PATIENT INFORMATION LEAFLET

Ondaset™

اونڈاسیٹ

(Ondansetron)

4mg/2ml and 8mg/4ml Injection

4ملی گرام/2ملی لیٹر اور 8ملی گرام/4ملی لیٹر انجکشن

Read this entire leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. WHAT ONDASET IS AND WHAT IT IS USED FOR:

Pharmacotherapeutic group: Selective Serotonin 5-HT3 receptor antagonist ATC code: A04AA01
Indicated for the following:

Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Cancer Chemotherapy

Ondaset Injection is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin. Ondaset is approved for patients aged 6 months and older.

Prevention of Postoperative Nausea and/or Vomiting

Ondaset Injection is indicated for the prevention of postoperative nausea and/or vomiting. As with other antiemetics, routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and/or vomiting will occur postoperatively. In patients in whom nausea and/or vomiting must be avoided postoperatively, Ondaset Injection is recommended even when the incidence of postoperative nausea and/or vomiting is low. For patients who do not receive prophylactic Ondaset Injection and experience nausea and/or vomiting postoperatively, Ondaset Injection may be given to prevent further episodes.
Ondaset is approved for patients aged 1 month and older.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE ONDASET:

Do not use Ondaset if

Ondansetron Injection is contraindicated for patients known to have hypersensitivity (e.g., anaphylaxis) to this product or any of its components. Anaphylactic reactions are known to occur 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 is administered with Ondansetron.

Warnings and Precautions

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis and bronchospasm, are known to occur in patients who have exhibited hypersensitivity to other selective 5-HT3 receptor antagonists.

QT Prolongation

Ondansetron prolongs the QT interval in a dose-dependent manner. In addition, Torsade de Pointes is known to occur in patients using Ondansetron. Avoid Ondansetron in patients with congenital long QT syndrome. ECG monitoring is recommended in patients with electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia), congestive heart failure, bradyarrhythmias, or patients taking other medicinal products that lead to QT prolongation.

Myocardial Ischemia

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

Serotonin Syndrome

The development of serotonin syndrome is known to occur with 5-HT3 receptor antagonists alone. Most cases are known to be associated with concomitant use of serotonergic drugs (e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors, mirtazapine, fentanyl, lithium, tramadol, and intravenous methylene blue). Some of the cases may be fatal. Serotonin syndrome occurring with overdose of Ondansetron alone is also known to occur.

The majority of cases of serotonin syndrome related to 5-HT3 receptor antagonist use occur in a post-anesthesia care unit or an infusion center. Patients should be monitored for the emergence of serotonin syndrome, especially with concomitant use of Ondansetron and other serotonergic drugs. If symptoms of serotonin syndrome occur, discontinue Ondansetron and initiate supportive treatment. Patients should be informed of the increased risk of serotonin syndrome, especially if Ondansetron is used concomitantly with other serotonergic drugs.

Masking of Progressive Ileus and Gastric Distension

The use of Ondansetron in patients following abdominal surgery or in patients with chemotherapy-induced nausea and vomiting may mask a progressive ileus and gastric distention.

Effect on Peristalsis

Ondansetron is not a drug that stimulates gastric or intestinal peristalsis. It should not be used instead of nasogastric suction.

Sub-Acute Intestinal Obstruction

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

Adenotonsillar Surgery

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.

Paediatric Population

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

Other medicines and Ondaset

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 interactions when ondansetron is administered with alcohol, temazepam, furosemide, alfentanil, tramadol, morphine, lidocaine, thiopental, or propofol.

Drugs Affecting Cytochrome P-450 Enzymes

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.

QT prolonging drugs, Cardiotoxic drugs, Antibiotics, Antifungals, Antiarrhythmics and Beta Blockers

Caution should be exercised when ondansetron is coadministered with drugs that prolong the QT interval and/or cause electrolyte abnormalities. Use of ondansetron with QT prolonging drugs may result in additional QT prolongation. Concomitant use of ondansetron with cardiotoxic drugs (e.g. anthracyclines (such as doxorubicin, daunorubicin) or trastuzumab), antibiotics (such aserythromycin), antifungals (such as ketoconazole), antiarrhythmics (such as amiodarone) and beta blockers (such asatenolol or timolol) may increase the risk of arrhythmias.

Apomorphine

Based on known data of profound hypotension and loss of consciousness when apomorphine is administered with Ondansetron, the concomitant use of apomorphine with ondansetron is contraindicated.

Phenytoin, Carbamazepine, and Rifampin

In patients treated with potent inducers of CYP3A4 (i.e., phenytoin, carbamazepine, and rifampin), the clearance of Ondansetron is significantly increased and Ondansetron blood concentrations decreased. However, on the basis of available data, no dosage adjustment for Ondansetron is recommended for patients on these drugs.

Tramadol

Although there is no data on pharmacokinetic drug interactions between Ondansetron and tramadol, available data from small studies indicate that concomitant use of Ondansetron may result in reduced analgesic activity of tramadol.

