SUMMARY OF PRODUCT CHARACTERISTICS

VONIZA 10 & 20 MG FILM-COATED TABLETS

1. Name of the medicinal product

Voniza 10mg tablet.

2. Qualitative and quantitative composition

Each film coated tablet contains Vonoprazan 10mg.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

Yellow colored, round-shaped, film coated tablet, both faces are plain. Free from any visible defects.

4. Clinical particulars

4.1 Therapeutic indications

Voniza 10 Tablet is a potassium-competitive acid blocker indicated for

Healing of Gastric ulcer, duodenal ulcer, reflux esophagitis, prevention of recurrence of gastric or duodenal ulcer during low-dose aspirin administration, prevention of recurrence of gastric or duodenal ulcer during on-steroidal anti-inflammatory drug (NSAID)administration Adjunct to Helicobacter pylori eradication in the following settings: Gastric ulcer, duodenal ulcer, gastric mucosa-associated lymphatic tissue (MALT)lymphoma, idiopathic thrombocytopenic purpura, the stomach after endoscopic resection of early-stage gastric cancer or Helicobacter pylori gastritis.

4.2 Posology and method of administration Posology

Gastric Ulcers and duodenal ulcers

The recommended adult oral dosage is Vonoprazan 20 mg once daily for 8 weeks for gastric ulcers and 6 weeks for duodenal ulcer.

Reflux esophagitis: The usual adult dose for oral use is 20mg of Vonoprazan once daily for a total of 4weeks of treatment. If that dosing proves insufficient, the administration should be extended, but for no longer than 8 weeks of treatment. For the maintenance therapy of reflux esophagitis showing recurrence and recrudescence, the dose for oral use is l0mg of Vonoprazan once daily. However, when the efficacy is inadequate, the dosage may be increase up to 20mg of Vonoprazan once daily.

Prevention of recurrence of gastric or duodenal ulcer during low-dose aspirin administration:

The usual adult dosage is one tablet of Vonoprazan 10mg once daily.

Prevention of recurrence of gastric or duodenal ulcer during non-steroidal anti-inflammatory drug (NSAID) administration:

The usual adult dosage is Vonoprazan 10mg once daily.

Adjunct to Helicobacter pylori eradication:

For adults, the following three-drug regimen should be administered orally at the same time twice daily for seven days: 20mg of Vonoprazan, 750mg of amoxicillin hydrate and 200mg of clarithromycin. The dose of clarithromycin may be increased as clinically warranted. However, dosage should not exceed 400mg twice daily

***Pediatric population*:**

The safety and effectiveness of Vonoprazan have not been established in pediatric patient.

***Elderly**:*

No dose adjustment is required.

***Renal impairment**:*

The recommended dosage of Voniza Tablet in adult patients with renal impairment is described in the table below.

1. Gastric Ulcers and duodenal ulcers

Estimated glomerular filtration rate (GFR)	**Recommended Dosage**
30 mL/minute or greater	Vonoprazan 20mg once daily
Less than 30 mL/minute	Vonoprazan 20mg once daily

2. Treatment of H. pylori Infection

Estimated glomerular filtration rate (GFR)	**Recommended Dosage**
30 mL/minute or greater	Vonoprazan 20mg once daily
Less than 30 mL/minute	Not Recommended

3. Maintenance of Healed Gastric Ulcers and duodenal ulcers.

The recommended dosage of Voniza tablet in adult patients with renal impairment is the same as for adult patients with normal renal function

Hepatic impairment*:*

The recommended dosage of Voniza Tablet in adult patients with Hepatic impairment is described in Table below

1. Gastric Ulcers and duodenal ulcers

Classification	**Recommended Dosage**
Child-Pugh Class A	Vonoprazan 20mg once daily
Child-Pugh Class B	Vonoprazan 10mg once daily
Child-Pugh Class C	Vonoprazan 10mg once daily

2. Treatment of H. pylori Infection

Classification	**Recommended Dosage**
Child-Pugh Class A	Vonoprazan 20mg once daily
Child-Pugh Class B	Not Recommended
Child-Pugh Class C	Not recommended

3. Maintenance of Healed Gastric Ulcers and duodenal ulcers.

The recommended dosage of Voniza tablet in adult patients with Hepatic impairment is the same as for adult patients with normal renal function.

Method of administration:

The recommended Voniza Tablet dosage should be administered orally with or without food. The tablet should be Swallowed as whole and not chew or crush.

Route of administration: Oral use.

