

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use DEXLANSOPRAZOLE DELAYED-RELEASE CAPSULES safely and effectively. See full prescribing information for DEXLANSOPRAZOLE DELAYED-RELEASE CAPSULES.

DEXLANSOPRAZOLE delayed-release capsules, for oral use Initial U. S. Approval: 1995 (lansoprazole)

RECENT MAJOR CHANGES

Warnings and Precautions, Severe Cutaneous Adverse Reactions (5.5) Hypomagnesemia and Mineral Metabolism (5.8)	03/2022 03/2022
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INDICATIONS AND USAGE

Dexlansoprazole is a proton pump inhibitor (PPI) indicated in patients 12 years of age and older for:

- Healing of all grades of erosive esophagitis (EE) (1, 1)
- Maintenance of healed EE and relief of heartburn (1, 2)
- Treatment of symptomatic non-erosive gastroesophageal reflux disease (GERD) (1, 3)

DOSE AND ADMINISTRATION

Recommended dosage in patients 12 years of age and older:

- See full prescribing information for complete dosing information for dexlansoprazole delayed-release capsules by indication and age group and dosage adjustment in patients with hepatic impairment (2.1, 2.2)

Administration Instructions (2.3)

- Take without regard to food.
- Swallow whole; do not chew.
- See full prescribing information for alternative administration options.

DOSE FORMS AND STRENGTHS

- Delayed-Release Capsules: 60 mg (3)

CONTRAINDICATIONS

- Patients with known hypersensitivity to any component of the formulation (4)
- Patients receiving rilpivirine-containing products (4, 7)

WARNINGS AND PRECAUTIONS

- **Gastric Malignancy:** In adults, symptomatic response with dexlansoprazole does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing (5.1)
- **Acute Tubulointerstitial Nephritis:** Discontinue treatment and evaluate patients (5.2)
- **Clostridium difficile-Associated Diarrhea:** PPI therapy may be associated with increased risk (5.3)

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- 1.2 Maintenance of Healed Erosive Esophagitis and Relief of Heartburn
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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Healing of Erosive Esophagitis

Dexlansoprazole delayed-release capsules are indicated in patients 12 years of age and older for healing of all grades of erosive esophagitis (EE) for up to eight weeks.

1.2 Maintenance of Healed Erosive Esophagitis and Relief of Heartburn

Dexlansoprazole delayed-release capsules are indicated in patients 12 years of age and older to maintain healing of EE and relief of heartburn for up to six months in adults and 16 weeks in patients 12 to 17 years of age.

1.3 Treatment of Symptomatic Non-Erosive Gastroesophageal Reflux Disease

Dexlansoprazole delayed-release capsules are indicated in patients 12 years of age and older for the treatment of heartburn associated with symptomatic non-erosive gastroesophageal reflux disease (GERD) for four weeks.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage in Patients 12 Years of Age and Older

Indication	Dosage of Dexlansoprazole Capsules	Duration
Healing of EE	One 60 mg capsule once daily.	Up to 8 weeks.
Maintenance of Healed EE and Relief of Heartburn	One 30 mg capsule once daily.	Controlled studies did not extend beyond 6 months in adults and 16 weeks in patients 12 to 17 years of age.
Symptomatic Non-Erosive GERD	One 30 mg capsule once daily.	4 weeks.

2.2 Dosage Adjustment in Patients with Hepatic Impairment for the Healing of Erosive Esophagitis

For patients with moderate hepatic impairment (Child-Pugh Class B), the recommended dosage is 30 mg dexlansoprazole delayed-release capsule once daily for up to eight weeks. Dexlansoprazole delayed-release capsules is not recommended in patients with severe hepatic impairment (Child-Pugh Class C) *[See Use in Specific Populations (6.6)].*

2.3 Important Administration Information

- Take without regard to food.
- Missed doses: If a dose is missed, administer as soon as possible. However, if the next scheduled dose is due, do not take the missed dose, and take the next dose on time. Do not take two doses at one time to make up for a missed dose.
- Swallow whole; do not chew.
- For patients who have trouble swallowing capsules, dexlansoprazole delayed-release capsules can be opened and administered with applesauce as follows:
 1. Place one tablespoonful of applesauce into a clean container.
 2. Open capsule.
 3. Sprinkle intact granules on applesauce.
 4. Swallow applesauce and granules immediately. Do not chew granules. Do not save the applesauce and granules for later use.
- Alternatively, the capsule can be administered with water via oral syringe or nasogastric (NG) tube.

Administration with Water in an Oral Syringe

1. Open the capsule and empty the granules into a clean container with 20 mL of water.
2. Withdraw the entire mixture into a syringe.
3. Gently swirl the syringe in order to keep granules from settling.
4. Administer the mixture immediately into the mouth. Do not save the water and granule mixture for later use.
5. Refill the syringe with 10 mL of water, swirl gently, and administer.
6. Refill the syringe again with 10 mL of water, swirl gently, and administer.

Administration with Water via a NG Tube (>16 French)

1. Open the capsule and empty the granules into a clean container with 20 mL of water.
2. Withdraw the entire mixture into a catheter-tip syringe.
3. Swirl the catheter-tip syringe gently in order to keep the granules from settling, and immediately inject the mixture through the NG tube into the stomach. Do not save the water and granule mixture for later use.
4. Refill the catheter-tip syringe with 10 mL of water, swirl gently, and flush the tube.
5. Refill the catheter-tip syringe again with 10 mL of water, swirl gently, and administer.

3 DOSAGE FORMS AND STRENGTHS

Dexlansoprazole Delayed-Release Capsules

- 60 mg strength is an opaque, green capsule with "par" imprinted on the cap and "148" imprinted on the body.

4 CONTRAINDICATIONS

- Dexlansoprazole delayed-release capsules are contraindicated in patients with known hypersensitivity to any component of the formulation *[See Description (11)]*. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, laryngospasm, acute tubulointerstitial nephritis and urticaria *[See Warnings and Precautions (5.2), Adverse Reactions (6.1), and Interactions (7)]*.
- PPIs, including dexlansoprazole delayed-release capsules, are contraindicated with rilpivirine-containing products *[See Drug Interactions (7)]*.

