For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only. XXXXXXX-9093

Tegoprazan Tablets 50 mg

TEGCISE™50

1. GENERIC NAME
Tegoprazan Tablets 50 mg
2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film coated tablets contains:
Tegoprazan..50mg
Excipients..q.s.
Colors: Titanium dioxide I.P. and Iron oxide Red NF
3. DOSAGE FORM AND STRENGTH
Tablets and 50 mg
4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Tegoprazan 50 mg is indicated for
- Treatment of Erosive Gastroesophageal Reflux Disease,
- Treatment of Non-Erosive Gastroesophageal Reflux Disease,
- Treatment of Gastric Ulcer

4.2 Posology and method of administration
Posology
Adult
Treatment of Erosive Gastroesophageal Reflux Disease
- 50 mg once daily for 4 weeks.
- For patients who do not heal or have persistent symptoms after 4 weeks, an additional 4-week treatment may be considered.

Treatment of Non-Erosive Gastroesophageal Reflux Disease
- 50 mg once daily for 4 weeks.

Treatment of Gastric Ulcer
- 50 mg once daily for 8 weeks.

Method of administration
Oral use.
Tegoprazan can be taken without regard to food.
4.3 Contraindications
- Patients with Hypersensitivity to tegoprazan, any of the product components or substituted benzimidazoles
- Patients who take atazanavir, nelfinavir or rilpivirine-containing products
- Pregnant women or nursing mothers

4.4 Special warnings and precautions for use
- Hepatic impairment: Safety and efficacy of tegoprazan have not been established in patients with hepatic impairment.
- Renal impairment: Safety and efficacy of tegoprazan have not been established in patients with renal impairment.
- Elderly people: In general, tegoprazan should be administered to the elderly patients with caution, keeping in mind the greater frequency of decreased physiological functions, such as liver or kidney.
- Pediatric Use: Clinical safety and efficacy of Tegoprazan in pediatric and adolescent have not been established

