules 30 mg three times daily / amoxicillin 1 gm three times daily

All treatments were for 14 days. H. pylori eradication was defined as two negative tests (culture and histology) at 4 to 6 weeks following the end of treatment. Triple therapy was shown to be more effective than all possible dual therapy combinations. Dual therapy was shown to be more effective than both monotherapies. Eradication of H. pylori has been shown to reduce the risk of duodenal ulcer recurrence. A randomized, double-blind clinical study performed in the U.S. in patients with H. pylori and duodenal ulcer disease (defined as an active ulcer or history of an ulcer within one year) compared the efficacy of lansoprazole triple therapy...
for 10 and 14 days. This study established that the 10-day triple therapy was equivalent to the 14-day triple therapy in eradicating H. pylori (Tables 11 and 12). [See Indications and Usage (1.2)]

### Table 11 H. pylori Eradication Rates – Triple Therapy (Lansoprazole amoxicillin/clarithromycin) Percent of Patients Cured [95% Confidence Interval]

(Selected patients)

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration</th>
<th>Triple Therapy Evaluable Analysis*</th>
<th>Triple Therapy Intent-to-Treat Analysis#</th>
</tr>
</thead>
<tbody>
<tr>
<td>M93-131</td>
<td>14 days</td>
<td>92 [80-97.7] (N=48)</td>
<td>86 [73.3-93.5] (N=55)</td>
</tr>
<tr>
<td>M95-392</td>
<td>14 days</td>
<td>86 [75.7-93.6] (N=66)</td>
<td>83 [72-90.8] (N=70)</td>
</tr>
<tr>
<td>M95-399*</td>
<td>14 days</td>
<td>85 [77-91] (N=113)</td>
<td>82 [73.9-88.1] (N=126)</td>
</tr>
<tr>
<td></td>
<td>10 days</td>
<td>84 [76-89.8] (N=123)</td>
<td>81 [73.9-87.6] (N=135)</td>
</tr>
</tbody>
</table>

*Based on evaluable patients with confirmed duodenal ulcer (active or within one year) and H. pylori infection at baseline defined as at least two of three positive endoscopic tests from CLOtest, histology and/or culture. Patients were included in the analysis if they completed the study. Additionally, if patients dropped out of the study due to an adverse event related to the study drug, they were included in the evaluable analysis as failures of therapy.

# Patients were included in the analysis if they had documented H. pylori infection at baseline as defined above and had a confirmed duodenal ulcer (active or within one year). All dropouts were included as failures of therapy.

†(p<0.05) versus lansoprazole/amoxicillin and lansoprazole/clarithromycin dual therapy.

‡(p<0.05) versus clarithromycin/amoxicillin dual therapy.

The 95% confidence interval for the difference in eradication rates, 10-day minus 14-day is (-10.5, 8.1) in the evaluable analysis and (-9.7, 9.1) in the intent-to-treat analysis.

### Table 12 H. pylori Eradication Rates – 14-Day Dual Therapy (lansoprazole/amoxicillin) Percent of Patients Cured [95% Confidence Interval]

(Selected patients)

<table>
<thead>
<tr>
<th>Study</th>
<th>Dual Therapy Evaluable Analysis*</th>
<th>Dual Therapy Intent-to-Treat Analysis#</th>
</tr>
</thead>
<tbody>
<tr>
<td>M93-131</td>
<td>77 [62.5-87.2] (N=51)</td>
<td>70 [56.8-81.2] (N=60)</td>
</tr>
<tr>
<td>M93-125</td>
<td>66 [51.9-77.5] (N=58)</td>
<td>61 [48.5-72.9] (N=67)</td>
</tr>
</tbody>
</table>

*Based on evaluable patients with confirmed duodenal ulcer (active or within one year) and H. pylori infection at baseline defined as at least two of three positive endoscopic tests from CLOtest, histology and/or culture. Patients were included in the analysis if they completed the study. Additionally, if patients dropped out of the study due to an adverse event related to the study drug, they were included in the analysis as failures of therapy.

# Patients were included in the analysis if they had documented H. pylori infection at baseline as defined above and had a confirmed duodenal ulcer (active or within one year). All dropouts were included as failures of therapy.

