4.0 DRUG AND EXCIPIENT PROFILE

4.1 DOMPERIDONE\textsuperscript{1-16}

<table>
<thead>
<tr>
<th><strong>Category</strong></th>
<th>Peripheral dopamine receptor antagonist; antiemetic.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Molecular Weight</strong></td>
<td>425.911 g/mol</td>
</tr>
<tr>
<td><strong>Molecular Formula</strong></td>
<td>C\textsubscript{22}H\textsubscript{24}ClN\textsubscript{5}O\textsubscript{2}</td>
</tr>
<tr>
<td><strong>Melting Point</strong></td>
<td>242.5 °C</td>
</tr>
<tr>
<td><strong>pK\textalpha</strong></td>
<td>7.9</td>
</tr>
<tr>
<td><strong>IUPAC Name</strong></td>
<td>5-chloro-1-(1-[3-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)propyl] piperidin-4-yl)-1H-benzo[d]imidazol-2(3H)-one</td>
</tr>
</tbody>
</table>

**Structure**

![Structure](image)

**Description**

Domperidone is a benzimidazole derivatives and a member of dopamine receptor antagonist.

**Dose**

Adult - 20 – 40 mg t.d.s ; Children - 0.3 mg / kg t.d.s.

**Solubility**

Very slightly soluble in water and alcohol, slightly soluble in methanol.

**Pharmacology**

Domperidone acts as a gastrointestinal emptying adjunct and peristaltic stimulant. The antiemetic properties are related to dopamine receptor blocking activity at both chemoreceptor trigger zone and gastric level. It shows affinity for the D2 and D3 dopamine receptors.

**Pharmacokinetics**

Absorbed from the GIT, undergoes first pass metabolism in liver. Bioavailability is 5% following oral administration. Metabolites are excreted in faeces and in the urine. Plasma half-life is 7 - 8 hours. Onset of action is within 1 hour of administration.

**Routes of Administration**

Oral, intravenous, rectal

**Indications**

As an anti-emetic for relief on nausea and vomiting of any cause. Radiation, uremia. Reflux oesophagitis.
**Drug Interactions**

This medication enhances movement in the digestive tract, it may affect the absorption and action of other medications. Opioid analgesics and antimuscarinics antagonize its effects.

### 4.2 GLICLAZIDE\(^1,2,17-23\)

**Category**
Hypoglycemic Agents, Sulfonylureas, Antidiabetic

**Molecular Weight**
323.412 g/mol

**Molecular Formula**
\(\text{C}_{15}\text{H}_{21}\text{N}_{3}\text{O}_{3}\text{S}\)

**Melting Range**
180 °C – 182 °C

**pKa**
14.13

**IUPAC Name**
\(N\)-(hexahydrocyclopenta\([c]\)pyrrol-2(1\(H\))-ylcarbamoyl)-4-methylbenzene sulfonamide

**Structure**

![Structure of Gliclazide](image)

**Description**
Gliclazide belongs to category of sulfonylurea compounds drugs.

Gliclazide is a type of second generation sulfonylurea.

**Dose**
Adult - 20 – 40 mg t.d.s; Children - 0.3 mg / kg t.d.s.

**Solubility**
Very slightly soluble in water and alcohol, sparingly soluble in dimethylformamide, slightly soluble in methanol.

**Pharmacology**
Gliclazide is a second generation sulphonylurea which acts as a hypoglycemic agent. It stimulates \(\beta\) cells of the islet of Langerhans in the pancreas to release insulin. It also enhances peripheral insulin sensitivity. Overall, it potentiates insulin release and improves insulin dynamics.

**Pharmacokinetics**
Rapidly and well absorbed but may have wide inter- and intra-individual variability. Peak plasma concentrations occur within 4-6 hours of oral administration. 94%, highly bound to plasma.
proteins. Extensively metabolized in the liver. Less than 1% of the orally administered dose appears unchanged in the urine.

**Routes of Administration**
Oral

**Indications**
For the treatment of NIDDM in conjunction with diet and exercise

**Drug Interactions**
Hyperglycemic action may be caused by chlorpromazine, glucocorticoids, and progestogens. Its hypoglycemic action may be potentiated by alcohol.

### 4.3 POLYETHYLENE GLYCOL \(^{24-28}\)

**Synonym**
Carbowax; Carbowax Sentry; Lipoxol; Lutrol E; PEG; Pluriol E; polyoxethylene glycol.

**Chemical Name**
\( \alpha \)-Hydro-\( \omega \)-hydroxypoly(oxy-1,2-ethanediyl

**Molecular Formula**
\( \text{HOCH}_2\text{(CH}_2\text{OCH}_2)_m\text{CH}_2\text{OH} \) where \( m \) represents the average number of oxyethylene groups.

