Artwork:	
Seroblock Tablets / Injection Leaflet	
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Martin Dow

Seroblock *Tablet/Injection*

Ondansetron
(as Ondansetron hydrochloride) USP

سیروبلاک ٹیبلیٹس/انجکشن
اَونڈنسٹرون
(اَونڈنسٹرون بطور ہائیڈروکلورائیڈ) یو ایس پی

1. COMPOSITION
Seroblock Tablets 8mg:
Each film-coated tablet contains:
Ondansetron HCl (USP)
eq. to ondansetron 8mg
Product conforms to USP Specification

Seroblock Injection 8mg/4ml:
Each 4ml Contains:
Ondansetron HCl (U.S.P)
eq. to ondansetron 8mg
Product conforms to U.S.P Specifications.

2. DESCRIPTION
The active ingredient in Seroblock Tablets and Injection is ondansetron hydrochloride as the dihydrate, the racemic form of ondansetron and a selective blocking agent of the serotonin 5-HT3 receptor type.

3. THERAPEUTIC INDICATIONS
Ondansetron Injection indicated for the prevention of:
- Nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy.
- Postoperative nausea and/or vomiting.

Ondansetron Tablets
- Ondansetron 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 (PONV).
- Ondansetron is indicated for the management of chemotherapy-induced nausea and vomiting (CINV) in children aged ≥6 months, and for the prevention and treatment of PONV in children aged ≥ 1 month.
- No studies have been conducted on the use of orally administered ondansetron in the prevention and treatment of PONV in children aged ≥1 month, administration by IV injection is recommended for this purpose.

4. DOSAGE AND ADMINISTRATION
Ondansetron Injection
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 is 0.15-mg/kg per dose for 3 doses (maximum of 16 mg per dose).

Caution: Dilution of Ondansetron 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 below.

Population	Recommended Single Dose	Administration Instructions	Timing of Administration
Adults and pediatric patients older than 12 years of age	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 more than 40 kg	4 mg	Infuse intravenously over at least 30 seconds and preferably longer (over 2 to 5 minutes).	
Pediatric patients 1 month to 12 years and 40 kg or less	0.1 mg/kg	Infuse intravenously over at least 30 seconds and preferably longer (over 2 to 5 minutes).	

Dosage in 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.

Ondansetron Tablets
Adults: The route of administration and dose of ondansetron should be flexible in the range of 8-32mg a day and selected as shown below. The selection of dose regimen should be determined by the severity of the emetogenic challenge.

INDICATION	DOSAGE REGIMEN
Highly Emetogenic Cancer Chemotherapy	Tablet: A single 24-mg dose administered 30 minutes before the start of single-day highly emetogenic chemotherapy, including cisplatin greater than or equal to 50 mg/m^2
Moderately Emetogenic Cancer Chemotherapy	Tablets: 8 mg administered 30 minutes before the start of chemotherapy, with a subsequent 8-mg dose 8 hours after the first dose. Then administer 8 mg twice a day (every 12 hours) for 1 to 2 days after completion of chemotherapy.
Radiotherapy	For total body irradiation: 8 mg administered 1 to 2 hours before each fraction of radiotherapy each day. For single high-dose fraction radiotherapy to the abdomen: 8 mg administered 1 to 2 hours before radiotherapy, with subsequent 8-mg doses every 8 hours after the first dose for 1 to 2 days after completion of radiotherapy. For daily fractionated radiotherapy to the abdomen: 8 mg administered 1 to 2 hours before radiotherapy, with subsequent 8-mg doses every 8 hours after the first dose for each day radiotherapy is given.
Postoperative	Tablets: 16 mg administered 1 hour before induction of anesthesia.

Pediatric Patients

INDICATION	DOSAGE REGIMEN
Moderately Emetogenic Cancer Chemotherapy	12 to 17 years of age: 8 mg administered 30 minutes before the start of chemotherapy, with a subsequent 8-mg dose 4 and 8 hours after the first dose. Then administer 8 mg three times a day for 1 to 2 days after completion of chemotherapy. 4 to 11 years of age: 4 mg administered 30 minutes before the start of chemotherapy, with a subsequent 4-mg dose 4 and 8 hours after the first dose. Then administer 4 mg three times a day for 1 to 2 days after completion of chemotherapy.

