DELEP 30mg, 60mg Capsules

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(Dexlansoprazole)

DESCRIPTION:

DELEP (Dexlansoprazole) dual delayed-release capsules, belong to a class of proton pump inhibitor, a compound that inhibits gastric acid secretion. Dexlansoprazole is the *R*-enantiomer of lansoprazole (a racemic mixture of the *R*- and *S*-enantiomers).

QUALITATIVE AND QUANTITATIVE COMPOSITION:

DELEP (Dexlansoprazole) is available for oral administration as:

1.DELEP 30mg Capsule

Each capsule contains:

Dexlansoprazole dual delayed release pellets eq. to Dexlansoprazole.....30mg

(Product Specs. : Innovator's)

2.DELEP 60mg Capsule

Each capsule contains:

Dexlansoprazole dual delayed release pellets eq. to Dexlansoprazole.....60mg

(Product Specs. : Innovator's)

CLINICAL PHARMACOLOGY:

Mechanism of Action:

Dexlansoprazole is a PPI that suppresses gastric acid secretion by specific inhibition of the (H+, K+)-ATPase in the gastric parietal cell. By acting specifically on the proton pump, dexlansoprazole blocks the final step of acid production.

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.

Absorption:

After oral administration of dexlansoprazole capsules to healthy subjects and symptomatic GERD patients, mean C_{max} and AUC values of dexlansoprazole increased approximately dose proportionally.

Effect on Food:

DELEP can be taken without regard to food, some patients may benefit from administering the dose prior to a meal if post-meal symptoms do not resolve under post-fed conditions.

Distribution:

Plasma protein binding of dexlansoprazole ranged from 96% to 99% in healthy subjects. The apparent volume of distribution 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 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 1 to 2 hours.

THERAPEUTIC INDICATIONS WITH DOSAGE AND ADMINISTRATION:

DELEP (Dexlansoprazole) is indicated in patients 12 years of age and older.

Indications	Recommended Dose	Duration
Healing of Erosive Esophagitis	60mg	Once daily for up to 8 weeks
Maintenance of Healed Erosive Esophagitis and relief of heart burn	30mg	*Once daily for up to 6 months
Symptomatic Non-Erosive Gastroesophageal Reflux Disease (GERD)	30mg	Once daily for 4 weeks

*Controlled Studies did not extend beyond 6 months.

Special Population:

Hepatic Impairment:

Dexlansoprazole 30mg should be considered for patients with moderate hepatic impairment (Child-Pugh Class B). No studies have been conducted in patients with severe hepatic impairment (Child-Pugh Class C).

Administration Advice:

-**DELEP** capsule can be taken without regard to food.

-**DELEP** capsule should be swallowed whole.

-**DELEP** capsule should not be chewed.

For patients who have difficulty swallowing capsules, follow the instructions below for administration:

Administration with Applesauce:

-Take one tablespoon of Applesauce, open and sprinkle the contents of capsule on it, swallow it whole.

-Do not chew and save it for later use.

Administration with Water in an Oral Syringe:

-Open and mix capsule contents with 20mL of water in a clean container

-Use an oral syringe to withdraw the mixture, gently swirl the syringe and administer it immediately into the mouth. Do not save it for later use.

-Refill the syringe with 10mL of water, swirl gently and administer. Repeat this step one more time.

Administration with Water via a Nasogastric Tube (≥16 French):

-Open and mix capsule contents with 20mL of water in a clean container

-Withdraw the entire mixture into a catheter-tip syringe, swirl the syringe gently and inject the mixture through nasogastric tube into the stomach immediately. Do not save the 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:

-In patients with known hypersensitivity to dexlansoprazole or to any excipient of the product.

-With rilpivirine-containing products.

WARNINGS AND PRECAUTIONS:

-Use of proton pump inhibitors (PPIs) may increase risk of Clostridium difficile-associated diarrhea, especially in hospitalized patients. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

-Increased incidence of osteoporosis-related bone fractures of the hip, spine or wrist may occur with PPI therapy. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the conditions being treated.

-Consider obtaining serum magnesium concentrations prior to beginning long-term PPI therapy, especially if taking concomitant digoxin, diuretics or other drugs known to cause hypomagnesemia.

-Discontinue dexlansoprazole, if acute interstitial nephritis develops during PPI therapy.

-Prolonged treatment may lead to vitamin B12 malabsorption and subsequent vitamin B12 deficiency.

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

Pregnancy:

Dexlansoprazole should be used during pregnancy only if clearly needed.

Nursing Mothers:

It is not known whether dexlansoprazole is excreted in human milk. As many drugs are excreted in human milk, 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.

DRUG INTERACTIONS:

Drugs with pH-Dependent Absorption Kinetics:

Dexlansoprazole can reduce the absorption of other drugs (e.g., ***ampicillin esters, ketoconazole/itraconazole, iron salts, erlotinib, and mycophenolate mofetil***) due to its effect on reducing intragastric acidity. Use concomitantly with caution.

