SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG PRODUCT

GetzomeInsta (Omeprazole + Sodium Bicarbonate) SachetRange.

Strength: 20mg+1680mg and 40mg+1680mg
Pharmaceutical/Dosage Form: Granules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Eachsachetcontains:
Omeprazole USP…….…… 20mg
Sodium bicarbonateUSP …….. 1680mg

Each sachet contains:
Omeprazole USP…….…… 40mg
Sodium bicarbonate USP …….. 1680mg

3. PHARMACEUTICAL FORM

White to off-white granular powder filled in a printed sachet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

GetzomeInsta (Omeprazole + Sodium bicarbonate) powder for oral suspension is indicated:

- In the treatment of Gastro-Esophageal Reflux Disease (GERD):
  - For the treatment of heart burn and other symptoms associated with GERD.
  - For the treatment of erosive esophagitis which has been diagnosed by endoscopy.
- In Short term treatment of active duodenal ulcer. Some patients may require an additional therapy.
- In Short term treatment of active benign gastric ulcer.
- For maintenance treatment of healing of erosive esophagitis.
- For reduction treatment of risk of upper gastrointestinal bleeding in critically ill patients.

4.2 Posology and Method of Administration

GetzomeInsta (Omeprazole + Sodium bicarbonate) powder for oral suspension as per recommended dosing given in below table.
GetzomeInsta (Omeprazole + Sodium bicarbonate) should be taken on an empty stomach at least one hour before a meal.

Recommended doses for Adults (18years & older)

INDICATION	RECOMMENDED	DOSE FREQUENCY
Short term treatment of active duodenal ulcer	20mg	Once daily for 4 weeks
Benign gastric ulcer	40mg	Once daily for 4-8 weeks
Reduction of risk of upper gastrointestinal bleeding in critically ill patients (40mg oral suspension only)	40mg	40mg initially followed by 40mg 6-8 hours later and 40mg daily thereafter for 14 days*
Gastroesophageal Reflux Disease (GERD)		
Symptomatic GERD (with no esophageal erosions)	20mg	Once daily for upto 4 weeks
Erosive esophagitis	20mg	Once daily for upto 4-8 weeks**
Maintenance of healing of erosive esophagitis	20mg	Once daily

*Most patients heal within 4 weeks. Some patients may require an additional 4 weeks of therapy.
**The efficacy of GETZOME INSTA (Omeprazole + Sodium bicarbonate) used for longer than 8 weeks in these patients has not been established. In the rare instance of a patient not responding to 8 weeks of treatment, it may be helpful to give upto an additional 4 weeks of treatment. If there is recurrence of erosive esophagitis or GERD, symptoms (e.g., heartburn), additional 4-8 week courses of omeprazole may be considered.

Since both 20mg and 40mg oral suspension sachets contain the same amount of sodium bicarbonate (1680mg), two sachets of GetzomeInsta(Omeprazole + Sodiumbicarbonate) 20mg are not equivalent to one sachet of GetzomeInsta(Omeprazole + Sodium bicarbonate) 40mg; therefore, two 20mg sachets of GetzomeInsta(Omeprazole + Sodium bicarbonate) should not be substituted for one sachet GetzomeInsta(Omeprazole + Sodium bicarbonate) 40mg.

Method of administration:
- Empty the sachet contents into a small cup containing 1-2 tablespoons (15 - 30mL) of water to form suspension.
- Stir well and drink immediately.
- Refill cup with water and drink.
- Do not use other liquids or foods.

4.3 Contraindications:

- Omeprazole is contraindicated in patients with known hypersensitivity to any component of the formulation.
- Sodium bicarbonate is contraindicated in patients with metabolic alkalosis and hypocalcemia.

4.4 Special warnings and special precautions for use

General:
- Symptomatic response to therapy with omeprazole does not preclude the presence of gastric malignancy.
- Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole.
- Omeprazole powder for oral suspension contains sodium in the form of sodium bicarbonate. This should be taken into consideration for patients on a sodium-restricted diet.
- Sodium bicarbonate should be used with caution in patients with Bartter's syndrome, hypokalemia, respiratory alkalosis, and problems with acid-basebalance. Long- term administration of bicarbonate with calcium or milk can cause milk-alkali syndrome.