†(p<0.05) versus lansoprazole alone.

‡(p<0.05) versus lansoprazole alone or amoxicillin alone.

### Long-Term Maintenance Treatment of Duodenal Ulcers

lansoprazole delayed-release capsules has been shown to prevent the recurrence of duodenal ulcers. Two independent, double-blind, multicenter, controlled trials were conducted in patients with endoscopically confirmed healed duodenal ulcers. Patients remained healed significantly longer and the number of recurrences of duodenal ulcers was significantly less in patients treated with lansoprazole delayed-release capsules than in patients treated with placebo over a 12-month period (Table 13). [See Indications and Usage (1.3)]

### Table 13: Endoscopic Remission Rates

<table>
<thead>
<tr>
<th>Trial</th>
<th>Drug</th>
<th>No. of Pts.</th>
<th>0-3 mo.</th>
<th>0-6 mo.</th>
<th>0-12 mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>lansoprazole delayed-release capsules 15 mg daily</td>
<td>86</td>
<td>90%*</td>
<td>87%*</td>
<td>84%*</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>83</td>
<td>49%</td>
<td>41%</td>
<td>39%</td>
</tr>
<tr>
<td>#2</td>
<td>lansoprazole delayed-release capsules 30 mg daily</td>
<td>18</td>
<td>94%*</td>
<td>94%*</td>
<td>85%*</td>
</tr>
<tr>
<td></td>
<td>lansoprazole delayed-release capsules 15 mg daily</td>
<td>15</td>
<td>87%*</td>
<td>79%*</td>
<td>70%*</td>
</tr>
</tbody>
</table>
In trial #2, no significant difference was noted between lansoprazole delayed-release capsules 15 mg and 30 mg in maintaining remission.

**Gastric Ulcer**

In a U.S. multicenter, double-blind, placebo-controlled study of 253 patients with endoscopically documented gastric ulcer, the percentage of patients healed at four and eight weeks was significantly higher with lansoprazole delayed-release capsules 15 mg and 30 mg once a day than with placebo (Table 14). [See Indications and Usage (1.4)]

Table 14: Gastric Ulcer Healing Rates

<table>
<thead>
<tr>
<th>Week</th>
<th>15 mg daily (N=65)</th>
<th>30 mg daily (N=63)</th>
<th>60 mg daily (N=61)</th>
<th>Placebo (N=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>64.6%*</td>
<td>58.1%*</td>
<td>53.3%*</td>
<td>37.5%</td>
</tr>
<tr>
<td>8</td>
<td>92.2%*</td>
<td>96.8%*</td>
<td>93.2%*</td>
<td>76.7%</td>
</tr>
</tbody>
</table>

*(p<0.05) versus placebo.

Patients treated with any lansoprazole delayed-release capsules dose reported significantly less day and night abdominal pain along with fewer days of antacid use and fewer antacid tablets used per day than the placebo group.

Independent substantiation of the effectiveness of lansoprazole delayed-release capsules 30 mg was provided by a meta-analysis of published and unpublished data.

**Healing of NSAID-Associated Gastric Ulcer**

In two U.S. and Canadian multicenter, double-blind, active-controlled studies in patients with endoscopically confirmed NSAID-associated gastric ulcer who continued their NSAID use, the percentage of patients healed after 8 weeks was statistically significantly higher with 30 mg of lansoprazole delayed-release capsules than with the active control. A total of 711 patients were enrolled in the study, and 701 patients were treated. Patients ranged in age from 18 to 88 years (median age 59 years), with 67% female patients and 33% male patients. Race was distributed as follows: 87% Caucasian, 8% Black, 5% Other. There was no statistically significant difference between lansoprazole delayed-release capsules 30 mg daily and the active control on symptom relief (i.e., abdominal pain) (Table 15). [See Indications and Usage (1.5)]

