Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Ondex 8 mg Injection
Generic name: Ondansetron Injection BP 8 mg/4 mL

2. Qualitative and quantitative composition

Each 4 mL ampoule contains ondansetron hydrochloride dihydrate BP equivalent to 8 mg of ondansetron.
Water for injections BP q.s.
For the full list of excipients, see section 6.1.
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3. Pharmaceutical form

Injection

4. Clinical particulars

4.1 Therapeutic indications

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

Paediatric population

Ondansetron is indicated for the management of chemotherapy-induced nausea and vomiting in children aged ≥ 6 months, and for the prevention and treatment of PONV in children aged ≥ 1 month.

4.2 Posology and method of administration

Intravenously or intramuscularly
Nausea and vomiting associated with chemotherapy and radiotherapy: Adults: The emetogenic potential of cancer treatment varies according to the doses and combinations of chemotherapy and radiotherapy regimens used. Ondansetron is administered orally, intravenously and also intramuscularly, fact that allows a flexibility in the route of administration and dosage. ONDEX dose ranging from 8 mg to 32 mg per day and is selected as shown below:
Mild emetogenic chemotherapy and radiotherapy: For patients receiving emetogenic chemotherapy or radiotherapy, ondansetron can be used either orally (as tablets or syrup) or by intravenous or intramuscular injection. The recommended dose of ONDEX is 8 mg and it is administered by a slow intravenous or intramuscular injection right before treatment. For protection against delayed or prolonged emesis after the first 24 hours, ondansetron
treatment must be continued with oral administration of 8 mg per 12 hours for up to 5 day.

Highly emetogenic chemotherapy: For patients receiving highly emetogenic chemotherapy, e.g. high-dose cisplatin, ondansetron can be used by

intravenous or intramuscular injection. A single dose of 8 mg of ONDEX may be administered by slow intravenous injection right before the chemotherapy, followed by either 8 mg every 2-4 hours for 2 more intravenous or intramuscular doses or by continuous intravenous infusion of 1 mg/h for up to 24 hours. Alternatively, 32 mg of ONDEX may be administered by intravenous infusion for at least
15. Doses higher than 8 mg and up to 32 mg, are administered only intravenously, diluted in
50 – 100 mL of saline or other compatible infusion fluid (see Package Leaflet) in not less
than 15 minutes. The selection of dose regimen should be determined by the severity of the emetogenic challenge. The efficacy of ONDEX in highly emetogenic chemotherapy may be enhanced by the addition of a single intravenous dose of 20 mg of dexamethasone sodium
phosphate, prior to chemotherapy. For protection against delayed or prolonged emesis after the first 24 hours, ondansetron treatment should be continued with oral administration, with the therapeutic regimen of 8 mg every 12 hours for up to 5 days. Children: ONDEX is
administered by a slow intravenous injection of 5mg/m2 or by continuous intravenous infusion for at least 15 minutes right before the start of the chemotherapy, followed by 4 mg
per 12 hours orally for up to 5 days.
Post-operative nausea and vomiting (PONV) Adults: For the prevention of PONV ONDEX

can be administered either orally (as tablets or syrup) or by intravenous or intramuscular injection. ONDEX may be administered as a single dose of 4 mg by slow intravenous or intramuscular injection during anaesthesia induction. For the treatment of established PONV, a single dose of 4 mg, by slow intravenous or intramuscular injection, is recommended.
Elderly patients: There is limited experience in the use of ONDEX in the prevention and treatment of PONV in elderly patients, however, ONDEX is well tolerated by patients over
65 years of age receiving chemotherapy. Patients with renal impairment: No alteration in daily dosage, dosage frequency and route of administration, is required. Patients with hepatic impairment: Clearance of ONDEX is significantly reduced and half-life in blood

- serum is significantly prolonged, in subjects with moderate or severe impairment of hepatic function. In such patients the total daily dose should not exceed 8 mg, either intravenously or orally. Patients with poor sparteine/debrisoquine metabolism

4.3 Contraindications

Hypersensitivity to the active substance or to other selective 5-HT3 receptor antagonists (e.g. granisetron, dolasetron).
Concomitant use with apomorphine (see section 4.5).

4.4 Special warnings and precautions for use

Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5-HT3 receptor antagonists.

Respiratory events should be treated symptomatically and clinicians should pay particular attention to them as precursors of hypersensitivity reactions.

