13-09-2021
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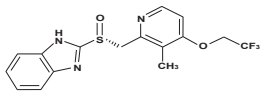
210mm

Delanzo™ DDR Capsules
(Dexlansoprazole)

COMPOSITION:
Delanzo™ DDR (Dexlansoprazole) is available for oral administration as:

Delanzo™ DDR Capsule 30mg	**Delanzo™ DDR Capsule 60mg**
Each capsule contains:	Each capsule contains:
Dexlansoprazole dual delayed release pellets MS eq. to Dexlansoprazole 30mg	Dexlansoprazole dual delayed release pellets MS eq. to Dexlansoprazole 60mg

DESCRIPTION:
Delanzo™ DDR (Dexlansoprazole), a proton pump inhibitor, is (+)-2-[(R)-([3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl] methyl} sulfinyl]-*1H* benzimidazole. Dexlansoprazole is the *R*-enantiomer of lansoprazole (a racemic mixture of the *R*- and *S*- enantiomers). Its molecular formula is $C_{16}H_{14}F_3N_3O_2S$ and the structural formula is:



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, mean Cmax and AUC values of dexlansoprazole increased approximately dose proportionally
Effect on Food
Dexlansoprazole can be taken without regard to food or the timing of 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 96.1% to 98.8% in healthy subjects. The apparent volume of distribution (Vz/F) after multiple doses in symptomatic GERD patients was 40L
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

SPECIAL POPULATION:
Pregnant Women
There are no adequate or well-controlled studies in pregnant women with dexlansoprazole. Exposure in clinical trials was very limited. Dexlansoprazole should not be administered to pregnant women unless the expected benefits outweigh the potential risks
Nursing Women
It is not known whether dexlansoprazole is excreted in human milk. As many drugs are excreted in human milk, dexlansoprazole should not be given to nursing mothers unless its use is considered essential. In this case nursing should be avoided
Paediatrics
The pharmacokinetics of dexlansoprazole in patients under the age of 12 years have not been studied
Geriatric Population
Dexlansoprazole exhibited higher systemic exposure (AUC) in geriatric subjects (34% higher) than younger patients. These differences were not clinically relevant. No dosage adjustment is necessary in geriatric patients
Hepatic Insufficiency
No adjustment for dexlansoprazole is necessary for patients with mild hepatic impairment (Child-Pugh Class A). 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)
Renal Insufficiency
The pharmacokinetics of dexlansoprazole are not expected to be altered in patients with renal impairment

THERAPEUTIC INDICATIONS:
Delanzo™ DDR (Dexlansoprazole) is indicated in patients 18 years of age and older:
- Healing of Erosive Esophagitis
- Maintenance of Healed Erosive Esophagitis and relief of Heartburn
- Symptomatic Non-Erosive Gastroesophageal Reflux Disease

DOSAGE AND ADMINISTRATION:

Indication	Recommended Dosage Regimen
Healing of Erosive Esophagitis	One 60mg capsule once daily for up to 8 weeks
Maintenance of Healed Erosive Esophagitis and Relief of Heartburn	One 30mg capsule once daily for up to 6 months
Symptomatic Non-Erosive Gastroesophageal Reflux Disease	One 30mg capsule once daily for 4 weeks

OR
As directed by the physician

Administration advice:
- Dexlansoprazole should be swallowed whole with plenty of water
- For patients that have difficulty swallowing capsules, the contents of a capsule can be sprinkled on one table spoon of applesauce, swallow applesauce and granules immediately. Do not chew granules. Do not save the applesauce and granules for later use

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. Do not save the water and granule mixture for later use. Refill the syringe with 10ml of water, swirl gently and administer
- Repeat this step one more time

CONTRAINDICATIONS:
Dexlansoprazole is contraindicated
- In patients with known hypersensitivity to dexlansoprazole or to any excipient of the product
- With rilpivirine-containing products

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ADVERSE REACTIONS:
Common:
Diarrhoea, abdominal pain, nausea, flatulence, constipation and headache