Table 15: NSAID-Associated Gastric Ulcer Healing Rates *

<table>
<thead>
<tr>
<th>Study #1</th>
<th>Lansoprazole 30 mg daily</th>
<th>Active Control ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>60% (53/88) ²</td>
<td>28% (23/83)</td>
</tr>
<tr>
<td>Week 8</td>
<td>79% (62/79) ²</td>
<td>55% (41/74)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study #2</th>
<th>Lansoprazole 30 mg daily</th>
<th>Active Control ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>53% (40/75)</td>
<td>38% (31/82)</td>
</tr>
<tr>
<td>Week 8</td>
<td>77% (47/61) ²</td>
<td>50% (33/66)</td>
</tr>
</tbody>
</table>

*Actual observed ulcer(s) healed at time points ± 2 days
†Dose for healing of gastric ulcer
‡(p<0.05) versus the active control

**Risk Reduction of NSAID-Associated Gastric Ulcer**

In one large U.S., multicenter, double-blind, placebo- and misoprostol-controlled (misoprostol blinded only to the endoscopist) study in patients who required chronic use of an NSAID and who had a history of an endoscopically documented gastric ulcer, the proportion of patients remaining free from gastric ulcer at 4, 8, and 12 weeks was significantly higher with 15 or 30 mg of lansoprazole than placebo. A total of 537 patients were enrolled in the study, and 535 patients were treated. Patients ranged in age from 23 to 89 years (median age 60 years), with 65% female patients and 35% male patients. Race was distributed as follows: 90% Caucasian, 6% Black, 4% other. The 30 mg dose of lansoprazole demonstrated no additional benefit in risk reduction of the NSAID-associated gastric ulcer than the 15 mg dose (Table 16). [See Indications and Usage (1.6)]
Table 16: Proportion of Patients Remaining Free of Gastric Ulcers *

<table>
<thead>
<tr>
<th>Week</th>
<th>Lansoprazole 15 mg daily (N=121)</th>
<th>Lansoprazole 30 mg daily (N=116)</th>
<th>Misoprostol 200 mcg four times daily (N=106)</th>
<th>Placebo (N=112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>90%</td>
<td>92%</td>
<td>96%</td>
<td>66%</td>
</tr>
<tr>
<td>8</td>
<td>86%</td>
<td>88%</td>
<td>95%</td>
<td>60%</td>
</tr>
<tr>
<td>12</td>
<td>80%</td>
<td>82%</td>
<td>93%</td>
<td>51%</td>
</tr>
</tbody>
</table>

(p<0.001) Lansoprazole 15 mg daily versus placebo; Lansoprazole 30 mg daily versus placebo; and misoprostol 200 mcg four times daily versus placebo.

(p<0.05) Misoprostol 200 mcg four times daily versus Lansoprazole 15 mg daily; and misoprostol 200 mcg four times daily versus Lansoprazole 30 mg daily.

*% = Life Table Estimate

Gastroesophageal Reflux Disease (GERD)

Symptomatic GERD: In a U.S. multicenter, double-blind, placebo-controlled study of 214 patients with frequent GERD symptoms, but no esophageal erosions by endoscopy, significantly greater relief of heartburn associated with GERD was observed with the administration of lansoprazole 15 mg once daily up to 8 weeks than with placebo. No significant additional benefit from lansoprazole 30 mg once daily was observed.

The intent-to-treat analyses demonstrated significant reduction in frequency and severity of day and night heartburn. Data for frequency and severity for the 8-week treatment period are presented in Table 17 and in Figures 1 and 2:

Table 17: Frequency of Heartburn

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (n=43)</th>
<th>Lansoprazole 15 mg (n=80)</th>
<th>Lansoprazole 30 mg (n=86)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Days without Heartburn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 1</td>
<td>0%</td>
<td>71%*</td>
<td>46%*</td>
</tr>
<tr>
<td>Week 4</td>
<td>11%</td>
<td>81%*</td>
<td>76%*</td>
</tr>
<tr>
<td>Week 8</td>
<td>13%</td>
<td>84%*</td>
<td>82%*</td>
</tr>
<tr>
<td>% of Nights without Heartburn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 1</td>
<td>17%</td>
<td>86%*</td>
<td>57%*</td>
</tr>
<tr>
<td>Week 4</td>
<td>25%</td>
<td>89%*</td>
<td>73%*</td>
</tr>
<tr>
<td>Week 8</td>
<td>36%</td>
<td>92%*</td>
<td>80%*</td>
</tr>
</tbody>
</table>

*(p<0.01) versus placebo.