4.3 Contraindications

Voniza tablet is contraindicated in patients with a known hypersensitivity to Vonoprazan or any component of Voniza tablet. Reactions have included anaphylactic shock [see Adverse Reactions Section)

Voniza tablet is contraindicated with Rilpivirine-containing products [see Drug Interactions (4.5]

4.4 Special warnings and precautions for use

1. Presence of Gastric Malignancy

In adults, symptomatic response to therapy with Voniza Tablet does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing in patients who have a suboptimal response or an early symptomatic relapse after completing treatment with Voniza Tablet. In older patients, also consider endoscopy.

2. Acute Tubulointerstitial Nephritis

Acute tubulointerstitial nephritis (TIN) has been reported with Vonoprazan .If suspected, discontinue Voniza Tablet and evaluate patients with suspected acute TIN.

3. Clostridioides difficile-Associated Diarrhea

Associated Diarrhea Published observational studies suggest that proton pump inhibitors (PPIs) may be associated with an increased risk of Clostridioides difficile-associated diarrhea (CDAD), especially in hospitalized patients. Voniza tablet blocks the proton pump to inhibit gastric acid production and, may also increase the risk of CDAD. Consider CDAD in patients with diarrhea that does not improve ,use the shortest duration of Voniza Tablet appropriate to the condition being treated.

4. 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 therapy (a year or longer). Bone fracture, including osteoporosis-related fracture, has also been reported with Vonoprazan. Use the shortest duration of Voniza tablet appropriate to the condition being treated [see Dosage and Administration]. Patients at risk for osteoporosis-related fractures should be managed according to the established treatment guidelines.

5. Severe Cutaneous Adverse Reactions

Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with Vonoprazan, discontinue Voniza tablet

at the first signs or symptoms of severe cutaneous adverse reactions or other signs of hypersensitivity and consider further evaluation.

6. Vitamin B12 (Cobalamin) Deficiency

Long-term use of acid-suppressing drugs can lead to malabsorption of Vitamin B12 caused by hypo or achlorhydria. Vitamin B12 deficiency has been reported post marketing with Vonoprazan. If clinical symptoms consistent with Vitamin B12 deficiency are observed in patients treated with Voniza Tablet consider further workup.

7. Hypomagnesemia and Mineral Metabolism

Hypomagnesemia has been reported post marketing with Vonoprazan [see Adverse Reactions]. Hypomagnesemia may lead to hypocalcemia and/or hypokalemia and may exacerbate underlying hypocalcemia in at-risk patients. Consider monitoring magnesium levels prior to initiation of Vonoprazan treatment and periodically in patients expected to be on prolonged treatment, in patients taking drugs that may have increased toxicity in the presence of hypomagnesemia (e.g., digoxin), or drugs that may cause hypomagnesemia (e.g., diuretics). Treatment of hypomagnesemia may require magnesium replacement and discontinuation of Voniza tablet. Consider monitoring magnesium and calcium levels prior to initiation of Vonoprazan and periodically while on treatment in patients with a preexisting risk of hypocalcemia (e.g., hypoparathyroidism). Supplement with magnesium and/or calcium, as necessary. If hypocalcemia is refractory to treatment, consider discontinuing Voniza tablet.

8. Interactions with Diagnostic Investigations for Neuroendocrine Tumors

Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors. Temporarily discontinue Voniza Tablet treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high.

9. Fundic Gland Polyps

Use of Vonoprazan is associated with a risk of fundic gland polyps that increases with long-term use, especially beyond one year. Fundic gland polyps have been reported with

Vonoprazan in clinical trials and post marketing use with PPIs. Most patients who developed fundic gland polyps were asymptomatic and fundic gland polyps were identified incidentally on endoscopy.

4.5 Interaction with other medicinal products and other forms of interaction Antiretroviral drugs

Vonoprazan reduces intragastric acidity which may alter the absorption of antiretroviral drugs leading to changes in the safety and/or effectiveness.

Concomitant use with Voniza Tablet and Rilpivirine-containing products is contraindicated.

Concomitant use with Voniza tablet and Atazanavir should be Avoided.

Other Drugs (e.g., iron salts, erlotinib, Dasatinib, nilotinib, mycophenolate mofetil, ketoconazole/itraconazole

Vonoprazan reduces intragastric acidity which may decrease the absorption of drugs reducing their effectiveness.

Certain CYP3A Substrates where minimal concentration changes may lead to serious toxicities

Vonoprazan is a weak CYP3A inhibitor. Vonoprazan may increase exposure of CYP3A4 substrates, which may increase the risk of adverse reactions related to these substrates.

