Dexlansoprazole MR Capsules 30 & 60 mg For Sale In India Only

DDR® 30/60

डीडीआर ३०/ डीडीआर ६०

To be sold by retail on the prescription of a Registered Medical Practitioner only.

PRESCRIBING INFORMATION

1. GENERIC NAME

Dexlansoprazole MR Capsules 30 mg

Dexlansoprazole MR Capsules 60 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dexlansoprazole MR Capsules 30 mg
Each HPMC capsule contains
Dexlansoprazole IP 30 mg
(as modified release pellets)
Colours: Titanium Dioxide IP, Sunset yellow supra FCF and approved colours used in capsule shell

Dexlansoprazole MR Capsules 60 mg
Each HPMC capsule contains
Dexlansoprazole IP 60 mg
(as modified release pellets)
Colours: Titanium Dioxide IP, Sunset yellow supra FCF and approved colours used in capsule shell

3. DOSAGE FORM AND STRENGHTS

Dexlansoprazole is available as 30 mg and 60 mg capsules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Dexlansoprazole is indicated for the treatment of

1. Healing of all grades of erosive esophagitis.
2. Maintaining healing of EE and relief of heartburn.
3. Treating heart burn associated with symptomatic non-erosive gastro esophageal reflux disease (GERD)

4.2 Posology and method of administration

Posology

Indication	Dosage of dexlansoprazole capsules	Duration
Healing of EE	One 60 mg capsule once daily	Up to 8 weeks
Maintaining healing of 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

Dosage adjustment in patients with hepatic impairment for the healing of erosive esophagitis

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)

Important administration information

- Take without regard to food.
- Missed doses: 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.
- Swallow whole; do not chew.
- For patients who have trouble swallowing capsules, dexlansoprazole capsules can be opened and administered with applesauce as follows:

1. Place one tablespoonful of applesauce into a clean container.
2. Open capsule.
3. Sprinkle intact granules on applesauce.
4. Swallow applesauce and granules immediately. Do not chew granules. Do not save the applesauce and granules for later use.

- Alternatively, the capsule can be administered with water via oral syringe or nasogastric (NG) tube.

- Administration with water in an oral syringe

1. Open the capsule and empty the granules into a clean container with 20 ml of water.
2. Withdraw the entire mixture into a syringe.
3. Gently swirl the syringe in order to keep granules from settling.
4. Administer the mixture immediately into the mouth. Do not save the water and Granule mixture for later use.
5. Refill the syringe with 10 ml of water, swirl gently, and administer.
6. Refill the syringe again with 10 ml of water, swirl gently, and administer.

- Administration with water via a NG tube (≥16 french)

1. Open the capsule and empty the granules into a clean container with 20 ml of water.
2. Withdraw the entire mixture into a catheter-tip syringe.
3. Swirl the catheter-tip syringe gently in order to keep the granules from settling, and immediately inject the mixture through the NG tube into the stomach. Do not save the water and granule mixture for later use.
4. Refill the catheter-tip syringe with 10 ml of water, swirl gently, and flush the tube.
5. Refill the catheter-tip syringe again with 10 ml of water, swirl gently, and administer.

4.3 Contraindications

- Dexlansoprazole is contraindicated in patients with known hypersensitivity to any component of the formulation. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, bronchospasm, acute tubulointerstitial nephritis and urticaria.
- PPIs, including dexlansoprazole, are contraindicated with rilpivirine-containing products

4.4 Special warnings and precautions for use

Presence of gastric malignancy

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.

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.

Cutaneous and systemic lupus erythematosus

Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in patients taking PPIs. These events have occurred as both new onset and an exacerbation of existing autoimmune disease. The majority of PPI-induced lupus erythematosus cases were cle.

The most common form of cle reported in patients treated with PPIs was sub-acute CLE (SCLE) and occurred within weeks to years after continuous drug therapy in patients ranging from infants to the elderly. Generally, histological findings were observed without organ involvement.

Systemic lupus erythematosus (SLE) is less commonly reported than CLE in patients receiving PPIs. PPIs-associated SLE is usually milder than nondrug induced SLE. Onset of SLE typically occurred within days to years after initiating treatment primarily in patients ranging from young adults to the elderly. The majority of patients presented with rash; however, arthralgia and cytopenia were also reported.

Avoid administration of PPIs for longer than medically indicated. If signs or symptoms consistent with CLE or SLE 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 PPIs alone in four to 12 weeks. Serological testing (e.g., ANA) may be positive and elevated serological test results may take longer to resolve than clinical manifestations.