General Precautions
1) In the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment with tegoprazan may alleviate symptoms and delay diagnosis.
2) 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. 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.
3) Patient should be monitored regularly when treated with tegoprazan for long term
4) Gastric polyp was observed with long term use of P-CABs and tegoprazan
5) Gastric ulcer: Clinical experience on long term use is insufficient. Do not administer for patient who do not require maintenance therapy
6) 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 appropriate dose and shortest duration of tegoprazan therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines.
7) Hypomagnesemia has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPIs. For patients expected to be on prolonged treatment or who take tegoprazan 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 treatment and periodically. Serious adverse reactions include tetany, arrhythmias, and seizures.
8) Decreased gastric acidity due to PPIs, increases counts of bacteria normally present in the gastrointestinal tract. Treatment with gastric acid suppressants may possibly increase the risk of gastrointestinal infections such as *Salmonella, Campylobacter and Clostridium difficile*. Published observational studies suggest that PPI therapy may be associated with an increased risk of *Clostridium difficile*-associated diarrhea (CDAD), especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve. CDAD has been reported with use of nearly all antibacterial agents. Patients should use the lowest dose and shortest duration of tegoprazan therapy appropriate to the condition being treated.
9) Fundic gland polyps: Risk of fundic gland polyps increases with long-term use of PPIs, especially beyond one year. Fundic gland polyps are mostly asymptomatic. Use the shortest duration and the lowest dose of PPI and tegoprazan according to symptoms.
4.5 Drug interactions
1. Effects of other drugs on tegoprazan
Tegoprazan is metabolized in liver by CYP3A4. *In vitro* studies have shown that ketoconazole, a CYP3A4 inhibitor, significantly inhibited the metabolism of tegoprazan, and while inhibitors of CYP1A2, CYP2C9, CYP2C19, CYP2D6 did not significantly reduced the metabolism of tegoprazan. Concomitant use of tegoprazan with CYP3A4 inhibitors may elevate exposure of tegoprazan.
Tegoprazan is a substrate of P-gp. *In vitro* studies have shown that the efflux ratio of tegoprazan was decreased by verapamil, a P-gp inhibitor. Co-administration of tegoprazan and P-gp inhibitors may result in increase of exposure by increasing gastrointestinal absorption of tegoprazan.
In healthy adult subjects, co-administration of tegoprazan with clarithromycin (substrates and inhibitors of CYP3A4 and P-gp) resulted in increase of $C_{ss,max}$ and AUC_{τ} of tegoprazan by 1.65 times and 2.5 times, respectively. AUC_{τ} of clarithromycin increased slightly by 1.25 times and there was no significant increase of $C_{ss,max}$. Neither adverse reactions nor adverse drug reaction clinically significant were observed.
In healthy adult subjects, co-administration of tegoprazan with metronidazole, tetracycline and bismuth resulted in decrease of the AUC_{0-12} and $C_{ss,max}$ of tegoprazan by 0.78 times and 0.75 times, respectively, and the AUC_{0-12} of tegoprazan metabolite M1 decreased by 0.77 times and $C_{ss,max}$ by 0.84 times, compared to when tegoprazan was administered alone. However, no clinically significant adverse reactions or adverse drug reactions were observed.
2. Effects of tegoprazan on other drugs
In vitro studies have shown that tegoprazan showed competitive inhibition against CYP2C8 and CYP3A4. But, the IC_{50} values were approximately 25-fold greater than the peak plasma concentration of the recommended human dose.
For OATP1B1, there was a difference in the inhibitory activity of tegoprazan depending on substrates and it is expected that the plasma concentrations of some drugs which are substrate for OATP1B1 may be increased slightly considering the $C_{ss,max}$ at the clinical doses.
As a result of co-administration of tegoprazan with metronidazole, tetracycline and bismuth to healthy adults, compared to the co-administration of metronidazole, tetracycline and bismuth, the pharmacokinetics of metronidazole was not affected, and the AUC_{0-6} of tetracycline was decreased by 0.62 times, $C_{ss,max}$ decreased by 0.64 times, AUC_{0-6} of bismuth increased by 1.55 times, and $C_{ss,max}$ increased by 1.38 times, but no clinically significant adverse reactions or adverse drug reactions were observed.
3. Drugs Dependent on Gastric pH for Absorption
Due to its effects on gastric acid secretion, tegoprazan can reduce the absorption of drugs where gastric pH is an important determinant of their bioavailability. Like with other drugs that decrease the intragastric acidity, the absorption of drugs such as ketoconazole, itraconazole, ampicillin ester, atazanavir, iron salts, erlotinib, gefitinib and mycophenolate mofetil (MMF) can decrease during treatment with tegoprazan. While absorption of drugs such as digoxin can increase during treatment with tegoprazan. Because tegoprazan inhibits gastric acid secretion, co-administration of atazanavir, nelfinavir and rilpivirin with tegoprazan is expected to decrease plasma concentration of atazanavir, nelfinavir or rilpivirin which is dependent on gastric pH for absorption, results in a loss of the therapeutic effect. Therefore, concomitant use of atazanavir, nelfinavir and rilpivirine with tegoprazan is contraindicated.
4. Tegoprazan is mainly metabolized by CYP3A4. Concomitant use of clarithromycin, a CYP3A4 inhibitor, with tegoprazan has increased AUCτ of tegoprazan and clarithromycin by 2.5 times and 1.25 times, respectively.
5. Tegoprazan has been shown to have no effects on the pharmacokinetic profiles of amoxicillin.
6. Tegoprazan has been shown to have no effects on the pharmacokinetic profiles of atorvastatin.
7. Concomitant use of tegoprazan and NSAIDs (Naproxen, Aceclofenac or Celecoxib) has been shown to have no clinically significant effects on the pharmacokinetic profiles.
4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)
Pregnant women
There is no safety data for exposure to tegoprazan in pregnant women. In an embryo-fetal development study, short supernumerary cervical ribs were observed with a higher incidence in rats. Therefore, tegoprazan is contraindicated during pregnancy.
Nursing mothers
As it is not known whether tegoprazan is excreted into human milk, discontinue nursing while taking tegoprazan. Excretion of tegoprazan into milk has been reported in rats.
Paediatric population
Clinical safety and efficacy or tegoprazan in pediatric and adolescent patients have not been established.
Geriatric use
In general, tegoprazan should be administered to the elderly patients with caution, keeping in mind the greater frequency of decreased physiological functions, such as liver or kidney.
4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed for tegoprazan, and the loss of this ability cannot be predicted from its pharmacological action. Nevertheless, when considering the patient's ability to drive and use machines, the clinical condition of the patient and the adverse reactions of the drug should be considered.
4.8 Undesirable effects
1) A total of 5 clinical studies were conducted with erosive gastroesophageal reflux disease and non-erosive gastroesophageal reflux disease and gastric ulcer patients. 360 patients were treated with tegoprazan 50 mg. Adverse reactions and adverse drug reactions (marked with*) reported during the clinical trials are as following;
Common adverse reactions reported (≥1%) in tegoprazan 50 mg treatment group are presented in Table 1
Table 1: Adverse reactions (%) reported in ≥1% patients from clinical trials

System Organ Class	Adversereactions
Gastrointestinal disorders	Nausea, diarrhoea, dyspepsia
Infections and Infestations	Nasopharyngitis, viral upper respiratory tract infection
General disorders and administration site conditions	Chest discomfort

