ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

<▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.>

1. NAME OF THE MEDICINAL PRODUCT

Fexuclue 40 mg Film-coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 40mg Film-coated tablet contains 40 mg Fexuprazan as hydrochloride

Excipient(s) with known effect
Each film-coated tablet contains 21 mg lactose (as monohydrate), see section 4.3.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Fexuclue film-coated tablet, 40mg is a pale-green, oblong film-coated tablet with a breaking line on the tablet. The 40 mg tablet has “40” on one side and “D.W” on the other side. The total weight of one Fexuclue film-coated tablet, 40 mg is 157.5 mg.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of erosive esophagitis (EE)

4.2 Posology and method of administration

The product is administered to adults as follows:
- Treatment of erosive esophagitis (EE)
1) 40 mg is administered orally once a day for 4 weeks.
2) In the case of patients with untreated esophagitis or symptoms persisting, the administration given for another 4 weeks. The Product can be administered with or without meals.

4.3 Contraindications

1) Patients who have a history of hypersensitivity to the Product or its components (refer to Section 6.1 List of excipients)
2) Patients taking a drug containing atazanavir, nelfinavir, or rilpivirine (refer to Section 4.5 Interaction with other medicinal products and other forms of interaction)
3) Pregnant and lactating women (refer to Section 4.6 Fertility, pregnancy and lactation)
4) Patients who have congenital conditions for lactose such as galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption, as this medicine contains lactose

4.4 Special warnings and precautions for use

The following patients should be administered with care

1) Patients with hepatic impairment (no experience of use)
2) Patients with renal impairment (no experience of use)
3) Elderly

This preparation contains *Tartrazine* that may cause allergic reactions in certain susceptible patients.

Pediatric Use
The clinical safety and efficacy of the Product in children and adolescents have not been established.

Geriatric Use
In general, physiological functions such as hepatic functions or renal functions are deteriorated in the elderly, so it should be administered carefully.

Use in Patients with Renal Impairment
The safety and efficacy of the Product in patients with renal impairment have not been established.

Use in Patients with Hepatic Impairment
The safety and efficacy of the Product in patients with hepatic impairment have not been established.

General Cautions
1) Since the Product may relieve symptoms of malignant tumors or delay the diagnosis, if a malignant tumor is suspected by warning symptoms (unintended significant weight loss, recurrent vomiting, dysphagia, hemoptysis, melena, etc.) and a gastric ulcer is present or suspected, it should be administered after confirming that it is not malignant.

2) The number of bacteria usually present in the gastrointestinal tract increases when acidity in the stomach decreases due to proton pump inhibitors (PPIs). The risk of infection of the gastrointestinal tract by bacteria such as *Salmonella*, *Campylobacter* and *Clostridium difficile* may slightly increase when treated with gastric acid inhibitors. This is associated with an increased risk of *Clostridium difficile* diarrhea and several observational studies have reported that this risk is increased, especially in hospitalized patients. This diagnosis should be considered when diarrhea does not improve. *Clostridium difficile* diarrhea has been reported with the used of almost all antimicrobial agents.

3) Proton Pump Inhibitor (PPI) treatment has been reported to have the potential of being associated with an increased risk of osteoporosis-related fractures of the hip, wrist and spine. The risk of fracture was increased in patients receiving high doses of PPIs (defined as repeated daily administration) and in patients with long-term use longer than a year. In the case of patients at risk of developing osteoporosis and osteoporotic fractures, appropriate clinical monitoring is recommended according to the latest clinical guidelines.

4) Hypomagnesemia was rarely reported in patients who had been under treatment with a proton pump inhibitor (PPI) for more than 3 months and the most frequent cases were treated for more than a year. In most patients, treatment of hypomagnesemia requires magnesium supplementation and discontinuation of PPI. Patents requiring long-term treatment or co-administering digoxin or drugs that cause hypomagnesemia (e.g., diuretics) require periodic monitoring of magnesium levels, including at the initiation of treatment. Serious adverse events include stiffness, arrhythmia and seizures.