Cyanocobalamin (vitamin b12) deficiency

Daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than three 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 in patients treated with dexlansoprazole.

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), healthcare professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.

Interactions with investigations for neuroendocrine tumors

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. If serial tests are performed (e.g., for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.

Interaction with methotrexate

Literature suggests that 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.

Fundic gland polyps

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.

4.5 Drug interactions

Tables 3 and 4 include drugs with clinically important drug interactions and interaction with diagnostics when administered concomitantly with dexlansoprazole and instructions for preventing or managing them. Consult the labeling of concomitantly used drugs to obtain further information about interactions with PPIs.

Table 3. Clinically relevant interactions affecting drugs coadministered with dexlansoprazole and interactions with diagnostics

Antiretrovirals	
Clinical impact:	The effect of PPIs on antiretroviral drugs is variable. The clinical importance and the mechanisms behind these interactions are not always known. 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. There are other antiretroviral drugs which do not result in clinically relevant interactions with dexlansoprazole.
Intervention:	Rilpivirine-containing products: concomitant use with dexlansoprazole is contraindicated.. Atazanavir: see prescribing information for atazanavir for dosing information. Nelfinavir: avoid concomitant use with dexlansoprazole. See prescribing information for nelfinavir. Saquinavir: see the prescribing information for saquinavir and monitor for potential saquinavir toxicities. Other antiretrovirals: see prescribing information.
Warfarin	
Clinical impact:	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.
Intervention:	Monitor INR and prothrombin time. Dose adjustment of warfarin may be needed to maintain target INR range. See prescribing information for warfarin.
Methotrexate	
Clinical impact:	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. No formal drug interaction studies of high- dose methotrexate with PPIs have been conducted.
Intervention:	A temporary withdrawal of dexlansoprazole may be considered in some patients receiving high-dose methotrexate.
Digoxin	
Clinical impact:	Potential for increased exposure of digoxin.
Intervention:	Monitor digoxin concentrations. Dose adjustment of digoxin may be needed to maintain therapeutic drug concentrations. See prescribing information for digoxin.
Drugs dependent on gastric pH for absorption (e.g., iron salts, erlotinib, dasatinib, nilotinib, mycophenolate mofetil, ketoconazole/itraconazole)	
Clinical impact:	Dexlansoprazole can reduce the absorption of other drugs due to its effect on reducing intragastric acidity.
Intervention:	Mycophenolate mofetil (MMF): 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 dexlansoprazole and MMF. Use dexlansoprazole with caution in transplant patients receiving MMF. See the prescribing information for other drugs dependent on gastric pH for absorption.
Tacrolimus	
Clinical impact:	Potentially increased exposure of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19.
Intervention:	Monitor tacrolimus whole blood trough concentrations. Dose adjustment of tacrolimus may be needed to maintain therapeutic drug concentrations. See prescribing information for tacrolimus.
Interactions with investigations of neuroendocrine tumors	
Clinical impact:	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.
Intervention:	Temporarily stop dexlansoprazole treatment at least 14 days before assessing CGA levels and consider repeating the test if initial CGA levels are high. If serial tests are performed (e.g., for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.
Interaction with secretin stimulation test	
Clinical impact:	Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma.
Intervention:	Temporarily stop dexlansoprazole treatment at least 30 days before assessing to a low gastrin levels to return to baseline.
False positive urine tests for THC	
Clinical impact:	There have been reports of false positive urine screening tests for tetra hydro cannabinol (THC) in patients receiving PPIs.
Intervention:	An alternative confirmatory method should be considered to verify positive results.

Table 4. Clinically relevant interactions affecting dexlansoprazole when coadministered with other drugs and substances

CYP2C19 or CYP3A4 inducers	
Clinical impact:	Decreased exposure of dexlansoprazole when used concomitantly with strong inducers.
Intervention:	St. John's wort, rifampin: avoid concomitant use with dexlansoprazole. Ritonavir-containing products
CYP2C19 or CYP3A4 inhibitors	
Clinical impact:	Increased exposure of dexlansoprazole is expected when used concomitantly with strong inhibitors.
Intervention:	Voriconazole

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

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.