**Category**
Ointment base; plasticizer; solvent; suppository base; tablet and capsule lubricant. Used to enhance the aqueous solubility or dissolution characteristics of poorly soluble compounds by making solid dispersions with an appropriate polyethylene glycol.

**Structural Formula**

\[
\text{HO-}\underset{\text{m}}{\text{(CH}}_2\text{O-CH}}_2\text{m}\text{-C-OH}
\]
**Description**

Solid grades (PEG>1000) are white or off-white in color, and range in consistency from pastes to waxy flakes. They have a faint, sweet odor. Grades of PEG 6000 and above are available as free-flowing milled powders. Liquid grades (PEG 200–600) occur as clear, colorless or slightly yellow-colored, viscous liquids. They have a slight but characteristic odor and a bitter, slightly burning taste. PEG 600 can occur as a solid at ambient temperatures.

<table>
<thead>
<tr>
<th>Properties</th>
<th>PEG 4000</th>
<th>PEG 6000</th>
<th>PEG 8000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance (25°C)</td>
<td>White flakes</td>
<td>White flakes</td>
<td>White flakes</td>
</tr>
<tr>
<td>pH value (1% water solution)</td>
<td>5.0~7.0</td>
<td>5.0~7.0</td>
<td>5.0~7.0</td>
</tr>
<tr>
<td>Moisture %</td>
<td>≤1.0</td>
<td>≤1.0</td>
<td>≤1.0</td>
</tr>
<tr>
<td>Viscosity (mm²/s)</td>
<td>6.0~9.0</td>
<td>11.0~16.0</td>
<td>16.0~20.0</td>
</tr>
<tr>
<td>Average molecular weight g/mol</td>
<td>3500~4500</td>
<td>5500~7500</td>
<td>750~8800</td>
</tr>
</tbody>
</table>

**4.4 POLYVINYL PYRROLIDONE**\(^{24,29}\)

- **Synonym**: Polyvinyl pyrrolidone; Povidone; PVP
- **Chemical Name**: 1-Ethenyl-2 pyrrolidone homopolymer
- **Molecular Formula**: \((C_6H_9NO)_n\)
- **Category**: Disintegrant, dissolution enhancer, suspending agent, tablet binder.
- ** Structural Formula**

![Structural Formula Image]
Chapter 4

Drug and Excipient Profile

Description

Povidone occurs as a fine, white to creamy white colored, odorless, hygroscopic powder. Povidone with K-values equal to or lower than 30 are manufactured by spray drying and occur as spheres. Povidone K 90 and higher K-values Povidone are manufactured by drum drying and occur as plates. USP describes Povidone as a synthetic polymer consisting of linear 1-vinyl-2-pyrrolidone groups, the differing degree of polymerization of which results in polymers of a various molecular weights. It is characterized by the viscosity.

<table>
<thead>
<tr>
<th>Molecular Weight</th>
<th>K-value</th>
<th>Approximate Molecular Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>2500</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>8000</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>10000</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>30000</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>50000</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>400000</td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>1000000</td>
<td></td>
</tr>
<tr>
<td>120</td>
<td>3000000</td>
<td></td>
</tr>
</tbody>
</table>

Properties

- **Clarity (10% in water)**: Clear
- **Nitrogen content (%)**: 12.0-12.8
- **Water (Karl Fischer %)**: ≤ 5.0
- **pH value (5% in water)**: 3.0-5.0

- **Applications**: Povidone is used as solubilizer in oral and parenteral formulations, and to enhance the dissolution of poorly soluble drugs from solid dosage forms. The solubility of poorly soluble active drugs may be increased by mixing with the Povidone.

4.5 SODIUM STARCH GLYCOLATE

**Synonym**: Carboxymethyl starch, sodium salt; caboxymethylamylum natricum, Explosol, Explotab, Glycolys, Primojel

**Chemical Name**: Sodium carboxymethyl starch

**Molecular Weight**: 500000-11000000
Chapter 4

Drug and Excipient Profile

<table>
<thead>
<tr>
<th>Category</th>
<th>Tablet and capsule disintegrant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural Formula</td>
<td><img src="image" alt="Structural Formula" /></td>
</tr>
</tbody>
</table>

**Description**

Sodium starch glycolate is a white or almost white free flowing very hygroscopic powder. Under microscope it is seen to consist of granules, irregularly shaped, ovoid or pear shaped, 30-100μm in size. Very fine, white or off white, free flowing powder; odorless or almost odorless.

