PREVACID® FDT
(Lansoprazole Fast Disintegrating Tablets)

PREVACID® FDT is a preparation of lansoprazole, a proton pump inhibitor.
PREVACID® FDT displays strong and sustained inhibition of gastric acid secretion by suppressing the activity of (H^+-K^+)-ATPase which exists locally in the parietal cells of gastric mucosa and plays an important role as a proton pump. Clinically, *PREVACID® FDT* attains a rapid and high healing ratio against gastric ulcer and duodenal ulcer, and the usefulness of the drug has been proven. It has also been proven to be a useful drug for treatment of stomal ulcer, reflux esophagitis and Zollinger-Ellison syndrome.

COMPOSITION
PREVACID® FDT are white to yellowish white uncoated tablets with orange to dark brown speckles for oral administration containing the active ingredient, lansoprazole in the form of enteric-coated microgranules and are available in two dosages strengths. *PREVACID® FDT* 15mg Tablets contains lansoprazole 15mg and *PREVACID® FDT* 30mg Tablets contains lansoprazole 30mg.

INDICATIONS
- Gastric ulcer, duodenal ulcer, stomal ulcer and reflux esophagitis.
- Relief of reflux-like symptoms (e.g. heartburn) and / or ulcer-like symptoms (e.g. upper epigastric pain) associated with acid-related dyspepsia.
- Treatment and prophylaxis of NSAID-associated benign gastric ulcer, duodenal ulcers and relief of symptoms in patients requiring continued NSAID treatment.
- Eradication of *H. pylori* from the upper gastrointestinal tract in patients with peptic ulcer (duodenal or benign gastric ulcer) when used in combination with appropriate antibiotics.
- Zollinger-Ellison syndrome (and other Pathological hypersecretory conditions)
- Short-term treatment of symptomatic GERD and erosive esophagitis for children (12-17 years of age)

DOSAGE AND ADMINISTRATION
Usually for adults, administer one tablet (30mg of lansoprazole) orally once a day.
In duodenal ulcer, 30mg once daily for 4 weeks. In gastric ulcer and stomal ulcer, 30mg once daily for 8 weeks. In reflux esophagitis, 30mg once daily for 4-8 weeks. In Zollinger-Ellison syndrome, the dosage should be adjusted according to the patient's signs and symptoms.

Eradication of *H. pylori*: The following combinations have been shown to be effective over 7 days. Prevacid tablet 30mg twice daily plus two of the following antibiotics: amoxicillin 1g twice daily or metronidazole 400mg twice daily and clarithromycin 250-500mg twice daily. The best eradication results are obtained when clarithromycin is combined with either amoxicillin or metronidazole. When used in combination with the recommended antibiotics, *PREVACID® FDT* is associated with *H. pylori* – eradication rates of up to 90%.

Acid related dyspepsia: 30mg once daily for 2-4 weeks*

Short term treatment of symptomatic GERD and Erosive Esophagitis (12-17 years): 30mg once daily for up to 8 weeks.

Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and relief of symptoms in patients requiring continued NSAID treatment: 15 or 30mg once daily for 4-8 weeks for treatment **. Prophylaxis: 15 or 30mg once daily.

Renal impairment: Dose adjustment is not required in patients with impaired renal function. However, a daily dosage of 30mg should not be exceeded.

Hepatic impairment:
Patients with moderate or severe liver disease should be kept under regular supervision and a 50% reduction of the daily dose is recommended.

Elderly: Ulcer healing rates in elderly patients are similar to those in a younger age group. The incidence rates of adverse events and laboratory test abnormalities are also similar to those seen in younger patients. For elderly patients, dosage and administration of lansoprazole need not be altered for a particular indication.

* *PREVACID® FDT 30mg once daily for 2-4 weeks depending on the severity and persistence of symptoms. Patients who do not respond after 4 weeks, or who relapse shortly afterwards, should be investigated.*

** *Most patients will be healed after 4 weeks; for those patients not fully healed, a further 4 weeks treatment can be given. For patients at particular risk or with ulcers that may be difficult to heal, the higher dose and / or the longer treatment duration should be used.*

PREVACID® FDT should not be chewed. Place the tablet on the tongue and allow it to disintegrate, with or without water, until the particles can be swallowed. The tablet typically disintegrates in less than 1 minute.