Figure 1

Figure 2

In two U.S., multicenter double-blind, ranitidine-controlled studies of 925 total patients with frequent GERD symptoms, but no esophageal erosions by endoscopy, lansoprazole 15 mg was superior to ranitidine 150 mg (twice daily) in decreasing the frequency
and severity of day and night heartburn associated with GERD for the 8-week treatment period. No significant additional benefit from lansoprazole 30 mg once daily was observed. [See Indications and Usage (1.7)]

**Erosive Esophagitis**

In a U.S. multicenter, double-blind, placebo-controlled study of 269 patients entering with an endoscopic diagnosis of esophagitis with mucosal grading of 2 or more and grades 3 and 4 signifying erosive disease, the percentages of patients with healing are presented in Table 18:

**Table 18: Erosive Esophagitis Healing Rates**

<table>
<thead>
<tr>
<th>Week</th>
<th>Lansoprazole</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15 mg daily</td>
<td>30 mg daily</td>
</tr>
<tr>
<td>4</td>
<td>(N=69)</td>
<td>(N=65)</td>
</tr>
<tr>
<td></td>
<td>67.6%*</td>
<td>81.3%*†</td>
</tr>
<tr>
<td>6</td>
<td>87.7%*</td>
<td>95.4%*</td>
</tr>
<tr>
<td>8</td>
<td>90.9%*</td>
<td>95.4%*</td>
</tr>
</tbody>
</table>

*(p<0.001) versus placebo. †(p<0.05) versus lansoprazole 15 mg.

In this study, all lansoprazole groups reported significantly greater relief of heartburn and less day and night abdominal pain along with fewer days of antacid use and fewer antacid tablets taken per day than the placebo group. Although all doses were effective, the earlier healing in the higher two doses suggests 30 mg daily as the recommended dose.

Lansoprazole was also compared in a U.S. multicenter, double-blind study to a low dose of ranitidine in 242 patients with erosive reflux esophagitis. Lansoprazoles at a dose of 30 mg was significantly more effective than ranitidine 150 mg twice daily as shown below (Table 19).

**Table 19: Erosive Esophagitis Healing Rates**

<table>
<thead>
<tr>
<th>Week</th>
<th>Lansoprazole 30 mg daily</th>
<th>Ranitidine 150 mg twice daily</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=115)</td>
<td>(N=127)</td>
</tr>
<tr>
<td>2</td>
<td>66.7%*</td>
<td>38.7%</td>
</tr>
<tr>
<td>4</td>
<td>82.5%*</td>
<td>52.0%</td>
</tr>
<tr>
<td>6</td>
<td>93.0%*</td>
<td>67.8%</td>
</tr>
<tr>
<td>8</td>
<td>92.1%*</td>
<td>69.9%</td>
</tr>
</tbody>
</table>

*(p<0.001) versus ranitidine.

In addition, patients treated with lansoprazole reported less day and nighttime heartburn and took less antacid tablets for fewer days than patients taking ranitidine 150 mg twice daily. Although this study demonstrates effectiveness of lansoprazole in healing erosive esophagitis, it does not represent an adequate comparison with ranitidine because the recommended ranitidine dose for esophagitis is 150 mg four times daily, twice the dose used in this study.

In the two trials described and in several smaller studies involving patients with moderate to severe erosive esophagitis, lansoprazole produced healing rates similar to those shown above.

In a U.S. multicenter, double-blind, active-controlled study, 30 mg of lansoprazole was compared with ranitidine 150 mg twice daily in 151 patients with erosive reflux esophagitis that was poorly responsive to a minimum of 12 weeks of treatment with at least one H2-receptor antagonist given at the dose indicated for symptom relief or greater, namely, cimetidine 800 mg/day, ranitidine 300 mg/day, famotidine 40 mg/day or nizatidine 300 mg/day. Lansoprazole 30 mg was more effective than ranitidine 150 mg twice daily in healing reflux esophagitis, and the percentage of patients with healing were as follows. This study does not constitute a comparison of the effectiveness of histamine H2-receptor antagonists with lansoprazole, as all patients had demonstrated unresponsiveness to the histamine H2-receptor antagonist mode of treatment. It does indicate, however, that lansoprazole may be useful in patients failing on a histamine H2-receptor antagonist (Table 20). [See Indications and Usage (1.7)]