In animal reproduction studies, oral administration of lansoprazole to rats during organogenesis through lactation at 1.8 times the maximum recommended human dexlansoprazole dose produced reductions in the offspring in femur weight, femur length, crown-rump length and growth plate thickness (males only) on postnatal day 21. These effects were associated with reduction in body weight gain. Advise pregnant women of the potential risk to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. A l pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the us general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

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. However, lansoprazole and its metabolites are present in rat milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for dexlansoprazole and any potential adverse effects on the breastfed child from dexlansoprazole or from the underlying maternal condition.

Pediatric use

The safety and effectiveness of dexlansoprazole have not been established in pediatric patients less than 12 years of age.

Geriatric use

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.

Hepatic impairment

No studies have been conducted in patients with severe hepatic impairment (child-pugh class c); the use of dexlansoprazole is not recommended for these patients.

4.7 Effects on ability to drive and use machines

Adverse drug reactions such as dizziness, vertigo, visual disturbances and somnolence may occur. Under these conditions the ability to react may be decreased.

4.8 Undesirable effects

The following serious adverse reactions are described below and elsewhere in labeling:

- Acute tubulointerstitial nephritis
- Clostridium difficile-associated diarrhea
- Bone fracture
- Cutaneous and systemic lupus erythematosus cyanocobalamin (vitamin b12) deficiency
- Hypomagnesemia
- Fundic gland polyps
- Risk of heart valve thickening in pediatric patients less than two years of age.

The following adverse reactions have been identified during postapproval of dexlansoprazole. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- **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, fundic gland polyps general disorders and administration site conditions: facial edema hepatobiliary disorders: drug-induced hepatitis
- **Immune system disorders**: anaphylactic shock (requiring emergency intervention), exfoliative dermatitis, stevens-jhohnson 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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. To report suspected adverse reactions, contact msn laboratories private limited at pharmacovigilance@msnlabs.com or through company website www.msnlabs.com->contact us->medical enquiry/ to report a side effect. You can also report side effects directly via the national pharmacovigilance programme of india by calling on 1800 180 3024 or you can report to msn labs on ++91- 40-38265229 (direct line); +91 7331134745 (whatapp). By reporting side effects, you can help provide more information on the safety of this product.

4.9 Overdose

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. Nonserious 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.

5. Pharmacological properties

5.1 Pharmacodynamic properties

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.

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. The results are summarized in table 5.

Table 5. Effect on 24 hour intragastric pH on day 5 after administration of dexlansoprazole or lansoprazole

Dexlansoprazole 60 mg	**Lansoprazole 30 mg**
Mean intragastric pH	
4.55	4.13
% time intragastric pH >4 (hours)	
71 (17 hours)	60 (14 hours)

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 30 and 60 mg dexlansoprazole. 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 pretreatment levels within one month of discontinuation of treatment.

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.

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, 60, or 90 mg for up to 12 months.

During lifetime exposure of rats dosed daily with up to 150 mg/kg/day of lansoprazole, marked hypergastrinemia was observed followed by ECL cell proliferation and formation of carcinoid tumors, especially in female rats.

Cardiac electrophysiology

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

5.2 Pharmacokinetic properties

Absorption

After oral administration of dexlansoprazole 30 or 60 mg to healthy subjects and symptomatic GERD patients, mean Cmax and AUC values of dexlansoprazole increased approximately dose proportionally.

When granules of dexlansoprazole 60 mg are mixed with water and dosed via NG tube or orally via syringe, the bioavailability (Cmax and AUC) of dexlansoprazole was similar to that when dexlansoprazole 60 mg was administered as an intact capsule.

Effect on food

In food-effect studies in healthy subjects receiving dexlansoprazole 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 20 mcg/ml. The apparent volume of distribution (vz/f) after multiple doses in symptomatic GERD patients was 40 l.

Elimination

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.

CYP2C19 is a polymorphic liver enzyme which exhibits three phenotypes in the metabolism of CYP2C19 substrates: extensive metabolizers (*1/*1), intermediate metabolizers (*1/mutant) and poor metabolizers (mutant/mutant). Dexlansoprazole is the major circulating component in plasma regardless of CYP2C19 metabolizer status. 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, no unchanged dexlansoprazole is excreted in urine. Following the administration of [^{14}C] dexlansoprazole to six healthy male subjects, approximately 50.7% (standard deviation (SD): 9.0%) of the administered radioactivity was excreted in urine and 47.6% (SD: 7.3%) in the feces. Apparent clearance (cl/f) in healthy subjects was 11.4 to 11.6 l/hour, respectively, after five days of 30 or 60 mg once daily administration.

