Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Loprot I.V Injection 40mg

2. Qualitative and quantitative composition

Each vial contains:
Omeprazole Sodium
equivalent to Omeprazole.....40mg

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Loprot I.V Injection 40mg-Injection

4. Clinical particulars

4.1 Therapeutic indications

LOPROT IV 40mg (Omeprazole) should be administered intravenously only either as an infusion or injection and should not be given by any other route. LOPROT IV 40mg (Omeprazole) is indicated for patients who are unable to take oral therapy for the short term (up to 5 days) treatment of:
(1) Gastro-oesophageal reflux disease.
(2) Peptic ulcer disease.
(3)Treatment and prophylaxis of NSAID associated ulceration.
(4) Duodenal ulcer.
(5) Zollinger-Ellison syndrome.
(6) Prophylaxis of acid aspiration.

4.2 Posology and method of administration

Indications:	Dosage:
1. Gastro-oesophageal reflux disease. 2. Peptic ulcer disease. 3. Treatment and prophylaxis of NSAID associated ulceration. 4. Duodenal ulcer.	LOPROT IV 40mg (Omeprazole) once daily for upto 5 days.
Zollinger-Ellison syndrome.	Initial dose of LOPROT IV 40mg (Omeprazole) given intravenously is 60mg daily. Higher daily doses may be required and the dose should be adjusted individually. Dose greater than 60mg should be given twice daily.
Prophylaxis of acid aspiration during general anesthesia.	Recommended dose of LOPROT IV 40mg (Omeprazole) is 40mg to be given slowly (over a period of 5 minutes) as an intravenous injection, in the evening before surgery and a further 40mg one hour before surgery.

Hepatic Impaired Patients: For patients with impaired hepatic function a daily dose of 10-20mg may be sufficient. INSTRUCTIONS FOR USE: Injection: For I.V. injection, reconstitute LOPROT IV 40mg (Omeprazole) with 10ml sterile water for injection to make a 10ml solution containing 4mg/ml
Omeprazole approximately. No other solvents for I.V. injection should be used. After reconstitution, LOPROT IV 40mg (Omeprazole) should be given as intravenous injection, slowly over a period of atleast 2.5 minutes at a maximum rate of 4ml/min. The reconstituted solution is stable for approximately 8 hours when stored in the original vial in a cool place.
Infusion: For I.V. infusion, reconstitute LOPROT IV 40mg (Omeprazole) with 10ml sterile water for injection to make a 10ml solution containing 4mg/ml Omeprazole approximately. Next add the 10ml reconstituted solution to 90ml of 0.9% w/v of sodium chloride solution for injection, 5% w/v of dextrose solution for injection or 5% w/v of mannitol to make 100ml solution containing 0.4mg/ml of Omeprazole approximately. No other solution should be used for infusion. The reconstituted infusion should be given intravenously over a period of 20-30 minutes. The prepared infusion solution (stored below 25°C) should be used within 3 hours of preparation and any unused portion should be discarded. From microbiological point of view, products should be used immediately while diluted infusion solution is approximately stable for 18 hours, when stored in a cool place, protected from sunlight provided that it has been reconstituted under controlled and validated aseptic conditions. The infusion solution should not be refrigerated. The reconstituted and diluted solutions should not be used if it contains visible particulate matter.

4.3 Contraindications

Omeprazole is contra-indicated in patients with known hypersensitivity to any component of the formulation.

4.4 Special warnings and precautions for use

General: When gastric ulcer is suspected, the possibility of malignancy should be excluded as treatment may alleviate symptoms and delay diagnosis. 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.
Pregnancy: There is no evidence of adverse events of Omeprazole on pregnancy or on the health of the fetus/newborn child when Omeprazole was given to pregnant women. However, administration should be done under caution.
Nursing Mothers: Omeprazole is excreted in breast milk. Thus a decision should be taken to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.5 Interaction with other medicinal products and other forms of interaction

In common with the use of other inhibitors of acid secretion or antacids, the

absorption of ketoconazole and itraconazole can decrease during treatment with Omeprazole due to decreased intragastric acidity during treatment with Omeprazole. With voriconazole, the plasma concentration of both drugs may be increased and a reduced dose of Omeprazole is recommended.
Omeprazole is metabolized by CYP2C19. Thus, when Omeprazole is combined with drugs metabolized by CYP2C19, such as diazepam, citalopram, imipramine, clomipramine, phenytoin and warfarin, the plasma concentrations of these drugs may be increased and a dose reduction could be needed.
Simultaneous treatment with Omeprazole and digoxin in healthy subjects lead to a 10% increase in the bioavailability of digoxin as a consequence of the increased intragastric pH.
Concomitant administration of Omeprazole and tacrolimus may increase the serum levels of tacrolimus. Omeprazole like other PPIs should not be co-administered with atazanavir.
Use of Omeprazole and Clarithromycin results in an approximate 30% increase in peak plasma concentrations of Omeprazole and an increase in its mean half life from 1.2 hours to 1.6 hours.