Frequent monitoring for concentrations and/or adverse reactions related to the substrate drugs when used with Vonoprazan should be done and Dosage reduction of substrate drugs may be needed.

CYP2C19 Substrates (e.g., clopidogrel, citalopram, cilostazol)

Vonoprazan is a CYP2C19 inhibitor. Vonoprazan may reduce plasma concentrations of the active metabolite of clopidogrel and may cause reduction in platelet inhibition. Vonoprazan may increase exposure of CYP2C19 substrate drugs (e.g., citalopram, cilostazol**).**

Carefully monitor the efficacy of clopidogrel and consider alternative anti-platelet therapy

Carefully monitor patients for adverse reactions associated with citalopram and cilostazol.

Chromogranin (CgA) Test for Neuroendocrine Tumors

Vonoprazan reduces intragastric acidity which increases CgA levels and may cause false positive results in diagnostic investigations for neuroendocrine tumors.

Assess CgA levels at least 14 days after stopping Vonoprazan treatment and repeat the test if initial CgA levels are high. If serial tests are performed (e.g., for monitoring), use the same commercial laboratory for testing, as reference ranges between tests may vary.

Interaction with Secretin Stimulation Test.

Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma

Temporarily stop Vonoprazan at least 14 days before assessing to allow gastrin levels to return to baseline.

4.6 Fertility, pregnancy and lactation Pregnancy

There are no adequate and well-controlled studies of Vonoprazan in pregnant women. Available data from pharmacovigilance reports with Vonoprazan-containing products use in pregnant women are not sufficient to evaluate for a drug-associated risk for major birth defects, miscarriage, or other adverse maternal or fetal outcomesregnancy

Breast-feeding

There are no data regarding the presence of Vonoprazan in human milk, the effects on the breastfeeding infant, or the effects on milk production. Vonoprazan and its metabolites are present in rat milk. Liver injury occurred in offspring from pregnant and lactating rats administered oral Vonoprazan at AUC exposures approximately equal to and greater than the MRHD When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because of the potential risk of adverse liver effects shown in animal studies with Vonoprazan, advise patients not to breastfeed during treatment with on Vonoprazan.

Fertility

Vonoprazan at oral doses up to 300 mg/kg/day in rats (approximately 133-times the MRHD based on AUC from a separate study in nonpregnant animals administered the same dose) was found to have no effect on fertility and reproductive performance.

4.7 Effects on ability to drive and use machines

Vonoprazan does not affect ability to drive or operate machinery.

4.8 Undesirable effects.

The following serious adverse reactions are described elsewhere in labeling:

- Acute Tubulointerstitial Nephritis [see Warnings and Precautions]
- Clostridioides difficile-Associated Diarrhea [see Warnings and Precautions]
- Bone Fracture [see Warnings and Precautions]
- Severe Cutaneous Adverse Reactions [see Warnings and Precautions]
- Vitamin B12 (Cobalamin) Deficiency [see Warnings and Precautions]
- Hypomagnesemia and Mineral Metabolism [see Warnings and Precautions]
- Fundic Gland Polyps [see Warnings and Precautions (5.9)]

The following side adverse rection were observed in 2%-3% of patients who received Vonoprazan for treatments of Erosive Esophagitis

Gastritis Diarrhea, Abdominal distension, Abdominal pain, Nausea, Dyspepsia Hypertension and Urinary tract infection.

Adverse reactions reported in 1% or less of Vonoprazan -treated patients for the healing or maintenance of healed erosive esophagitis or for the relief of heartburn associated with non-erosive gastroesophageal reflux disease in the United States trials are:

Blood and lymphatic system disorders: anemia, lymphocytosis

Cardiac disorders: tachycardia

Ear and labyrinth disorders: vertigo

Gastrointestinal disorders: duodenal polyp, dry mouth, dysphagia, eructation, flatulence, gastric polyps, vomiting

General disorders and administrative site conditions: asthenia, peripheral edema

Investigations: increased liver enzymes

Metabolism and nutritional disorders: diabetes mellitus

Musculoskeletal system: bone fracture

Nervous system disorders: dizziness, headache, syncope

Psychiatric disorders: depression, insomnia

Renal and urinary disorders: tubulointerstitial nephritis

Skin and subcutaneous tissue disorders: eczema, rash, urticaria

In Treatment of H. pylori Infection below adverse effects were observed

Adverse reactions reported in at least 2% of patients

Diarrhea , Dysgeusia , Vulvovaginal candidiasis, Abdominal pain, Headache ,Hypertension ,Nasopharyngitis