Elderly: There is limited experience in use of ondansetron in the prevention and treatment of post-operative nausea and vomiting in the elderly, however it is well tolerated in patients over 65 years receiving chemotherapy.
Dosage in Hepatic Impairment: In patients with severe hepatic impairment (Child-Pugh score of 10 or greater), do not exceed a total daily dose of 8 mg.
Patients with Renal Impairment: No alteration of daily dosage or frequency of dosing, or route of administration are required.

5. CONTRAINDICATIONS
- ONDANSETRON is contraindicated in patients known to be hypersensitive to ondansetron, other selective 5-HT3 receptor antagonists (e.g. granisetron, dolasetron) and any of the components of the formulation.
- Receiving concomitant apomorphine due to the risk of profound hypotension and loss of consciousness.

6. SPECIALWARNINGS AND PRECAUTIONS
- Hypersensitivity reactions, including anaphylaxis and bronchospasm, have been reported in patients who have exhibited hypersensitivity to other selective 5-HT3 receptor antagonists. If hypersensitivity reactions occur, discontinue use of ONDANSETRON; treat promptly per standard of care and monitor until signs and symptoms resolve.
- **QT Prolongation:** 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 has been reported in patients treated with ondansetron. In some cases, predominantly during intravenous administration, the symptoms appeared immediately after administration but recovered with prompt treatment. Therefore, caution should be exercised during and after administration of ondansetron.
- Serotonin Syndrome: Reported with 5-HT3 receptor antagonists alone but particularly with concomitant use of serotonergic drugs. Symptoms associated with serotonin syndrome may include the following combination of signs and symptoms: mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, with or without gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). If such symptoms occur, discontinue Ondansetron and initiate supportive treatment. If concomitant use of Ondansetron with other serotonergic drugs is clinically warranted, patients should be made aware of a potential increased risk for serotonin syndrome.
- The use of ONDANSETRON in patients following abdominal surgery or in patients with chemotherapy-induced nausea and vomiting may mask a progressive ileus and/or gastric distension. Monitor for decreased bowel activity, particularly in patients with risk factors for gastrointestinal obstruction. ONDANSETRON is not a drug that stimulates gastric or intestinal peristalsis. It should not be used instead of nasogastric suction.
- 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.
- Pediatric patients receiving ondansetron with hepatotoxic chemotherapeutic agents should be monitored closely for impaired hepatic function.

7. ADVERSE REACTIONS
Post-marketing Experience
Common: Headache, Sensation of warmth or flushing, Constipation, Local IV injection site reactions.
Uncommon: Movement disorders (including extrapyramidal reactions (such as oculogyric crisis, dystonic reactions and dyskinesia) have been observed without definitive evidence of persistent clinical sequelae; seizures. Arrhythmias, chest pain with or without ST segment depression, bradycardia. Hypotension, Hiccups and Asymptomatic increases in liver function tests.
Rare: Immediate hypersensitivity reactions sometimes severe, including anaphylaxis, Dizziness predominantly during rapid IV administration, Transient visual disturbances (e.g. blurred vision) predominantly during rapid intravenous administration and QTc prolongation (including Torsade de pointes).
Frequency not known: Rarely and predominantly with intravenous ondansetron, transient ECG changes including QT interval prolongation have been reported. Rare cases of hypersensitivity reactions, sometimes severe (e.g., anaphylactic reactions, angioedema, bronchospasm, shortness of breath, hypotension, laryngeal edema, stridor) have also been reported. Laryngospasm, shock, and cardiopulmonary arrest have occurred during allergic reactions in patients receiving injectable ondansetron. Liver enzyme abnormalities. Oculogyric crisis, appearing alone, as well as with other dystonic reactions. Urticaria, Stevens-Johnson syndrome, and toxic epidermal necrolysis. Cases of transient blindness, predominantly during intravenous administration, have been reported. These cases of transient blindness were reported to resolve within a few minutes up to 48 hours.

8. DRUG INTERACTIONS
- Serotonergic Drugs: Serotonin syndrome (including altered mental status, autonomic instability, and neuromuscular symptoms) has been described following the concomitant use of 5-HT3 receptor antagonists and other serotonergic drugs, including SSRIs and serotonin and SNRIs. Monitor for the emergence of serotonin syndrome. If symptoms occur, discontinue ONDANSETRON and initiate supportive treatment.