Alternatively, for children or other patients who have difficulty swallowing tablets, *PREVACID® FDT* can be delivered in two different ways.

PREVACID® FDT ***– Oral Syringe***
For administration via oral syringe, *PREVACID® FDT* can be administered as follows:

- Place a 15mg tablet in oral syringe and draw up approximately 4mL of water, or place a 30mg tablet in oral syringe and draw up approximately 10mL of water.
- Shake gently to allow for quick dispersal.
- After the tablet has dispersed, administer the contents within 15 minutes.
- Refill the syringe with approximately 2mL (5mL for the 30mg tablet) of water, shake gently, and administer any remaining contents.

PREVACID® FDT ***– Nasogastric Tube Administration (≥8 French)***
For administration via nasogastric tube, *PREVACID® FDT* can be administered as follows:

- Place 15mg tablet in a syringe and draw up 4mL of water, or place a 30mg tablet in a syringe and draw up 10mL of water.
- Shake gently to allow for a quick dispersal.
- After the tablet has dispersed, inject through the nasogastric tube into the stomach within 15 minutes.
- Refill the syringe with approximately 5mL of water, shake gently, and flush the nasogastric tube.

WARNINGS AND PRECAUTIONS

Before using *PREVACID® FDT* with antibiotics to eradicate *H. pylori*, prescribers should refer to the full prescribing information of the respective antibiotic for guidance.

Careful administration: (*PREVACID® FDT* should be administered with caution to the following patients.)

a) Patients with a past history of drughypersensitivity
b) Elderly patients (See 5: Usage in the Elderly.)
c) Patients with impaired renal and hepatic function (See 6: Usage in impaired renal and hepatic function)
d) The possibility of malignancy should be excluded when gastric ulcer is suspected, as symptoms may be alleviated and diagnosis delayed.

Regular Surveillance

Patients on proton pump inhibitor treatment (particularly those treated for long term) should be kept under regular surveillance.

Severe Cutaneous Adverse Reactions

Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP) and erythema multiforme have been reported in association with the use of PPIs (see ADVERSE REACTION). Discontinue lansoprazole at the first signs or symptoms of severe cutaneous adverse reactions or other signs of hypersensitivity and consider further evaluation.

Subacute Cutaneous Lupus Erythematosus (SCLE)

Proton pump inhibitors are associated with very infrequent cases of subacute cutaneous lupus erythematosus (SCLE). If lesions occur, especially in sun exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the healthcare professional should consider stopping the product. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Bone fracture: Proton pump inhibitors, especially if used in high doses and over long durations (>1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly in the elderly or in presence of other recognized risk factors. Observational studies suggest PPI may increase the overall risk of fracture by 10-40%. Some of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

Clostridium difficile diarrhea: Published observational studies suggest that PPI therapy 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 drug and shortest duration of PPI therapy appropriate to the condition being treated.

Hypomagnesemia: Severe hypomagnesaemia has been reported in patients treated with PPI like this product for at least three months, and in most cases for a year. Serious manifestations of hypomagenesia such as fatigue, tetany, delirium, convulsions, dizziness, arrhythmias and seizures can occur but they may begin insidiously and be overlooked. Hypomagnesemia may lead to hypocalcemia and/or hypokalemia (see Adverse Reaction). In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPI with digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Vitamin B12 Deficiency: Daily treatment with any acid-suppressing medications over a prolonged period of time (e.g. longer than 3 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. Cyanocobalamin deficiency should be considered in patients with Zollinger-Ellison syndrome and other pathological hypersecretory conditions requiring long-term treatment, individuals with reduced body stores or risk factors for reduced vitamin B12 absorption (such as the elderly) on long-term therapy or if relevant clinical symptoms are observed.

Interference with laboratory tests: Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. If the patient(s) are due to have a test on Chromogranin A level, *PREVACID® FDT* treatment should be stopped for at least 5 days before CgA measurements to avoid this interference (see section Pharmacodynamic). If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

HIV Protease Inhibitors: Co-administration of lansoprazole is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH such as atazanavir, nelfinavir; due to significant reduction in their bioavailability.

