**PROSOGAN® FD** Enteric Coated **Tablet**
LANSOPRAZOLE 15 and 30 mg

## 1 NAME OF THE MEDICINAL PRODUCT

PROSOGAN® FD Enteric Coated Tablet

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Prosogan FD Enteric Coated Tablet 15 mg

Each tablet contains 15 mg Lansoprazole.

2.2 Prosogan FD Enteric Coated Tablet 30 mg

Each tablet contains 30 mg Lansoprazole.

## 3 PHARMACEUTICAL FORM

3.1 Prosogan FD Enteric Coated Tablet 15 mg are white to yellowish-white uncoated tablet speckled with red-orange to dark brown, with "15" debossed on one side of the tablet.

3.2 Prosogan FD Enteric Coated Tablet 30 mg are white to yellowish-white uncoated tablet speckled with red-orange to dark brown, with "30" debossed on one side of the tablet.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

- Duodenal ulcer.
- Benign gastric ulcer.
- Reflux esophagitis.
- Treatment of NSAID-associated gastric ulcer.

### 4.2 Posology and method of administration

Dosage :
- Duodenal ulcer : Prosogan FD Enteric Coated Tablet 30 mg once daily for 4 weeks.
- Benign gastric ulcer : Prosogan FD Enteric Coated Tablet 30 mg once daily for 8 weeks.
- Reflux esophagitis : Prosogan FD Enteric Coated Tablet 30 mg once daily for 4 weeks.
- Treatment of NSAID-associated gastric ulcer : Prosogan FD Enteric Coated Tablet 30 mg once daily for 8 weeks.

Administration :
For oral administration
Prosogan FD Enteric Coated Tablet should be placed on the tongue and gently sucked. The tablet rapidly disperses in the mouth, releasing the gastro-resistant microgranules which are swallowed with the patient's saliva. Alternatively, the tablet can be swallowed whole with a drink of water.
The tablets should not be crushed or chewed.

To achieve the optimal acid inhibitory effect, and hence most rapid healing and symptom relief, once daily should be administered in the morning before food.

Alternatively, for other patients who have difficulty swallowing tablets, Prosogan FD tablet can be delivered in different way :
Nasogastric tube administration
For administration via a nasogastric tube, Prosogan FD Enteric Coated Tablet can be administered as follow :
- Place a 15 mg tablet in a syringe and draw up 4 mL of water, or place a 30 mg tablet in a syringe and draw up 10 mL 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 5 mL of water, shake gently, and flush the nasogastric tube.

- Elderly : Dose adjustment is not required in the elderly. The normal daily dosage should not be exceeded.
- Impaired hepatic and renal function : Prosogan FD Enteric Coated Tablet is metabolized substantially by the liver. Clinical trials in patients with liver disease indicate that metabolism of Prosogan FD Enteric Coated Tablet is prolonged when daily doses of 30 mg are administered to patients with severe hepatic impairment. Consider dose adjustment in patients with severe liver impairment and a 50% reduction of the daily dose is recommended. These patients should be kept under regular supervision.
- There is no need to alter the dosage in patients with mild to moderate impairment of hepatic function or impaired renal function.

## 4.3 Contraindication
Hypersensitivity to the active ingredients or to any of the excipients.

## 4.4 Special warnings and special precautions for use

In common with other anti-ulcer therapies, the possibility of malignancy should be excluded when gastric ulcer is suspected, as symptoms may be alleviated and diagnosis delayed.
Similarly, the possibility of serious underlying disease such as malignancy should be excluded before treatment for dyspepsia commences, particularly in patients of middle age or older who have new or recently changed dyspeptic symptoms.

Prosogan FD Enteric Coated Tablet should be used with caution in patients with severe hepatic dysfunction. These patients should be kept under regular supervision, and a daily dosage of 30 mg should not be exceeded.

**Clostridium difficile** : PPI therapy may be associated with an increased risk of Clostridium difficile infection.
Decreased gastric acidity due to any means, including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing drugs may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter*.

**Bone fracture** : PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine. The risk of fractures was increased in patients who received high-dose, defined as multiple daily doses, and long term PPI therapy (a year or longer).

**Hypomagnesemia** : has rarely been reported 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. Hypomagnesemia may lead to hypocalcemia and/or hypokalemia *(see Undesirable Effects, 4.8)*. In most patients, treatment of hypomagnesemia and hypomagnesemia associated hypocalcemia and/or hypokalemia required magnesium replacement and discontinuation of the PPI.