- Ondansetron does not itself appear to induce or inhibit the cytochrome P-450 drug-metabolizing enzyme system of the liver. Because ondansetron is metabolized by hepatic cytochrome P-450 drug-metabolizing enzymes (CYP3A4, CYP2D6, CYP1A2), inducers or inhibitors of these enzymes may change the clearance and, hence, the half-life of ondansetron. In patients treated with potent inducers of CYP3A4 (i.e., phenytoin, carbamazepine, and rifampin), the clearance of ondansetron was significantly increased and ondansetron blood concentrations were decreased. However, on the basis of available data, no dosage adjustment for ONDANSETRON is recommended for patients on these drugs.

- Monitor patients to ensure adequate pain control when ondansetron is administered with tramadol.

- Concomitant use of ondansetron with cardiotoxic drugs (e.g. anthracyclines such as doxorubicin, daunorubicin or trastuzimab), antibiotics (such as erythromycin), antifungals (such as ketoconazole), antiarrhythmics (such as amiodarone) and beta blockers (such as atenolol or timolol) may increase the risk of arrhythmias. Caution should be exercised when ondansetron is co-administered with drugs that prolong the QT interval and/or cause electrolyte abnormalities.

9. PREGNANCY AND LACTATION
Pregnancy: Available data do not reliably inform the association of Ondansetron and adverse fetal outcomes. In human epidemiological studies, an increase in orofacial clefts was observed in infants of women administered ondansetron during the first trimester of pregnancy. Regarding cardiac malformations the epidemiological studies showed conflicting results. The use of ondansetron in pregnancy is not recommended.

Breast Feeding: It is not known whether ondansetron is present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Ondansetron. It is therefore recommended that mothers receiving ondansetron should not breast-feed their babies.

10. CLINICAL PHARMACOLOGY
Pharmacotherapeutic group: Antiemetics and Antinauseants.
Mode of action: Ondansetron is a selective 5-HT3 receptor antagonist. While its mechanism of action has not been fully characterized, ondansetron is not a dopamine-receptor antagonist. Serotonin receptors of the 5-HT3 type are present both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postrema. It is not certain whether ondansetron's antiemetic action is mediated centrally, peripherally, or in both sites. However, cytotoxic chemotherapy appears to be associated with release of serotonin from the enterochromaffin cells of the small intestine. In humans, urinary 5-hydroxyindoleacetic acid (5-HIAA) excretion increases after cisplatin administration in parallel with the onset of emesis. The released serotonin may stimulate the vagal afferents through the 5-HT3 receptors and initiate the vomiting reflex.

11. OVERDOSAGE
There is no specific antidote for ondansetron overdose. Patients should be managed with appropriate supportive therapy. 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.

In addition to the adverse reactions listed above, the following adverse reactions have been described in the setting of ondansetron overdose: "Sudden blindness" (amaurosis) of 2 to 3 minutes' duration plus severe constipation occurred in one patient that was administered 72 mg of ondansetron intravenously as a single dose. Hypotension (and faintness) occurred in a patient that took 48 mg of Ondansetron tablets. Following infusion of 32 mg over only a 4-minute period, a vasovagal episode with transient second-degree heart block was observed. In all instances, the adverse reactions resolved completely.

Pediatric cases consistent with serotonin syndrome have been reported after inadvertent oral overdoses of ondansetron (exceeding estimated ingestion of 5 mg per kg) in young children. Patients required supportive care, including intubation in some cases, with complete recovery without sequelae within 1 to 2 days.

12. HOW SUPPLIED
Presentation
Seroblock Tablets 8mg: Available pack of 10's tablets.
Seroblock Injection 8mg/4ml: Available in 1ml ampoule in the carton.

Dosage:
As prescribed by the physician.

Instructions Tablets:
Store below 25 °C. Protect from light and heat.
Keep all medicines out of the reach of children.

Instructions Injection:
Store in a cool & dry place between 2°C-30°C.
Protect from light and heat.
Keep all medicines out of the reach of children.

عمومی خوراک:
ڈاکٹری ہدایت کے مطابق استعمال کریں۔

ہدایات ٹیبلیٹس:
25° ڈگری سنٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
روشنی گرمی اور نمی سے محفوظ رکھیں۔ بچوں کی پہنچ سے دور رکھیں۔

ہدایات انجکشن:
دو اکھٹی اور خشک جگہ 2°C تا 30°C ڈگری کے درمیان درجہ حرارت پر رکھیں۔
روشنی اور گرمی سے محفوظ رکھیں۔ بچوں کی پہنچ سے دور رکھیں۔

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Manufactured by:
Wilshire Laboratories (Pvt) Limited
124/1 Industrial Estate, Kot Lakhpat,
Lahore, Pakistan.