Less common adverse reactions reported in <1% patients after administration of tegoprazan 50 mg from clinical studies are listed below by System Organ Class;
Gastrointestinal Disorders: abdominal pain upper*, abdominal discomfort*, constipation*, abdominal pain*, abdominal distension*, vomiting, eructation, abdominal pain lower, gastric ulcer*, anal haemorrhage*, erosive duodenitis*, flatulence*, gastric polyps*, gastroesophageal reflux disease*, intestinal metaplasia, haematemesis, haemorrhoids, melaena*
Infections and Infestations: folliculitis*, nasopharyngitis*, gastroenteritis bacterial, latent tuberculosis
Investigations: alanine aminotransferase increased*, gamma-glutamyltransferase increased*, blood bilirubin increased, aspartate aminotransferase increased*, blood creatine phosphokinase increased*, blood urine present*, red blood cells urine positive*, blood gastrin increased*, blood triglycerides increased*
General Disorders and Administration Site Conditions: fatigue*
Injury, Poisoning and Procedural Complications: ligament sprain, concussion, excoriation, foot fracture, joint injury, muscle strain
Musculoskeletal and Connective Tissue Disorders: myalgia*, arthralgia, tendonitis*
Nervous System Disorders: headache*, dizziness
Skin and Subcutaneous Tissue Disorders: angioedema, dermatitis, seborrhoeic dermatitis*
Respiratory, Thoracic and Mediastinal Disorders: cough*, oropharyngeal pain, throat irritation
Reproductive System and Breast Disorders: vaginal discharge, vulvovaginal pruritus, breast calcifications*, adenomyosis, ovarian cyst
Hepatobiliary Disorders: bile duct stone, hepatic cyst
Renal and Urinary Disorders: hypertonic bladder, nocturia*, renal cyst
Neoplasms Benign, Malignant and Unspecified: adenocarcinoma gastric, breast cancer, gastrointestinal tract adenoma*, uterine leiomyoma
Cardiac Disorders: ventricular extrasystoles*
Blood and Lymphatic System Disorders: lymphadenitis*, anaemia*
Psychiatric Disorders: insomnia*
Surgical and Medical Procedures: dental implantation
Ear and Labyrinth Disorders: ear pain*
Metabolism and nutrition disorders: diabetes mellitus
Vascular disorder: hypertension
Endocrine disorders: thyroid cyst*
2) Two clinical studies were conducted in patients with peptic ulcer and/or chronic atrophic gastritis who were positive for *H. pylori*. 314 patients were treated with tegoprazan 50 mg, in combination with amoxicillin 1 g and clarithromycin 500 mg. Adverse reactions and adverse drug reactions (marked with *) reported during the clinical trial is as following;
Common adverse reactions reported (≥1%) in tegoprazan 50 mg in combination with amoxicillin 1 g and clarithromycin 500 mg treatment group are presented in Table 2.
Table 2: Adverse reactions (%) reported in ≥1% patients from clinical trials

System Organ Class	Adverse reactions
Gastrointestinal Disorders	Diarrhoea*, aabdominal pain upper*, abdominal distension*, dyspepsia*, nausea*, abdominal pain*
Nervous System Disorders	Dysgeusia*, headache*
Skin and Subcutaneous Tissue Disorders	Urticaria*

Less common adverse reactions reported in <1% patients after administration of tegoprazan 50 mg in combination with amoxicillin 1g and clarithromycin 500mg from clinical study is listed below by System Organ Class;
Gastrointestinal Disorders: constipation*, dry mouth*, abdominal discomfort*, anal incontinence*, duodenitis, haematochezia, paraesthesia oral*, vomiting
Nervous System Disorders: dizziness*, migraine*, somnolence*, taste disorder*
Skin and Subcutaneous Tissue Disorders: pruritus*, erythema*, rash*, drug eruption*, toxic skin eruption*
Infections and Infestations: nasopharyngitis, cystitis, herpes zoster, folliculitis*, hordeolum, sinusitis, tonsillitis*
Investigations: Blood creatine phosphokinase increased*, aspartate aminotransferase increased, blood triglycerides increased, blood lactate dehydrogenase increased*
General Disorders and Administration Site Conditions: asthenia*, chest pain*
Musculoskeletal and Connective Tissue Disorders: back pain, myalgia*, musculoskeletal stiffness*
Respiratory, Thoracic and Mediastinal Disorders: dysphonia, cough, oropharyngeal pain
Cardiac Disorders: palpitations*
Vascular Disorders: hot flush*, flushing*
Eye Disorders: choroiditis*, retinal disorder*
Psychiatric Disorders: insomnia*
Neoplasms Benign, Malignant and Unspecified (including cysts and polyps): colon adenoma
Hepatobiliary Disorders: hepatic steatosis
Metabolism and Nutrition Disorders: type 2 diabetes mellitus
3) One global phase 3 clinical study was conducted in patients with erosive gastroesophageal reflux disease in India, Russia and South Africa. A total 128 subjects received Tegoprazan 50 mg.
Adverse reactions and adverse drug reactions (marked with *) reported during the clinical trials are as following;
Common adverse reactions reported (≥1%) in tegoprazan 50 mg treatment group are presented in Table 3
Table 3: Adverse Reactions (%) reported in ≥1% patients with Tegoprazan 50 mg