Ondansetron prolongs the QT interval in a dose-dependent manner (see section 5.1). In addition, post-marketing cases of Torsade de Pointes have been reported in patients using ondansetron. Ondansetron should be avoided in patients with congenital long QT syndrome and administered with caution to patients who have, or may develop, prolongation of QTc. These conditions include patients with electrolyte abnormalities, congestive heart failure or bradyarrhythmias, and patients taking other medicinal products that lead to QT prolongation or electrolyte abnormalities.

Cases of myocardial ischaemia have been reported in patients treated with ondansetron. In some patients, especially with intravenous administration, symptoms appeared immediately after administration. Patients should be alerted to the signs and symptoms of myocardial ischaemia.

Hypokalaemia and hypomagnesaemia should be corrected prior to ondansetron administration.

There have been post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following concomitant use of ondansetron and other serotonergic medicinal products, including selective serotonin reuptake inhibitors (SSRIs) and serotonin noradrenaline reuptake inhibitors (SNRIs). If concomitant treatment is clinically warranted, appropriate observation of the patient is advised.

As ondansetron is known to increase large bowel transit time, patients with signs of subacute intestinal obstruction should be monitored following administration.

In patients undergoing adenotonsillar surgery, prevention of nausea and vomiting with ondansetron may mask occult bleeding; such patients should therefore be followed carefully after ondansetron.

Paediatric population

Paediatric patients receiving ondansetron with hepatotoxic chemotherapeutic agents should be monitored closely for impaired hepatic function.

When calculating the dose on an mg/kg basis and administering three doses at 4-hourly intervals, the total daily dose will be higher than if one single dose of 5mg/m^2 followed by an oral dose is given. The comparative efficacy of these two different dosing regimens has not been investigated in clinical trials. Cross-trial comparison indicates similar efficacy for both regimens (section 5.1).

This medicine contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially
'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of ondansetron on other medicinal products

There is no evidence that ondansetron either induces or inhibits the metabolism of other medicinal products commonly co-administered with it. Specific studies have shown that ondansetron does not interact with alcohol, temazepam, furosemide, alfentanil, morphine, lidocaine, propofol or thiopental.

Effects of other medicinal products on ondansetron

Ondansetron is metabolised by multiple hepatic cytochrome P450 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.

Caution should be exercised when ondansetron is co-administered with medicinal products that prolong the QT interval and/or cause electrolyte abnormalities (see section 4.4). Use with QT-prolonging medicinal products may result in additional QT prolongation. Concomitant use with cardiotoxic medicinal products (e.g. anthracyclines such as doxorubicin and daunorubicin, or trastuzumab), antibiotics (such as erythromycin or ketoconazole), antiarrhythmics (such as amiodarone) and beta-blockers (such as atenolol or timolol) may increase the risk of arrhythmias.

Serotonergic medicinal products: post-marketing reports describe serotonin syndrome following concomitant use of ondansetron and other serotonergic medicinal products, including SSRIs and SNRIs (see section 4.4).

Apomorphine: based on reports of profound hypotension and loss of consciousness when ondansetron was administered with apomorphine hydrochloride, concomitant use with apomorphine is contraindicated.

Phenytoin, carbamazepine and rifampicin: in patients treated with these potent inducers of CYP3A4, 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

Women of childbearing potential

Women of childbearing potential should consider the use of contraception.

Pregnancy

Based on human experience from epidemiological studies, ondansetron is suspected to cause orofacial malformations when administered during the first trimester of pregnancy. In one cohort study including 1.8 million pregnancies, first-trimester ondansetron use was associated with an increased risk of oral clefts (3 additional cases per 10,000 women treated; adjusted relative risk 1.24, 95% CI 1.03–1.48). The available epidemiological studies on cardiac malformations show conflicting results. Animal studies do not indicate direct or indirect harmful effects

with respect to reproductive toxicity. Ondansetron should not be used during the first trimester of pregnancy.

Breast-feeding

Tests have shown that ondansetron passes into the milk of lactating animals (see section 5.3). It is therefore recommended that mothers receiving ondansetron should not breast-feed their infants.

4.7 Effects on ability to drive and use machines

4.8 Undesirable effects

Cardiac disorders

Uncommon: chest pain with or without ST segment depression, cardiac arrhythmias and bradycardia. Chest pain and cardiac arrhythmias may be fatal in individual cases.

Rare: transitory changes in the electrocardiogram, QTc prolongation (including Torsade de Pointes).