Serotonergic Drugs

Serotonin syndrome (including altered mental status, autonomic instability, and neuromuscular symptoms) is known to occur following the concomitant use of 5-HT3 receptor antagonists and other serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs).

Chemotherapy

In humans, carmustine, etoposide, and cisplatin do not affect the pharmacokinetics of Ondansetron.

Temazepam

The coadministration of Ondansetron had no effect on the pharmacokinetics and pharmacodynamics of temazepam.

Alfentanil and Atracurium

Ondansetron does not alter the respiratory depressant effects produced by alfentanil or the degree of neuromuscular blockade produced by atracurium. Interactions with general or local anesthetics are not known.

Ondaset with food and drink

Ondansetron can be taken with or without food.

Pregnancy Breast-feeding and Fertility

Based on human experience from epidemiological studies, ondansetron is suspected to cause orofacial malformations when administered during the first trimester of pregnancy. Ondansetron should not be used during the first trimester of pregnancy.

It is not known whether Ondansetron is present in human milk. There is no data on the effects of Ondansetron on the breast-fed infant or the effects on milk production. Tests have shown that ondansetron passes into the milk of lactating animals. It is therefore recommended that mothers receiving Ondansetron should not breast-feed their babies, or the developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for Ondansetron and any potential adverse effects on the breast-fed infant from Ondansetron or from the underlying maternal condition.
There is no information on the effects of ondansetron on human fertility.

Driving and using machines

In psychomotor testing Ondansetron does not impair performance nor cause sedation. No detrimental effects on such activities are predicted from the pharmacology of Ondansetron.

3. HOW TO USE ONDASET:

Dosage

Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Chemotherapy

The recommended dosage for adult and pediatric patients 6 months of age and older for prevention of nausea and vomiting associated with emetogenic chemotherapy should be administered immediately before chemotherapy as a single intravenous dose of 0.15 mg/kg per dose for 3 doses (maximum of 16 mg per dose). The single intravenous dose must not exceed 8 mg.

Caution: Dilution of Ondaset Injection is required in adult and pediatric patients prior to administration. Infuse intravenously over 15 minutes beginning 30 minutes before the start of emetogenic chemotherapy and then repeat 4 and 8 hours after the first dose.

Prevention of Postoperative Nausea and Vomiting

The recommended dose and administration instructions for adult and pediatric patients 1 month of age and older for prevention of postoperative nausea and vomiting are shown in Table 1.

Population	Recommended Single Dose	Administration Instructions	Timing of Administration
Adults and pediatric patients older than 12 years of	4 mg	May be administered intravenously or intramuscularly: • Intravenously: infuse Undiluted Syringe contents (4 mg) over at least 30 seconds and preferably longer (over 2 to 5 minutes). •Intramuscularly: inject undiluted syringe contents (4 mg)	Administer immediately before induction of anesthesia, or postoperatively if the patient did not receive prophylactic antiemetics and experiences nausea and/or vomiting occurring within 2 hours after surgery
Pediatric patients 1 month to 12 years and 40 kg or greater	4 mg	Infuse intravenously over at least 30 seconds and preferably longer (over 2 to 5 minutes).	
Pediatric patients 1 month to 12 years less than 40 kg	0.1 mg/kg	Infuse intravenously over at least 30 seconds and preferably longer (over 2 to 5 minutes).	

Administration Requirement

Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Chemotherapy

• Dilution of Ondaset Injection in 50 mL of 5% Dextrose
Injection or 0.9% Sodium Chloride Injection is required before administration to adult and pediatric patients for the prevention of nausea and vomiting associated with emetogenic chemotherapy.
For pediatric patients between 6 months and 1 year of age and/or 10 kg or less: Depending on the fluid needs of the patient, Ondansetron Injection may be diluted in 10 to 50 mL of 5% Dextrose Injection or 0.9% Sodium Chloride Injection.

• Occasionally, Ondansetron precipitates at the stopper / vial interface in vials stored upright. Potency and safety are not affected. If a precipitate is observed, resolubilize by shaking the vial vigorously.

• Do not mix Ondaset Injection with solutions for which physical and chemical compatibility has not been established. In particular, this applies to alkaline solutions as a precipitate may form.

• Inspect the diluted Ondaset Injection solution for
particulate matter and discoloration before administration; discard if present.

• Storage: After dilution, do not use beyond 24 hours.
Although Ondaset Injection is chemically and physically stable when diluted as recommended, sterile precautions should be observed because diluents generally do not contain preservative.

• Compatibility: Ondaset Injection is compatible and stable
at room temperature under normal lighting conditions for 48 hours after dilution with the following intravenous fluids: 0.9% Sodium Chloride Injection, 5% Dextrose Injection, 5% Dextrose and 0.9% Sodium Chloride Injection, 5% Dextrose and 0.45% Sodium Chloride Injection, and 3% Sodium Chloride Injection.

Prevention of Postoperative Nausea and Vomiting

• Dilution of Ondaset Injection is not required before
administration to adult and pediatric patients.