5 WARNINGS AND PRECAUTIONS

Dexlansoprazole Delayed-Release Capsules, 60 mg contain FD&C Yellow # 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow # 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

5.1 Presence of Gastric Malignancy

In adults, symptomatic response to therapy with dexlansoprazole does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing in adult patients who have a suboptimal response or an early symptomatic relapse after completing treatment with a PPI. In older patients, also consider an endoscopy.

5.2 Acute Tubulointerstitial Nephritis

Acute tubulointerstitial nephritis (TIN) has been observed in patients taking PPIs and may occur at any point during PPI therapy. Patients may present with varying signs and symptoms from symptomatic hypersensitivity reactions to non-specific symptoms of decreased renal function (e.g., malaise, nausea, anorexia). In reported case series, some patients were diagnosed on biopsy and in the absence of extra-renal manifestations (e.g., fever, rash or arthralgia).

Discontinue dexlansoprazole and evaluate patients with suspected acute TIN *[See Contraindications (4)]*.

5.3 *Clostridium difficile*-Associated Diarrhea

Published observational studies suggest that PPI therapy like dexlansoprazole may be associated with an increased risk of *Clostridium difficile*-associated diarrhea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve *[See Adverse Reactions (6.2)]*.

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

5.4 Bone Fracture

Several published observational studies suggest that 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 (3 year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the conditions being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines *[See Dosage and Administration (2), Adverse Reactions (6.2)]*.

5.5 Severe Cutaneous Adverse Reactions

Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with the use of PPIs *[See Adverse Reactions (6.2)]*. Discontinue dexlansoprazole delayed-release capsules at the first signs or symptoms of severe cutaneous adverse reactions or other signs of hypersensitivity and consider further evaluation.

5.6 Cutaneous and Systemic Lupus Erythematosus

Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in patients taking PPIs. These events have occurred as both new onset and an exacerbation of existing autoimmune disease. The majority of PPI-induced lupus erythematosus cases were CLE.

The most common form of CLE reported in patients treated with PPIs was subacute CLE (SACLE) and occurred within weeks to years after continuous drug therapy in patients ranging from infants to the elderly. Generally, histological findings were observed without organ involvement.

Systemic lupus erythematosus (SLE) is less commonly reported than CLE in patients receiving PPIs. PPI-associated SLE is usually milder than nondrug induced SLE. Onset of SLE typically occurred within days to years after initiating treatment primarily in patients ranging from young adults to the elderly. The majority of patients presented with rash; however, arthralgia and arthralgia were also reported.

Avoid administration of PPIs for longer than medically indicated. If signs or symptoms consistent with CLE or SLE are noted in patients receiving dexlansoprazole delayed-release capsules, discontinue the drug and refer the patient to the appropriate specialist for evaluation. Most patients improve with discontinuation of the PPI alone in 4 to 12 weeks. Serological testing (e.g., ANA) may be positive and elevated serological test results may take longer to resolve than clinical manifestations.

5.7 Cyanocobalamin (Vitamin B12) Deficiency

Daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than three years) may lead to malabsorption of cyanocobalamin (Vitamin B12) caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency are observed in patients treated with dexlansoprazole.

5.8 Hypomagnesemia and Mineral Metabolism

Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. Hypomagnesemia may lead to hypocalcemia and/or hypokalemia and may exacerbate underlying hypocalcemia in at-risk patients. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically *[See Adverse Reactions (6.2)]*.

Consider monitoring magnesium and calcium levels prior to initiation of dexlansoprazole delayed-release capsules and periodically while on treatment in patients with a preexisting risk of hypocalcemia (e.g., hypoparathyroidism). Supplement with magnesium and/or calcium as necessary. If hypocalcemia is refractory to treatment, consider discontinuing the PPI.

5.9 Interactions with Investigations for Neuroendocrine Tumors

Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors. Healthcare providers should temporarily stop dexlansoprazole treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g., for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary *[See Drug Interactions (7), Clinical Pharmacology (12.2)]*.

5.10 Interaction with Methotrexate

Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of the PPI may be considered in some patients *[See Drug Interactions (7)]*.

5.11 Fundic Gland Polyps

PPI use is associated with an increased risk of fundic gland polyps that increases with long-term use, especially beyond one year. Most PPI users who developed fundic gland polyps were asymptomatic and fundic gland polyps were identified incidentally on endoscopy. Use the shortest duration of PPI therapy appropriate to the condition being treated.

5.12 Risk of Heart Valve Thickening in Pediatric Patients Less Than Two Years of Age

Dexlansoprazole is not recommended in pediatric patients less than two years of age. Nonclinical studies in juvenile rats with lansoprazole have demonstrated an adverse effect of heart valve thickening. Dexlansoprazole is the R-enantiomer of lansoprazole *[See Use in Specific Populations (6.4)]*.

- **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 (5.4)
- **Severe Cutaneous Adverse Reactions:** Discontinue at the first signs or symptoms of severe cutaneous adverse reactions or other signs of hypersensitivity and consider further evaluation (5.5)
- **Cutaneous and Systemic Lupus Erythematosus:** Mostly cutaneous; new onset or exacerbation of existing disease; discontinue dexlansoprazole delayed-release capsules and refer to specialist for evaluation (5.6)
- **Cyanocobalamin (Vitamin B12) Deficiency:** Daily long-term use (e.g., longer than 3 years) may lead to malabsorption or a deficiency of cyanocobalamin (5.7)
- **Hypomagnesemia and Mineral Metabolism:** Reported rarely with prolonged treatment with PPIs (5.8)
- **Interactions with Investigations for Neuroendocrine Tumors:** Increases in intragastric pH may result in hypergastrinemia and enterochromaffin-like cell hyperplasia and increased chromogranin A levels which may interfere with diagnostic investigations for neuroendocrine tumors (5.9, 7)
- **Interaction with Methotrexate:** Concomitant use with PPIs may elevate and/or prolong serum concentrations of methotrexate and/or its metabolite, possibly leading to toxicity. With high-dose methotrexate administration, consider a temporary withdrawal of dexlansoprazole delayed-release capsules (5.10, 7)
- **Fundic Gland Polyps:** Risk increases with long-term use, especially beyond 1 year. Use the shortest duration of therapy (5.11)
- **Risk of Heart Valve Thickening in Pediatric Patients Less than Two Years of Age:** Dexlansoprazole is not recommended in pediatric patients less than 2 years of age (5.12, 8.4)