4.5 Interaction with other medicinal products and other forms of interaction

1) Since the administration of the Product raises the pH in the stomach, it can interact with drug absorption in the case of oral drugs, where the pH of the stomach is an important determinant of bioavailability. Therefore, the use of the Product may reduce the bioavailability of drugs that depends on the gastric pH, such as atazanavir and nelfinavir.

2) The Product is mainly metabolized by CYP3A4 and partially by CYP2B6, CYP2C19 and CYP2D6.

3) When 80 mg of the Product and clarithromycin were co-administered, the AUCτ of the Product and clarithromycin were shown to be 1.1 times and 0.77 times, respectively, which were not clinically significant.
4) When the Product, clarithromycin and amoxicillin were co-administered, the AUCτ of amoxicillin was

shown to be 0.86 times, but it was not clinically significant.

4.6 Fertility, pregnancy and lactation

1) Pregnant women
There are no clinical trial data of the Product in pregnant and lactating women. As a result of embryo-fetal development tests in rats and rabbits, maternal body weight and feed intake decreased, but there was no effect on embryo-fetal development. For safety reasons, the use of the Product during pregnancy is prohibited.

2) Lactating women
Breastfeeding should be discontinued if the Product is used as it is not known if the Product will pass to breast milk in lactating women. In animal studies (rats), it has been reported that the Product passes into breast milk.

4.7 Effects on ability to drive and use machines

Fexuprazan is not expected to adversely affect the ability to drive or use machines. Adverse drug reactions such as dizziness and visual disturbances may occur. If affected, patients should not drive or operate machines.'

4.8 Undesirable effects

A total of two clinical trials were conducted in patients with erosive esophagitis (EE). Of the subjects who participated in the clinical trials, 183 received 40 mg of the Product. Adverse events reported in clinical trials are as follows. Adverse events (1% or more) and adverse drug reactions (*) commonly reported in the Product administration group are shown in the following Table 1.

Table 1. Adverse events reported by 1% or more in clinical trials

System Organ Class (SOC)	Adverse event
Gastrointestinal disorders	Dyspepsia*, diarrhea*, nausea*, abdominal discomfort*, chronic gastritis, gastritis, erosive gastritis
Skin and subcutaneous tissue disorders	Erythema*, pruritus*
Nervous system disorders	Headache*
Musculoskeletal and connective tissue disorders	Back pain

Other adverse events reported in clinical trials with an incidence of less than 1% after administration of the Product are listed according to the major system organ class as follows.
- Gastrointestinal disorders: Hiatal hernia, Brunner's gland hyperplasia
- Infections and infestations: Bronchitis, herpes simplex, influenza, periodontitis, pharyngitis, vaginal infection
- Skin and subcutaneous tissue disorders: Dermatitis contact, swelling face*
- General disorders and administration site conditions: Chest discomfort, feeling abnormal*, edema, pain, pyrexia
- Nervous system disorders: Dizziness, dysgeusia*
- Musculoskeletal and connective tissue disorders: Myalgia*, musculoskeletal pain, neck pain
- Eye disorders: Cataract, conjunctival hemorrhage*, retinal tear
- Ear and labyrinth disorders: Ear discomfort*
- Respiratory, thoracic and mediastinal disorders: Rhinorrhea
- Metabolic and nutritional disorders: Hypertriglyceridemia

4.9 Overdose

No cases of severe overdose of the Product have been reported. In clinical trials, there has been experience of single dose of the Product up to 320 mg. In the event of overdose, the patient should be monitored for symptoms of toxicity and if necessary, general adjuvant treatment should be provided.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC: A02BC10 (Fexuprazan)

Pharmacological actions

The Product has a mechanism of action to inhibit gastric acid secretion by controlling H+/K+-ATPase in parietal cells of stomach in a K+ ion-dependent and reversible manner. The Product directly inhibits the proton pump without undergoing acid-induced activity.