Not known: myocardial ischaemia (see section 4.4).

Vascular disorders

Common: sensations of flushing or warmth. Uncommon: hypotension.

Respiratory, thoracic and mediastinal disorders

Uncommon: hiccups.

Gastrointestinal disorders

Common: ondansetron is known to increase large bowel transit time and may cause constipation in some patients.

Hepatobiliary disorders

Uncommon: asymptomatic increases in liver function tests were observed. These reactions were frequently observed in patients undergoing chemotherapy with cisplatin.

Skin and subcutaneous tissue disorders

Uncommon: hypersensitivity reactions around the injection site (e.g. rash, urticaria, itching) may occur, sometimes extending along the drug administration vein.

General disorders and administration site conditions

Common: local reactions at the intravenous injection site.

Paediatric population

The adverse event profile in children and adolescents was comparable to that seen in adults.

Reporting of suspected adverse reactions

Healthcare professionals are asked to report any suspected adverse reactions via the Pharmacy and Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS): https://pv.pharmacyboardkenya.org

4.9 Overdose

Little is known at present about overdose with ondansetron; however, a limited number of patients have received overdoses. In the majority of cases, symptoms were similar to those already reported in patients receiving recommended doses (see section 4.8). Manifestations reported

include visual disturbances, severe constipation, hypotension and a vasovagal episode with transient second degree AV block. In all instances the events resolved completely. Ondansetron prolongs the QT interval in a dose-dependent fashion; ECG monitoring is recommended in cases of overdose.

There is no specific antidote for ondansetron. In all cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate. The use of ipecacuanha to treat overdose with ondansetron is not recommended, as patients are unlikely to respond due to the anti-emetic action of ondansetron itself.

Paediatric population

Paediatric cases consistent with serotonin syndrome have been reported after inadvertent oral overdoses of ondansetron (exceeding an estimated ingestion of 4 mg/kg) in infants and children aged 12 months to 2 years.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antiemetics and antinauseants, serotonin (5-HT3) antagonists. ATC code: A04AA01.

Mechanism of action

Ondansetron is a potent, highly selective 5-HT3 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 5-HT in the small intestine, initiating a vomiting reflex by activating vagal afferents via 5-HT3 receptors; ondansetron blocks the initiation of this reflex. Activation of vagal afferents may also cause release of 5-HT in the area postrema, located on the floor of the fourth ventricle, which may also promote emesis through a central mechanism. The effect of ondansetron in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy is therefore probably due to antagonism of 5-HT3 receptors on neurons located in both the peripheral and central nervous systems. 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.

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

Effect on the QTc interval

The effect of ondansetron on the QTc interval was evaluated in a double-blind, randomised, placebo- and positive- (moxifloxacin) controlled crossover study in 58 healthy adult men and women. Ondansetron doses included 8 mg and 32 mg infused intravenously over 15 minutes. At the highest tested dose of 32 mg, the maximum mean (upper limit of 90% CI) difference in QTcF from placebo after baseline correction was 19.6 (21.5) msec. At the lower tested dose of 8 mg, the corresponding value was 5.8 (7.8) msec. In this study there were no QTcF measurements greater than 480 msec and no QTcF prolongation greater than 60 msec. No significant changes were seen in the measured PR or QRS intervals.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of ondansetron are unchanged on repeat dosing. A direct correlation of plasma concentration and anti-emetic effect has not been established.

Absorption

Following oral administration, ondansetron is passively and completely absorbed from the gastrointestinal tract and undergoes first-pass metabolism; bioavailability is about 60%. Peak plasma concentrations of about 30 ng/mL are attained approximately 1.5 hours after an 8 mg dose. For doses above 8 mg, the increase in systemic exposure with dose is greater than proportional, which may reflect some reduction in first-pass metabolism at higher oral doses. Bioavailability following oral administration is slightly enhanced by the presence of food but unaffected by antacids.

A 4 mg intravenous infusion given over 5 minutes results in peak plasma concentrations of about 65 ng/mL. Following intramuscular administration, peak plasma concentrations of about 25 ng/mL are attained within 10 minutes of injection.

Distribution

The disposition of ondansetron following oral, intramuscular and intravenous dosing is similar, with a steady-state volume of distribution of about 140 L. Equivalent systemic exposure is achieved after intramuscular and intravenous administration. Ondansetron is not highly protein bound (70–76%).

