SUMMARY OF PRODUCT CHARACTERISTICS

1. **Name of drug product:**

1.1 Name of the medicinal product

NEOMIT (Ondansetron Injection USP)

1.2 Strength

2 mg /ml – 2 ml

1.3 Pharmaceutical dosage form:

Solution for Injection.

2. **Qualitative and quantitative composition**

Each mL contains:
Ondansetron Hydrochloride Dihydrate USP
Eq. to Ondansetron 2mg

For full list of excipients, see section 6.1

3. **Pharmaceutical form**

A clear colourless solution

4. **Clinical Particulars**

4.1 Therapeutic indications

Ondansetron Hydrochloride is indicated for the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy, and for the prevention and treatment of post-operative nausea and vomiting.

Paediatric population:

Ondansetron is indicated for the management of chemotherapy-induced nausea and vomiting (CINV) in children aged $\geq$ 6 months, and for the prevention and treatment of PONV in children aged $\geq$ 1 month

4.2 Posology and method of administration

Adults:

The emetogenic potential of cancer treatment varies according to the doses and combinations of chemotherapy and radiotherapy regimens used. The route of administration and dose of ondansetron hydrochloride should be flexible in the range of 8-32 mg a day and selected as shown below.

Emetogenic chemotherapy and radiotherapy:

Ondansetron hydrochloride can be given either by rectal, oral (tablets or syrup), intravenous or intramuscular administration. For most patients receiving emetogenic chemotherapy or radiotherapy, ondansetron hydrochloride 8 mg should be administered as a slow intravenous or intramuscular injection immediately before treatment, followed by 8 mg orally twelve hourly.
To protect against delayed or prolonged emesis after the first 24 hours, oral or rectal treatment with ondansetron hydrochloride should be continued for up to 5 days after a course of treatment.

Highly emetogenic chemotherapy:

For patients receiving highly emetogenic chemotherapy, e.g. high-dose cisplatin, ondansetron hydrochloride can be given either by rectal, intravenous or intramuscular administration.
Ondansetron hydrochloride has been shown to be equally effective in the following dose schedules over the first 24 hours of chemotherapy:

- A single dose of 8 mg by slow intravenous or intramuscular injection immediately before chemotherapy
- A dose of 8 mg by slow intravenous or intramuscular injection immediately before chemotherapy, followed by two further intravenous or intramuscular doses of 8 mg two or four hours apart, or by a constant infusion of 1 mg/hour for up to 24 hours
- A single dose of 32 mg diluted in 50-100 ml of saline or other compatible infusion fluid (see Pharmaceutical Precautions) and infused over not less than 15 minutes immediately before chemotherapy

The selection of dose regimen should be determined by the severity of the emetogenic challenge. The efficacy of ondansetron hydrochloride in highly emetogenic chemotherapy may be enhanced by the addition of a single intravenous dose of dexamethasone sodium phosphate, 20 mg administered prior to chemotherapy.
To protect against delayed or prolonged emesis after the first 24 hours, oral or rectal treatment with ondansetron hydrochloride should be continued for up to 5 days after a course of treatment.

Children:

Ondansetron hydrochloride may be administered as a single intravenous dose of 5 mg/m^2 immediately before chemotherapy, followed by 4 mg orally twelve hours later. 4 mg orally twice daily should be continued for up to 5 days after a course of treatment.

Elderly:

Ondansetron hydrochloride is well tolerated by patients over 65 years and no alteration of dosage, dosing frequency or route of administration are required.

Patients with renal impairment:

No alteration of daily dosage, frequency of dosing or route of administration are required. **Patients with hepatic impairment:** Clearance of ondansetron hydrochloride is significantly reduced and serum half-life significantly prolonged in subjects with moderate or severe impairment of hepatic function. In such patients a total daily dose of 8 mg should not be exceeded.

Post-operative nausea and vomiting (PONV):

Adults:

For the prevention of PONV ondansetron hydrochloride can be administered orally or by intravenous or intramuscular injection. Ondansetron hydrochloride may be administered as a single dose of 4 mg given by intramuscular or slow intravenous injection at induction of anaesthesia. For treatment of established PONV a single dose of 4 mg given by intramuscular or slow intravenous injection is recommended.