**Table 20: Reflux Esophagitis Healing Rates in Patients Poorly Responsive to Histamine H2-Receptor Antagonist Therapy**

<table>
<thead>
<tr>
<th>Week</th>
<th>Lansoprazole 30 mg daily</th>
<th>Ranitidine 150 mg twice daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>74.7%*</td>
<td>42.6%</td>
</tr>
</tbody>
</table>

*(p<0.001) versus ranitidine.
**Long-Term Maintenance Treatment of Erosive Esophagitis**

Two independent, double-blind, multicenter, controlled trials were conducted in patients with endoscopically confirmed healed esophagitis. Patients remained in remission significantly longer and the number of recurrences of erosive esophagitis was significantly less in patients treated with lansoprazole than in patients treated with placebo over a 12-month period (Table 21).

### Table 21: Endoscopic Remission Rates

<table>
<thead>
<tr>
<th>Trial</th>
<th>Drug</th>
<th>No. of Pts.</th>
<th>0-3 mo.</th>
<th>0-6 mo.</th>
<th>0-12 mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>Lansoprazole 15 mg daily</td>
<td>59</td>
<td>83%*</td>
<td>81%*</td>
<td>79%*</td>
</tr>
<tr>
<td></td>
<td>Lansoprazole 30 mg daily</td>
<td>56</td>
<td>93%*</td>
<td>93%*</td>
<td>90%*</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>55</td>
<td>31%</td>
<td>27%</td>
<td>24%</td>
</tr>
<tr>
<td>#2</td>
<td>Lansoprazole 15 mg daily</td>
<td>50</td>
<td>74%*</td>
<td>72%*</td>
<td>67%*</td>
</tr>
<tr>
<td></td>
<td>Lansoprazole 30 mg daily</td>
<td>49</td>
<td>75%*</td>
<td>72%*</td>
<td>55%*</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>47</td>
<td>16%</td>
<td>13%</td>
<td>13%</td>
</tr>
</tbody>
</table>

*% = Life Table Estimate

*(p ≤ 0.001) versus placebo.

Regardless of initial grade of erosive esophagitis, lansoprazole 15 mg and 30 mg were similar in maintaining remission. In a U.S., randomized, double-blind, study, lansoprazole 15 mg daily (n = 100) was compared with ranitidine 150 mg twice daily (n = 106), at the recommended dosage, in patients with endoscopically-proven healed erosive esophagitis over a 12-month period. Treatment with lansoprazoles resulted in patients remaining healed (Grade 0 lesions) of erosive esophagitis for significantly longer periods of time than those treated with ranitidine (p < 0.001). In addition, lansoprazoles was significantly more effective than ranitidine in providing complete relief of both daytime and nighttime heartburn. Patients treated with lansoprazoles remained asymptomatic for a significantly longer period of time than patients treated with ranitidine. [See Indications and Usage (1.8)]

### Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome

In open studies of 57 patients with pathological hypersecretory conditions, such as Zollinger-Ellison syndrome (ZES) with or without multiple endocrine adenomas, lansoprazole significantly inhibited gastric acid secretion and controlled associated symptoms of diarrhea, anorexia and pain. Doses ranging from 15 mg every other day to 180 mg per day maintained basal acid secretion below 10 mEq/hr in patients without prior gastric surgery and below 5 mEq/hr in patients with prior gastric surgery.

Initial doses were titrated to the individual patient need, and adjustments were necessary with time in some patients. [See Dosage and Administration (2.1)] lansoprazole was well tolerated at these high dose levels for prolonged periods (greater than four years in some patients). In most ZES patients, serum gastrin levels were not modified by lansoprazole. However, in some patients, serum gastrin increased to levels greater than those present prior to initiation of lansoprazole therapy. [See Indications and Usage (1.9)]

### 15 REFERENCE


### 16 HOW SUPPLIED/STORAGE AND HANDLING

Lansoprazole delayed release capsules USP, 15 mg are white to pale yellow colored enteric coated pellets filled in size ‘3’ hard gelatin capsules with opaque pink colored cap and opaque green colored body, imprinted ‘RDY’ on cap and ‘398’ on body with white ink. They are supplied in bottles of 30’s, 60’s, 90’s, 100’s, 500’s and unit dose package of 10 (1 x 10).