1) Clinical studies

(1) Erosive esophagitis: A randomized, double-blind, comparative phase 3 clinical trial with 40 mg of the Product or 40 mg of Esomeprazole administered orally once daily for up to 8 weeks was conducted in 218 patients with erosive esophagitis. As a study result, the cumulative healing rate at Week 8 is shown in the table below and the non-inferiority of the Product to esomeprazole group was confirmed (Table 2).

Table 2. Cumulative healing rate at Week 8 in patients with erosive esophagitis (PPS; Per Protocol Set)**

	Product 40 mg (N=107)	Esomeprazole 40 mg (N=111)
Cumulative Healing Rate n (%)	106(99.07)	110(99.10)
	0.89[a] [-0.86, 2.64][b] 0.3378[c]	

a) Healing rate difference, % (baseline LA grade correction, Cochran Mantel-Haenszel Method)
b) 95% confidence interval of healing rate difference, c) p-value
* Non-inferiority margin: -10%
** Study number: DW_DWP14012301

5.2 Pharmacokinetic properties

1) Absorption

When single administration of 10~320 mg of the Product carried out in healthy adults, it was rapidly absorbed and the maximum plasma concentration reached at a median value of 1.75~3.5 hours after administration. Blood drug concentration increased as the dose increased. When 20~160 mg of the Product was repeatedly administered orally for 7 days, the drug concentration in the steady state and terminal elimination half-life were similar to that of the single administration. There was no accumulation of *in vivo* exposure after repeated administration and the drug concentration in blood tended to increase in proportion to the dose increase. As a result of orally administering 160 mg of the Product to healthy adult males after fasting and high-fat diet to evaluate the dietary effect on bioavailability, there were no significant differences in *in vivo* exposure and pharmacodynamic endpoints (retention time above pH 4 in the stomach).

2) Distribution

The *in vitro* plasma protein binding rates in human plasma were 94.3% and 92.8% at concentrations of 1 and 10 μg/mL, respectively.

3) Metabolism

The Product is mainly metabolized by CYP3A4, the main metabolite is metabolite M14 and this metabolite is ineffective.

4) Excretion

The amounts of unchanged forms excreted from urine and feces after intravenous administration in rats were 0.61% and 34.22%. After oral administration of the ^{14}C marker of the Product to rats, the excretion recovery rate at 120 hours was 98.9%, where the recovery rates of urine and feces were 18.8% and 80.1%, respectively. After single oral administration to biliary tract intubated rats, the bile was excreted at 88.0% at 48 hours and the total recovery rate was 98.2%. After oral administration of the 14C marker of the Product to dogs, the fecal recovery rate at 168 hours was 96.7%, where the recovery rates of urine and feces were 38.8% and 57.9%, respectively.

After oral administration of the Product to healthy adult males, the mean elimination half-life of unchanged

forms and metabolite M14 were 9.7 hours and 14.2 hours, respectively. The urine excretions and elimination rate of the unchanged form were about 0.6% and 0.63 L/hr, respectively.

5) Drug -Drug Interaction
(1) Drugs that may affect the plasma concentration of the Product
① The Product is a substrate of CYP3A4 and when the Product and a CYP3A4 inhibitor were administered in combination, the increase in exposure of the Product may be slight.
The AUC_T of the Product increased slightly to 1.1 times as a result of co-administration of 80 mg of the Product and 500 mg as clarithromycin twice a day for 7 days in healthy adult males.
(2) Drugs whose plasma concentration may be changed by the Product
① The Product showed competitive inhibitory effect against CYP3A4 in *in vitro*, but its IC_{50} (11.7 μM) was about 100 times higher than the maximum plasma concentration in the clinical dose (40mg basis).
② As a result of co-administration of three preparations, 80 mg of the Product, 1 g as amoxicillin and500 mg as clarithromycin twice a day for 7 days to healthy adult males, the AUC_T and Css,max of clarithromycin were decreased to 23% and 28%, respectively and the AUC_T and Css,max of amoxicillin were decreased to 14% and 33%, respectively.
③ The Product showed competitive inhibitory effect against MATE1, MATE2K and OCT1 in *in vitro*, but it is unlikely to increase the blood concentration of the transporter substrate drug when considering the maximum plasma concentration at the clinical dose (40 mg basis).