PREGNANCY (CATEGORY B) AND LACTATION

Pregnancy - Lansoprazole should be administered to pregnant women with caution only if needed. *Lactation* - It is unknown whether lansoprazole is excreted in human breast milk. During treatment with lansoprazole, nursing should be avoided if the administration of this drug is necessary for the mother.

Use in children

12 to 17 years of age

In an uncontrolled, open-label, U.S. multicenter study, 87 adolescent patients (12-17 years of age) with symptomatic GERD were treated with *PREVACID® FDT* for 8 to 12 weeks. Baseline upper endoscopies classified these patients into two groups: 64 (74%) nonerosive GERD and 23 (26%) erosive esophagitis (EE). The nonerosive GERD patients received *PREVACID® FDT* 15mg q.d. for 8 weeks and the EE patients received *PREVACID® FDT* 30mg q.d. for 8 to 12 weeks. At baseline, 89% of these patients had mild to moderate overall GERD symptoms (assessed by investigator interviews). During 8 weeks of *PREVACID® FDT* treatment, adolescent patients experienced a 63% reduction in frequency and a 69% reduction in severity of GERD symptoms based on diary results.

Twenty-one of 22 (95.5%) adolescent erosive esophagitis patients were healed after 8 weeks of *PREVACID® FDT* treatment. One patient remained unhealed after 12 weeks of treatment.

In pediatric patients age 12 to 17

GERD	Final Visit % (n/N)
Symptomatic GERD (All patients) Improvement in Overall GERD Symptoms[a]	73.2% (60/82)[b]
Nonerosive GERD Improvement in Overall GERD Symptoms[a]	71.2% (42/59)[b]
Erosive Esophagitis Improvement in Overall GERD Symptoms[a] Healing Rate[c]	78.3% (18/23) 95.5% (21/22)[c]

a Symptoms assessed by patients diary (parents / caregivers as necessary).

b No data available for 5 patients.

c Data from one healed patients were excluded from this analysis due to timing of final endoscopy.

In these 87 adolescent patients, increases in serum gastrin levels were similar to those observed in adult studies, median fasting serum gastrin levels increased 42% from 45pg/mL at baseline to 64 pg/mL [interquartile range (25^{th} – 75^{th} percentile) of 44 – 88pg/mL] at the final visit. (Normal serum gastrin levels are 25 to 111pg/mL).

The safety of *PREVACID® FDT* has been assessed in these 87 adolescent patients. Of the 87 adolescent patients with GERD, 6% (5/87) took *PREVACID® FDT* for <6 weeks, 93% (81/87) for 6-10 weeks, and 1% (1/87) for >10 weeks.
The most frequently reported (at least 3%) treatment-related adverse events in these patients were headache (7%), abdominal pain (5%), nausea (3%) and dizziness (3%). Treatment-related dizziness, reported in this package insert as occurring in <1% of adult patients, was reported in this study by 3 adolescent patients with nonerosive GERD, who had dizziness concurrently with other events (such as migraine, dyspnea, and vomiting).

DRUG INTERACTION
Lansoprazole is metabolized through the cytochrome P450 system, specifically through the CYP3A and CYP2C19 isozymes. Studies have shown that lansoprazole does not have clinically significant interactions with other drugs metabolized by the cytochrome P450 system such as warfarin, antipyrine, indomethacin, ibuprofen, phenytoin, propanolol, prednisolone, diazepam, clarithromycin, or terfenadine in healthy subjects. These compounds are metabolized through various cytochrome P450 isozymes including CYP1A2, CYP2C9, CYP2C19, CYP2D6 and CYP3A. When lansoprazole was administered concomitantly with theophylline (CYP1A2, CYP3A), a minor increase (10%) in the clearance of theophylline was seen. Because of the small magnitude and the direction of the effect on theophylline clearance, this interaction has not been considered to be clinically significant. Nonetheless, individual patients may require additional titration of their theophylline dosage when lansoprazole is started or stopped to ensure clinically effective blood levels.
In a study of healthy subjects neither the pharmacokinetics of warfarin enantiomers nor prothrombin time were affected following single or multiple 60mg doses of lansoprazole. However, there have been reports of increased International Normalized Ratio (INR) and prothrombin time in patients receiving proton pump inhibitors, including lansoprazole, and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with proton pump inhibitors and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time. Lansoprazole has also been shown to have no clinically significant interaction with amoxicillin. In a single-dose crossover study examining lansoprazole 30mg and omeprazole 20mg each administered alone and concomitantly with sucralfate 1gram, absorption of the proton pump inhibitors was delayed and their bioavailability was reduced by 17% and 16%, respectively, when administered concomitantly with sucralfate. Therefore, proton pump inhibitors should be taken at least 30 minutes prior to sucralfate. In clinical trials, antacids were administered concomitantly with *PREVACID® FDT* this did not interfere with its effect. Lansoprazole causes a profound and long-lasting inhibition of gastric acid secretion; therefore, it is theoretically possible that lansoprazole may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g., ketoconazole, ampicillin esters, iron salts, digoxin).