System Organ Class	Adverse reactions
Gastrointestinal Disorders	Abdominal Discomfort*, Abdominal Distension*, Abdominal Pain*, Abdominal Pain Upper*, Constipation*, Diarrhoea*, Dry Mouth*, Eructation*, Flatulance*, Nausea*
General Disorders And Administration Site Conditions	Non cardiac chest pain
Nervous System Disorders	Dizziness*, Dysgeusia*, headache*

Less common Adverse reactions and adverse drug reactions (marked with *) reported in <1% patients after administration of tegoprazan 50 mg from this clinical study is listed below by System Organ Class;
Gastrointestinal Disorders: Dyspepsia*, Tongue coated*, Tongue Discomfort*, Vomiting*
General Disorders And Administration Site Conditions: Non-Cardiac Chest Pain*, Feeling abnormal*, Pyrexia*
Infections and Infestations: Urinary Tract Infection*
Investigations: Bilirubin Conjugated Increased*, Blood Bilirubin Increased*, Blood Creatine Phosphokinase Increased*, Blood Triglycerides Increased*, Protein Urine Present*
Metabolism and Nutrition Disorders: Decreased Appetite*
Musculoskeletal and Connective Tissue Disorders: Neck pain*
Renal and Urinary Disorders: Crystalluria*
Respiratory, Thoracic and Mediastinal Disorders: Asthma*, Cough*, Dry Throat*
Reporting of 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. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com.
4.9 Overdose
There have been no reports of significant overdose with tegoprazan. In clinical trials, there have been cases where up to 400 mg of this drug has been administered to healthy adults. In the event of an overdose with tegoprazan, the patients should be monitored for poisoning symptoms and treatment should be supportive if necessary.
5. PHARMACOLOGICAL PROPERTIES
5.1 Mechanism of action
Tegoprazan is a potassium-competitive acid blocker (P-CAB) that reversibly blocks gastric acid secretion by competitively binding with potassium to the proton pumps(H+/K+-ATPase) present in gastric wall cells.
5.2 Pharmacodynamics properties
Tegoprazan is a potassium-competitive acid blocker (P-CAB) that reversibly blocks gastric acid secretion by competitively binding with potassium to the proton pumps(H+/K+-ATPase) present in gastric wall cells.
Tegoprazan binds in a concentration-dependent manner and blocks gastric acid secretion. Binding has reversibility. Tegoprazan inhibits the proton pump directly without activation by acid.
Clinical studies
1) Erosive Gastroesophageal Reflux Disease
A randomized, double-blind, active-controlled, comparative phase III study was conducted in 302 patients with erosive gastroesophageal reflux disease to evaluate Tegoprazan 50 mg, 100 mg or esomeprazole 40 mg for up to 8 weeks. The cumulative healing rate at week 8 was 98.91%(91 patients/92 patients), 98.90%(90 patients/91 patients), and 98.86%(87 patients/88 patients), respectively, in the Tegoprazan 50 mg, 100 mg and esomeprazole 40 mg treatment groups, demonstrating non-inferiority. (Table 4).
Table 4: Cumulative healing rate of Erosive Gastroesophageal Reflux Disease at week 8

	Tegoprazan		Esomeprazole
	50 mg	100 mg	40 mg
PPS	N=92	N=91	N=88
ERD Healing Rate [%(N)]	98.91 (91)	98.90 (90)	98.86 (87)
Difference with 95% confidence interval	0.05 [-3.02,3.11]	0.04 [-3.04,3.12]	
*p-value**	< 0.0001	< 0.0001	

* Non-inferiority margin -10%, significance level 0.025(one-sided test), PPS: Per Protocol Set
A phase 3 randomized double blind study was conducted to evaluate efficacy and safety of Tegoprazan 50 mg in comparison to esomeprazole 40 mg in 255 patients with erosive gastroesophageal reflux disease from India, Russia, and South Africa. The cumulative endoscopic healing rate for Tegoprazan arm was (99.1 %) [95% CI: 95.25: 99.98] was higher as compared to Esomeprazole arm (97.2 %) [95% CI: 92.17: 99.43].
Tegoprazan was non-inferior to Esomeprazole (p-value <0.0001) (Table 5).
Table 5: Cumulative healing rate of Erosive Gastroesophageal Reflux Disease at week 8

	Tegoprazan50mg	Esomeprazole40mg
PPS	N=115	N=109
ERD Healing Rate [%(N)]	114 (99.1%)	106 (97.2%)
Difference with 95% confidence interval	1.88 (-1.63:5.39)	
*p-value**	< 0.0001	