Bottles of 30    NDC 55111-398-30
Bottles of 60    NDC 55111-398-60
Bottles of 90    NDC 55111-398-90
Bottles of 100   NDC 55111-398-01
Bottles of 500   NDC 55111-398-05
Unit Dosage Package of 10 (1x10)  NDC 55111-398-79

Lansoprazole delayed release capsules USP, 30 mg are white to pale yellow colored enteric coated pellets filled in size ‘1’ hard gelatin capsules with opaque pink colored cap and opaque black colored body, imprinted ‘RDY’ on cap and ‘399’ on body with white ink. They are supplied in bottles of 30’s, 60’s, 90’s, 100’s, 500’s and unit dose package of 10 (1 x 10).

Bottles of 30    NDC 55111-399-30
Bottles of 60    NDC 55111-399-60
Bottles of 90    NDC 55111-399-90
Store at 20°–25° C (68°–77° F); [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION
Patient should be informed of the following:

17.1 Information for Patients
Lansoprazole is available as a capsule and is available in 15 mg and 30 mg strengths. Directions for use specific to the route and available methods of administration is presented below. [See Dosage and Administration (2.3)]
- Lansoprazole should be taken before eating.
- Lansoprazole products SHOULD NOT BE CRUSHED OR CHEWED.

Administration Options

1 Lansoprazole Delayed-Release Capsules
- Lansoprazole delayed-release capsules should be swallowed whole.
- Alternatively, for patients who have difficulty swallowing capsules, lansoprazole delayed-release capsules can be opened and administered as follows:
  - Open capsule.
  - Sprinkle intact granules on one tablespoon of either applesauce, ENSURE pudding, cottage cheese, yogurt or strained pears.
  - Swallow immediately.
- Lansoprazole
  - Open capsule.
  - Sprinkle intact granules into a small volume of either apple juice, orange juice or tomato juice (60 mL – approximately 2 ounces).
  - Mix briefly.
  - Swallow immediately.
  - To ensure complete delivery of the dose, the glass should be rinsed with two or more volumes of juice and the contents swallowed immediately.
- Lansoprazole delayed-release capsules – Nasogastric Tube (≥16 French) Administration
  - For patients who have a nasogastric tube in place, lansoprazole delayed-release capsules can be administered as follows:
    - Open capsule.
    - Mix intact granules into 40 mL of apple juice. DO NOT USE OTHER LIQUIDS.
    - Inject through the nasogastric tube into the stomach.
    - Flush with additional apple juice to clear the tube.

USE IN OTHER FOODS AND LIQUIDS HAS NOT BEEN STUDIED CLINICALLY AND IS THEREFORE NOT RECOMMENDED.

FDA-APPROVED PATIENT LABELING
Patient Information
Lansoprazole Delayed-Release Capsules USP

Read the information that comes with lansoprazole delayed-release capsules before you start taking it 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 are lansoprazole delayed-release capsules?
Lansoprazole delayed-release capsules are a prescription medicine called a proton pump inhibitor (PPI). Lansoprazole delayed-release capsules reduces the amount of acid in your stomach.

Lansoprazole delayed-release capsules are used in adults:
• for 4 weeks to heal ulcers in the first part of the small bowel (duodenal ulcers).
• for up to 12 months to stop healed duodenal ulcers from coming back. for up to 8 weeks to heal stomach ulcers.
• for up to 8 weeks to heal stomach ulcers in some people taking medicines called non-steroidal anti-inflammatory drugs (NSAIDs).
• for reducing the risk of stomach ulcers in some people taking NSAIDs.
• for reducing the risk of stomach infections (Helicobacter pylori), along with antibiotics amoxicillin and clarithromycin.
• for up to 8 weeks for the relief of heartburn and other symptoms of gastroesophageal reflux disease (GERD).