HIV Protease Inhibitors: Co-administration of lansoprazole is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH such as atazanavir, nelfinavir; due to significant reduction in their bioavailability.

Methotrexate: Concomitant use with high-dose Methotrexate may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities.

Clopidogrel: Concomitant administration of lansoprazole and clopidogrel in healthy subjects had no clinically important effect on exposure to the active metabolite of clopidogrel or clopidogrel-induced platelet inhibition. No dose adjustment of clopidogrel is necessary when administered with an approved dose of lansoprazole.

Warfarin: Co-administration of lansoprazole 60 mg and warfarin did not affect the pharmacokinetics of warfarin or INR. However, there have been reports of 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. Patients treated with lansoprazole and warfarin concomitantly may need to be monitored for increase in INR and prothrombin time.

Tacrolimus: Concomitant administration of lansoprazole and tacrolimus may increase whole blood levels of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19.

Drugs that Inhibit or Induce CYP2C19 : (Tacrolimus, Fluvoxamine)*:* Concomitant administration of lansoprazole and tacrolimus may increase whole blood levels of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19. Inhibitors of CYP2C19 such as fluvoxamine would likely increase the systemic exposure of to lansoprazole. Inducers of CYP2C19 would likely decrease the systemic exposure to lansoprazole.

CONTRAINDICATION

PREVACID® FDT is contradicted in patients with known hypersensitivity to any component of the formulation of *PREVACID ® FDT.*

ADVERSE REACTION

a) Hypersensitivity: Anaphylactic reactions* (generalized rash, facial edema, dyspnea, etc.) may rarely occur, and shock has consequently occurred in certain cases. Toxic epidermal necrolysis* (Lyell syndrome) and oculomucocutaneous syndrome (Stevens-Johnson syndrome*) may occur. Therefore, close observation should be made, and if any abnormality is observed, *PREVACID® FDT* should be discontinued and appropriate measures taken. Rash and pruritus may infrequently occur.

b) Hepatic: Severe hepatic dysfunction with jaundice, hepatitis, etc., may rarely occur. Therefore, close observation should be made. If any abnormality is observed, *PREVACID® FDT* should be discontinued and appropriate measures taken. The elevation of GOT, GPT, alkaline-P, LDH or γ-GTP may infrequently occur.

c) Blood: Agranulocytosis*, pancytopenia* or hemolytic anemia may rarely occur. Anemia, leucopenia*, eosinophilia or thrombocytopenia* may infrequently occur. Therefore, close observation should be made, and if any abnormality is observed, such appropriate measures as discontinuation of *PREVACID® FDT* should be taken.

d) Gastrointestinal: Constipation, diarrhea, dry mouth or abdominal distension may infrequently occur. Nausea, vomiting, microscopic colitis*(frequency 'not known'), anorexia, Fundic gland polyps (benign) (frequency 'common'), abdominal pain, candidiasis, stomatitis, glossitis or taste abnormality may rarely occur. With the exception of patients being treated for the eradication of *Helicobacter* pylori infection, if diarrhea persists, administration of *PREVACID® FDT should* be discontinued, due to the possibility of microscopic colitis with thickening of the collagen bundle or infiltration of inflammatory cells noted in the large intestine submucosa. In majority of cases, symptoms of microscopic colitis resolve on discontinuation of *PREVACID® FDT.* Serious colitis accompanied with bloody stools, such as pseudomembranous colitis, may occur due to amoxicillin or clarithromycin being used for *Helicobacter pylori* eradication. If abdominal pain and frequent diarrhea occur, appropriate measures, such as immediate discontinuation of the treatment, should be taken. Heartburn and gastroesophageal reflux were observed (<1%) in the clinical studies on *Helicobacter pylori* eradication.

