DXL®
(Dexlansoprazole)

Highnoon

COMPOSITION
DXL 30mg Capsule: Each capsule contains: Dexlansoprazole dual delayed-release pellets eq. to Dexlansoprazole 30mg
DXL 60mg Capsule: Each capsule contains: Dexlansoprazole dual delayed-release pellets eq. to Dexlansoprazole 60mg

DESCRIPTION
Dexlansoprazole is a compound that inhibits gastric acid secretion. It is the R-isomer of the proton pump inhibitor lansoprazole.

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.

PHARMACOKINETICS
After an oral dose of delayed release formulation of dexlansoprazole, peak plasma concentration occurs 1 to 2 hours after dosing, followed by a second peak within 4 to 5 hours. Plasma protein binding varies from about 96% to 99%. Dexlansoprazole is extensively metabolized in the liver to inactive metabolites. Oxidative metabolites are formed by cytochrome P450 isoenzymes, CYP2C19 and CYP3A4. Dexlansoprazole has half-life of about 1 to 2 hours. Metabolites are excreted in the urine and feces.

INDICATIONS AND USAGE
It is indicated in;
- Healing of erosive esophagitis.
- Maintenance of healed erosive esophagitis and relief of heartburn.
- Treatment of symptomatic non-erosive gastroesophageal reflux disease

DOSAGE AND ADMINISTRATION
- An oral dose of 60 mg capsule is given once daily for up to eight weeks for healing of all grades of erosive esophagitis in patients 12 years of age and older. Once erosion have healed 30mg once daily is given for maintenance.
- An oral dose of 30 mg capsule once daily are indicated in patients 12 years of age and older to maintain healing of erosive esophagitis and relief of heartburn for up to six months in adults and 16 weeks in patients 12 to 17 years of age.
- An oral dose of 30 mg capsule is given once daily for four weeks for the treatment of heartburn associated with symptomatic non-erosive gastroesophageal reflux disease (GERD) in patients 12 years of age and older.
- It can taken without regard to food.

CONTRAINDICATIONS
- It 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 dexolansaprazole, are contraindicated with rilpivirine-containing products.

ADVERSE REACTIONS
The reported adverse effects are acute interstitial nephritis, Clostridium Difficile-Associated Diarrhea, bone fracture, Cutaneous and Systemic Lupus Erythematosus, Cyanocobalamin (Vitamin B- 12) Deficiency and Hypomagnesemia.
The other reported adverse events are diarrhea, abdominal pain, nausea, upper respiratory tract infection, vomiting, flatulence, anemia, lymphadenopathy, autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, angina, arrhythmia, bradycardia, chest pain, edema, myocardial infarction, palpitation, tachycardia, ear pain, tinnitus, vertigo, deafness, goiter, eye irritation, eye swelling, blurred vision, abdominal discomfort, abdominal tenderness, abnormal feces, anal discomfort, Barrett's esophagus, bezoar, bowel sounds abnormal, 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, oral edema, pancreatitis, retching, asthenia, chest pain, chills, feeling abnormal, inflammation, mucosal inflammation, nodule, pain, pyrexia, biliary colic, cholelithiasis, drug-induced hepatitis, hepatomegaly, hypersensitivity, candida infections, influenza, nasopharyngitis, oral herpes, pharyngitis, sinusitis, viral infection, vulvo-vaginal infection, fractures, joint sprains, 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, urticaria, deep vein thrombosis, hot flush, anaphylactic shock (requiring emergency intervention), exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis (some fatal) and hypertension. The additional reported adverse events are; anaphylaxis, auditory hallucination, B-cell lymphoma, bursitis, central obesity, cholecystitis acute, dehydration, diabetes mellitus, dysphonia, epistaxis, folliculitis, gout, herpes zoster, hyperlipidemia, hypothyroidism, increased neutrophils, MCHC decrease, neutropenia, rectal tenesmus, restless legs syndrome, facial edema, somnolence, nasopharyngitis, cerebrovascular accident, transient ischemic attack, pharyngeal edema, throat tightness, generalized rash, leukocytoclastic vasculitis, oropharyngeal pain, tonsillitis and heart value thickening.