Less Common Adverse Reactions

Other adverse reactions reported in less than 2% of patients treated with Vonoprazan , amoxicillin, and clarithromycin are listed below by body system:

Blood and lymphatic system disorders: anemia, leukocytosis, leukopenia, neutropenia

Cardiac disorders: QT prolongation, tachycardia Eye disorders: orbital edema

Gastrointestinal disorders: abdominal distension, constipation, dry mouth, duodenal polyp, duodenal ulcer, dyspepsia, flatulence, gastric ulcer, gastroesophageal reflux disease, hematochezia, large intestine polyp, rectal polyp, nausea, stomatitis, tongue discomfort, vomiting

General disorders and administration site conditions: fatigue, pyrexia Immune system disorders: drug hypersensitivity Infections and infestations: anal fungal infection, gastrointestinal viral infection, oral fungal infection, pneumonia, tongue fungal infection, upper respiratory tract infection, urinary tract infection, viral infection Investigations: increased liver function test Metabolism and nutrition disorders: decreased appetite Musculoskeletal system: bone fracture Nervous system disorders: ageusia, dizziness, tension headache Psychiatric disorders: anxiety, depression, insomnia Renal and urinary disorders: renal hypertrophy, tubulointerstitial nephritis Reproductive system and breast disorders: vaginal discharge Respiratory, thoracic and mediastinal disorders: cough, nasal polyps, oropharyngeal pain Skin and subcutaneous tissue disorders: dermatitis, dry skin, and rash.

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions .

4.9 Overdose

No cases of overdose have been reported. However, the following information may prove useful:

5. Pharmacological properties

Pharmacotherapeutic group: Potassium-Competitive acid blocker

ATC code: A02BC08

5.1 Pharmacodynamic properties

Vonoprazan suppresses basal and stimulated gastric acid secretion at the secretory surface of the gastric parietal cell through inhibition of the H+, K+-ATPase enzyme system in a potassium-competitive manner. Because this enzyme is regarded as the acid (proton) pump within the parietal cell, Vonoprazan has been characterized as a type of gastric proton-pump inhibitor, in that it blocks the final step of acid production. Vonoprazan does not require activation by acid. Vonoprazan may selectively concentrate in the parietal cells in both the resting and stimulated states. Vonoprazan binds to the active pumps in a noncovalent and reversible manner

Antisecretory Activity

Following a single 10 mg or 20 mg dose of Vonoprazan, the onset of the antisecretory effect as measured by intragastric pH occurs within 2 to 3 hours. The elevated intragastric pH levels compared to placebo increase with dose and are maintained for over 24 hours after dosing. The inhibitory effect of Vonoprazan on acid secretion increases with repeated daily dosing and steady state is achieved by Day 4. The antisecretory effect of Vonoprazan decreases following drug discontinuation although intragastric pH remained elevated compared to placebo for 24 to 48 hours following the dose on Day 7. The effects of Vonoprazan 10 observed, which is consistent with the pharmacological action of a potassium-competitive acid blocker. No neoplastic changes were observed.

5.2 Pharmacokinetic properties Absorption

Vonoprazan exhibits time independent pharmacokinetics and steady state concentrations are achieved by Day 3 to 4. After multiple doses of Vonoprazan ranging from 10 to 40 mg (twice the maximum recommended dose) once daily for 7 days in healthy subjects, Cmax and area under the plasma concentration time curve (AUC) values for Vonoprazan increased in an approximately dose proportional manner. There is little accumulation in plasma after once daily multiple doses, with an accumulation index ratio of less than 1.2 based on AUC for doses ranging from 10 to 40 mg (twice the maximum recommended dose). Steady state plasma exposure of Vonoprazan following 20 mg twice daily dosing (AUC0-12h = 273

hr*ng/mL, N=10) was approximately 1.8-fold higher compared to the mean estimate from the same subjects on Day 1 (AUC0-12h = 155 hr*ng/mL, N=10).

Effect of Food

In a food effect study in healthy subjects (N=24) who received Vonoprazan 20 mg, a high-fat meal resulted in a 5% increase in Cmax, a 15% increase in AUC, and a delay in median Tmax of 2 hours. These changes are not considered to be clinically significant [see Dosage and Administration (2.4)].

Distribution

Plasma protein binding of Vonoprazan ranged from 85 to 88% in healthy subjects and was independent of concentration from 0.1 to 10 mcg/mL. Elimination Metabolism Vonoprazan is metabolized to inactive metabolites via multiple pathways by a combination of cytochrome P450 (CYP) isoforms (CYP3A4/5, CYP2B6, CYP2C19, CYP2C9 and CYP2D6) along with sulfo- and glucuronosyl-transferases. CYP2C19 polymorphisms have been evaluated in clinical studies and there were no considerable differences in the pharmacokinetics of Vonoprazan based on CYP2C19 metabolizer status.