Children (aged 2 years and over):

For prevention of PONV in paediatric patients having surgery performed under general anaesthesia, ondansetron may be administered by slow intravenous injection at a dose of 0.1 mg/kg up to a maximum of 4 mg, either prior to, at or after induction of anaesthesia.

For treatment of established PONV in paediatric patients, ondansetron may be administered by slow intravenous injection at a dose of 0.1 mg/kg up to a maximum of 4 mg. There is limited data on the use of ondansetron hydrochloride in the prevention and treatment of PONV in children under 2 years of age.

Elderly:

There is limited experience in the use of ondansetron hydrochloride in the prevention and treatment of PONV in the elderly, however ondansetron hydrochloride is well tolerated in patients over 65 years receiving chemotherapy.

Patients with renal impairment:

No alteration of daily dosage, frequency of dosing or route of administration are required.

Patients with hepatic impairment:

Clearance of ondansetron hydrochloride is significantly reduced and serum half-life significantly prolonged in subjects with moderate or severe impairment of hepatic function. In such patients a total daily dose of 8 mg should not be exceeded.

Patients with poor sparteine / debrisoquine metabolism:

The elimination half-life of ondansetron is not altered in subjects classified as poor metabolisers of sparteine and debrisoquine. Consequently in such patients repeat dosing will give drug exposure levels no different from those of the general population. No alteration of daily dosage or frequency of dosing are required.

4.3 Contraindications

Hypersensitivity to any component of the preparation.

4.4 Special warnings and precautions for use

Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5HT3 receptor antagonists. As ondansetron is known to increase large bowel transit time, patients with signs of subacute intestinal obstruction should be monitored following administration. This medicinal product contains less than 1 mmol sodium (23 mg) per ampoule, i.e. essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of

There is no evidence that ondansetron either induces or inhibits the metabolism of other drugs commonly co-administered with it. Specific studies have shown that there are no pharmacokinetic interactions when ondansetron is administered with alcohol, temazepan, furosemide, tramadol or propofol.

Ondansetron is metabolised by multiple hepatic cytochrome P-450 enzymes: CYP3A4, CYP2D6 and CYP1A2. Due to the multiplicity of metabolic enzymes capable of metabolising ondansetron, enzyme inhibition or reduced activity of one enzyme (e.g. CYP2D6 genetic deficiency) is normally compensated by other enzymes and should result in little or no significant change in overall ondansetron clearance or dose requirement.

Phenytoin, Carbamazepine and Rifampicin: In patients treated with potent inducers of CYP3A4 (i.e. phenytoin, carbamazepine,

and rifampicin), the oral clearance of ondansetron was increased and ondansetron blood concentrations were decreased.
Tramadol: Data from small studies indicate that ondansetron may reduce the analgesic effect of tramadol.

4.6 Pregnancy and lactation

The safety of ondansetron for use in human pregnancy has not been established. Evaluation of experimental animal studies does not indicate direct or indirect harmful effects with respect to the development of the embryo, or foetus, the course of gestation and peri- and post-natal development. However, as animal studies are not always predictive of human response, the use of ondansetron in pregnancy is not recommended.
Tests have shown that ondansetron passes into the milk of lactating animals. It is therefore recommended that mothers receiving ondansetron hydrochloride should not breast-feed their babies.

4.7 Effects on ability to drive and operate machines

In psychomotor testing ondansetron does not impair performance nor cause sedation.

