Exlant®
(Dexlansoprazole)
Delayed Release Capsules

30mg
60mg
Capsules

ایکس لینٹ
(ڈیکسلینسوپرازول)
کیپسولز

۳۰ ملی گرام
۶۰ ملی گرام

QUALITATIVE AND QUANTITATIVE COMPOSITION

Exlant® 30mg capsules:
Each capsule contains:
Dexlansoprazole dual delayed release pellets eq. to
Dexlansoprazole.....30mg
Innovator's Specification
Exlant® 60mg capsules:
Each capsule contains:
Dexlansoprazole dual delayed release pellets eq. to
Dexlansoprazole.....60mg
Innovator's Specification

DESCRIPTION

The active ingredient is dexlansoprazole, a proton pump inhibitor, is (+)-2-[(R)- {[3-methyl-4-(2,2,2-trifluoroetoxy) 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 empirical formula is: C16H14F3N3O2S. Dexlansoprazole is a white to nearly white crystalline powder. Dexlansoprazole is stable when exposed to light. Dexlansoprazole is more stable in neutral and alkaline conditions than acidic conditions.

CLINICAL PHARMACOLOGY

Mechanism of Action: Dexlansoprazole belongs to a class of anti-secretory 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: Serum Gastrin Effects:** Studies shows that the mean fasting gastrin concentrations increased from baseline during treatment with dexlansoprazole. Increased gastrin 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. **Cardiac Electrophysiology:** Studies shows that at a dose five times the maximum recommended dose, dexlansoprazole does not prolong the QT interval to any clinically relevant extent. **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. 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 30mg or 60mg capsules although mean AUCt and Cmax values of dexlansoprazole were slightly higher (less than 10%) on Day 5 than on Day 1. **Absorption:** After oral administration of dexlansoprazole 30mg or 60mg capsules to healthy subjects and symptomatic GERD patients, mean Cmax and AUC values of dexlansoprazole increased approximately dose proportionally. **Effect of Food:** Patient 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 and was independent of concentration from 0.01 to 20mcg/mL. 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. Because dexlansoprazole is metabolized by CYP2C19 and CYP3A4, inducers and inhibitors of these enzymes may potentially alter exposure of dexlansoprazole. **Excretion:** Following the administration of dexlansoprazole capsule, no unchanged dexlansoprazole is excreted in urine. **Pharmacogenomics:** Effect of CYP2C19 Polymorphism on Systemic Exposure of Dexlansoprazole Systemic exposure of dexlansoprazole is generally higher in intermediate and poor metabolizers.

INDICATIONS AND USAGE

Dexlansoprazole is a proton pump inhibitor used to treat:
1. Healing of EE(Erosive esophagitis). 2. Maintenance of Healed EE and Relief of Heartburn. 3. Symptomatic Non-Erosive GERD (Gastroesophageal reflux disease)

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 Renantiomer. Contraindicated with rilpivirine-containing products.

INTERACTIONS

Anti-retrovirals: Decreased exposure of rilpivirine, atazanavir and nelfinavir when use concomitantly with dexlansoprazole may reduce antiviral effect and promote drug resistance. While increased exposure of saquinavir may increase toxicity of antiretroviral drugs. **Warfarin:** Increased INR and prothrombin time in patients receiving PPIs and warfarin. Monitor INR and prothrombin. **Methotrexate:** Concomitant use of PPIs with methotrexate (at high doses)may elevate and prolong serum concentrations of methotrexate or its metabolite hydroxy methotrexate, leading to methotrexate toxicities. **Digoxin:** Potential for increased exposure of digoxin. Dose adjustment of digoxin may be needed to maintain therapeutic drug concentrations. Drugs dependent on Gastric pH for absorption(e.g.,iron salts, erlotinib, dasatinib, nilotinib, mycophenoloate mofetil,ketoconazole /itraconazole): Dexlansoprazole can reduce the absorption of drugs due to its effect on reducing intragastric acidity. **Tacrolimus:** Dose adjustment is needed. **CYP2C19 or CYP3A4 inducers:** Decreased exposure of dexlansoprazole when used concomitantly with strong inducers. **CYP2C19 or CYP3A4 inhibitors:** Increased exposure of dexlansoprazole when used concomitantly with strong inhibitors. **Cytochrome P 450 Interactions:** Dexlansoprazole is metabolized, in part, by CYP2C19 and CYP3A4. **Clopidogrel:** Clopidogrel is metabolized to its active metabolite in part by CYP2C19. The mean AUC of the active metabolite of clopidogrel was reduced by approximately 9% (mean AUC ratio was 91%, with 90% CI of 86-97%) when dexlansoprazole was co-administered compared to administration of clopidogrel alone. **Alcohol:** Avoid using alcohol with dexlansoprazole.

