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 – 4 ml

1.3 Pharmaceutical dosage form:

Solution for Injection.

2. Qualitative and quantitative composition

Sr. No.	Particulars	Grade	Qty. /ml	Function
1.	Ondansetron Hydrochloride Dihydrate USP equivalent to Ondansetron	USP	2mg	Active

For the Excipients, refer 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.

4.2 Posology and method of administration

Route of administration: Intramuscular/ Intravenous

Adults:

Chemotherapy and radiotherapy - Highly emetogenic regimens, single dose of 8 mg by slow I.V. Injection immediately prior to chemotherapy or 8mg by slow I.V. Injection prior to chemotherapy followed by either two doses of 8mg by l.V.
Injection repeated 2-4 hours apart or by 1mg per hour by I.V. for upto 24 hours or single dose of 32 mg in 50-100 ml saline infused over 15 minutes prior to chemotherapy. After first 24 hours, follow by 8 mg orally twice daily for upto 5 days. In case of radiotherapy ondansetron may be given 8 mg. 1 to 2 hours, before therapy, followed by 8 mg orally 12 hourly after radiotherapy for 5 days. Efficacy may be enhanced by the addition of dexamethasone 20 mg I.V. prior to chemotherapy. Less emetogenic regimens or radiotherapy - 8 mg by slow I.V. Injection immediately prior to chemotherapy or orally 1-2 hours before followed by 8 mg orally twelve hourly. After first 24 hours, follow by 8 mg orally twice daily for up to 5 days. In case of post-operative nausea & vomiting, it can be given prophylactically as a single dose of

4 mg. by slow intravenous Infusion at induction of anaesthesia or 8 mg orally 60 min. prior to anaesthesia (followed by two-eight hourly doses of 8 mg) For treatment of established post-operative nausea & vomiting, Ondansetron can be given as single undiluted dose of 4 mg by slow Intravenous Infusion.

CHILDREN: (4-18 years)

A recommended dose is 5 mg per m2 body-surface intravenously over 15 minutes immediately before chemotherapy followed by 4 mg orally every 12 hours for Up to 5 days.

RECOMMENDED INFUSION SOLUTIONS:

Intravenous solutions should be prepared at the time of infusion with the following recommended infusion solution:

1) Sodium Chloride Intravenous Infusion 0.9% w/v
2) Dextrose Intravenous Infusion 5% w/v
3) Mannitol Intravenous Infusion 10% w/v
4) Ringer Intravenous Infusion
5) Potassium Chloride 0.3% w/v and Glucose 5% w/v

4.3 Contraindications

Ondansetron injection is contraindicated for patients known to have hypersensitivity to the drug (e.g., anaphylaxis) to this product or any of its components. Anaphylactic reactions have been reported in patients taking ondansetron. The concomitant use of apomorphine with ondansetron is contraindicated based on reports of profound hypotension and loss of consciousness when apomorphine was administered with ondansetron.

4.4 Special warnings and precautions for use

Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective $5HT_3$ receptor antagonists. As ondansetron is known to increase large bowel transit time, patients with signs of subacute intestinal obstruction should be monitored following administration. In patients with adenotonsillar surgery prevention of nausea and vomiting with ondansetron may mask occult bleeding. Therefore, such patients should be followed carefully after ondansetron. Since there is little experience to date of the use of ondansetron in cardiac patients, caution should be exercised if ondansetron is co-administered with anaesthetics to patients with arrhythmias or cardiac conduction disorders or to patients who are being treated with antiarrhythmic agents or betablockers. The solution for injection contains less than 1 mmol sodium (23 mg) per ampoule, i.e. essentially 'sodium- free'. Ondansetron solution for injection should not be used in children with a total body surface below 0.6 m2. The medicinal product should not be used for children younger than two years, as for these patients the experience is limited.

Effects on driving and machinery operation:

Ondansetron 2 mg/ml has no or negligible influence on the ability to drive and use machines. In psychomotor testing ondansetron does not impair performance nor cause sedation.

4.5 Interaction with other medicinal products

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

With reference literature reproduction studies have been performed in pregnant rats and rabbits at Intravenous (I.V.) doses upto 4mg/kg per day and have revealed no evidence of impaired fertility or harm to the fetus due to Ondansetron. There are however, no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Lactation :

Tests have shown that Ondansetron is excreted in the breast milk of rats. It is therefore recommended that mothers receiving Ondansetron should not breast-feed their babies. Caution should be excercised when Ondansetron is administered to nursing woman.

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

The commonest side effects that have been reported are constipation and headache. Other side effects that have been rarely reported are hypersensitivity reactions like skin rash, tachycardia, angina and ECG alterations, possible extrapyramidal reactions, hypokalemia and increased levels of aspartate transaminase (AST) and alanine transaminase (ALT).

4.9 Overdosage

Little information is at present known about overdosage with Ondansetron. Symptomatic and supportive therapy should be given as appropriate. There is no specific antidote for overdose with Ondansetron.

5. Pharmacological properties

5.1 Pharmacodynamics properties

Ondansetron is a potent, highly selective and competitive antagonist of the 5HT3 receptors, a subclass of serotonin receptors, located on peripheral neurons and within the CNS. Chemotherapeutic agents and radiotherapy may cause release of 5HT

(serotonin) from enter ochromaffin cells in the visceral mucosa and initiate the emesis reflex and its accompanying feeling of nausea. Ondansetron selectively blocks the excitation of the presynaptic 5HT3 receptors of the peripheral neurons in this reflex

and may exert additional actions within the CNS on 5HT3 receptors mediating the actions of vagal input to the area postrema. Ondansetron thus prevents nausea and vomiting induced by cancer chemotherapy and radiotherapy. Ondansetron does not have any extra-pyramidal side effects.

5.2 Pharmacokinetic properties

An Intravenous Infusion of 8mg Ondansetron over 5 minutes gives peak plasma values of 80 to 100 mcg/L; which fall steadily over the subsequent 15 hours. The bioavailability of oral Ondansetron is approximately 60%. The drug is extensively metabolised and metabolites are excreted in feces and urine, following oral administration of 8mg the time to peak concentration is approximately 1.6 hours. The elimination half-life is approximately 3 hours though this may be prolonged to approximately 5 hours in the elderly. Plasma protein binding is 70-76%. Ondansetron is rapidly cleared by the body and less than 10% of the drug is excreted unchanged.

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 8 mg/4 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

Five flint ampoules of 5ml with black band snap off packed in a blister.

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):

07282/09068/NMR/2021

9. Date of first authorization/ Renewal of the authorization:
13/04/2022

10. Date of revision of the text:
July,2023

11. Reference - Ondansetron 2 mg/ml Solution for Injection - Summary of Product Characteristics (SmPC) - https://www.medicines.org.uk/emc/product/6469/smpc#gref