<table>
<thead>
<tr>
<th>Properties</th>
<th>IP</th>
<th>USP 26-NF21</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>5.5 - 7.5</td>
<td>5.5 - 7.5</td>
</tr>
<tr>
<td>Loss on Drying, NMT %</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Iron, NMT %</td>
<td>0.002</td>
<td>0.002</td>
</tr>
<tr>
<td>Heavy Metals, NMT %</td>
<td>0.002</td>
<td>0.002</td>
</tr>
<tr>
<td>Sodium Chloride, NMT %</td>
<td>10</td>
<td>7</td>
</tr>
</tbody>
</table>

**Applications**

Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant in capsule and tablet formulations. It is commonly used in tablets.

4.6 KYRON\(^{28, 31,32}\)

Kyron is derived from the polymer cross-linked polyacrylic used in the pharmaceutical industry to mask the taste of bitter medicine to achieve stability and drugs. It is white to off white fine powder, swellable in water. KYRON T 314 is derived from cross linked polymer of polycarboxylic acid as per USP/NF and has a K+ ionic form. It is a very high purity polymer used in pharmaceutical formulation as a super fast disintegrant as well as dissolution improver in solid dosage form like tablet, capsule, pellets etc. It is suitable for the both wet granulation as well as direct compression system for tablet formulations. Different grades of Kyron with specifications showed in table 4.1.

Table 4.1: Different grades of Kyron with specifications.
**KYRON GRADES**

<table>
<thead>
<tr>
<th>Specification</th>
<th>T-104</th>
<th>T-114</th>
<th>T-134</th>
<th>T-154</th>
<th>T-159</th>
<th>T-123</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacopoeia</td>
<td>In house</td>
<td>In house</td>
<td>Polacrill potassium USP</td>
<td>Sodium polystyrene Sulphonate USP</td>
<td>In house</td>
<td>In house</td>
</tr>
<tr>
<td>Type</td>
<td>Weak acid</td>
<td>Weak acid</td>
<td>Weak acid</td>
<td>Strong acid</td>
<td>Strong acid</td>
<td>Weak base</td>
</tr>
<tr>
<td>Functionality</td>
<td>-COO</td>
<td>-COO</td>
<td>-COO</td>
<td>-SO₃</td>
<td>-SO₃</td>
<td>Secondary amine</td>
</tr>
<tr>
<td>Ionic Form</td>
<td>Hydrogen</td>
<td>Hydrogen</td>
<td>Potassium</td>
<td>Sodium</td>
<td>Hydrogen</td>
<td>Free base</td>
</tr>
<tr>
<td>Matrix</td>
<td>Polyacrylic copolymer</td>
<td>Polyacrylic copolymer</td>
<td>Polyacrylic copolymer</td>
<td>Polystyrene copolymer</td>
<td>Polystyrene copolymer</td>
<td>Polystyrene copolymer</td>
</tr>
<tr>
<td>Moisture content (%)</td>
<td>&lt;10</td>
<td>&lt;5</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Appearance</td>
<td>White to off white free flowing powder</td>
<td>White to off white free flowing powder</td>
<td>White to off white free flowing powder</td>
<td>off White to golden yellow free flowing powder</td>
<td>off White to golden yellow free flowing powder</td>
<td>White to off white free flowing powder</td>
</tr>
</tbody>
</table>

### 4.7 MANNITOL

1,24,27,28,33,34,35

**Synonym**
Cordycepic acid, Emprove, manna sugar, D-mannite, peralitol.

**Chemical Name**
D-mannitol

**Molecular Formula**
C₆H₁₄O₆

**Molecular Weight**
182.17

**Category**
Diluent, plasticizer, sweetening agent, tablet and capsule diluent, therapeutic agent, tonicity agent.

**Structure**

![Mannitol Structure](image)

**Description**
It is a hexahydric alcohol related to mannose and is isomeric with alcohol. It occurs as a white, odorless, crystalline powder, or free flowing granules. It has a sweet taste, approximately as sweet as glucose and half as sweet as sucrose and imparts a cooling sensation in mouth.

**Applications**
It is widely used as diluent in tablet formulations. It is not hygroscopic hence can be used with moisture sensitive active ingredients. It may be used...
used with direct compression with the wet granulation.

Solubility

1 in 5.5 in water, 1 in 18 in glycerine and 1 in 83 in ethanol at 20°C

4.8 ASPARTAME 1,24,27,28,36,37,38

Synonym
Aspartamum, aspartyl phenylalanine methyl ester.