GERD happens when acid from your stomach enters 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. In some cases, acid can damage the lining of your esophagus. This damage is called erosive esophagitis.
• for 8 weeks to heal the acid-related damage to the lining of the esophagus (called erosive esophagitis) and to relieve symptoms, such as heartburn pain. If needed, your doctor may prescribe an additional 8 weeks of lansoprazole delayed-release capsules.
• to stop erosive esophagitis from coming back (studies lasted 12 months).
• for the long-term treatment of conditions where your stomach makes too much acid. This includes a condition called Zollinger-Ellison syndrome.

Lansoprazole delayed-release capsules are used in children and adolescents (ages 1 to 17):
• for up to 12 weeks to treat GERD and erosive esophagitis, in children 1 to 11 years old.
• for up to 8 weeks to treat GERD and erosive esophagitis, in adolescents 12 to 17 years old.

Lansoprazole delayed-release capsules are not recommended for children under the age of 1 year.
Lansoprazole delayed-release capsules may help your acid-related symptoms, but you could still have serious stomach problems. Talk with your doctor.

Who should not take lansoprazole delayed-release capsules?
Do not take lansoprazole delayed-release capsules if you are allergic to lansoprazole delayed-release capsules or any of its ingredients. See the end of this leaflet for a complete list of ingredients in lansoprazole delayed-release capsules.

What should I tell my doctor before taking lansoprazole delayed-release capsules?
Before you take lansoprazole delayed-release capsules, tell your doctor if you:
• have liver problems
• have any other medical conditions
• are pregnant or plan to become pregnant. It is not known if lansoprazole delayed-release capsules will harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant.
• are breast-feeding or planning to breast-feed. You and your doctor should decide if you will take lansoprazole delayed-release capsules or breast-feed. You should not do both without first talking with your doctor.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Lansoprazole delayed-release capsules may affect how other medicines work, and other medicines may affect how lansoprazole delayed-release capsules works. Especially tell your doctor if you take:
• ampicillin sodium (Unasyn) or ampicillin trihydrate (Principen)
• atazanavir (Reyataz)
• digoxin (Lanoxicaps, Lanoxin)
• a product that contains iron
• ketoconazole (Nizoral)
• warfarin (Coumadin, Jantoven)
• tacrolimus (Prograf)
• theophylline (Theo-24, Theolair)

Ask your doctor or pharmacist if you are not sure if your medicine is listed above.

How should I take lansoprazole delayed-release capsules?
• Take lansoprazole delayed-release capsules exactly as prescribed by your doctor.

• Do not change your dose or stop taking lansoprazole delayed-release capsules without talking to your doctor first.

• You should take lansoprazole delayed-release capsules before eating.

• Lansoprazole delayed-release capsules can be swallowed whole, do not crush or chew them. They can also be opened and sprinkled into approximately ¼ cup apple, tomato or orange juice, or on 1 tablespoon applesauce, Ensure® pudding, cottage cheese, yogurt or strained pears only. See “Patient Instructions for Use” at the end of this leaflet for instructions on how to take lansoprazole delayed-release capsules with these foods, and how to mix and give lansoprazole delayed-release capsules through a nasogastric tube.

• If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose. Just take the next dose at your regular time. Do not take 2 doses at the same time. If you are not sure about dosing, call your doctor.

• If you take too much lansoprazole delayed-release capsules, call your doctor right away.

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

Serious allergic reactions. Tell your doctor if you get any of the following symptoms with lansoprazole delayed-release capsules.
• rash
• face swelling
• throat tightness
• difficulty breathing

Your doctor may stop lansoprazole delayed-release capsules if these symptoms happen.

The most common side effects of lansoprazole delayed-release capsules in adults and children include:
• diarrhea
• stomach pain
• nausea
• constipation
• headache
• dizziness

People who are taking multiple daily doses of proton pump inhibitor medicines for a long period of time may have an increased risk of fractures of the hip, wrist or spine.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of lansoprazole delayed-release capsules. For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

How should I store lansoprazole delayed-release capsules?
• Store lansoprazole delayed-release capsules at room temperature between 20° to 25° C (68° to 77° F)

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

General information about lansoprazole delayed-release capsules
Medicines are sometimes prescribed for conditions other than those listed in a Patient Information Leaflet. Do not use lansoprazole delayed-release capsules for conditions for which it was not prescribed. Do not give lansoprazole delayed-release capsules to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information Leaflet provides a summary of the most important information about lansoprazole 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, call 1-888-375-3784.