ADVERSE REACTIONS

The most common adverse reactions are:

- Adults (>2%): diarrhea, abdominal pain, nausea, upper respiratory tract infection, vomiting, and flatulence (6.1)
 - Pediatric: Patients 12 to 17 years of age (<5%): headache, abdominal pain, diarrhea, nasopharyngitis, and oropharyngeal pain (6.1)
- To report SUSPECTED ADVERSE REACTIONS, contact Par Pharmaceutical at 1-800-828-3393 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

See full prescribing information for a list of clinically important drug interactions (7)

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Based on animal data, may cause adverse effects on fetal bone growth and development (8.1)
- **Pediatrics:** Based on data with lansoprazole, dexlansoprazole is not effective in patients with symptomatic GERD 1 month to less than 1 year of age and nonclinical studies have demonstrated adverse effects in juvenile rats (8.4)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Table 3: Clinically Relevant Interactions Affecting Drugs Coadministered with Dexlansoprazole and Interactions with Diagnostics Continued...

Methotrexate	
<i>Clinical Impact:</i>	Concomitant use of PPIs with methotrexate (primarily at high dose) may elevate and prolong serum concentrations of methotrexate and/or its metabolite hydroxymethotrexate, possibly leading to methotrexate toxicities. No formal drug interaction studies of high-dose methotrexate with PPIs have been conducted <i>[See Warnings and Precautions (5.10)]</i> .
<i>Intervention:</i>	A temporary withdrawal of dexlansoprazole may be considered in some patients receiving high-dose methotrexate.

Digoxin	
<i>Clinical Impact:</i>	Potential for increased exposure of digoxin.
<i>Intervention:</i>	Monitor digoxin concentrations. Dose adjustment of digoxin may be needed to maintain therapeutic drug concentrations. See prescribing information for digoxin.

Drugs Dependent on Gastric pH for Absorption (e.g., iron salts, erlotinib, dasatinib, nilotinib, mycophenolate mofetil, ketoconazole/itraconazole)

<i>Clinical Impact:</i>	Dexlansoprazole can reduce the absorption of other drugs due to its effect on reducing intragastric acidity.
<i>Intervention:</i>	Mycophenolate mofetil (MMF): Coadministration of PPIs in healthy subjects and in transplant patients receiving MMF has been reported to reduce the exposure to the active metabolite, mycophenolic acid (MPA), possibly due to a decrease in MMF solubility at an increased gastric pH. The clinical relevance of reduced MPA exposure on organ rejection has not been established in transplant patients receiving dexlansoprazole and MMF. Use dexlansoprazole with caution in transplant patients receiving MMF. See the prescribing information for other drugs dependent on gastric pH for absorption.

Tacrolimus

<i>Clinical Impact:</i>	Potentially increased exposure of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19.
<i>Intervention:</i>	Monitor tacrolimus whole blood trough concentrations. Dose adjustment of tacrolimus may be needed to maintain therapeutic drug concentrations. See prescribing information for tacrolimus.

Interactions with Investigations of Neuroendocrine Tumors

<i>Clinical Impact:</i>	CgA levels increase secondary to PPI-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors <i>[See Warnings and Precautions (5.9), Clinical Pharmacology (12.2)]</i> .
<i>Intervention:</i>	Temporarily stop dexlansoprazole treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g., for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.

Interaction with Secretin Stimulation Test

<i>Clinical Impact:</i>	Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma.
<i>Intervention:</i>	Temporarily stop dexlansoprazole treatment at least 30 days before assessing to allow gastrin levels to return to baseline <i>[See Clinical Pharmacology (12.2)]</i> .

False Positive Urine Tests for THC

<i>Clinical Impact:</i>	There have been reports of false positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving PPIs.
<i>Intervention:</i>	An alternative confirmatory method should be considered to verify positive results.

Table 4: Clinically Relevant Interactions Affecting Dexlansoprazole When Coadministered with Other Drugs and Substances

CYP2C19 or CYP3A4 Inducers	
<i>Clinical Impact:</i>	Decreased exposure of dexlansoprazole when used concomitantly with strong inducers <i>[See Clinical Pharmacology (12.3)]</i> .
<i>Intervention:</i>	St. John's Wort, rifampin: Avoid concomitant use with dexlansoprazole. Ritonavir-containing products: See prescribing information.

CYP2C19 or CYP3A4 Inhibitors

<i>Clinical Impact:</i>	Increased exposure of dexlansoprazole is expected when used concomitantly with strong inhibitors <i>[See Clinical Pharmacology (12.3)]</i> .
<i>Intervention:</i>	Voriconazole: See prescribing information.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no studies with dexlansoprazole use in pregnant women to inform a drug-associated risk. Dexlansoprazole is the R-enantiomer of lansoprazole, and published observational studies of lansoprazole used during pregnancy did not demonstrate an association of adverse pregnancy-related outcomes with lansoprazole *[See Data]*.

In animal reproduction studies, oral administration of lansoprazole to rats during organogenesis through lactation at 1.8 times the maximum recommended human dexlansoprazole dose produced reductions in the offspring in femur weight, femur length, crown-rump length and growth plate thickness (males only) on postnatal Day 21 *[see Data]*. These effects were associated with reduction in body weight gain. Advise pregnant women of the potential risk to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Human Data

Dexlansoprazole is the R-enantiomer of lansoprazole. Available data from published observational studies failed to demonstrate an association of adverse pregnancy-related outcomes and lansoprazole use. Methodological limitations of these observational studies cannot definitively establish or exclude any drug-associated risk during pregnancy. In a prospective study by the European Network of Teratology Information Services, outcomes from a group of 82 pregnant women administered median daily doses of 30 mg of lansoprazole were compared to a control group of 688 pregnant women who did not take any PPIs. There was no difference in the rate of major malformations between women exposed to PPIs and the control group, corresponding to a Relative Risk (RR)=1.04, [95% Confidence Interval (CI) 0.25 to 4.21]. In a population-based retrospective cohort study covering all live births in Denmark from 1996 to 2008, there was no significant increase in major birth defects during analysis of first trimester exposure to lansoprazole in 794 live births. A meta-analysis that compared 1,530 pregnant women exposed to PPIs in at least the first trimester with 133,410 unexposed pregnant women showed no significant increase in risk for congenital malformations or spontaneous abortion with exposure to PPIs (for major malformations Odds Ratio (OR)=1.12, [95% CI 0.86 to 1.45] and for spontaneous abortions OR=1.29, [95% CI 0.84 to 1.97]).

