Redexa®
(Dexlansoprazole)

ریڈیکسا

COMPOSITION
REDEXA (Dexlansoprazole) is available for oral administration as:

REDEXA 30mg Capsules
Each capsule contains:
Dexlansoprazole Dual Delayed Release Pellets Eq. to Dexlansoprazole.....30mg
(As per innovator's specs.)

REDEXA 60mg Capsules
Each capsule contains:
Dexlansoprazole Dual Delayed Release Pellets Eq. to Dexlansoprazole.....60mg
(As per innovator's specs.)

DESCRIPTION
The active ingredient in REDEXA (dexlansoprazole) delayed-release capsules, a proton pump inhibitor, is (+)-2-[(R)-{[3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl] methyl} sulfinyl]-1H-benzimidazole, a compound that inhibits gastric acid secretion. Dexlansoprazole is the R-enantiomer of lansoprazole (a racemic mixture of the R- and S-enantiomers). Its molecular formula is $C_{16}H_{14}F_3N_3O_2S$.

CLINICAL PHARMACOLOGY

Mechanism of Action
Dexlansoprazole belongs to a class of antisecretory 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.

Pharmacodynamics

Antisecretory Activity
The effects of Dexlansoprazole 60 mg (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.

Serum Gastrin Effects
The effect of Dexlansoprazole on serum gastrin concentrations was evaluated in approximately 3460 patients in clinical trials up to eight weeks and in 1023 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 doses. 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 pre-treatment levels within one month of discontinuation of treatment.

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 for up to 12 months.

Pharmacokinetics

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

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.

Absorption
After oral administration of dexlansoprazole capsules to healthy subjects and symptomatic GERD patients, mean Cmax and AUC values of dexlansoprazole increased approximately dose proportionally.

Effect on Food
In healthy subjects receiving dexlansoprazole capsules under various fed conditions compared to fasting, increases in Cmax ranged from 12% to 55%, increases in AUC ranged from 9% to 37% and Tmax varied (ranging from a decrease of 0.7 hours to an increase of three hours).

Distribution
Plasma protein binding of dexlansoprazole ranged from 96% to 99% in healthy subjects. The apparent volume of distribution (Vz/F) after multiple doses in symptomatic GERD patients was 40 L.

Metabolism
Dexlansoprazole is extensively metabolized in the liver by oxidation, reduction and subsequent formation of sulfate, glucuronide 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.

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 capsule, no unchanged dexlansoprazole is excreted in urine. Apparent clearance (CL/F) in healthy subjects was 11.4 to 11.6 L/hour respectively, after five days of 30mg or 60mg once daily administration. Dexlansoprazole is eliminated with a half-life of approximately one to two hours in healthy subjects and in patients with symptomatic GERD.

INDICATIONS

Healing of Erosive Esophagitis
Dexlansoprazole is indicated in patients 12 years of age and older for healing of all grades of erosive esophagitis (EE) for up to eight weeks.

Maintenance of Healed Erosive Esophagitis and Relief of Heartburn
Dexlansoprazole is 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.

Treatment of Symptomatic Non-Erosive Gastroesophageal Reflux Disease
Dexlansoprazole is 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.

DOSAGE AND ADMINISTRATION

Recommended Dosage in Patients 12 Years of Age and Older

Recommended Dexlansoprazole Capsules Dosage Regimen by Indication 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.

Dose adjustment

Renal impairment
No dosage adjustment of dexlansoprazole is necessary in patients with renal impairment. The pharmacokinetics of dexlansoprazole in patients with renal impairment are not expected to be altered since 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

Hepatic impairment
No adjustment for REDEXA is necessary for patients with mild hepatic impairment (Child-Pugh Class A). Consider a maximum daily dose of 30 mg for patients with moderate hepatic impairment (Child-Pugh Class B). REDEXA is not recommended in patients with severe hepatic impairment (Child-Pugh Class C)

Elderly
Dexlansoprazole exhibited higher systemic exposure (AUC) in geriatric subjects (34% higher) than younger patients.

Administration requirements:
• Dexlansoprazole can be taken without regard to food.
• Dexlansoprazole should be swallowed whole.
• For patients that have difficulty swallowing capsules, the contents of a capsule can be sprinkled on applesauce or empty the content of capsule into a clean container with 20mL of water and withdraw the entire mixture into an oral syringe. Administer immediately into the mouth. Refill the syringe with 10mL of water, swirl gently and administer. Repeat this step one more time.

Administration with water via a nasogastric tube:
• Open the capsule and empty the content of capsule into a clean container with 20mL of water.
• Withdraw the entire mixture into a catheter-tip syringe, swirl the syringe gently in order to keep the granules from settling and immediately inject the mixture through the nasogastric tube into the stomach.
• Do not save the water and granule mixture for later use.
• Refill the syringe with 10mL of water, swirl gently and flush the tube.
• Refill the syringe again with 10mL of water, swirl gently and administer.

CONTRAINDICATIONS
• Dexlansoprazole is contraindicated in patients with known hypersensitivity to any component of the formulation. Hypersensitivity reactions, including anaphylaxis have been reported. Acute interstitial nephritis (AIN) has been reported with other proton pump inhibitors (PPIs), including lansoprazole of which dexlansoprazole is the R-enantiomer.