* Non-inferiority margin -10%, significance level 0.025(one-sided test), PPS: Per Protocol Set
2) Non-Erosive Gastroesophageal Reflux Disease
A randomized, double-blind, placebo-controlled, phase III study was conducted in 324 patients with non-erosive gastroesophageal reflux disease to evaluate Tegoprazan 50 mg, 100 mg or placebo for 4 weeks. The rate of patients with complete resolution of main symptoms, heartburn and reflux of gastric acid, at week 4 was 42.45%(45 patients/106 patients), 48.48%(48 patients/99 patients), 24.24%(24 patients/99 patients), respectively in treatment group of Tegoprazan 50 mg, 100 mg and placebo, demonstrating superiority (Table 6).
Table 6: Percentages of patients with complete resolution of main symptoms at week 4 in non-erosive gastroesophageal reflux disease

	Tegoprazan		Placebo
	50 mg	100 mg	
FAS	N = 106	N = 99	N = 99
Symptom resoution [%(N)]	42.45 (45)	48.48 (48)	24.24 (24)
*p-value**	0.0058	0.0004	

* Chi-square test, significance level 0.05(two-sided test), FAS; Full Analysis Set
3) Gastric Ulcer
A randomized, double-blind, active-controlled, comparative phase III study was conducted in 306 patients with gastric ulcer to evaluate Tegoprazan 50 mg, 100 mg or lansoprazole 30 mg for up to 8 weeks. The cumulative healing rate at week 8 was 100.00%(88 patients/88 patients), 97.85%(91 patients/93 patients), and 100.00%(85 patients/85 patients), respectively, in the Tegoprazan 50 mg, 100 mg and 30 mg lansoprazole treatment groups, demonstrating non-inferiority. (Table 7).

Table 7: Cumulative healing rate of Gastric Ulcer at week 8

	Tegoprazan		Lansoprazole
	50mg	100mg	30mg
PPS	N = 88	N = 93	N = 85
GU Healing Rate [%(N)]	100.00 (88)	97.85 (91)	100.00 (85)
Difference with 95% confidence interval	0.00	-2.15 [-7.66,2.43]	
p-value*		< 0.0001	