Animal Data

An embryo-fetal development study conducted in rabbits at oral dexlansoprazole doses up to 30 mg/kg/day (approximately nine times the maximum recommended human dexlansoprazole dose [60 mg/day] based on body surface area) during organogenesis showed no effects on fetuses due to dexlansoprazole. In addition, embryo-fetal development studies performed in rats with lansoprazole at doses up to 150 mg/kg/day (40 times the recommended human lansoprazole dose based on body surface area) during organogenesis and in rabbits with oral lansoprazole at doses up to 30 mg/kg/day (16 times the recommended human lansoprazole dose based on body surface area) during organogenesis revealed no effects on fetuses due to lansoprazole.

A pre- and postnatal developmental toxicity study in rats with additional endpoints to evaluate bone development was performed with lansoprazole at oral doses of 10 to 100 mg/kg/day (0.2 to 1.8 times the maximum recommended human dexlansoprazole dose of 60 mg based on dexlansoprazole AUC [area under the plasma concentration-time curve] administered during organogenesis through lactation. Maternal effects observed at 100 mg/kg/day (1.8 times the maximum recommended human dexlansoprazole dose of 60 mg based on dexlansoprazole AUC) included increased gestation period, decreased body weight gain during gestation, and decreased food consumption. The number of stillbirths was increased at this dose, which may have been secondary to maternal toxicity. Body weight of pups was reduced at 100 mg/kg/day starting on postnatal Day 11. Femur weight, femur length, and crown-rump length were reduced at 100 mg/kg/day on postnatal Day 21. Femur weight was still decreased in the 100 mg/kg/day group at age 17 to 18 weeks. Growth plate thickness was decreased in the 100 mg/kg/day males on postnatal Day 21, and was increased in the 30 and 100 mg/kg/day males at age 17 to 18 weeks. The effects on bone parameters were associated with reduction in body weight gain.

8.2 Lactation

Risk Summary

There is no information regarding the presence of dexlansoprazole in human milk, the effects on the breastfed infant, or the effects on milk production. However, lansoprazole and its metabolites are present in rat milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for dexlansoprazole and any potential adverse effects on the breastfed child from dexlansoprazole or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of dexlansoprazole have been established in pediatric patients 12 years to 17 years of age for the healing of all grades of EE, the maintenance of healed EE, and relief of heartburn associated with symptomatic non-erosive GERD. Use of dexlansoprazole in this age group is supported by evidence from adequate and well-controlled studies of dexlansoprazole in adults with additional safety, efficacy and pharmacokinetic data in pediatric patients 12 to 17 years of age. The adverse reaction profile in patients 12 to 17 years of age was similar to adults *[See Dosage and Administration (2.1), Adverse Reactions (6.1), Clinical Pharmacology (12.3), Clinical Studies (14)]*.

The safety and effectiveness of dexlansoprazole have not been established in pediatric patients less than 12 years of age. Dexlansoprazole is not recommended in pediatric patients less than two years of age *[See Warnings and Precautions (5.12)]*. Nonclinical studies in juvenile rats treated with lansoprazole (the racemic mixture) have demonstrated adverse effects of heart valve thickening and bone changes at dexlansoprazole exposures which are expected to be similar to or higher than the dexlansoprazole exposure in pediatric patients one year to two years of age, as described below in *Juvenile Animal Toxicity Data*.

The use of dexlansoprazole is not recommended for the treatment of symptomatic GERD in pediatric patients one month to less than one year of age because lansoprazole was not shown to be effective in a multicenter, double-blind controlled trial.

Juvenile Animal Toxicity Data

Heart Valve Thickening</

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Dexlansoprazole belongs to a class of antsecretory compounds, the substituted benzimidazoles, that suppress gastric acid secretion by specific inhibition of the (H⁺, K⁺)-ATPase at the secretory surface of the gastric parietal cell. Because this enzyme is regarded as the acid (proton) pump within the parietal cell, dexlansoprazole has been characterized as a gastric proton-pump inhibitor, in that it blocks the final step of acid production.

12.2 Pharmacokinetics

Antisecretory Activity

The effects of dexlansoprazole 60 mg capsules (n=20) or lansoprazole 30 mg (n=23) once daily for five days on 24-hour intragastric pH were assessed in healthy subjects in a multiple-dose crossover study. The results are summarized in *Table 5*.

	Dexlansoprazole 60 mg capsules	Lansoprazole 30 mg
Mean Intragastric pH		
	4.55	4.13
% Time Intragastric pH > 4 (hours)		
	71 (17 hours)	60 (14 hours)

Serum Gastrin Effects

The effect of dexlansoprazole on serum gastrin concentrations was evaluated in approximately 3,480 patients in clinical trials up to eight weeks and in 1,023 patients for up to six to 12 months. The mean fasting gastrin concentrations increased from baseline during treatment with dexlansoprazole 30 mg and 60 mg capsules. In patients treated for more than six months, mean serum gastrin levels increased during approximately the first three months of treatment and were stable for the remainder of treatment. Mean serum gastrin levels returned to pretreatment levels within one month of discontinuation of treatment.

Increased gastric causes enterochromaffin-like cell hyperplasia and increased serum CgA levels. The increased CgA levels may cause false positive results in diagnostic investigations for neuroendocrine tumors. [See *Warnings and Precautions (5.9)*.]

Enterochromaffin-Like Cell (ECL) Effects

There were no reports of ECL cell hyperplasia in gastric biopsy specimens obtained from 653 patients treated with dexlansoprazole 30 mg, 60 mg or 90 mg capsules for up to 12 months.