e) Psychoneurotic: Headache or sleepiness may infrequently occur. Depressed state, insomnia, dizziness or tremor may rarely occur.

f) Metabolism and nutrition disorders: Hyponatremia*, Hypomagnesaemia*(frequency 'not known'), vitamin B12 deficiency,
Hypocalcemia*ƒ and Hypokalemia*ƒ

g) Renal: Tubulointerstitial nephritis (TIN) (with possible progression to renal failure), interstitial nephritis.

h) Musculoskeletal disorders (frequency “uncommon”): Fracture of the hip, wrist or spine.

i) Skin and subcutaneous tissue disorders: Rash, Pruritus, Cutaneous lupus erythematosus*, Steven-Johnson Syndrome*, Toxic Epidermal Necrolysis*, Drug reaction with eosinophilia and systemic symptoms (DRESS)*, Acute generalized exanthematous pustulosis*, Erythema multiforme*, Subacute cutaneous lupus erythematosus (SCLE)*(frequency ‘not known’)

j) Infections and infestations: Clostridium difficile associated diarrhea.

k) Others: Interstitial pneumonia may rarely occur. Therefore, if fever, coughing, dyspnea, abnormal lung sound (crepitation), etc., are observed such examinations as chest X-ray should immediately be performed, and PREVACID® FDT should be discontinued. Appropriate measures, such as treatment with a corticosteroid preparation, should be taken. Fever or elevation of total cholesterol and uric acid may infrequently occur. Gynecomastia, blurred vision, edema, weakness, malaise, numbness of tongue or lips, numbness of limbs, arthralgia, muscle pain or alopecia may rarely occur. Increased triglyceride, positive urinary protein, or positive urine sugar were observed (1-5%) in the clinical studies on Helicobacter pylori eradication.

*Postmarketing events

†Hypocalcemia and/or hypokalemia may be related to the occurrence of hypomagnesemia (see WARNINGS AND PRECAUTIONS).

CLINICAL PHARMACOLOGY

Pharmacokinetics and Metabolism

PREVACID® FDT contains an enteric-coated granule formulation of lansoprazole. Absorption of lansoprazole begins only after the granules leave the stomach. Absorption is rapid, with mean peak plasma levels of lansoprazole occurring after approximately 1.7 hours. Peak plasma concentration of lansoprazole (C_{max}) and the area under the plasma concentration curve (AUC) of lansoprazole are approximately proportional in doses from 15mg to 60mg after single-oral administration. Lansoprazole does not accumulate and its pharmacokinetics are unaltered by multiple dosing.

Absorption

The absorption of lansoprazole is rapid, with mean C_{max} occurring approximately 1.7 hours after oral dosing, and relatively complete with absolute bioavailability over 80%. In healthy subjects, the mean (±SD) plasma half-life was

1.5 (±1.0) hours. Both C_{max} and AUC are diminished by about 50% to 70% if the drug is given 30 minutes after food as opposed to the fasting condition. There is no significant food effect if the drug is given before meals.

Distribution

Lansoprazole is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 0.05 to 5.0µg/mL.

Metabolism

Lansoprazole is extensively metabolized in the liver. Two metabolites have been identified in measurable quantities in plasma (the hydroxylated sulfinyl and sulfone derivatives of lansoprazole). These metabolites have very little or no antisecretory activity. Lansoprazole is thought to be transformed into two active species which inhibit acid secretion by (H^+, K^+)ATPase within the parietal cell canaliculus, but are not present in the systemic circulation. The plasma elimination of half-life of lansoprazole does not reflect its duration of suppression of gastric acid secretion. Thus, the plasma elimination half-life is less than two hours, while the acid inhibitory effect lasts more than 24 hours.

Elimination

Following single-dose oral administration of lansoprazole, virtually no unchanged lansoprazole was excreted in the urine. In one study, after a single oral dose of ^{14}C-lansoprazole, approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the feces. This implies a significant biliary excretion of the metabolites of lansoprazole.

Special Populations

Geriatric

The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased approximately 50% to 100%. Because the mean half-life in the elderly remains between 1.9 to 2.9 hours, repeated once daily dosing does not result in accumulation of lansoprazole. Peak plasma levels were not increased in the elderly.