* Non-inferiority margin -8.54%, significance level 0.025(one-sided test), PPS: Per Protocol Set
5.3 Pharmacokinetic properties
Absorption
T_{max} of tegoprazan following single oral dose to healthy adults was ranged from 0.5 to 1.5 hours across the doses tested 50~400 mg. After single administration, the mean peak plasma concentration (C_{max}) and mean exposure level (AUC) tended to increase dose portionally within the administration dose range. After 7 days of repeated administration, the mean peak plasma concentration of each dose group was similar or decreased in comparison with that of single administration.
Food effects on bioavailability were evaluated after administration of 200 mg of oral tegoprazan fasting and after meals to healthy adults. Although there was a tendency to delay the T_{max} and decrease the C_{max} after food intake, there was no significant difference on the AUC_{last} and pharmacodynamic parameter (the maintenance time of intragastric acidity above pH 4).
Food effects on bioavailability were evaluated after administration of 50 mg of oral tegoprazan fasting, before meals or after meals to healthy adults. Although there was a tendency to delay the T_{max} and decrease the C_{max} after food intake, there was no significant difference on the AUC_{last} and pharmacodynamic parameter (the maintenance time of intragastric acidity above pH 4).
Distribution
The proportion of *in vitro* non-protein-binding drug was 8.7 ~ 9.0% human in the concentration range of 1 ~ 10 μM.
Metabolism and Excretion
Tegoprazan is mainly metabolized by CYP3A4. The main metabolite is metabolite M1 (dealkylated metabolite).
After intravenous administration of tegoprazan to rats and dogs, amount of unchanged tegoprazan excreted in urine was less than 1%. After oral administration of [^{14}C]-tegoprazan to rats, recovery of radioactivity at 168 hours (of dosing) were 93% and 97% in the female and male, respectively. 22% to 24% of the total radioactivity was excreted in urine, and 65% to 69% was eliminated in feces in both female and male rats. After oral administration to rats with biliary intubation, tegoprazan was excreted 41.4% in bile acid, 25.7% in urine and 28.4% in feces. And the total recovery of radioactivity was 97.7%. Less than 1% of unchanged tegoprazan was found 1% in bile acid and urine, 15% was in feces. 6% of metabolite M1 was found in feces.
Following the administration of tegoprazan to healthy male subjects, the plasma elimination half-life of unchanged tegoprazan and metabolite M1 were 4.1 hours and 22.8 hours, respectively. Urinary excretion rate of the unchanged tegoprazan was approximately 4.1% and the clearance was 1.1L/hr. Urinary excretion rate of the major metabolite M1 was about 2.3% and the clearance was 0.5L/hr.
6. NON CLINICAL PROPERTIES
6.1 Animal Toxicology and Pharmacology
Pharmacology
Tegoprazan is a Potassium-Competitive Acid Blocker (P-CAB), which directly inhibit gastric H+/K+-ATPase in K+-competitive and reversible manner, thus, do not require the acid activation process to exhibit its inhibitory action for H+/K+-ATPase.
The inhibitory activity of Tegoprazan was studied *in vitro* using H+/K+-ATPase in ion-tight and ion leaky vesicles. The *in vitro* study results shows that Tegoprazan exhibited a high selectivity for the gastric acid H+/K+-ATPase. In the *in vivo* Heidenhain pouch dog model, oral administration of Tegoprazan strongly suppressed gastric acid secretion in dose-dependent manner. Tegoprazan potently inhibited gastroesophageal reflux disease (GERD) in two experimental rat models for GERD established by dual ligation of the forestomach and the pyloric ring in rat stomach. In three rat models of naproxen-induced, ethanol-induced, WIRS-induced peptic ulcer, Tegoprazan significantly inhibited gastric lesion formation.
The standard safety pharmacology studies were conducted and Tegoprazan had no effects on the CNS, respiratory or cardiovascular systems.
Toxicology
1) Mutagenesis
Tegoprazan was negative in the bacterial reverse mutation test using *Salmonella* and *E. coli*. Tegoprazan was positive in the CHL cell chromosome aberration assay, but negative in the *in vivo* micronucleus test using rat bone marrow cells not to induce micronucleus.
2) Carcinogenesis
In a 2 year carcinogenicity study in rats, gastrointestinal neuroendocrine tumor was observed in the male 15 mg/kg/day(about 4.8 times AUC of the recommended human dose) group and the female 6 mg/kg/day(about 6.8 times AUC of the recommended human dose).
3) Impairment of Fertility
No effects on fertility and early embryonic development were observed up to a high dose of 500 mg/kg/day. As a result of the embryo-fetal development studies, short supernumerary cervical ribs were observed with a higher incidence in rats. The NOAEL for maternal rats was determined to be 500 mg/kg/day, which was 369 times the AUC of the human recommended dose, and the NOEL for embryos and fetuses was determined to be 20 mg/kg/day, which was 15.6 times the AUC of the human recommended dose.
There were no effects on fetal development despite abortions and weight loss symptoms in the maximum dose(10mg/kg/day) group of rabbit. The NOAEL for maternal rabbits was determined to be 5mg/kg/day, which was 2 times the AUC of the human recommended dose, and the NOAEL for embryos and fetuses was determined to be 10 mg/kg/day, which was 4.8 times the AUC of the human recommended dose.
In a pre- and post-natal development study and maternal function study in rats, tegoprazan and metabolite M1 were shown to be excreted in breast milk. And the NOAEL was determined to be 20 mg/kg/day, which was 8 times the AUC of the human recommended dose on the basis of the decreased survival rate of the first filial rats at 60mg/kg/day, the maximal dose.
7. DESCRIPTION
Solubility: Tegoprazan is freely soluble in Methanol, Ethanol, slightly soluble in Acetonitrile, sparingly soluble in 50% Acetonitrile, practically insoluble in water, very slightly soluble in water at pH 4.0, and practically insoluble at pH 6.8.
pKa: 5.2±0.2, 12.0±0.2
Molecular weight: 387.38 g/mol
International nonproprietary or generic or chemical name: 7-{[(4S)-5,7-difluoro-3,4-dihydro-2H-1-benzopyran-4-yl]oxy}-N,N,2-trimethyl-1H-1,3-benzodiazole-5-carboxamide
Molecular Formula: $C_{20}H_{19}F_2N_3O_3$
Pharmacotherapeutic group: Potassium competitive acid blocker (P-CAB)
8. PHARMACEUTICAL PARTICULARS
8.1 Incompatibilities
Not applicable.
8.2 Shelf life
36 months
8.3 Packaging Information
Blister Pack
8.4 Storage and handing instructions
Store below 30°C.
Keep out of reach of children.
9. PATIENTS COUNSELLING INFORMATION
This medicine is intended for adult patients only
Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or health care provider
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms of illness are the same as yours.
- If you get any side effects, talk to your doctor or health care provider. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?
1. What Tegoprazan is and what it is used for
2. What you need to know before you take Tegoprazan
3. How to take Tegoprazan
4. Possible side effects
5. How to store Tegoprazan
6. Contents of the pack and other information
1. What Tegoprazan is and what it is used for
Tegoprazan is a high-selective potassium-competitive acid blocker (P-CAB) with a fast onset of action and the ability to control gastric pH for a prolonged period of time. Tegoprazan's strong and continued effect is due to its ability to be slowly cleared from the gastric glands and exertion of effects independent of acid levels. It has also been observed to be efficacious independent of food intake.
Tegoprazan 50 mg is indicated for
- Treatment of Erosive Gastroesophageal Reflux Disease (which can include heartburn. It is caused when acid and food from your stomach escapes into your food pipe (oesophagus).),
- Treatment of Non-Erosive Gastroesophageal Reflux Disease,
- Treatment of Gastric Ulcer (Ulcers in your stomach).