DRUG INTERACTIONS
- The effect of PPIs on antiretroviral drugs is variable. Decreased exposure of some antiretroviral drugs (e.g., rilpivirine, atazanavir, and nelfinavir) when used concomitantly with dexlansoprazole may reduce antiviral effect and promote the development of drug resistance. Increased exposure of other antiretroviral drugs (e.g., saquinavir) when used concomitantly with dexlansoprazole may increase toxicity of the antiretroviral drugs.
- Avoid concomitant use of dexlansoprazole with Rilpivirine-containing products, Atazanavir, Nelfinavir, Saquinavir and other antiretrovirals drugs.
- 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. Monitor INR and prothrombin time. Dose adjustment of warfarin may be needed to maintain target INR range.
- 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. A temporary withdrawal of dexlansoprazole may be considered in some patients receiving high-dose methotrexate.
- Potential for increased exposure of digoxin. Monitor digoxin concentrations. Dose adjustment of digoxin may be needed to maintain therapeutic drug concentrations.
- Dexlansoprazole can reduce the absorption of drugs i.e. drugs dependent on gastric pH for absorption (e.g., iron salts, erlotinib, dasatinib, nilotinib, mycophenolate mofetil, ketoconazole/ itraconazole).
- Use dexlansoprazole with caution in transplant patients receiving mycophenolate mofetil.
- Potentially increased exposure of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19. Monitor tacrolimus whole blood trough concentrations. Dose adjustment of tacrolimus may be needed to maintain therapeutic drug concentrations.
- 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 and consider repeating the test if initial CgA levels are high.
- 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.
- There have been reports of false positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving PPIs. An alternative confirmatory method should be considered to verify positive results.
- Decreased exposure of dexlansoprazole when used concomitantly with strong inducers CYP2C19 or CYP3A4 Inducers. St. John's Wort, rifampin. Avoid concomitant use with dexlansoprazole (Ritonavir-containing products).
- Increased exposure of dexlansoprazole is expected when used concomitantly with strong inhibitors CYP2C19 or CYP3A4 Inhibitors (Voriconazole).
- Alcohol may modify the release rate of dexlansoprazole, possibly leading to decreased efficacy. Avoid alcoholic beverages when taking dexlansoprazole.

WARNINGS AND PRECAUTIONS
- Before giving PPI to patient the possibility of the malignancy should be excluded since these drugs may mask symptoms and delay diagnosis. 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.
- 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.
- 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.
- 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 accordingly. Regular monitoring of bone density should be monitored.
- Avoid administration of PPIs for longer than medically indicated. If signs or symptoms consistent with cutaneous lupus erythematosus or systemic lupus erythematosus are noted in patients receiving dexlansoprazole, 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.
- 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. 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. 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.
- 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.
- The 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.
- PPIs should be used with caution in hepatic impairment.
- 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.
- 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.
- Severe cutaneous adverse reactions including Steven Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic syndrome symptom (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in associate with the use of PPIs. Discontinue omeprazole as first sign and symptom of severe cutaneous adverse reaction or other signs of hypersensitivity and consider further evaluation.
- PPI use is associated with an increased risk of fundic gland polyps that increase 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.

USE IN SPECIFIC POPULATIONS
Pregnancy
There are no studies with dexlansoprazole use in pregnant women to inform a drug-associated risk.

Lactation
Since many drugs are excreted in milk, and because of the potential for adverse reactions to nursing infants from dexlansoprazole, a decision should be made to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use
The safety and effectiveness of dexlansoprazole have not been established in pediatric patients less than 12 years of age. 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.
The adverse reaction profile in patients 12 to 17 years of age was similar to adults
Dexlansoprazole is not recommended in pediatric patients less than two years of age.
Heart valve thickening and bone changes may occur.
It is not recommended for the treatment of symptomatic GERD in pediatric patients one month to less than one year of age

Hepatic Impairment
No dosage adjustment for dexlansoprazole capsules is necessary for patients with mild hepatic impairment (Child-Pugh Class A). Patients with moderate hepatic impairment (Child-Pugh Class B), the recommended dosage is 30 mg once daily for up to eight weeks. Dexlansoprazole is not recommended in patients with severe hepatic impairment (Child-Pugh Class C).

OVERDOSAGE
In the event of over-exposure, treatment should be symptomatic and supportive. Dexlansoprazole is not expected to be removed from the circulation by hemodialysis.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

PRESENTATION
DXL 30mg Capsules: Alu. Alu. Blister Pack of 3 x 10's.
DXL 60mg Capsules: Alu. Alu. Blister Pack of 3 x 10's.

ڈی ایکس ایل®
(ڈیکسلانسو پرازول)

خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
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