6. DRUG AND ADDITIVE PROFILE

LANSOPRAZOLE \(^{108,109,110,111,112}\)

Brand Name:

Prevacid, Ogast, Lansox

IUPAC Name :

\[2-((3\text{-methyl}-4(2,2,2\text{-trifluoroethoxy})\text{pyridin-2-yl})\text{methane}sulfinyl)-1H-1,3-\text{benzodiazole}\]

Molecular Formula:

\(\text{C}_{16}\text{H}_{14}\text{F}_{3}\text{N}_{3}\text{O}_{2}\text{S}\)

Molecular Structure:

![Fig.6.1 Structure of Lansoprazole](image)

Molecular Weight:

369.363g/mol

Physical Appearance:

White to brownish – white powder
Melting point:
178-182 °C

Solubility:
Very slightly soluble in acetonitrile, soluble in absolute ethanol, soluble in ethanol, practically insoluble in buffer solution pH 7.

Pharmacodynamics
Lansoprazole acts by inhibiting, specifically, the hydrogen/potassium ATPase (proton pump) of the parietal cell in the stomach. This is the terminal step in acid production. This produces reduction of gastric acidity, which in turn heals peptic ulceration.

Pharmacokinetics

Absorption
Peak plasma levels occur within 1.5 to 2 hours following oral administration of lansoprazole. It has high bioavailability (80-90%).

Distribution
Its plasma protein binding is high at 97%.

Metabolism
Lansoprazole is metabolised substantially by the liver.

Elimination
The plasma elimination half-life ranges from 1 to 2 hours after single or multiple doses in healthy subjects. Lansoprazole is excreted by both the renal and biliary route.
**Therapeutic Uses**

Lansoprazole is effective in

- treatment of acid-related disorders of the upper GIT
- Gastro Oesophageal Reflux Disease
- combination with antibiotics in the eradication of bacteria *H. pylori*
- healing and maintenance for patients with benign gastric ulcer & duodenal ulcer
- relief of symptoms (heartburn, epigastric pain) related with acid-related dyspepsia.
- treatment of NSAID-associated benign gastric ulcers, duodenal ulcers
- long term management Zollinger-Ellison syndrome.

**DOSING PARAMETERS**

The dosing parameters at different conditions were given below:

- Acid-related dyspepsia: 15mg or 30mg once daily for 2-4 weeks
- Duodenal ulcer: 30mg once daily for 4 weeks.
- Benign gastric ulcer: 30mg once daily for 8 weeks.
- For prevention of relapse the recommended maintenance dose: 15mg once daily.
- NSAID benign gastric & duodenal ulcers: 15mg or 30mg once daily for 4 or 8 weeks.
- For patients at particular risk or with ulcers that may be difficult to heal, the higher
- dose and/or the longer treatment duration should be used.
- Gastro Oesophageal Reflux Disease: 30mg once daily for 4 weeks
• Hypersecretory conditions: 60mg initial dose once daily
• Patients requiring 120mg or more per day, dose to be divided & administered twice
• To achieve the optimal and rapid healing, lansoprazole single should be administered in the morning before food. Lansoprazole 'twice daily' should be administered once in the morning before food, and once in the evening.

Drug Interactions

The possible drug interactions of lansoprazole were given below
• Drug interaction may be produced with drugs like oral contraceptives, phenytoin, carbamazepine, theophylline, or warfarin which are metabolized by liver.
• Antacids and sucralfate may reduce the bioavailability of lansoprazole and so, not be taken within an hour of lansoprazole.

Adverse Drug Reactions

The adverse drug reactions were
• Common adverse effects: headache, dizziness, fatigue
• Gastrointestinal effects: diarrhoea, constipation, abdominal pain, nausea, vomiting
• Dermatological reactions: skin rashes, urticaria and pruritus
• Hypersensitivity reactions: angioedema, wheezing, anaphylaxis
• Haematological: thrombocytopenia, agranulocytosis, eosinophilia, leucopenia
• Very rare: colitis, jaundice, hepatitis. Gynaecomastia, impotence, blurred vision
Precautions / Warnings

Lansoprazole is metabolised substantially by the liver. It is therefore recommended that the daily dose for patients with severe liver disease is adjusted to 15mg or 30mg. There is no need to alter the dose in patients with mild to moderate hepatic or renal failure.

Decreased gastric acidity 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.

The use of lansoprazole should be avoided during pregnancy and lactation unless considered essential.

Contraindications

The use of lansoprazole is contra-indicated in patients with a history of hypersensitivity.

Storage:

Store in tightly closed container at room temperature.

Preparations

Lansoprazole is available as 15mg and 30mg tablets and capsules. Tablets are available as fast dissolving. It is also available as oral suspension in 15 and 30mg unit dose. It is also available as powdered form for intravenous injection in the dose of 30mg.
ADDITIVES PROFILE

POLYMER PROFILE: CHITOSAN

Synonyms: 2-Amino-2-deoxy-(1,4)-b-D-glucopyranan; deacetylated chitin
Chemical name: Poly-b-(1,4)-2-Amino-2-deoxy-D-glucose

Molecular structure:

![Fig. 6.2 Structure of Chitosan](image)

Mol. Wt: Vary from 10,000–10,00,000
Description: Odorless, white or creamy-white powder or flakes
Density: 1.35–1.40 g/cm³
Solubility: sparingly soluble in water; insoluble in ethanol (95%), other organic solvents. Soluble in dil. & conc. solutions of most organic acids.
Acidity/alkalinity: pH = 4.0–6.0 (1% w/v aqueous solution)
Tg: 2038 °C
Storage: Stable material at room temperature
Stored in a tightly closed container in a cool, dry place.
Applications: Coating agent; disintegrant; film-forming agent; mucoadhesive; viscosity-increasing agent. In drug delivery
Incompatibilities: Chitosan is incompatible with strong oxidizing agents.
POLYMER PROFILE: PLGA