During lifetime exposure of rats dosed daily with up to 150 mg/kg/day of lansoprazole, marked hypergastrinemia was observed followed by ECL cell proliferation and formation of carcinoid tumors, especially in female rats [see *Nonclinical Toxicology (13.1)*].

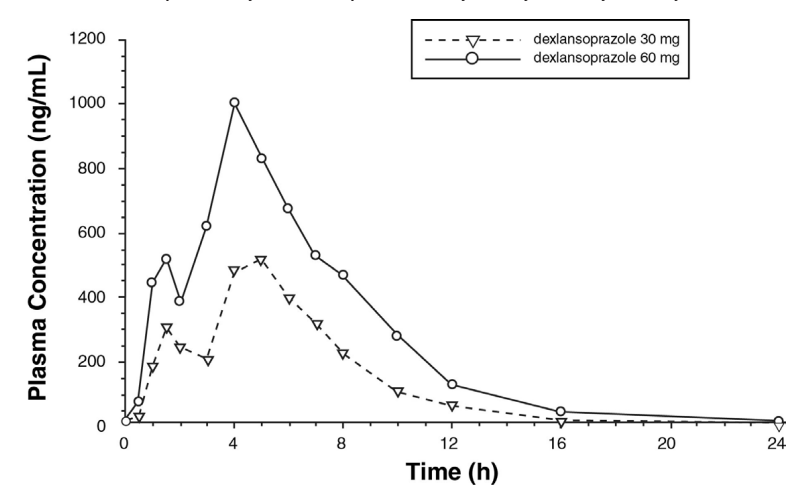
Cardiac Electrophysiology

At a dose five times the maximum recommended dose, dexlansoprazole does not prolong the QT interval to any clinically relevant extent.

12.3 Pharmacokinetics

The dual delayed-release formulation of dexlansoprazole capsules results in a dexlansoprazole plasma concentration-time profile with two distinct peaks; the first peak occurs one to two hours after administration, followed by a second peak within four to five hours (see *Figure 7*). Dexlansoprazole is eliminated with a half-life of approximately one to two hours in healthy subjects and in patients with symptomatic GERD. No accumulation of dexlansoprazole occurs after multiple, once daily doses of dexlansoprazole 30 mg or 60 mg capsules although mean AUC₀₋₂₄ and C_{max} values of dexlansoprazole were slightly higher (less than 10%) on Day 5 than on Day 1.

Figure 1: Mean Plasma Dexlansoprazole Concentration - Time Profile Following Oral Administration of 30 mg or 60 mg Dexlansoprazole Delayed-Release Capsules Once Daily for 5 Days in Healthy Adult Subjects



The pharmacokinetics of dexlansoprazole are highly variable, with percent coefficient of variation (%CV) values for C_{max}, AUC, and CL/F of greater than 30% (see *Table 6*).

Table 6: Mean (%CV) Pharmacokinetic Parameters for Adult Subjects on Day 5 After Administration of Dexlansoprazole Delayed-Release Capsules

Dose (mg)	C _{max} (ng/mL)	AUC ₀₋₂₄ (ng-h/mL)	CL/F (L/h)
30	658 (40%) (N=44)	3275 (47%) (N=43)	11.4 (48%) (N=43)
60	1,397 (51%) (N=79)	6,529 (60%) (N=73)	11.6 (46%) (N=41)

Absorption

After oral administration of dexlansoprazole 30 mg or 60 mg capsules to healthy subjects and symptomatic GERD patients, mean C_{max} and AUC values of dexlansoprazole increased approximately dose proportionally (see *Figure 1*).

When granules of dexlansoprazole 60 mg capsules are mixed with water and dosed via NG tube or orally via syringe, the bioavailability (C_{max} and AUC) of dexlansoprazole was similar to that when dexlansoprazole 60 mg was administered as an intact capsule [see *Dosage and Administration (2.3)*].

Effect on Food

In food-effect studies in healthy subjects receiving dexlansoprazole capsules under various fed conditions compared to fasting, increases in C_{max} ranged from 12 to 55%, increases in AUC ranged from 9 to 37%, and T_{max} varied (ranging from a decrease of 0.7 hours to an increase of three hours) [see *Dosage and Administration (2.3)*].

Distribution

Plasma protein binding of dexlansoprazole ranged from 96 to 99% in healthy subjects and was independent of concentration from 0.01 to 20 mcg/mL. The apparent volume of distribution (V_F) after multiple doses in symptomatic GERD patients was 40 L.

Elimination

Metabolism

Dexlansoprazole is extensively metabolized in the liver by oxidation, reduction, and subsequent formation of sulfate, glyconjugate and glutathione conjugates to inactive metabolites. Oxidative metabolites are formed by the cytochrome P450 (CYP) enzyme system including hydroxylation mainly by CYP2C19, and oxidation to the sulfone by CYP3A4.

CYP2C19 is a polymorphic liver enzyme which exhibits three phenotypes in the metabolism of CYP2C19 substrates: extensive metabolizers (*1/*1), intermediate metabolizers (*1/*mutant) and poor metabolizers (mutant/*mutant). Dexlansoprazole is the major circulating component in plasma regardless of CYP2C19 metabolizer status. In CYP2C19 intermediate and extensive metabolizers, the major plasma metabolites are 5-hydroxy dexlansoprazole and its glucuronide conjugate, while in CYP2C19 poor metabolizers dexlansoprazole sulfone is the major plasma metabolite.

Excretion

Following the administration of dexlansoprazole delayed-release capsules, no unchanged dexlansoprazole is excreted in urine. Following the administration of [¹⁴C] dexlansoprazole to six healthy male subjects, approximately 50.7% (standard deviation (SD): 9%) of the administered radioactivity was excreted in urine and 47.6% (SD: 7.3%) in the feces. Apparent clearance (CL/F) in healthy subjects was 11.4 to 11.6 L/h, respectively, after five days of 30 or 60 mg once daily administration.

Specific Populations

Age: Pediatric Population

The pharmacokinetics of dexlansoprazole in patients under the age of 12 years have not been studied.