**HIV Protease inhibitors** : co-administration of Prosogan FD Enteric Coated Tablet 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.

**Influence on Vitamin B12 Absorption**: Daily treatment with any acid-suppressing medications over a prolonged period of time (several years) may lead to malabsorption of cyanocobalamin (vitamin B12) caused by hypo- or achlorhydria. 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.

**Gastric Malignancy**: Symptomatic response to lansoprazole does not preclude the presence of gastric malignancy.
**Interference with laboratory tests:** Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, proton pump inhibitor treatment should be stopped 14 days before CgA measurements.

**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 Undesirable Effects, 4.8)*. 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 in rare cases with the occurrence 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.

**Formulations Containing Lactose**
Since Prosogan FD Enteric Coated Tablet contain Lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

## 4.5 Interaction with other medications and other forms of interaction

Prosogan FD Enteric Coated Tablet is hepatically metabolized and studies indicate that it is a weak inducer of cytochrome P450. There is the possibility of interaction with drugs which are metabolized by the liver. Caution should be exercised when oral contraceptives and preparations such as phenytoin, carbamazepine or warfarin are taken concomitantly with the administration of Prosogan FD tablet.

Patient monitoring should be taken in co-administration of PROSOGAN FD Enteric Coated Tablet with theophylline.

No clinically significant effects on NSAIDs or diazepam have been found.

Antacids and sucralfate may reduce the bioavailability of Prosogan FD Enteric Coated Tablet and should, therefore, not be taken within an hour of Prosogan FD Enteric Coated Tablet.

**Drugs with pH Dependent Absorption Pharmacokinetics** : Prosogan FD Enteric Coated Tablet may interfere with the absorption of other drugs where gastric pH is an important determinant of oral bioavailability.

**HIV Protease inhibitors** : Co-administration of Prosogan FD Enteric Coated Tablet 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 Prosogan FD Enteric Coated Tablet 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 Prosogan FD Enteric Coated Tablet.

**Tacrolimus**: Concomitant administration of Prosogan FD Enteric Coated Tablet 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**: Inhibitors of CYP2C19 such as fluvoxamine would likely increase the systemic exposure to lansoprazole. Inducers of CYP2C19 would likely decrease the systemic exposure to Prosogan FD Enteric Coated Tablet.

## 4.6 Pregnancy and Lactation

There is insufficient experience to recommend the use of Prosogan FD Enteric Coated Tablet in pregnancy. Animal studies do not reveal any teratogenic effect. Reproduction studies indicate slightly reduced litter survival and weights in rats and rabbits given very high doses of Prosogan FD Enteric Coated Tablet. The use of Prosogan FD Enteric Coated Tablet in pregnancy should be avoided.
Animal studies indicate that Prosogan FD Enteric Coated Tablet is secreted into breast milk. There is no information on the secretion of Prosogan FD Enteric Coated Tablet into breast milk in humans. The use of Prosogan FD Enteric Coated Tablet during breast feeding should be avoided unless considered essential.

## 4.7 Effects on ability to drive and use machines

Prosogan FD Enteric Coated Tablet is not expected to adversely affect the ability to drive or use machines.

## 4.8 Undesirable effects

**Adverse Drug Reactions**
Prosogan FD Enteric Coated Tablet is well-tolerated, with adverse events generally being mild and transient.
The most commonly reported adverse events are headache, dizziness, fatigue and malaise.
Gastrointestinal effects include diarrhoea, constipation, abdominal pain, nausea, vomiting, flatulence, dry or sore mouth or throat and microscopic colitis*.

As with other PPIs , very rare, cases of colitis have been reported. In severe and/or protracted cases of diarrhoea, discontinuation of therapy should be considered. In the majority of cases symptoms resolve on discontinuation of therapy.

Alterations in liver function test value and, rarely, jaundice or hepatitis, elevation of AST (GOT), ALT (GPT), Alkaline-P, LDH and γ–GTP values have been reported.

Dermatological reactions include skin rashes, urticaria and pruritus. The generally resolve on discontinuation of drug therapy. Serious dermatological reactions are rare but there have been occasional reports of Steven-Johnson syndrome*, toxic epidermal necrolysis* and cutaneous lupus erythematosus* or bullous rashes including erythema multiforme* and Drug reaction with eosinophilia and systemic symptoms (DRESS)*and Acute generalized exanthematous pustulosis (AGEP)*. Cases of hair thinning and photosensitivity have also been reported.