4.8 Undesirable effects

Ondansetron is known to increase large bowel transit time and may cause constipation in some patients. The following side effects can occur: headache, a sensation of flushing or warmth, hiccups and occasional asymptomatic increases in liver function tests. There have been rare reports of immediate hypersensitivity reactions sometimes severe including anaphylaxis. Rare cases of transient visual disturbances (e.g. blurred vision) and dizziness have been reported during rapid intravenous administration of ondansetron. There have been rare reports suggestive of involuntary movement disorders such as extrapyramidal reactions e.g. oculogyric crisis/dystonic reactions without definitive evidence of persistent clinical sequelae and seizures have been rarely observed although no known pharmacological mechanism can account for ondansetron causing these effects. Chest pain with or without ST segment depression, cardiac arrhythmias, hypotension and bradycardia have been rarely reported.
Occasionally, hypersensitivity reactions around the injection site (e.g. rash, urticaria, itching) may occur, sometimes extending along the drug administration vein.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reaction to the National Regulatory Authority's reporting systems.

4.9 Overdosage

Little is known at present about overdosage with ondansetron, however, a limited number of patients received overdoses. Manifestations that have been reported include visual disturbances, severe constipation, hypotension and a vasovagal episode with transient second degree AV block. In all instances, the events resolved completely. There is no specific antidote for ondansetron, therefore in all cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiemetics and Antinauseants – Serotonin (5HT3) antagonists, ATC code: A04A A01.

Ondansetron is a potent, highly selective 5HT3 receptor-antagonist. Its precise mode of action in the control of nausea and vomiting is not known. Chemotherapeutic agents and radiotherapy may cause release of 5HT in the small intestine initiating a vomiting reflex by activating vagal afferents via 5HT3 receptors. Ondansetron blocks the initiation of this reflex. Activation of vagal afferents may also cause a release of 5HT in the area postrema, located on the floor of the fourth ventricle, and this may also promote emesis through a central mechanism. Thus, the effect of ondansetron in the management of the nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy is probably due to antagonism of 5HT3 receptors on neurons located both in the peripheral and central nervous system. The mechanisms of action in post-operative nausea and vomiting are not known but there may be common pathways with cytotoxic induced nausea and vomiting.

prolactin concentrations. The role of ondansetron in opiate-induced emesis is not yet established.

5.2 Pharmacokinetic properties

The disposition of ondansetron following oral, intramuscular (IM) and intravenous (IV) dosing is similar with a terminal half-life of about 3 hours and steady state volume of distribution of about 140 litres. Equivalent systemic exposure is achieved after IM and IV administration of ondansetron. A 4 mg intravenous infusion of ondansetron given over 5 minutes results in peak plasma concentrations of about 65 ng/ml. Following intramuscular administration of ondansetron, peak plasma concentrations of about 25 ng/ml are attained within 10 minutes of injection.

Ondansetron is not highly protein bound (70-76%). Ondansetron is cleared from the systemic circulation predominantly by hepatic metabolism through multiple enzymatic pathways. Less than 5% of the absorbed dose is excreted unchanged in the urine. The absence of the enzyme CYP2D6 (the debrisoquine polymorphism) has no effect on ondansetron's pharmacokinetics. The pharmacokinetic properties of ondansetron are unchanged on repeat dosing.

5.3 Pre-clinical Safety Data

Not applicable since Ondansetron Injection has been used in clinical practice for many years and its effects in man are well known.

6. Pharmaceutical particulars

6.1 List of excipients

Citric Acid USP
Sodium Citrate USP
Sodium Chloride USP
Water for Injection USP, (Bulk)

6.2 Incompatibilities

Ondansetron 4 mg/2 ml Solution for Injection should not be administered in the same syringe or infusion as any other medication.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30°C. Protected from light. Do not freeze.

6.5 Nature and contents of container

2ml flint Black OPC dotted with blue band above. Such 5 ampoules are packed in blister. Such 2 Blisters are packed in Carton along with leaflet.

6.6. Special Precautions for Handling and Disposal Use as directed by a physician.

7. Marketing authorization holder:

M/s. NEON LABORATORIES LIMITED
140, Damji Shamji Industrial Complex,
28, Mahal Industrial Estate, M.
Caves Road, Andheri (E),
Mumbai – 400 093.
INDIA

8. Marketing Authorization Number (s):H2019/CTD3662/778ER

9. Date of first authorization/ Renewal of the authorization: 2025

10. Date of revision of the text: Dec 2025