Patients 12 to 17 Years of Age

The pharmacokinetics of dexlansoprazole were studied in 36 patients 12 to 17 years of age with symptomatic GERD in a multicenter trial. Patients were randomized to receive dexlansoprazole 30 mg or 60 mg once daily for seven days. The dexlansoprazole mean C_{max} and AUC in patients 12 to 17 years of age were 105 and 88%, respectively, compared to those observed in adults at the 30 mg dose, and were 81 and 78%, respectively, at the 60 mg dose (see *Tables 6 and 7*).

Table 7: Mean (%CV) Pharmacokinetic Parameters in Patients 12 to 17 Years of Age with Symptomatic GERD on Day 7 After Administration of Dexlansoprazole Once Daily for 7 Days

Dose	C _{max} (ng/mL)	AUC ₀₋₂₄ (ng-h/mL)	CL/F (L/h)
30 mg (N=17)	691 (53)	2,886 (47)	12.8 (48)
60 mg (N=18)	1,136 (51)	5,120 (58)	15.3 (49)

Age: Geriatric Population

The terminal elimination half-life of dexlansoprazole is significantly increased in geriatric subjects compared to younger subjects (2.2 and 1.5 hours, respectively). Dexlansoprazole exhibited higher systemic exposure (AUC) in geriatric subjects (34% higher) than younger subjects [see *Use in Specific Populations (8.5)*].

Sex

In a study of 12 male and 12 female healthy subjects who received a single dose of dexlansoprazole 60 mg capsules, females had higher systemic exposure (AUC) (43% higher) than males. This difference in exposure between males and females does not represent a significant safety concern.

Renal Impairment

Dexlansoprazole is extensively metabolized in the liver to inactive metabolites, and no parent drug is recovered in the urine following an oral dose of dexlansoprazole. Therefore, the pharmacokinetics of dexlansoprazole are not expected to be altered in patients with renal impairment, and no studies were conducted in patients with renal impairment. In addition, the pharmacokinetics of lansoprazole were not clinically different in patients with mild, moderate or severe renal impairment compared to healthy subjects with normal renal function.

Hepatic Impairment

In a study of 12 patients with moderate hepatic impairment (Child-Pugh Class B) who received a single dose of 60 mg dexlansoprazole capsules, the systemic exposure (AUC) of bound and unbound dexlansoprazole was approximately two times greater compared to subjects with normal hepatic function. This difference in exposure was not due to a difference in protein binding. No studies have been conducted in patients with severe hepatic impairment (Child-Pugh Class C) [see *Dosage and Administration (2.2)*, *Use in Specific Populations (8.6)*].

Drug-Drug Interactions

Effect of Dexlansoprazole on Other Drugs

Cytochrome P 450 Interactions

Dexlansoprazole is metabolized, in part, by CYP2C19 and CYP3A4 [see *Clinical Pharmacology (12.3)*].

In vitro studies have shown that dexlansoprazole is not likely to inhibit CYP isozymes 1A1, 1A2, 2A6, 2B6, 2C8, 2D9, 2D6, 2E1 or 2A4. As such, no clinically relevant interactions with drugs metabolized by these CYP enzymes would be expected. Furthermore, *in vivo* studies showed that dexlansoprazole did not have an impact on the pharmacokinetics of coadministered pefloxacin (CYP2C8 substrate) or theophylline (CYP1A2 substrate). The subjects' CYP1A2 genotypes in the drug-drug interaction study with theophylline were not determined. Although *in vitro* studies indicated that dexlansoprazole has the potential to inhibit CYP2C19 *in vivo*, an *in vivo* drug-drug interaction study in mainly CYP2C19 extensive and intermediate metabolizers has shown that dexlansoprazole does not affect the pharmacokinetics of diazepam (CYP2C19 substrate).

Clopidogrel

Clopidogrel is metabolized to its active metabolite in part by CYP2C19. A study of healthy subjects who were CYP2C19 extensive metabolizers, receiving once daily administration of clopidogrel 75 mg alone or concomitantly with dexlansoprazole 60 mg capsules (n=40), for nine days was conducted. The mean AUC of the active metabolite of clopidogrel was reduced by approximately 9% (mean AUC ratio was 91%, with 90% CI of 86 to 97%) when dexlansoprazole was coadministered compared to administration of clopidogrel alone. Pharmacodynamic parameters were also measured and demonstrated that the change in inhibition of platelet aggregation (induced by 5 mM ADP) was related to the change in the exposure to clopidogrel active metabolite. The effect on exposure to the active metabolite of clopidogrel and on clopidogrel-induced platelet inhibition is not considered clinically important.

Effect of Other Drugs on Dexlansoprazole

Because dexlansoprazole is metabolized by CYP2C19 and CYP3A4, inducers and inhibitors of these enzymes may potentially alter exposure of dexlansoprazole.

12.5 Pharmacogenomics

Effect of CYP2C19 Polymorphism on Systemic Exposure of Dexlansoprazole

Systemic exposure of dexlansoprazole is generally higher in intermediate and poor metabolizers. In male Japanese subjects who received a single dose of dexlansoprazole 30 mg or 60 mg capsules (N=2 to 6 subjects/group), mean dexlansoprazole C_{max} and AUC values were up to two times higher in intermediate compared to extensive metabolizers, in poor metabolizers, mean C_{max} was up to four times higher and mean AUC was up to 12 times higher compared to extensive metabolizers. Though such study was not conducted in Caucasians and African Americans, it is expected dexlansoprazole exposure in these races will be affected by CYP2C19 phenotypes as well.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of dexlansoprazole was assessed with lansoprazole studies. In two, 24 month carcinogenicity studies, Sprague-Dawley rats were treated orally with lansoprazole at doses of 5 to 150 mg/kg/day, about one 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 lansoprazole 30 mg/day.

Lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids in both male and female rats [see *Clinical Pharmacology (12.2)*].

In rats, lansoprazole 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 (four to 10 times the recommended human lansoprazole 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 orally with lansoprazole doses of 15 to 600 mg/kg/day, two to 60 times the recommended human lansoprazole dose based on BSA. Lansoprazole produced a dose-related increase 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 lansoprazole/kg/day (40 to 80 times the recommended human lansoprazole dose based on BSA) and female mice treated with 150 to 600 mg lansoprazole/kg/day (20 to 80 times the recommended human lansoprazole 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 lansoprazole dose based on BSA).