Less Common:
Anemia, lymphadenopathy, angina, arrhythmia, bradycardia, chest pain, edema, myocardial infarction, palpitation, tachycardia, ear pain, tinnitus, vertigo, goiter, eye irritation, eye swelling, abdominal discomfort, abdominal tenderness, abnormal feces, anal discomfort, Barrett's esophagus, bezoar, abnormal bowel sounds, breath odor, colitis microscopic, colonic polyp, constipation, dry mouth, duodenitis, dyspepsia, dysphagia, enteritis, eructation, esophagitis, gastric polyp, gastritis, gastroenteritis, gastrointestinal disorders, gastrointestinal hypermotility disorders, GERD, GI ulcers and perforation, hematemesis, hematochezia, hemorrhoids, impaired gastric emptying, irritable bowel syndrome, mucus stools, oral mucosal blistering, painful defecation, proctitis, paresthesia oral, rectal hemorrhage, retching, asthenia, chest pain, chills, feeling abnormal, inflammation, mucosal inflammation, nodule, pain, pyrexia, biliary colic, cholelithiasis, hepatomegaly, hypersensitivity, candida infections, influenza, nasopharyngitis, oral herpes, pharyngitis, sinusitis, viral infection, vulvo-vaginal infection, procedural pain, sunburn, ALP increased, ALT increased, AST increased, bilirubin decreased/increased, blood creatinine increased, blood gastrin increased, blood glucose increased, blood potassium increased, liver function test abnormal, platelet count decreased, total protein increased, weight increase, appetite changes, hypercalcemia, hypokalemia, arthralgia, arthritis, muscle cramps, musculoskeletal pain, myalgia, 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, dyspareunia, menorrhagia, menstrual disorder, aspiration, asthma, bronchitis, cough, dyspnea, hiccups, hyperventilation, respiratory tract congestion, sore throat, acne, dermatitis, erythema, pruritus, rash, skin lesion, urticarial, deep vein thrombosis, hot flush, hypertension, anaphylaxis, 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

DRUG INTERACTIONS:
Drugs with pH-Dependent Absorption Pharmacokinetics: (e.g., Ampicillin esters, digoxin, iron salts, ketoconazole)
Dexlansoprazole can reduce the absorption of other drugs due to its effect on reducing intragastric acidity
Cytochrome P 450 Interactions
Dexlansoprazole is metabolized, in part, by CYP2C19 and CYP3A4
Warfarin
Patients treated with PPIs and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time
Concomitant Use of Antacids with Dexlansoprazole
No formal drug-drug interaction studies were conducted with dexlansoprazole and antacids. Antacids may be used concomitantly, if required
Theophylline
Individual patients should monitor their theophylline level while taking the two drugs concomitantly
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
Clopidogrel
No dose adjustment of clopidogrel is necessary when administered with an approved dose of dexlansoprazole
Methotrexate
Concomitant use of PPIs with methotrexate may elevate and prolong serum concentrations of methotrexate and/or its metabolite hydroxymethotrexate
Rilpivirine
Co-administration is contraindicated due to significant decrease in rilpivirine exposure and loss of therapeutic effect
Atazanavir
Co-administration of dexlansoprazole with atazanavir is not recommended
Nelfinavir
Co-administration of dexlansoprazole with nelfinavir is not recommended
Saquinavir
Co-administration of saquinavir requires caution and monitoring, alongwith potential dose reduction of saquinavir, due to increased saquinavir exposure and thus the risk of saquinavir-related toxicities
False Positive Urine Test for THC
There have been reports of fasle positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving PPIs
Interaction with Secretin Stimulation Test
Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma

OVERDOSAGE:
There have been no reports of significant overdose of dexlansoprazole. Multiple doses of dexlansoprazole 120mg and a single dose of dexlansoprazole 300mg 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 60mg. Non-serious adverse reactions observed with twice daily doses of dexlansoprazole 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

SHELF LIFE:
See expiry on the pack

AVAILABILITY:
Delanzo™DDR Capsule 30mg in a pack of 30's
Delanzo™DDR Capsule 60mg in a pack of 30's

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light and humidity
Store between 15 to 30°C
Improper storage may deteriorate the medicine

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com
Mfg. Lic. No. 000072

ڈیلینزو™ ڈی ڈی آر کیپسول
(ڈیکسلینزوپرازول)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو گرمی، روشنی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری
سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہوجائیگی۔

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