5.3 Preclinical safety data

(1) Genotoxicity
The Product was negative in all of the bacterial reverse mutation tests using *Salmonella* and *E. coli*, chromosomal abnormality tests using CHO cell lines and micronucleus tests using rats.

(2) Reproductive toxicity
As a result of fertility and early embryo development tests in rats, there was no effect on fertility and early embryo development up to a dose of 50 mg/kg/day. As a result of the embryo-fetal development test in rats, a decrease in feed intake and weight was observed in the group administered with more than 30 mg/kg/day. The weight of the fetus decreased by 5%, but there was no effect on development or growth delay. The no-effect levels (NOELs) of embryo-fetal and the maternal were confirmed to be 60 mg/kg/day (about 19.8 times the clinical dose of 40 mg AUC) and 15 mg/kg/day (7.5 times the clinical dose 40 mg AUC), respectively. As a result of the embryo-fetal development test in rabbits, a decrease in feed intake and weight and constipation symptoms were observed in the group administered with more than 15 mg/kg/day. However, there was no effect on development or growth delay. The no-effect levels (NOELs) of the maternal and embryo-fetal were confirmed to be 10 mg/kg/day (0.6 times the clinical dose of 40 mg AUC) and 15 mg/kg/day (1.7 times the clinical dose 40 mg AUC), respectively. As a result of prenatal development and maternal function evaluation tests in rats, there was no effect on the offspring immediately after childbirth by the Product, but it was transferred to maternal milk and the body weight decreased during the breastfeeding period in the administration dose of more than 7.5 mg/kg/day (3.7 times the clinical dose 40 mg AUC). However, no dysfunctions including behavior, development, sexual maturity and genital organs of the offspring even at the high dose of 30 mg/kg/day (17.2 times the clinical dose 40 mg AUC).

(3) Carcinogenicity
In a carcinogenicity study administered orally in rats for 2 years, gastric neuroendocrine tumors were observed at 10 mg/kg/day (about 3.7 times based on the clinical dose 40mg/day AUC) for males and 5 mg/kg/day (about 4.1 times based on the clinical dose 40mg/day AUC) for females. In the 26-week carcinogenicity test in RasH2 mice, gastric benign adenomas were observed at 60 mg/kg/day in males (about 26.9 times based on the clinical dose 40mg/day AUC).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Lactose monohydrate
Microcrystalline cellulose

Croscarmellose sodium
Magnesium stearate
Ferric oxide yellow
Opadry white 03B28796
Opadry AMB2 Green 88A610038

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at temperatures not exceeding 30ºC.

1) Keep out of reach of children.
2) Be aware that changing it to another container may cause an accident or is not desirable in terms of quality maintenance.

6.5 Nature and contents of container

Fexuclue film-coated tablet, 40mg is packaged in soft aluminum foil (PVC/AL/NY) and hard aluminum foil (Al+VMCH adhesive) blisters. Each blister packaging unit has 7 tablets per PTP plate.

7. PRODUCT REGISTRATION HOLDER

TAEVAS LIFE SCIENCES SDN. BHD.
Suite 163E, Level 16, Gurney Paragon Office Tower, Jalan Kelawei, 10250 George Town, Pulau Pinang, Malaysia

8. MANUFACTURER

Daewoong Pharmaceutical Co., Ltd.
1, Osongsaengmyeong 2-ro, Osong-eup, Heungdeok-gu, Cheongju-si, Chungcheongbuk-do, Republic of Korea

9. DATE OF REVISION

Date of Revision: June 2026