• PPIs, including dexlansoprazole, are contraindicated with rilpivirine-containing products.

WARNING AND PRECAUTIONS

Gastric Malignancy
Symptomatic response with dexlansoprazole does not preclude the presence of gastric malignancy.

Acute Interstitial Nephritis
Acute interstitial nephritis has been observed in patients taking PPIs including lansoprazole. Acute interstitial nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue dexlansoprazole if acute interstitial nephritis develops.

Cyanocobalamin (vitamin B12) Deficiency
Daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than 3 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.

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

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 (a 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

Hypomagnesemia
Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI.
For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.

Concomitant Use of Dexlansoprazole with Methotrexate
Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of the PPI may be considered in some patients.

ADVERSE REACTIONS
Blood and Lymphatic System Disorders: autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura

Ear and Labyrinth Disorders: deafness
Eye Disorders: blurred vision
Gastrointestinal Disorders: oral edema, pancreatitis
General Disorders and Administration Site Conditions: facial edema
Hepatobiliary Disorders: drug-induced hepatitis
Immune System Disorders: anaphylactic shock (requiring emergency intervention), exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis (some fatal)
Infections and Infestations: Clostridium difficile associated diarrhea
Metabolism and Nutrition Disorders: hypomagnesemia, hyponatremia
Musculoskeletal System Disorders: bone fracture
Nervous System Disorders: cerebrovascular accident, transient ischemic attack
Renal and Urinary Disorders: Acute renal failure
Respiratory, Thoracic and Mediastinal Disorders: pharyngeal edema, throat tightness
Skin and Subcutaneous Tissue Disorders: generalized rash, leukocytoclastic vasculitis

DRUG INTERACTIONS

Drugs with pH-Dependent Absorption Kinetics
Due to its effects on gastric acid secretion, dexlansoprazole can reduce the absorption of drugs where gastric pH is an important determinant of their bioavailability. Like with other drugs that decrease the intragastric acidity, the absorption of drugs such as ampicillin esters, ketoconazole, atazanavir, iron salts, erlotinib, and mycophenolate mofetil (MMF) can decrease, while the absorption of drugs such as digoxin can increase during treatment with dexlansoprazole.

dexlansoprazole is 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, dexlansoprazole should not be co-administered with atazanavir.

Co-administration 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 PPIs and MMF. Use DEXLANSOPRAZOLE with caution in transplant patients receiving MMF.

Warfarin
Co-administration of dexlansoprazole 90 mg and warfarin 25 mg did not affect the pharmacokinetics of warfarin or INR. 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 dexlansoprazole and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time.

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

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

USE IN SPECIAL POPULATIONS

Pregnancy
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 use during pregnancy did not demonstrate an association of adverse pregnancy-related outcomes with lansoprazole.

Nursing Mothers
It is not known whether dexlansoprazole is excreted in human milk. However, lansoprazole and its metabolites are present in rat milk following the administration of lansoprazole. As many drugs are excreted in human milk, 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 the drug, taking into account the importance of the drug to the mother.

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, and treatment 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.

Geriatric Use
In clinical studies of dexlansoprazole, 11% of patients were aged 65 years and over. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified significant differences in responses between geriatric and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Renal Impairment
No dosage adjustment of dexlansoprazole is necessary in patients with renal impairment. The pharmacokinetics of dexlansoprazole in patients with renal impairment are not expected to be altered since 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.

Hepatic impairment
For patients with moderate hepatic impairment (Child-Pugh Class B), the recommended dosage is 30 mg DEXLANSOPRAZOLE once daily for up to eight weeks. dexlansoprazole is not recommended in patients with severe hepatic impairment (Child-Pugh Class C).

OVER DOSAGE
There have been no reports of significant overdose with dexlansoprazole. Multiple doses of Dexlansoprazole 120 mg and a single dose of dexlansoprazole 300 mg did not result in death or other severe adverse events. However, serious adverse events of hypertension have been reported in association with twice daily doses of dexlansoprazole 60 mg. Non-serious adverse reactions observed with twice daily doses of dexlansoprazole 60 mg include hot flashes, contusion, oropharyngeal pain, and weight loss. Dexlansoprazole is not expected to be removed from the circulation by hemodialysis.
In the event of over-exposure, treatment should be symptomatic and supportive.

PRESENTATION
REDEXA 30 mg: Pack of 30 Dual Delayed Release Capsules
REDEXA 60 mg: Pack of 30 Dual Delayed Release Capsules

INSTRUCTIONS
Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.
For suspected adverse drug reaction, email us at reports@pharmevo.biz

For more information on our products
call PharmAssist helpline 0800-82222
Monday to Friday 9:00 am to 6:00 pm
or email us at : pharmassist@pharmevo.biz

ہدایات:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کی جائے۔
روشنی، گرمی اور نمی سے محفوظ، 30°C سے کم درجہ حرارت پر رکھیں۔
دوا کے ممکنہ منفی اثرات کے متعلق reports@pharmevo.biz پر مطلع کریں۔

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Our dream, a healthier society

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