Synonyms: Resomer

Molecular formula: \[((\text{C}_6\text{H}_8\text{O}_4)x(\text{C}_4\text{H}_4\text{O}_4)y)n\]

Molecular structure:

\[
\text{HO} \quad \text{O} \quad \text{[O]} \quad \text{O} \quad \text{H} \\
x \quad \text{[O]} \quad \text{y}
\]

\(x = \text{no. of lactic acid units, } y = \text{no. of glycolic acid units}\)

Fig. 6.3. Structure of PLGA

Wt. Avg. mol. wt: Varies from 5000 to 20000

Description: It is a biocompatible/biodegradable polymer synthesized from lactic acid and glycolic acid. Amorphous in nature

Solubility: Soluble in acetone, ethylacetate, but insoluble in water, methanol and ethanol.

Tg: 40-60°C

Degradation: Degraded into glycolic and lactic acids in body by hydrolysis.

Storage: Stored in a temperature of -20°C.

Applications: It can be successfully used for sustained release formulations. It can be used for preparation of microspheres, nanoparticles for effective and targeted delivery of drugs.
TRI-POLY PHOSPHATE \textsuperscript{120,121}

Synonyms: Sodium tripolyphosphate, polygon, STPP

IUPAC Name: pentosodium triphosphate

Molecular Formula: Na\textsubscript{5}P\textsubscript{3}O\textsubscript{10}

Molecular Structure:

Fig 6.4 Structure of Sodium tri-polyphosphate

Molecular Weight: 367.86

Appearance: White or colorless crystal powder.

Storage: Keep in dry and windy condition

Uses: Component of commercial detergents. Preservative for seafood, meats, poultry, and animal feeds.

GLACIAL ACETIC ACID \textsuperscript{120,121}

Synonyms: E260, ethanoic acid, methane carboxylic acid, vinegar

Chemical Name: Ethanolic acid

Empirical Formula: C\textsubscript{2}H\textsubscript{4}O\textsubscript{2}

Chemical structure

Fig. 6.5 Structure of Glacial acetic acid
Molecular Weight: 60.05

Description: crystalline mass or a clear, colorless volatile solution with a pungent odor.

Boiling point: 118°C

Dissociation constant: $pK_a = 4.76$

Flash point: 398°C (closed cup); 578°C (open cup).

Melting point: 178°C

Refractive index: ND 20 = 1.3718

Solubility: miscible with ethanol, ether, glycerin, water, and other fixed and volatile oils.

Specific gravity: 1.045

Storage: Airtight container in a cool and dry place.

Uses: Acidifying agent.

Incompatibilities: with alkaline substances.

**PLURONIC F68**

Synonyms: Lutrol, Monolan, poloxalkol, polyethylene–propylene glycol copolymer

Empirical Formula: HO(C2H4O)a(C3H6O)b(C2H4O)aH.

Uses: Dispersing agent, emulsifying and coemulsifying agent, solubilizing agent

Description: odourless, white, waxy, free-flowing prilled granules, or as cast solids.

Density: 1.06 g/cm³ at 258°C

Flash point: 2608°C

HLB value: 0.5–30; 29 for poloxamer 188.
Melting point: 578°C for poloxamer 188

Viscosity (dynamic): 1000 mPa s (1000 cP) as a melt at 778°C for poloxamer 188.

Storage: Stored in a well-closed container in a cool, dry place.

**ACETONE**<sup>120,121</sup>

Synonyms: dimethyl ketone, dimethyl formaldehyde

Chemical name: 2-Propanone

Molecular formula: C₃H₆O

Molecular weight: 58.08

Description: Colourless volatile liquid.

Solubility: Miscible in water and ethanol.

Odour: Fruity

Boiling point: 56.2°C

Melting point: 94.35°C

Density: 0.7899 g/ml

Applications: Used as solvent in formulation of microspheres and nanoparticles. Widely used as a solvent in production of various compounds like methacrylic acid, bisphenol etc.

**POLYSORBATE 80**<sup>120,121</sup>

Synonym: Polysorbate 80, Alkest, Crillet 4

Formula: C₆₄H₁₂₄O₂₆

Molecular weight: 1310 daltons
<table>
<thead>
<tr>
<th><strong>Description:</strong></th>
<th>Non-ionic surfactant obtained from polyethoxylated sorbitan and oleic acid. Amber colour viscous liquid.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Solubility:</strong></td>
<td>Soluble in water, methanol and ethanol. Insoluble in mineral oil.</td>
</tr>
<tr>
<td><strong>Relative density:</strong></td>
<td>1.07 (RT)</td>
</tr>
<tr>
<td><strong>Viscosity:</strong></td>
<td>400 to 620 cps</td>
</tr>
<tr>
<td><strong>Melting point:</strong></td>
<td>-20.5°C</td>
</tr>
<tr>
<td><strong>HLB Value:</strong></td>
<td>15</td>
</tr>
<tr>
<td><strong>Surface tension:</strong></td>
<td>42.5 dynes/cm</td>
</tr>
<tr>
<td><strong>CMC:</strong></td>
<td>13 to 15 mg/litre</td>
</tr>
<tr>
<td><strong>Applications:</strong></td>
<td>Emulsifier, stabilizer.</td>
</tr>
</tbody>
</table>