Excretion

Following oral administration of radiolabeled Vonoprazan, approximately 67% of the radiolabeled dose (8% as unchanged Vonoprazan) was recovered in urine and 31% (1.4% as unchanged Vonoprazan) was recovered in feces.

Specific Populations

Geriatric Patients

No clinically meaningful differences in the pharmacokinetics of Vonoprazan are predicted in patients 65 years of age and older compared to younger adult patients. Sex, Race or Ethnicity There were no clinically significant differences in the pharmacokinetics of Vonoprazan based on sex or race/ethnicity.

Patients with Renal impairment

The pharmacokinetics of Vonoprazan administered as a single 20 mg dose in patients with mild [eGFR 60 to were 1.3-fold greater compared to estimates from subjects with normal renal function [see Dosage and Administration (4.2)]. Protein binding of Vonoprazan is not

affected by impaired renal function. In patients requiring dialysis, Vonoprazan was present in the dialysate and represented 0.94% of the dose administered.

Patients with Hepatic Impairment

The pharmacokinetics of Vonoprazan administered as a single 20 mg dose in patients with mild [Child-Pugh Class A (N=8)], moderate [Child-Pugh Class B (N=8)], or severe [Child-Pugh Class C (N=6)] hepatic impairment were compared to those with normal hepatic function (N=12). Compared to subjects with normal hepatic function, systemic exposure (AUC0-inf) of Vonoprazan was 1.2-, 2.4-, and 2.6-times greater in patients with mild, moderate, and severe hepatic impairment, respectively [see Dosage and Administration (4.2)]. Protein binding of Vonoprazan is not affected by impaired hepatic function.

Drug Interaction Studies

In Vitro Studies

Cytochrome P450 (CYP450) Enzymes

In vitro studies have shown that Vonoprazan directly and time-dependently inhibits CYP2B6, CYP2C19, and CYP3A4/5.

Transporter Systems

Vonoprazan inhibits multidrug and toxin extrusion protein 1 (MATE1) and organic cation transporter 1 (OCT1), but only at concentrations higher than clinically relevant.

Clinical Studies Combination Therapy with Vonoprazan, Amoxicillin, and Clarithromycin

When Vonoprazan 20 mg, amoxicillin 750 mg and clarithromycin 400 mg were co-administered twice daily for 7 days (N=11), there was no effect on pharmacokinetics of amoxicillin compared to amoxicillin alone. However, Vonoprazan Cmax and AUC0-12h increased by 87% and 85%, respectively, and clarithromycin Cmax and AUC0-12h increased by 64% and 45% respectively, compared to administration of each component alone.

Effect of Vonoprazan on CYP3A4 Substrates

When a single oral dose of midazolam 2 mg was administered following Vonoprazan 20 mg twice daily for 7 days (N=20), midazolam AUC0-inf increased 93% compared to administration of midazolam alone.

Effect of CYP3A Inhibitors on Vonoprazan

When a single dose of 40 mg Vonoprazan (twice the maximum recommended dose) was administered with clarithromycin 500 mg twice daily for 7 days (N=16), Vonoprazan AUC0-inf increased 58% compared to administration of Vonoprazan alone.

Coadministration of Vonoprazan with NSAIDs or Low Dose Aspirin

When a single dose of 40 mg Vonoprazan (twice the maximum recommended dose) was co-administered with diclofenac 25 mg, meloxicam 10 mg, or aspirin 100 mg, there were no clinically meaningful changes in exposure of Vonoprazan, diclofenac, meloxicam, or aspirin compared to administration of each drug alone.

6. Pharmaceutical particulars

6.1 List of excipients Tablet core:

Mannitol

Microcrystalline Cellulose (PH101)

Croscarmellose Sodium

Hydroxypropyl Cellulose (Klucel LF)

Fumaric Acid

Magnesium Stearate

Film Coating

Opadry-OY-L 22920(Yellow)Ph Grade

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years. (24 months)

6.4 Special precautions for storage

Store below 30^0c, protect from light and moisture.

6.5 Nature and contents of container

Alu/Alu blister pack, packed in inner cartons**.**

Pack size :30's

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorizations holder

Square Pharmaceutical EPZ Limited.

8. Marketing authorization number(s)

CTD12147/26760

9. Date of first authorization/renewal of the authorization

04-03-2026

10. Date of revision of the text

04-03-2026