Biotransformation

Ondansetron is cleared from the systemic circulation predominantly by hepatic metabolism through multiple enzymatic pathways. The absence of the enzyme CYP2D6 (the debrisoquine polymorphism) has no effect on the pharmacokinetics of ondansetron.

Elimination

Less than 5% of the absorbed dose is excreted unchanged in the urine. The terminal half-life is about 3 hours.

Special populations

Children and adolescents (aged 1 month to 17 years): in paediatric patients aged 1 to 4 months (n = 19) undergoing surgery, weight-normalised clearance was approximately 30% slower than in patients aged 5 to 24 months (n = 22) but comparable to patients aged 3 to 12 years. The half-life in patients aged 1 to 4 months averaged 6.7 hours compared with 2.9 hours for patients in the 5 to 24 month and 3 to 12 year age ranges. These differences can be explained in part by the higher percentage of total body water in neonates and infants and a higher volume of distribution for water-soluble medicinal products such as ondansetron.

In a study of 21 paediatric patients aged 3 to 12 years undergoing elective surgery under general anaesthesia, the absolute values for both clearance and volume of distribution following a single intravenous dose of 2 mg (3–7 years) or 4 mg (8–12 years) were reduced. The magnitude of change was age-related, with clearance falling from about 300 mL/min at 12 years of age to 100 mL/min at 3 years, and volume of distribution falling from about 75 L at 12 years to 17 L at 3 years. Use of weight-

based dosing (0.1 mg/kg up to a maximum of 4 mg) compensates for these changes and is effective in normalising systemic exposure in paediatric patients.
Based on population pharmacokinetic parameters for subjects aged 1 month to 48 months, administration of a 0.15 mg/kg intravenous dose every 4 hours for 3 doses would result in systemic exposure (AUC) comparable to that observed in paediatric surgery subjects aged 5 to 24 months and in previous paediatric studies in cancer (aged 4 to 18 years) and surgical (aged 3 to 12 years) subjects at similar doses.
Population pharmacokinetic analysis was performed on 428 subjects (cancer patients, surgery patients and healthy volunteers) aged 1 month to 44 years following intravenous administration. Systemic exposure in children and adolescents was comparable to adults, with the exception of infants aged 1 to 4 months. Volume of distribution was related to age and was lower in adults than in infants and children. Clearance was related to weight but not to age, with the exception of infants aged 1 to 4 months. Since patients less than 6 months of age receive only a single dose in PONV, a decreased clearance is not likely to be clinically relevant.
Elderly: studies in healthy elderly volunteers have shown slight age-related increases in both oral bioavailability (65%) and half-life (5 hours).
Renal impairment: in patients with renal impairment (creatinine clearance 15–60 mL/min), both systemic clearance and volume of distribution are reduced following intravenous administration, resulting in a slight but clinically insignificant increase in elimination half-life (5.4 hours). A study in patients with severe renal impairment requiring regular haemodialysis (studied between dialyses) showed the pharmacokinetics of ondansetron to be essentially unchanged following intravenous administration.
Gender: gender differences were shown in the disposition of ondansetron, with females having a greater rate and extent of absorption following an oral dose and reduced systemic clearance and volume of distribution (adjusted for weight).

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated-dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.
Ondansetron and its metabolites accumulate in the milk of rats, with a milk/plasma ratio of 5.2:1.
A study in cloned human cardiac ion channels has shown that ondansetron has the potential to affect cardiac repolarisation via blockade of hERG potassium channels. The clinical relevance of this finding is uncertain.

6. Pharmaceutical Particulars

6.1 List of Excipients

6.2 Incompatibilities

None known.

6.3 Shelf-Life
36 months.

6.4 Special Precautions for storage
Keep the ampoules in the outer carton in order to protect from light.

6.5 Nature and Content of container
4 mL × 5 ampoules packed in one mono carton.

6.6 Special precautions for disposal and other handling

7. Marketing Authorization Holder
National Pharmacy Limited
P.O. Box 17843-00500, Nairobi, Kenya.
Manufacturer
OM Biomedic Pvt. Ltd.
Plot No. 68, 69 & 82, 83, Sector-6A, IIE, SIDCUL, Haridwar (Uttarakhand), India.

8. Marketing Authorization Number
H2025/CTD11077/24403

9. Date of first authorization/renewal of the authorization
2025 May 26

10. Date of revision of the text
2025 May 26