4.6 Pregnancy and Lactation

Pregnancy
Results from three prospective epidemiological studies (more than 1000 exposed outcomes) indicate no adverse effects of omeprazole on pregnancy or on the health of the foetus/newborn child. Omeprazole can be used during pregnancy.
Breastfeeding
Omeprazole is excreted in breast milk but is not likely to influence the child when therapeutic doses are used. Fertility
Animal studies with the racemic mixture omeprazole, do not indicate effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Loprot I.V Injection is not likely to affect the ability to drive or use machines.

4.8 Undesirable effects

Omeprazole is well tolerated and the adverse reactions have generally been mild and reversible.

Common: Central and peripheral nervous system; Headache. Gastrointestinal; Diarrhea, constipation, abdominal pain, nausea/vomiting and flatulence.

Uncommon: Central and peripheral nervous system; Dizziness, paraesthesia, somnolence, insomnia and vertigo. Hepatic; Increased liver enzymes. Skin; Rash and/or pruritis, urticaria.

Other; Malaise.

Rare: Central and peripheral nervous system; Reversible mental confusion, agitation, aggression, depression and hallucinations, predominantly in severely ill patients.

Endocrine; Gynecomastia.

Gastrointestinal; Dry mouth, stomatitis and gastrointestinal candidiasis. Hematological; Leukopenia, thrombocytopenia, agranulocytosis and pancytopenia.

Hepatic; Encephalopathy in patients with pre-existing severe liver disease, hepatitis with or without jaundice, hepatic failure and increased liver enzymes.

Musculoskeletal; Arthritic and myalgic symptoms and muscular weakness. Reproductive system; Impotence, breast disorders.

Skin; Photosensitivity, bullous eruption erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and alopecia.

Others; Hypersensitivity reactions e.g. angioedema, fever, bronchospasm, interstitial nephritis and anaphylactic shock. Increased sweating, peripheral edema, blurred vision, taste disturbance and hyponatremia. Isolated cases of irreversible visual impairment have been reported in critically ill patients particularly at high doses, however no casual relationship has been established. Gastro-duodenal carcinoids have been reported in patients with Zollinger-Ellison syndrome on long term treatment with Omeprazole.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via the relevant national regulatory authority pharmacovigilance.

4.9 Overdose

Symptoms were transient and no serious clinical outcome has been reported with Omeprazole overdose. No specific antidote for Omeprazole overdose is known. Omeprazole is extensively bound to plasma proteins and is therefore, not readily dialyzable. In the event of overdose, treatment should be symptomatic and supportive.

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 new class of anti-secretory compounds, the substituted benzimidazoles that do not exhibit anti-cholinergic or histamine antagonistic properties. It inhibits secretion of gastric

acid by irreversibly blocking the enzyme system of hydrogen/potassium adenosine triphosphate (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

Distribution: The apparent volume of distribution in healthy subjects is approximately 0.3L/kg. The plasma protein binding of Omeprazole is about 95%.

Metabolism & Excretion: 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 (80%) is eliminated in the urine and the remainder is recoverable in the feces. The elimination half-life in plasma following I.V. administration of Omeprazole is approximately 40 minutes. The total plasma clearance is 0.3 to 0.6L/min. There is no change in half-life during treatment.

Special Populations: Pediatric: There is limited experience with Omeprazole administered intravenously in children. Geriatric: In elderly patients the volume of distribution is slightly decreased as compared to healthy patients. A slight decrease in elimination rate and an increase in bioavailability are also likely to occur in elderly patients. Dose adjustment is not needed in the elderly.

Renal Insufficiency: The distribution volume in patients with reduced renal function is similar to that seen in healthy patients. Dose adjustment is not needed in patients with impaired renal function.

Hepatic Insufficiency: In patients with impaired liver function the volume of distribution is slightly decreased, while the plasma half life of Omeprazole is increased.

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

Disodium Edetate
Sodium Hydroxide
Water for Injection

6.2 Incompatibilities
Infusions with low pH should not be used for diluting LOPROT IV 40mg (Omeprazole) as discoloration of solution can occur.

6.3 Shelf-Life
24 months

6.4 Special Precautions for storage
Store below 25□C.
Protect from light and moisture. Keep out of the reach of children.

6.5 Nature and Content of container
LOPROT IV 40mg (Omeprazole) lyophilized powder for injection is available as one vial plus 10ml sterile water for injection.

6.6 Special precautions for disposal and other handling
No special requirements

7. Marketing Authorization Holder
Nabiqasim Industries Pvt Ltd

8. Marketing Authorization Number

H2022/CTD6846/13110

9. Date of first authorization/renewal of the authorization

2022 September 06

10. Date of revision of the text

2022 September 06