Antiretrovirals:

-***Rilpivirine, atazanavir and nelfinavir:*** When used concomitantly with dexlansoprazole may reduce antiviral effect and promote the development of drug resistance. Avoid concomitant use with dexlansoprazole.

-***Saquinavir:*** When used concomitantly with dexlansoprazole may increase exposure and thus toxicity of the antiretroviral drugs. Monitor for potential saquinavir toxicities.

Digoxin:

Potential for increased exposure of digoxin. Monitor digoxin concentration.

Warfarin:

Concomitant use of PPIs with warfarin may increase INR and prothrombin time which may lead to abnormal bleeding and even death. Monitor for increases in INR and prothrombin time.

Tacrolimus:

Potentially increased whole blood levels of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19. Careful monitoring suggested.

Methotrexate:

Concomitant use of PPIs with high dose methotrexate may elevate and prolong serum concentrations of methotrexate and/or its metabolite hydroxymethotrexate, possibly leading to methotrexate toxicities.

A temporary withdrawal of PPIs may be considered in some patients receiving high-dose methotrexate.

CYP2C19 or CYP3A4 Inducers (St. John's Wort, Rifampin):

Decreased exposure of dexlansoprazole.

CYP2C19 or CYP3A4 Inhibitors:

Increased exposure of dexlansoprazole.

Interactions with Investigations of Neuroendocrine Tumors:

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.

Temporarily stop dexlansoprazole treatment at least 14 days before assessing CgA levels.

Interaction with Secretin Stimulation Test:

Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma. Temporarily stop dexlansoprazole treatment at least 30 days before assessing to allow gastrin levels to return to baseline.

False Positive Urine Tests for THC:

There have been reports of false positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving PPIs. An alternative confirmatory method should be considered.

ADVERSE REACTIONS:

Common:

Diarrhea, abdominal pain, nausea, upper respiratory tract infection, vomiting and flatulence.

Less Common:

Anemia, angina, arrhythmia, bradycardia, chest pain, edema, myocardial infarction, palpitation, tachycardia, ear pain, tinnitus, vertigo, goiter, eye irritation, eye swelling, abdominal discomfort, abdominal tenderness, Barrett's esophagus, bezoar, abnormal bowel sounds, breath odor, colonic polyp, constipation, dry mouth, duodenitis, dyspepsia, dysphagia, enteritis , esophagitis, gastric polyp, gastritis, gastroenteritis, gastrointestinal disorders, GERD, GI ulcers and perforation, hemorrhoids, impaired gastric emptying, irritable bowel syndrome, mucus stools, rectal hemorrhage, asthenia, chills, mucosal inflammation, nodule, pain, pyrexia, biliary colic, cholelithiasis, hepatomegaly, hypersensitivity, candida infections, influenza, nasopharyngitis, oral herpes, sinusitis, viral infection, vulvo-vaginal infection, fractures, joint sprains, procedural pain, sunburn, increased liver enzymes, bilirubin decreased/increased, blood creatinine increased, blood gastrin increased, blood glucose increased, blood potassium increased platelet count decreased, total protein increased, weight increase, appetite changes, hypercalcemia, hypokalemia, arthralgia, arthritis, muscle cramps, musculoskeletal pain, altered taste, convulsion, dizziness, headaches, migraine, memory impairment, paresthesia, psychomotor hyperactivity, tremor, trigeminal neuralgia, abnormal dreams, anxiety, depression, insomnia, libido changes, dysuria, micturition urgency, dysmenorrhea, menorrhagia, menstrual disorder, aspiration, asthma, bronchitis, cough, dyspnea, hiccups, hyperventilation, respiratory tract congestion, sore throat, acne, dermatitis, erythema, pruritus, rash, deep vein thrombosis, hot flush, hypertension, auditory hallucination, B-cell lymphoma, bursitis, central obesity, acute cholecystitis, dehydration, diabetes mellitus, dysphonia, epistaxis, folliculitis, gout, herpes zoster, hyperlipidemia, hypothyroidism, increased neutrophils, MCHC decrease, neutropenia, rectal tenesmus, restless legs syndrome, somnolence, tonsillitis.

OVERDOSAGE:

There have been no reports of significant overdose of **DELEP**. Serious adverse events of hypertension have been reported in association with twice daily doses of **DELEP** 60mg. Non-serious adverse reactions observed with twice daily doses of **DELEP** 60mg include hot flashes, contusion, oropharyngeal pain, and weight loss. Dexlansoprazole is not expected to be removed from the circulation by hemodialysis. If an overdose occurs, treatment should be symptomatic and supportive.

INSTRUCTIONS:

-Store below 30˚C.

-Protect from light & moisture.

-Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

HOW SUPPLIED:

DELEP (Dexlansoprazole) 30mg Capsules are available in blister pack of 30's.

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غذا کے ہمراہ یا خالی پیٹ - ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایت نامہ اور دوا کو بچوں کی پہنچ سے دور محفوظ جگہ پر رکھیں۔

روشنی اور نمی سے بچائیں۔

اس دوا کو صرف معالج کی تجویز کے مطابق فروخت کریں۔

SIGMA PHARMA

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