USE IN SPECIFIC POPULATION

Pregnancy: There are no studies with dexlansoprazole use in pregnant women to inform a drug-associated risk. **Lactation:** There is no information regarding the presence of dexlansoprazole in human milk, the effects on the breastfed infant, or the effects on milk production. **Pediatric Use:** Safety and effectiveness of dexlansoprazole have not been established in pediatric patients. The use of dexlansoprazole is not recommended for symptomatic non-erosive GERD in pediatric patients less than 1 year of age because studies in this class of drugs have not demonstrated efficacy. **Geriatric Use:** Greater sensitivity of some older individuals is there. The terminal elimination half-life of dexlansoprazole is significantly increased in geriatric 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. **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. **Hepatic Impairment:** Patients with moderate hepatic impairment (Child-Pugh Class B) who received a single oral dose of 60mg dexlansoprazole capsules, the systemic exposure (AUC) of bound and unbound dexlansoprazole was approximately two times greater compared to normal hepatic function. For adult patients with moderate hepatic impairment, (Child-Pugh Class B), the recommended dosage is 30mg dexlansoprazole capsule once daily for up to 8 weeks. The use of dexlansoprazole is not recommended in patients with severe hepatic impairment (Child-Pugh Class C). No dos-age adjustment for dexlansoprazole capsules is necessary for patients with mild hepatic impairment (Child-Pugh Class A). **Gender:** Females have higher systemic exposure (AUC) (43% higher) than males who received a single oral dose of dexlansoprazole 60mg capsules.

PRECAUTIONS

Presence of 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 B-12) 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 B-12) caused by hypo- or achlorhydria. **Clostridium Difficile Associated Diarrhea:** PPI therapy like dexlansoprazole may be associated with an increased risk of Clostridium difficile associated diarrhea, especially in hospitalized patients. This diagnosis should be con-sidered for diarrhea that does not improve. **Bone Fracture:** PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine. **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.Treatment of hypomagnesemia required magnesium replacement and discon-tinuation of the PPI. **Interactions with Investigations for Neuroendocrine Tumors:** Dexlansoprazole may cause interaction. **Interaction with Methotrexate:** 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.

ADVERSE REACTIONS

The following serious adverse reactions are described below: Acute Interstitial Nephritis, Cyanocobalamin (Vitamin B-12) Deficiency, Clostridium difficile Associated Diarrhea Bone Fracture and Hypomagnesemia.

DOSAGE AND ADMINISTRATION

Exlant Capsules Adult Dosing Recommendations		
Indications	**Dosage**	**Duration**
Healing of EE(Erosive esophagitis)	One 60mg once daily	upto 8 weeks
Maintenance of Healed EE and Relief of Heartburn	One 30mg once daily	Controlled studies didn't extend beyond 6 months in adults and 16 weeks in patients 12 to 17 years
Symptomatic Non-Erosive GERD	One 30mg once daily	4 weeks

•Take without regard to food. Swallow whole; do not chew.
•Alternatively, the capsule can be administered with water via oral syringe or nasogastric (NG) tube. **Overdosage:** There have been no reports of significant overdose of dexlansoprazole. 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. In the event of over-exposure, treatment should be symptomatic and supportive. **Missed dose:** 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.

INSTRUCTIONS:

Dosage as directed by the physician.
Store at 25°C ,excursions permitted to 15°C to 30°C.
Protect from sunlight and moisture.
Keep all medicines out of the reach of children.

PRESENTATION

Exlant 30mg Capsules are available in blister pack of 3 x 10's.
Exlant 60mg Capsules are available in blister pack of 3 x 10's.

علامات/طریقہ استعمال:

ایکس لیٹ پروٹون پمپ انہیبٹر ہے جو کہ سینے کی جلن اور اس سے منسلک امراض کے علاج کے لئے تجویز کردہ ہے۔

مضر اثرات:

ایکیوٹ انٹرسٹیشیل نیفرائٹس، وٹامن بی-۱۲ کی کمی، ہائپومیگنیسیمیا سے مشروط دست، اوسٹیوپوروسس سے منسلک ہڈیوں کا فریکچر۔

احتیاطی تدابیر:

علاج سے پہلے حساس مریضوں کی تشخیص ضروری ہے۔
۱۲ سال سے کم عمر کے بچوں اور جگر کے پیچیدہ امراض میں مبتلا مریضوں میں ایکس لیٹ کا استعمال ممنوع ہے۔ بزرگ احتیاط سے استعمال کریں۔

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۲۵ ڈگری سینٹی گریڈ پر رکھیں،
محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔
سورج کی روشنی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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