2. What you need to know before you use Tegoprazan
Do not take Tegoprazan if you are:
- allergic to tegoprazan, or any of the product components or substituted benzimidazoles
- taking a medicine containing atazanavir, nelfinavir or rilpivirine
- pregnant or breast feeding

Warnings and precautions
Talk to your doctor or pharmacist before taking this medicine, or during treatment, especially if you:
- are allergic to tegoprazan, or any of the product components or substituted benzimidazoles .
- In elderly patients, keeping in mind the greater frequency of decreased physiological functions, such as liver or kidney.

Children and adolescents
Clinical safety and efficacy of tegoprazan in pediatric and adolescent patients have not been established
Other medicines and Tegoprazan tablets
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, including herbal medicines. This is especially important in case you are taking any of the following medicines:
- drugs that decrease the intragastric acidity, the absorption of drugs such as ketoconazole, itraconazole, ampicillin ester, atazanavir, iron salts, erlotinib, gefitinib and mycophenolate mofetil (MMF) can decrease during treatment with tegoprazan. While absorption of drugs such as digoxin can increase during treatment with tegoprazan.
- clarithromycin, a CYP3A4 inhibitor, with tegoprazan has increased AUCτ of tegoprazan and clarithromycin by 2.5 times and 1.25 times, respectively.

If you are not sure if any of the above applies to you, talk to your doctor or pharmacist before taking tegoprazan tablets
Pregnancy and breast-feeding
- Do not use this medicine if you are pregnant or think you may be pregnant
- Do not use this medicine if you are breast-feeding or planning to breast-feed

If you are pregnant or breast feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
Driving and using machines
No studies on the effects on the ability to drive and use machines have been performed for tegoprazan.
3. How to take Tegoprazan.
Always take this medicine exactly as your doctor has told you. Check with your doctor or health care provider if you are not sure.
How much to take
For 'erosive gastroesophageal reflux disease' (GERD)
- The usual dose is 50 mg tablet once a day for up to 4 weeks

If your condition did not improve after 4 weeks treatment, your doctor may tell you to continue treatment for additional 4 weeks.
For 'non-erosive gastroesophageal reflux disease' (NERD)
- The usual dose is 50 mg tablet once a day for up to 4 weeks

For 'ulcers of the stomach' (peptic ulcers)
- The usual dose is 50 mg tablet once a day for up to 8 weeks

If you take more Tegoprazan than you should
If you take more than you should, talk to a doctor or go to a hospital straight away. Take the medicine pack with you.
If you forget to take Tegoprazan
Do not take a double dose to make up for a forgotten dose. If you miss one dose, take your next dose on the day after the missed dose. If you miss two or more doses, contact your doctor.
If you stop taking Tegoprazan
If you stop taking this medicine you will lose the effects of the medicine. You should not stop this medicine unless told to do so by your doctor.
If you have any further questions on the use of this medicine, ask your doctor or health care provider.
4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.
The side effects are usually mild and improve without you having to stop taking this medicine
Adverse reactions reported in clinical studies conducted in patients with erosive gastroesophageal reflux disease and non-erosive gastroesophageal reflux disease and gastric ulcer
Common (affects more than 1%)
- Nausea,
- diarrhoea,
- dyspepsia,
- Nasopharyngitis,
- viral upper respiratory tract infection,
- Chest discomfort.

Less common (affects less than 1%)
- abdominal pain upper, abdominal discomfort, constipation, abdominal pain, abdominal distension, vomiting, eructation, abdominal pain lower, gastric ulcer, anal haemorrhage, erosive duodenitis, flatulence, gastric polyps, gastroesophageal reflux disease, intestinal metaplasia, haematemesis, haemorrhoids, melaena,
- folliculitis, nasopharyngitis, gastroenteritis bacterial, latent tuberculosis,
- alanine aminotransferase increased, gamma-glutamyltransferase increased, blood bilirubin increased, aspartate aminotransferase increased, blood creatine phosphokinase increased, blood urine present, red blood cells urine positive, blood gastrin increased, blood triglycerides increased,
- fatigue,
- ligament sprain, concussion, excoriation, foot fracture, joint injury, muscle strain,
- muscle pain (myalgia), joint pains (arthralgia), tendon inflammation (tendonitis),
- headache, dizziness,
- angioedema, dermatitis, seborrhoeic dermatitis,
- cough, oropharyngeal pain, throat irritation,
- vaginal discharge, vulvovaginal pruritus, breast calcifications, adenomyosis, ovarian cyst,
- bile duct stone, hepatic cyst,
- hypertonic bladder, nocturia, renal cyst,
- adenocarcinoma gastric, breast cancer, gastrointestinal tract adenoma, uterine leiomyoma,
- ventricular extrasystoles,
- lymphadenitis, anaemia,
- insomnia,
- dental implantation,
- ear pain,
- diabetes mellitus,
- hypertension,
- thyroid cyst.