Chemical Name
N-L-α-aspartyl-L-phenylalanine-1-methyl ester

Molecular Formula
C₁₄H₁₈N₂O₅

Molecular Weight
294.30

Category
Sweetening agent

Structure

Description
It is an off white, almost odorless crystalline powder with an intensely sweet taste.

Applications
It enhances flavor systems and can be used to mask some unpleasant taste characteristics. Approximate sweetening power is 180-200 times that of sucrose.

Solubility
Slightly soluble in ethanol (95%), sparingly soluble in water. At 20°C the solubility is 1% w/v at the isoelectric point pH 5.2. Solubility increases at higher temperature and in acidic pH.

4.9 TALC 1,24,27,28

Synonym
Hydrous magnesium calcium silicate, , magnesium hydrogen metasilicate, , purified French chalk, soapstone, steatite, talcum.

Chemical Name
Talc

Formula
Mg₆(Si₂O₅)₄(OH)₄

Category
Anticaking agent, glidants, tablet and capsule diluent, tablet and capsule lubricant.
Description: It is very fine, white, odorless, impalpable, unctuous, crystalline powder. It adheres to skin and is soft to touch and free of grittiness.

Applications: Used in oral solid dosage forms as lubricant and diluent. Talc is used as lubricant in tablet formulations.

Solubility: Practically insoluble in dilute acids and alkalis, organic solvents and water.

4.10 AVICEL\textsuperscript{24,27,28}

Synonym: Avicel PH, cellulose gel, hellulosum microcrystallinum, crystalline cellulose, E460, Emocel

Chemical Name: Cellulose

Formula: \((\text{C}_6\text{H}_{10}\text{O}_5)n\sim36000\) where \(n\sim220\)

Category: Adsorbent, suspending agent, tablet and capsule diluent, tablet disintegrand.

Structural Formula:

![Structural Formula of Cellulose](image)

Description: It is a purified, practically depolymerised cellulose that occurs as a white, odorless, tasteless, crystalline powder composed of porous particles.

Applications: It is used as binder and diluent in tablet formulations. It can be used with the wet granulation and direct compression. It also has disintegrant properties that make it useful in tableting.

Solubility: Slightly soluble in 5% sodium hydroxide solution, practically insoluble in water, dilute acids and most organic solvents.

4.11 MAGNESIUM STEARATE\textsuperscript{1,24,27,28,39,40}

Synonym: Dibasic magnesium stearate, magnesium distearate, magnesium octadeconate, octadecanoic acid magnesium salt.

Chemical Name: Octadecanoic acid magnesium salt
Chapter 4

Drug and Excipient Profile

**Molecular Formula**  \( \text{C}_{36}\text{H}_{70}\text{MgO}_4 \)

**Molecular Weight**  591.24

**Category**  Tablet and capsule lubricant

**Structure**

\[
\text{Mg}^{2+} \quad \text{O}^{-} \quad \text{C}-\text{O}^{-} \quad \text{C}-\text{O}^{-}
\]

**Description**  It is a very fine, light white, precipitated or milled, low bulk density, having a faint odor of stearic acid and a characteristic taste.

**Applications**  It is used as lubricant in tablet and capsule manufacture in concentration of 0.25% and 5.0% w/w.

**Solubility**  Practically insoluble in ethanol, ether, slightly soluble in warm benzene and warm ethanol (95%), sparingly soluble in water.

### 4.12 CROSSCARMELLOSE SODIUM

**Synonym**  Ac-di-sol, carmellose natricum conexum, cfrosslinked carboxymethylcellulose sodium, explocel, modified cellulose gum, Nymcel, Primellose.

**Chemical Name**  Cellulose, carboxymethyl ether, sodium salt, crosslinked.

**Category**  Tablet and capsule disintegrant

**Structural Formula**

\[
\text{CH}_3\text{COH}_3\text{COONa} \quad \text{OH} \quad \text{OH} \quad \text{OH} \quad \text{CH}_2\text{COH}_3\text{COONa}
\]

**Description**  It occurs as white, odorless, tasteless, granular powder. It is hygroscopic after drying.
**Applications**

It is used in oral formulations as disintegrant for capsules, tablets and granules. It can be used with both direct compression and wet granulation.

**Solubility**

Insoluble in water, although crosscarmellose swells 4-8 times its original volume on contact with water. Practically insoluble in acetone, ethanol and toluene.
REFERENCES

2. Swann IL, Thompson EN, Qureshi K, "Domperidone or metoclopramide in preventing chemotherapeutically induced nausea and vomiting", BMJ. 1979; 6199: 1188.
27. Indian Pharmacopeia. Indian Pharmacopeial commission Ghaziabad;Vol-III-2007; 300,744,1337,1391,1779,3365.