4.5 Interaction with other medicaments

- Omeprazole can prolong the elimination of diazepam, warfarin andphenytoin, drugs that are metabolized by oxidation in the liver. There have been reports of increased INR and prothrombin time in patients receiving proton pump inhibitors, including omeprazole, 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 may need to be monitored for increases in INR and prothrombin time. Although in normal subjects no interaction with theophylline or propranolol was found, there have been clinical reports of interaction with other drugs metabolized via the cytochrome P-450 system (e.g., cyclosporine, disulfiram, benzodiazepines). Patients should be monitored to determine if it is necessary to adjust the dosage of these drugs when taken concomitantly with omeprazole.
- Because of its profound and long-lasting inhibition of gastric acid secretion, it is theoretically possible that omeprazole may interfere with absorption of drugs where gastric pH is an important determinant of their bioavailability (e.g., ketoconazole, ampicillin esters, and iron salts).
- Concomitant administration of omeprazole and atazanavir has been reported to reduce the plasma levels of atazanavir.
- Concomitant administration of omeprazole and tacrolimus may increase the serum levels of tacrolimus.
- Co-administration of omeprazole and clarithromycin have resulted in increases of plasma levels of omeprazole, clarithromycin, and 14-hydroxy-clarithromycin.

4.6Fertility, Pregnancy and Lactation

Pregnancy:
There are no adequate and well controlled studies on the use of omeprazole in pregnant women. Omeprazole should be used during pregnancy only if the potential benefit to pregnant women justifies the potential risk to the fetus.

Nursing Mothers:
Omeprazole is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from omeprazole; a decision should be made whether, to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. In addition, sodium bicarbonate should be used with caution in nursing mothers.

4.7 Effects on ability to drive and use machines

Omeprazole + Sodium Bicarbonate is not likely to affect the ability to drive or use machines. Adverse drug reactions such as dizziness and visual disturbances may occur (see section 4.8). If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

The following adverse reactions were reported:

- ***Body As a Whole***
  Allergic reactions, including, rarely anaphylaxis, fever, pain, fatigue, malaise and abdominal swelling.

- ***Cardiovascular***
  Chest pain or angina, tachycardia, bradycardia, palpitation, elevated blood pressure, and peripheral edema.

- ***Gastrointestinal***
  Pancreatitis (sometimes fatal), anorexia, irritable colon, flatulence, fecal discoloration, esophageal candidiasis, mucosal atrophy of the tongue, dry mouth and stomatitis. During treatment with omeprazole, gastric fundic gland polyps have been noted rarely. These polyps are benign and appear to be reversible when treatment is discontinued.

- ***Hepatic***
  Mild and, rarely, marked elevations of liver function tests [ALT (SGPT), AST (SGOT), g-glutamyltranspeptidase, alkaline phosphatase, and bilirubin (jaundice)]. In rare instances, overt liver disease has occurred, including hepatocellular, cholestatic, or mixed hepatitis, liver necrosis (sometimes fatal), hepatic failure (sometimes fatal), and hepatic encephalopathy.

- ***Metabolic/Nutritional***
  Hyponatremia, hypoglycemia and weight gain.

- ***Musculoskeletal***
  Muscle cramps, myalgia, muscle weakness, joint pain, and leg pain.

- ***Nervous System/Psychiatric***
  Psychic disturbances including depression, agitation, aggression, hallucinations, confusion, insomnia, nervousness, tremors, apathy, somnolence, anxiety, dream abnormalities, vertigo, paresthesia and hemifacial dysesthesia.

- ***Respiratory***
  Epistaxis and pharyngeal pain.

- ***Skin***
  Rash and rarely, cases of severe generalized skin reactions including toxic epidermal necrolysis (TEN; sometimes fatal), Stevens-Johnson syndrome, and erythema multiforme (some severe); purpura and/or petechiae (sometimes with rechallenge); skin inflammation, urticaria, angioedema, pruritus, photosensitivity, alopecia, dry skin and hyperhydrosis.

- ***Special Senses***
  Tinnitus and taste perversion.

- ***Ocular***
  Blurred vision, ocular irritation, dry eye syndrome, optic atrophy, anterior ischemic optic neuropathy, optic neuritis and double vision.

- ***Urogenital***
  Interstitial nephritis (sometimes with positive rechallenge), urinary tract infection, microscopic pyuria, urinary frequency, elevated serum creatinine, proteinuria, hematuria, glycosuria, testicular pain, and gynecomastia.

- ***Hematologic***
  Rare instances of pancytopenia, agranulocytosis (sometimes fatal), thrombocytopenia, neutropenia, leukopenia, anemia, leucocytosis and hemolytic anemia have been reported.
  Additional adverse reactions that could be caused by sodium bicarbonate, include metabolic alkalosis, seizures and tetany.

4.8 Overdosage

In doses ranged up to 2400mg, manifestations were variable, but included confusion, drowsiness, blurred vision, tachycardia, nausea, vomiting, diaphoresis, flushing, headache, dry mouth, and other adverse reactions similar to those seen in normal clinical experience. No specific antidote for omeprazole overdosage is known. Omeprazole is extensively protein bound and is, therefore, not readily dialyzable. In the event of overdosage, treatment should be symptomatic and supportive. In addition, a sodium bicarbonate overdose may cause hypocalcemia, hypokalemia, hypernatremia, and seizures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of Action:

Omeprazole reduces gastric acid secretion through a unique mechanism of action. Omeprazole belongs to a class of anti-secretory compounds - the substituted benzimidazoles that do not exhibit anti-cholinergic or H_2 histamine antagonistic properties. It inhibits secretion of gastric acid by irreversibly blocking the enzyme system of hydrogen/potassium adenosine triphosphatase (H+/K+ATPase), the proton pump of the gastric parietal cell. This effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus.