6. Nonclinical properties

The carcinogenic potential of dexlansoprazole was assessed using lansoprazole studies. In two, 24 month carcinogenicity studies, sprague-dawley rats were treated orally with lansoprazole at doses of 5 to 150 mg/kg/day, about one to 40 times the exposure on a body surface (mg/m^2) basis of a 50 kg person of average height [1.46 m^2 body surface area (BSA)] given the recommended human dose of lansoprazole 30 mg/day.

Lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids in both male and female rats.

In rats, lansoprazole also increased the incidence of intestinal metaplasia of the gastric epithelium in both sexes. In male rats, lansoprazole produced a dose-related increase of testicular interstitial ce l adenomas. The incidence of these adenomas in rats receiving doses of 15 to 150 mg/kg/day (four to 40 times the recommended human lansoprazole dose based on BSA) exceeded the low background incidence (range = 1.4 to 10%) for this strain of rat.

In a 24 month carcinogenicity study, cd-1 mice were treated orally with lansoprazole doses of 15 to 600 mg/kg/day, two to 80 times the recommended human lansoprazole dose based on BSA. Lansoprazole produced a dose-related increased incidence of gastric ECL cell hyperplasia. It also produced an increased incidence of liver tumors (hepatocellular adenoma plus carcinoma). The tumor incidences in male mice treated with 300 and 600 mg lansoprazole/kg/day (40 to 80 times the recommended human lansoprazole dose based on BSA) and female mice treated with 150 to 600 mg lansoprazole/kg/day (20 to 80 times the recommended human lansoprazole dose based on bsa) exceeded the ranges of background incidences in historical controls for this strain of mice. Lansoprazole treatment produced adenoma of rete testis in male mice receiving 75 to 600 mg/kg/day (10 to 80 times the recommended human lansoprazole dose based on BSA).

A 26 week p53 (+/-) transgenic mouse carcinogenicity study of lansoprazole was not positive.

Lansoprazole was positive in the AMES test and the in vitro human lymphocyte chromosomal aberration assay. Lansoprazole was not genotoxic in the ex vivo rat hepatocyte unscheduled DNA synthesis (UDS) test, the in vivo mouse micronucleus test or the rat bone marrow cell chromosomal aberration test.

Dexlansoprazole was positive in the AMES test and in the in vitro chromosome aberration test using chinese hamster lung cells. Dexlansoprazole was negative in the in vivo mouse micronucleus test.

The potential effects of dexlansoprazole on fertility and reproductive performance were assessed using lansoprazole studies. Lansoprazole at oral doses up to 150 mg/kg/day (40 times the recommended human lansoprazole dose based on BSA) was found to have no effect on fertility and reproductive performance of male and female rats.

7. Pharmaceutical particulars

7.1 Incompatibilities

Not applicable.

7.2 Special precautions for disposal and other handling

7.3 Packing information

DDR 30: Blister pack of 10 capsules

DDR 60: Blister pack of 10 capsules

7.4 Storage and handling instructions

Store below 25°C. Protect from light and moisture.

8. Patient counseling information

Advise the patient to read the prescribing information.

Adverse reactions

Advise patients to report to their healthcare provider if they experience any signs or symptoms consistent with:

- Hypersensitivity reactions
- Acute tubulointerstitial nephritis
- Clostridium difficile-associated diarrhea
- Bone fracture
- Cutaneous and systemic lupus erythematosus
- Cyanocobalamin (vitamin b12) deficiency
- Hypomagnesemia

Drug interactions

Advise patients to report to their healthcare provider if they are taking rilpivirine- containing products or high-dose methotrexate.

Pregnancy

Advise a pregnant woman of the potential risk to a fetus. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy.

Administration

- Take without regard to food.
- Missed doses: 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.
- Swallow whole; do not chew.
- Can be opened and sprinkled on applesauce for patients who have trouble swallowing the capsule.
- Alternatively, the capsule can be administered with water via oral syringe or ng tube, as described in the instructions for use.

9. Details of manufacturer

MSN Laboratories Private Limited,
Formulations Division, Unit-06,
Sy. No. (Parts of), 745,811-813,824 & 825,
Burgul Village, Farooqnagar Mandal,
Ranga Reddy District, Pincode 509202,
Telangana State, india.

10. DETAILS OF MANUFACTURING LICENCE NUMBER

Mfg. Lic. No.: TS/RR/2024-116346

11. Date of revision

October -2021

630004-00