**Patient Instructions for Use**

**Lansoprazole Delayed-Release Capsules**

* Swallow lansoprazole delayed-release capsules whole. Do not crush or chew them.

* If you have trouble swallowing a whole capsule, you can open the capsule and take it with the foods or juices listed below.

For taking lansoprazole delayed-release capsules with applesauce, ENSURE pudding, cottage cheese, yogurt or strained pears:

- Open the capsule.
- Sprinkle the granules on one tablespoon of either applesauce, ENSURE pudding, cottage cheese, yogurt or strained pears.
- Swallow right away.

For taking lansoprazole delayed-release capsules with apple juice, orange juice or tomato juice:

- Open the capsule.
- Sprinkle the granules into 60 mL (about ¼ cup) of either apple juice, orange juice or tomato juice.
- Stir briefly.
- Swallow right away.
- To make sure that the entire dose is taken, rinse the glass with 1/2 cup or more of juice to get out any leftover granules. Swallow the juice right away.

For giving lansoprazole delayed-release capsules through a nasogastric tube (NG tube) ≥16 French, as prescribed by your doctor:

- Open the capsule and empty the granules into a syringe. Do not break or crush the granules.
- Mix with 40 mL of apple juice. DO NOT USE OTHER LIQUIDS.
- Attach the syringe to the NG tube and give the medicine in the syringe through the NG tube into the stomach.
- After giving the granules, flush the NG tube with more apple juice to clear the tube.

USE IN OTHER FOODS AND LIQUIDS IS NOT RECOMMENDED.

**What is in lansoprazole delayed-release capsules?**

**Active ingredient:** Lansoprazole.

**Inactive ingredients in lansoprazole delayed-release capsules:**

Ammonium hydroxide, hydroxypropyl cellulose, low substituted hydroxypropyl cellulose, magnesium carbonate, methacrylic acid copolymer, polyethylene glycol, polysorbate 80, propylene glycol, shellac, simethicone, starch, sucrose, sugar spheres, talc, and titanium dioxide.

Components of the gelatin capsule include gelatin, iron oxide red, iron oxide yellow, FD&C Blue 2, sodium lauryl sulphate and titanium dioxide for 15 mg capsules and gelatin, iron oxide black, iron oxide red, iron oxide yellow, sodium lauryl sulphate and titanium dioxide for 30 mg capsules.

To reorder additional Patient Information Leaflets, please contact Dr. Reddy's Customer Service at 1-866-733-3952.

All trademark names are the property of their respective owners.

Rx only

Manufactured by:

**Dr. Reddy's Laboratories Limited**

Bachepalli – 502 325 INDIA

Issued: 0910

**PACKAGE LABEL.PRINCIPAL DISPLAY PANEL SECTION**

Lansoprazole Delayed- Release Capsules USP, 15 mg Container Label
Each pink and green capsule contains: 15 mg of lansoprazole USP, as enteric-coated pellets. Each capsule is imprinted with RDY and 398 for product identification. See enclosure for full prescribing information. Keep out of the reach of children. Protect from moisture. Store at 20°–25°C (68°–77°F); [See USP Controlled Room Temperature]. This unit-dose package is not child-resistant. Retain blisters in carton until time of use.
Lansoprazole Delayed-Release Capsules USP, 30 mg - Carton Label
Lansoprazole
Delayed-Release
Capsules USP, 30 mg
Rx Only

Each pink and black capsule contains: 30 mg of lansoprazole USP, as enteric-coated pellets. Each capsule is imprinted with RDY and 399 for product identification.
See enclosure for full prescribing information.
Keep out of the reach of children.
Protect from moisture.
Store at 20°-25°C (68°-77°F); [See USP Controlled Room Temperature].
This unit-dose package is not child-resistant.
Retain blisters in carton until time of use.

10 Capsules Unit Dose
(1 blistercard containing 10 capsules)

NDC 55111-399-79

Manufactured by
Dr. Reddy's Laboratories Limited
Rachapally - 502 265 INDIA

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