Pediatric

The pharmacokinetics of lansoprazole were studies in pediatric patients with GERD aged 12 to 17 years. In adolescent subjects aged 12 to 17 years, subjects were randomized to receive lansoprazole at 15mg or 30mg q.d. Mean C_{max} and AUC values of lansoprazole was not affected by bodyweight or age; and nearly dose-proportional increases in Mean C_{max} and AUC values were observed. Overall, lansoprazole pharmacokinetic patients aged 12 to 17 years were similar to those observed in healthy adult subjects.

Gender

In a study comparing 12 male and 6 female human subjects, no gender differences were found in pharmacokinetics and intragastric pH results.

Renal Insufficiency

In patients with severe renal insufficiency, plasma protein binding decreased by 1.0%-1.5% after administration of 60mg of lansoprazole. Patients with renal insufficiency had a shortened elimination half-life and decreased total AUC (free and bound). AUC for free lansoprazole in plasma, however, was not related to the degree of renal impairment, and C_{max} and T_{max} were not different from subjects with healthy kidneys. No dose adjustment is necessary in patients with renal insufficiency.

Hepatic Insufficiency

In patients with various degrees of chronic hepatic disease, the mean plasma half-life of the drug was prolonged from 1.5 hours to 3.2-7.2 hours. An increase in mean AUC of up to 500% was observed at steady state in hepatically-impaired patients compared to healthy subjects. Dose reduction in patients with severe hepatic disease should be considered.

Race

The pooled mean pharmacokinetic parameters of lansoprazole from twelve U.S. Phase 1 studies (N=513) were compared to the mean pharmacokinetic parameters from two Asian studies (N=20). The mean AUCs of lansoprazole in Asian subjects were approximately twice those seen in pooled U.S. data; however, the inter-individual variability was high. The C_{max} values were comparable.

Pharmacodynamics

Mechanism of Action

Lansoprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or histamine H_2-receptor antagonist properties, but that suppress gastric acid secretion by specific inhibition of the (H^+, K^+)-ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the parietal cell, lansoprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus.

Serum Gastrin Effects

In over 2100 patients, median fasting serum gastrin levels increased 50% to 100% from baseline but remained within normal range after treatment with 15 to 60 mg of oral lansoprazole. These elevations reached a plateau within two months of therapy and returned to pretreatment levels within four weeks after discontinuation of therapy.

Increased gastrin causes enterochromaffin-like cell hyperplasia and increased serum CgA levels. During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also CgA increases due to decreased gastric acidity.The increased CgA levels may interfere with investigations for neuroendocrine tumours.

Available published evidence suggests that proton pump inhibitors should be discontinued between 5 days and 2 weeks prior to CgA measurements. This is to allow CgA levels that might be spuriously elevated following PPI treatment to return to reference range.

OVERDOSAGE

Oral doses up to 5000mg/kg in rats (approximately 1300 times the recommended human dose based on body surface area) and mice (about 675.7 times the recommended human dose based on body surface area) did not produce deaths or any clinical signs. Lansoprazole is not removed from the circulation by hemodialysis. In one reported case of overdose, the patient consumed 600mg of lansoprazole with no adverse reaction.

PRECAUTION FOR *PREVACID ® FDT*

1. The tablets of *PREVACID® FDT* is orally dispersed, but the ingredients are not absorbed through oral mucous membrane. Therefore, this tablet should be swallowed with saliva or water after placing the tablet on the tongue.
2. This product is more fragile compared with the tablets heretofore in use.
3. Use the tablet as soon as possible after unsealing, even before the expiration date.

PACKAGING

Available in pack size of 28.

STORAGE

Store below 30°C in the original packaging.

EXPIRATION

3 years after manufacture.

Manufactured by Kokando Co, Ltd, 9-1, Umezawa-cho 2 chome, Toyama 930-0055, Japan

Product Registration holder: Takeda Malaysia Sdn Bhd, Unit TB-L13-1, Level 13, Tower B, Plaza 33, No. 1, Jalan Kemajuan, Seksyen 13, 46200 Petaling Jaya, Selangor, Malaysia.

Date of Revision

Version: 3
Reference: CCDS v28.0
Last revision date: January 2023