A 26 week p53 (+/-) transgenic mouse carcinogenicity study of lansoprazole was not positive.

Lansoprazole was positive in the Ames test and the *in vitro* human lymphocyte chromosomal aberration assay. Lansoprazole was not genotoxic in 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.

Dexlansoprazole was positive in the Ames test and in the *in vitro* chromosome aberration test using Chinese hamster lung cells. Dexlansoprazole was negative in the *in vivo* mouse micronucleus test.

The potential effects of dexlansoprazole on fertility and reproductive performance were assessed using lansoprazole studies. Lansoprazole at oral doses up to 150 mg/kg/day (40 times the recommended human lansoprazole dose based on BSA) was found to have no effect on fertility and reproductive performance of male and female rats.

14 CLINICAL STUDIES

14.1 Healing of Erosive Esophagitis in Adults

Two multicenter, double-blind, active-controlled, randomized, eight week studies were conducted in patients with endoscopically confirmed EE. Severity of the disease was classified based on the Los Angeles Classification Grading System (Grades A to D). Patients were randomized to one of the following three treatment groups: Dexlansoprazole 60 mg once daily, dexlansoprazole 30 mg once daily or lansoprazole 30 mg once daily. Patients who were *H. pylori* positive or who had Barrett's Esophagus and/or definite dysplastic changes at baseline were excluded from these studies. A total of 4,092 patients were enrolled and ranged in age from 18 to 90 years (median age 48 years) with 54% male. Race was distributed as follows: 87% Caucasian, 5% Black and 8% Other. Based on the Los Angeles Classification, 71% of patients had mild EE (Grades A and B) and 29% of patients had moderate to severe EE (Grades C and D) before treatment.

The studies were designed to test noninferiority. If noninferiority was demonstrated then superiority would be tested. Although noninferiority was demonstrated in both studies, the finding of superiority in one study was not replicated in the other. The proportion of patients with healed EE at Week 4 or 8 is presented below in *Table 8*.

Study	Number of Patients (N) ¹	Treatment Group (daily)	Week 4 % Healed	Week 8 ¹ % Healed	(95% CI) for the Treatment Difference (Dexlansoprazole–Lansoprazole) by Week 8
1	657	Dexlansoprazole 60 mg capsules	70	87	(-1.5, 6.1) ⁴
	648	Lansoprazole 30 mg	65	85	
2	639	Dexlansoprazole 60 mg capsules	66	85	(2.2, 10.5) ⁴
	656	Lansoprazole 30 mg	65	79	

CI = Confidence interval
Based on crude rate estimates, patients who did not have endoscopically documented healed EE and prematurely discontinued were considered not healed.
¹Patients with at least one postbaseline endoscopy.
²Primary efficacy endpoint.
³Demonstrated noninferiority to lansoprazole.
Dexlansoprazole 90 mg once daily was studied and did not provide additional clinical benefit over dexlansoprazole 60 mg once daily.

14.2 Maintenance of Healed Erosive Esophagitis and Relief of Heartburn in Adults

A multicenter, double-blind, placebo-controlled, randomized study was conducted in patients who successfully completed an EE study and showed endoscopically confirmed healed EE. Maintenance of healing and symptom resolution over a six month period was evaluated with dexlansoprazole 30 mg or 60 mg capsules once daily compared to placebo. A total of 445 patients were enrolled and ranged in age from 18 to 85 years (median age 49 years), with 52% female. Race was distributed as follows: 90% Caucasian, 5% Black and 5% Other.

Sixty-six percent of patients treated with 30 mg of dexlansoprazole capsules remained healed over the six month time period as confirmed by endoscopy (see *Table 9*).

Number of Patients (N) ¹	Treatment Group (daily)	Maintenance Rate (%)
125	Dexlansoprazole 30 mg capsules	66.4 ²
119	Placebo	14.3

*Based on crude rate estimates, patients who did not have endoscopically documented relapse and prematurely discontinued were considered not healed.
¹Patients with at least one postbaseline endoscopy
²Statistically significant vs placebo

Dexlansoprazole 60 mg capsules once daily was studied and did not provide additional clinical benefit over dexlansoprazole 30 mg capsules once daily.

The effect of dexlansoprazole 30 mg capsules on maintenance of relief of heartburn was also evaluated. Upon entry into the maintenance study, a majority of patients' baseline heartburn severity was rated as none. Dexlansoprazole 30 mg capsules demonstrated a statistically significantly higher percent of 24-hour heartburn-free periods compared to placebo over the six month treatment period (see *Table 10*). The majority of patients treated with placebo discontinued due to relapse of EE between Month 2 and Month 6.

Treatment Group (daily)	Overall Treatment*		Month 1		Month 6	
	N	Heartburn-Free 24 hour Periods (%)	N	Heartburn-Free 24 hour Periods (%)	N	Heartburn-Free 24 hour Periods (%)
Dexlansoprazole 30 mg capsules	132	96.1 ¹	126	96.7	80	98.3
Placebo	141	28.6	117	28.6	23	73.3

*Secondary efficacy endpoint
¹Statistically significant vs placebo

14.3 Treatment of Symptomatic Non-Erosive GERD in Adults

A multicenter, double-blind, placebo-controlled, randomized, four week study was conducted in patients with a diagnosis of symptomatic non-erosive GERD made primarily by presentation of symptoms. These patients who identified heartburn as their primary symptom, had a history of heartburn for six months or longer, had heartburn on at least four of seven days immediately prior to randomization and had no esophageal erosions as confirmed by endoscopy. However, patients with symptoms which were not acid-related may not have been excluded using these inclusion criteria. Patients were randomized to one of the following treatment groups: Dexlansoprazole 30 mg daily, 60 mg daily, or placebo. A total of 947 patients were enrolled and ranged in age from 18 to 86 years (median age 48 years) with 71% female. Race was distributed as follows: 82% Caucasian, 14% Black and 4% Other.