5.2 Pharmacokinetic Properties

Absorption:

Omeprazole is acid-labile and is administered orally on an empty stomach 1 hour prior to a meal. The absorption of omeprazole is rapid, with mean peak plasma levels being 1954ng/mL (33%) occurring at about 30 minutes (range 10 to 90 minutes) after a single dose or repeated-dose administration. Absolute bioavailability of omeprazole powder for oral suspension is about 30-40% at doses 20-40mg due in large part to presystemic metabolism. When powder for oral suspension is administered 1 hour after a meal, the omeprazole AUC is reduced by approximately 24% relative to administered 1 hour prior to meal.

Distribution:

Omeprazole is bound to plasma proteins. Protein binding is approximately 95%.

Metabolism & Elimination:

Following absorption, omeprazole is almost completely metabolized in the liver, primarily by the cytochrome P450 isoenzyme CYP2C19 to form hydroxy-omeprazole and to a small extent by CYP3A4 to form omeprazole sulfone. These metabolites are inactive and excreted mostly in the urine and to a lesser extent in the bile. The majority of the dose (77%) was eliminated in the urine. The remainder of the dose was recoverable in the feces. The mean plasma omeprazole half-life is approximately 1 hour (ranging from 0.4 to 3.2 hours) and the total body clearance is 500-600mL/min.

Special population:

Pediatric

The pharmacokinetics of omeprazole has not been studied in patients < 18 years of age.

Geriatric

The elimination rate of omeprazole was somewhat decreased in the elderly, and bioavailability was increased. Omeprazole was 76% bioavailable when a single 40mg oral dose of omeprazole (buffered solution) was administered to healthy elderly subjects, versus 58% in young subjects given the same dose. The plasma clearance of omeprazole was 250mL/min (about half that of young subjects) and its plasma half-life averaged one hour, similar to that of young healthy subjects.

Renal Insufficiency

In patients with chronic renal impairment, whose creatinine clearance ranged between 10 and 62mL/min/1.73m2, the disposition of omeprazole from a buffered solution was very similar to that in healthy subjects, although there was a slight increase in bioavailability. Because urinary excretion is a primary route of excretion of omeprazole metabolites, their elimination slowed in proportion to the decreased creatinine clearance.

Hepatic Insufficiency

In patients with chronic hepatic diseases, the bioavailability of Omeprazole from a buffered solution increased to approximately 100% and the mean plasma half-life of the drug increased to nearly 3hours compared to the mean half-life of 1 hour in normal subjects. Plasma clearance averaged 70mL/min, compared to a value of 500-600mL/min in normal subject.

5.3 Preclinical Safety data

Gastric ECL-cell hyperplasia and carcinoids, have been observed in life-long studies in rats treated with omeprazole. These changes are the result of sustained hypergastrinaemia secondary to acid inhibition. Similar findings have been made after treatment with H2-receptor antagonists, proton pump inhibitors and after partial fundectomy. Thus, these changes are not from a direct effect of any individual active substance

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Mannitol, Xanthan gum,Mint Flavor, Sucralose.

6.2 Incompatibilities

Not applicable

6.3 Shelf-life

3Years
The expiration dates refer to the product correctly stored in the required conditions.

6.4 Nature and contents of container

GetzomeInsta (Omeprazole + Sodium Bicarbonate) 20mg+1680mgis available in Alu Sachet packs of 1 x 10's with a package insert in a unit carton.
GetzomeInsta (Omeprazole + Sodium Bicarbonate) 40mg+1680mg is available in Alu Sachet packs of 1 x 10's with a package insert in a unit carton.

6.5 Instructions for use/handling

- Store below 30°C.
- Protect from sunlight & moisture.
- Keep out of reach of children.

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

Getz Pharma (Private) Limited
29-30/27, Korangi Industrial Area Karachi 74900, Pakistan
Tel: (92-21) 111-111-511
Fax: (92-21) 5057592

8. DRUG PRODUCT MANUFACTURER

Getz Pharma (Private) Limited
29-30/27, Korangi Industrial Area Karachi 74900, Pakistan
Tel: (92-21) 111-111-511
Fax: (92-21) 5057592

9. NAFDAC REGISTRATION NUMBER

A4-9827 – GetzomeInsta 20mg+1680mg
A4-9826 – GetzomeInsta 40mg+1680mg