Adverse reactions reported in clinical studies conducted in patients with peptic ulcer and/or chronic atrophic gastritis who were positive for *H. pylori*
Common (affects more than 1%)
- diarrhoea,
- abdominal pain upper,
- abdominal distension
- dyspepsia,
- nausea,
- abdominal pain
- bad taste in mouth (Dysguesia) and
- headache
- rash (urticaria)

Less common (affects less than 1%)
- constipation, dry mouth, abdominal discomfort, anal incontinence, duodenitis, haematochezia, paraesthesia oral, vomiting
- dizziness, migraine, somnolence, taste disorder
- pruritus, erythema, rash, drug eruption, toxic skin eruption
- nasopharyngitis, cystitis, herpes zoster, folliculitis, sinusitis, tonsillitis
- Blood creatine phosphokinase increased, aspartate aminotransferase increased, blood triglycerides increased, blood lactate dehydrogenase increased
- Weakness (asthenia), chest pain
- back pain, myalgia (muscle pain), musculoskeletal stiffness
- dysphonia, cough, oropharyngeal pain (pain in throat)
- palpitations (abnormal rapid or irregular heart beat)
- hot flush, flushing
- choroiditis, retinal disorder (eye symptoms)
- insomnia (sleep disorder)
- colon adenoma
- hepatic steatosis (fatty liver disease)
- type 2 diabetes mellitus

Adverse reactions reported in clinical studies conducted in patients with erosive gastroesophageal reflux disease
Common side effects:
- abdominal discomfort
- abdominal distension
- abdominal pain
- abdominal pain upper
- constipation
- diarrhoea
- dry mouth
- eructation
- flatulence
- nausea
- non cardiac chest pain
- dizziness
- dysgeusia
- headache

Less common effects:
- dyspepsia
- tongue coated
- tongue discomfort
- vomiting
- non-cardiac chest pain
- feeling abnormal
- pyrexia
- urinary tract infection
- bilirubin conjugated increased, blood bilirubin increased, blood creatine phosphokinase increased, blood triglycerides increased, protein urine present
- decreased appetite
- neck pain
- crystalluria (crystals in the urine)
- asthma
- cough
- dry throat

Reporting of 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. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com.
5. How to store Tegoprazan
Store below 30°C.
Keep out of reach of children.
6. Contents of the pack and other information
Tegoprazan Tablets 50 mg are light pink oblong tablets engraved with "KI50" on one side and "I" on the other side. The tablets are provided in blister packs.
Each pack contains one or three blister, each blister with 10 tablets. This gives a total of 10 or 30 tablets per pack.
10. DETAILS OF MANUFACTURER
Manufactured by: HK inno.N Corporation
239, Osongsaengmyeong 2-ro, Osong-eup,
Heungdeok-gu, Cheongju-si, Chungcheongbuk-do,
Republic of Korea (South Korea)
Imported by:
Dr. Reddy's Laboratories Limited,
Global Distribution Centre, Survey No. 41, Bachupally (V),
Bachupally (M), Medchal - Malkajgiri (Dist.), Hyderabad - 500 090, Telangana, INDIA.
11. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE
License No. IL/FF-000915 RC/FF-002397; Issued date 14-07-2025.
12. DATE OF REVISION
September 2025

MARKETED BY :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

107186

TM - Trademark under registration

IN/TEGCISE 50mg/AUG-2025/01/PI

PRODUCT NAME :	Tegcise	COUNTRY : Domestic P2P	LOCATION : Dr. Reddy's Lab.	SUPERSEDES A/W NO. :		
ITEM / PACK :	Insert	NO. OF COLORS : 1	SUBSTRATE :			
DESIGN STYLE :	Front	PANTONE SHADE Nos. :	REMARK :			
CODE :	XXXXXXX-9093	Black	Activities	Department	Name	Signature	Date
DIMENSION (MM) :	170 x 730 mm		Prepared By	Pkg.Dev			
ART WORK SIZE :	S/S		Reviewed By	Pkg.Dev			
DATE :	22-09-2025		Reviewed By	CR			
			Approved By	Quality			

This colour proof is not colour binding. Follow pantone shade reference for actual colour matching.

PRODUCT NAME :	Tegcise	COUNTRY : Domestic P2P	LOCATION : Dr. Reddy's Lab.	SUPERSEDES A/W NO. :		
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