Dexlansoprazole 30 mg capsules provided statistically significantly greater percent of days with heartburn-free 24-hour periods over placebo as assessed by daily diary over four weeks (see *Table 11*). Dexlansoprazole 60 mg capsules once daily was studied and provided no additional clinical benefit over dexlansoprazole 30 mg capsules once daily.

Table 11: Median Percentages of 24 Hour Heartburn-Free Periods During the 4 Week Treatment Period of the Symptomatic Non-Erosive GERD Study in Adults

N	Treatment Group (daily)	Heartburn-Free 24-hour Periods (%)	
		Dexlansoprazole 30 mg capsule	Placebo
312	Dexlansoprazole 30 mg capsule	54.9 ¹	18.5
310	Placebo		

*Statistically significant vs placebo
A higher percentage of patients on dexlansoprazole 30 mg capsules had heartburn-free 24-hour periods compared to placebo as early as the first three days of treatment and this was sustained throughout the treatment period (percentage of patients on Day 3: dexlansoprazole 38% versus placebo 15%; on Day 28: dexlansoprazole 63% versus placebo 40%).

14.4 Pediatric GERD

Use of dexlansoprazole in patients 12 to 17 years of age is supported by evidence from adequate and well-controlled studies of dexlansoprazole capsules in adults, with additional safety, efficacy, and pharmacokinetic data from studies performed in pediatric patients.

Healing of EE, Maintenance of Healed EE and Relief of Heartburn

In a multicenter, 36 week trial, 62 patients 12 to 17 years of age with a documented history of GERD for at least three months and endoscopically-proven erosive esophagitis (EE) were enrolled to evaluate the healing of EE, maintenance of healed EE and relief of heartburn, followed by an additional 12 weeks without treatment.

The median age was 15 years, with males accounting for 61% of the patients. Based on the Los Angeles Classification Grading Scale, 97% of patients had mild EE (Grades A and B), and 3% of patients had moderate to severe EE (Grades C and D) before treatment.

In the first eight weeks, 62 patients were treated with dexlansoprazole 60 mg capsules once daily to evaluate the healing of EE. Of the 62 patients, 53 patients completed the eight week trial, and 51 (88%) patients achieved healing of EE, as confirmed by endoscopy, over eight weeks of treatment (see *Table 12*).

	Dexlansoprazole 60 mg Capsules
Proportion of randomized patients healed (n (%) 95% CI	51/62 (82%) (70, 91) ¹
Proportion of evaluable patients healed* (n (%) 95% CI	51/58 (88%) (77, 95) ¹

* Includes only patients who underwent postbaseline endoscopy.
¹ Reported are the exact confidence limits.

After the initial eight weeks of treatment, all 51 patients with healed EE were randomized to receive treatment with dexlansoprazole 30 mg capsules or placebo, once daily for an additional 16 weeks to evaluate maintenance of healing and symptom resolution. Maintenance of healing was assessed by endoscopy at Week 24. Of the 51 patients randomized, 13 patients discontinued early. Of these, five patients did not undergo postbaseline endoscopy. Eighteen of 22 (82%) evaluable patients treated with dexlansoprazole 30 mg capsules remained healed over the 16 week treatment period as confirmed by endoscopy, compared with 14 of 24 (58%) in placebo (see *Table 13*).

	Dexlansoprazole 30 mg Capsules	Placebo
Proportion of randomized patients who maintained healing of EE (n (%) 95% CI	18/25 (72%) (61, 88) ¹	14/26 (54%) (33, 73) ¹
Proportion of evaluable patients who maintained healing of EE ¹ (n (%) 95% CI	18/22 (82%) (60, 95) ¹	14/24 (58%) (37, 78) ¹

* Following eight weeks of initial therapy and 16 weeks of maintenance therapy.
¹ Includes patients with at least one postbaseline endoscopy.
² Reported are the exact confidence limits.

Relief of heartburn was assessed in randomized patients during the 16 week maintenance period. The median percentage of 24-hour heartburn-free periods was 87% for those receiving dexlansoprazole 30 mg capsules compared to 68% for those receiving placebo.

Out of the 32 patients who maintained healing of EE at the end of the 16 week maintenance period, 27 patients (16 treated with dexlansoprazole and 11 treated with placebo during the double-blind phase) were followed for an additional 12 weeks without therapy. Twenty-four of the 27 patients completed the 12 week follow-up period. One patient required treatment with acid suppression therapy.

Treatment of Symptomatic Non-Erosive GERD

In a single-arm, open-label, multicenter trial, 104 pediatric patients 12 to 17 years of age with symptomatic non-erosive GERD were treated with dexlansoprazole 30 mg capsules once daily, for four weeks to evaluate safety and effectiveness. Patients had a documented history of GERD symptoms for at least three months prior to screening, reported heartburn on at least three out of seven days during screening, and had no esophageal erosions as confirmed by endoscopy. The median age was 15 years, with females accounting for 70% of the patients. During the four week treatment period, the median percentage of 24-hour heartburn free periods was 47%.

Dexlansoprazole Delayed-Release Capsules, 60 mg, are opaque, green with "par" imprinted on the cap and "148" imprinted on the body.

NDC Number Size
49884-148-11 Bottle of 30
49884-148-09 Bottle of 90

Store at 20° to 25° C (68° to 77°F); excursions permitted to 15° to 30° C (59° to 86°F) [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Adverse Reactions

Advise patients to report to their healthcare provider if they experience any signs or symptoms consistent with:

- Hypersensitivity Reactions [see *Contraindications (4)*]
- Acute Tubulointerstitial Nephritis [see *Warnings and Precautions (5.2)*]
- Clostridium difficile*-Associated Diarrhea [see *Warnings and Precautions (5.3)*]
- Bone Fracture [see *Warnings and Precautions (5.4)*]
- Severe Cutaneous Adverse Reactions [see *Warnings and Precautions (5.5)*]
- Cutaneous and Systemic Lupus Erythematosus [see *Warnings and Precautions (5.6)*]
- Cyanocobalamin (Vitamin B12) Deficiency [see *Warnings and Precautions (5.7)*]
- Hypomagnesemia and Mineral Metabolism [see