• Inspect Ondaset Injection visually for particulate matter
and discoloration before administration; discard if present.

If you use more Ondaset than you should

In the case of an overdose, there is no specific antidote for Ondansetron. Patients should be managed with appropriate supportive therapy.

If you forget to use Ondaset

Take a missed dose as soon as possible. If it is almost time for the next dose, skip the missed dose and take the next dose at the regular scheduled time. Do not take 2 doses at the same time.

If you stop using Ondaset

Ondansetron must be taken precisely as directed by a doctor. If you suddenly stop taking the drug when you need it, you might experience episodes of nausea or vomiting.

Dosage Adjustment

Hepatic Impairment

In patients with severe hepatic impairment (Child-Pugh score of 10 or greater), a single maximal daily dose of 8 mg infused over 15 minutes beginning 30 minutes before the start of the emetogenic chemotherapy is recommended. There is no experience beyond first-day administration of Ondansetron in these patients.

Renal Impairment

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

Elderly

No dose adjustment is required in elderly patients.

4. POSSIBLE SIDE EFFECTS:

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1000 to <1/100), rare (≥ 1/10,000 to <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data). Very common, common and uncommon events were generally determined from clinical trial data. The incidence in placebo was taken into account. Rare, very rare and not known events were generally determined from post-marketing spontaneous data.

The following frequencies are estimated at the standard recommended doses of ondansetron.

The adverse event profiles in children and adolescents were comparable to that seen in adults.

Immune system disorders

Rare	Immediate hypersensitivity reactions sometimes severe, including anaphylaxis.

Nervous system disorders

Very common	Headache
Uncommon	Seizures, movement disorders (including such as dystonic reactions, oculogyric crisis and dyskinesia) (1)

Nervous system disorders

Rare	Dizziness predominantly during rapid IV administration.

Eye disorders

Rare	Transient visual disturbances (e.g. blurred vision) predominantly during IV administration.
Very rare	Transient blindness predominantly during IV administration (2).

Cardiac disorders

Uncommon	Arrhythmias, chest pain with or without ST segment depression, bradycardia.
Rare	QTc prolongation (including Torsade de Pointes).
Not known	Myocardial ischemia*

Vascular disorders

Common	Sensation of warmth or flushing.
Uncommon	Hypotension.

Respiratory, thoracic and mediastinal disorders

Uncommon	Hiccups.

Gastrointestinal disorders

Common	Constipation

Hepatobiliary disorders

Uncommon	Asymptomatic increases in liver function tests (3).

General disorders and administration site conditions

Common	Local IV injection site reactions.

1. Observed without definitive evidence of persistent
clinical sequelae.
2. The majority of the blindness cases reported resolved within 20 minutes. Most patients had received chemotherapeutic agents, which included cisplatin. Some cases of transient blindness were reported as cortical in origin.
3. These events were observed commonly in patients receiving chemotherapy with cisplatin.
* These types of adverse drug reactions have been derived from post-marketing experience with Ondansetron via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, itis not possible to reliably estimate their frequency which is therefore categorized as not known.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. You can also report side effects via Website: https://aspin.com.pk/drug-safety/. Or to DRAP through MED Vigilance E-Reporting System of DRAP available online at https://primaryreporting.who-umc.org/pk.

PHARMACEUTICAL INFORMATION

Shelf life

2 years

5. HOW TO STORE:

As prescribed by the physician.
Do not store above 30°C.
Protect from sunlight and heat.
Do not freeze.
Keep out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.

ہدایات :

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۳۰ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں۔
سورج کی روشنی اور گرمی سے بچائیں۔
منجمد ہونے سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔

6. CONTENTS OF THE PACK AND OTHER INFORMATION:

6.1 What Ondaset Contains

Ondaset 4mg/2ml Injection IM/IV:

Each 2ml contains:
Ondansetron as Hydrochloride Dihydrate 4mg
(USP Specifications)

Ondaset 8mg/4ml Injection IM/IV

Each 4ml contains:
Ondansetron as Hydrochloride Dihydrate 8mg
(USP Specifications)

The other Ingredients are Sodium chloride, Sodium citrate Dihydrate, Citric Acid Monohydrate, Water for Injection

6.2 What Ondaset looks like and contents of the pack

Clear colorless solution free from foreign particles.
Ondaset (Ondansetron) 4mg/2ml injection is available in a pack of 2ml x 5's.
Ondaset (Ondansetron) 8mg/4ml injection is available in a pack of 4ml x 1's.

6.3 Marketing Authorization Holder and Manufacturer:

6.3.1 Manufactured by:
AGP Limited
B-23-C, S.I.T.E., Karachi, Pakistan.

6.3.2 Manufactured for:

ASPIN
An OBS Group Company

Aspin Pharma (Pvt.) Ltd.
Plot No. 10 & 25, Sector No. 20, Korangi Industrial Area, Karachi - 74900, Pakistan.
www.aspin.com.pk

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