Other hypersensitivity reactions include angioedema, wheezing, and very rarely, anaphylaxis*.
Cases of Tubulointerstitial nephritis (TIN) have been reported with possible progression to renal failure.

Haematological effects (thrombocytopenia*, agranulocytosis*, eosinophilia, leucopenia* and pancytopenia*) have occurred rarely. Bruising, purpura and petechiae have also been reported.

Other reactions include arthralgia, myalgia, depression, peripheral oedema and, rarely, paraesthesia, blurred vision, taste disturbance, vertigo, confusion and hallucinations.
Gynaecomastia and impotence have been reported rarely.
Metabolism and nutrition disorders: Hyponatremia*, Hypomagnesaemia*, Hypocalcemia*† and Hypokalemia*†

* Postmarketing events
† Hypocalcemia and/or hypokalemia may be related to the occurrence of hypomagnesemia *(see Special Warnings and Special Precautions for Use, 4.4)*

## 4.9 Overdose

There is no information on the effect of overdosage. Prosogan FD Enteric Coated Tablet is not removed from the circulation by hemodialysis. However, Prosogan FD Enteric Coated Tablet has been given at doses up to 120 mg /day without significant adverse effects. Symptomatic and supportive therapy should be given as appropriate.

# 5 Pharmacological Properties

MECHANISM OF ACTION
Prosogan FD Enteric Coated Tablet is a class of proton pump inhibitors. Its mode of action is to inhibit specifically the $H^+$ / $K^+$ ATPase (proton pump) of the parietal cell in the stomach, the terminal step in acid production.

Lansoprazole exhibits high (80-90%) bioavailability with a single dose. As a result, effective acid inhibition is achieved rapidly. Peak plasma levels occurred within 1.5 to 2.0 hours. The plasma elimination half-life ranges from 1 to 2 hours following single or multiple doses in healthy subjects. There is no evidence of accumulation following multiple doses in healthy subjects. The plasma protein binding is 97%.

**Preclinical safety data**

Gastric tumours have been observed in life-long studies in rats.
An increased incidence of spontaneous retinal atrophy has been observed in life-long studies in rats. These lesions which are common to albino laboratory rats have not been observed in monkeys or dogs or life-long studies in mice. They are considered to be rat specific. No such treatment related changes have been observed in patients treated continuously for long periods.

**Juvenile Animal Studies:**
Five juvenile animal studies were conducted with lansoprazole which revealed no treatment related differences between juvenile and adult animals.
During a further 8-week juvenile rat study, cardiac valve thickening occurred at approximately 11-fold the expected human exposure, based on AUC. The findings reversed or trended towards reversibility after a 4-week drug-free recovery period. In a follow-up lansoprazole developmental sensitivity study, juvenile rats younger than postnatal Day 21 (age equivalent to approximately 2 years in humans) were more sensitive to the development of heart valve thickening, with valve thickening occurring at lower exposure (approximately 4-fold the expected human exposure based on AUC) in animals dosed starting at postnatal Day 14 (age equivalent to approximately 1 year in humans).

## 6 Pharmaceutical Particulars

### 6.1 List of excipients

Each tablet contains enteric-coated granules consisting of the active ingredient, lansoprazole, and the excipients.
The examples of main excipients are;
Lactose monohydrate, magnesium carbonate, hydroxypropylcellulose, microcrystalline cellulose, hypromellose, titanium dioxide, mannitol, methacrylic acid copolymer LD, polyacrylate, talc, macrogol, polysorbate 80, aspartame, flavoring, glyceryl monostearate, ferric oxide, anhydrous citric acid, crospovidone.

### 6.2 Incompatibilities

None

### 6.3 Shelf life

3 years

### 6.4 Special precautions for storage

Store below 30°C

### 6.5 Nature and contents of container

Box 28 Tablets (2 blisters @ 14 tablets).

**Registration number**
Prosogan FD Enteric Coated Tablet 15 mg. Reg. No. DKI1952000115A1
Prosogan FD Enteric Coated Tablet 30 mg. Reg. No. DKI1952000115B1

**ON MEDICAL PRESCRIPTION ONLY**
**HARUS DENGAN RESEP DOKTER**

Manufactured and released by Kokando Company Limited, Toyama, Japan
for Takeda Pharmaceutical Company Limited, Osaka, Japan
Imported & packed by PT. Takeda Indonesia, Bekasi, Indonesia

Based on CCDS version 28.0 dtd 19 May 2022