210mm

ONTIV™ Tablet

(Ondansetron Hydrochloride)

QUALITATIVE AND QUANTITATIVE COMPOSITION

ONTIV™ 8mg Tablet
Each film coated tablet contains:
Ondansetron Hydrochloride Dihydrate USP
equivalent to Ondansetron.....8mg

PHARMACEUTICAL FORM

Tablet.

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS:
Adults:
ONTIV™ is indicated for the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy.
ONTIV™ is indicated for the prevention of postoperative nausea and vomiting (PONV). For treatment of established PONV, administration by injection is recommended.

POSOLOGY AND METHOD OF ADMINISTRATION:
Adults:
Chemotherapy and radiotherapy induced nausea and vomiting (CINV and RINV):
The emetogenic potential of cancer treatment varies according to the doses and combinations of chemotherapy and radiotherapy regimens used.
Emetogenic chemotherapy and radiotherapy:
ONTIV™ can be given orally.
The recommended oral dose is 8mg taken 1-2 hours before chemotherapy or radiation treatment, followed by 8mg every 12 hours for a maximum of 5 days to protect against delayed or prolonged emesis.
For highly emetogenic chemotherapy a single dose of up to 24mg ondansetron taken with 12mg oral dexamethasone sodium phosphate, 1 to 2 hours before chemotherapy, may be used.
To protect against delayed or prolonged emesis after the first 24 hours, oral treatment with ondansetron may be continued for up to 5 days after a course of treatment.
The recommended dose for oral administration is 8mg to be taken twice daily.
Dosing by BSA:
Oral dosing can commence 12 hours later and may be continued for up to 5 days. The total dose over 24 hours (given as divided doses) must not exceed the adult dose of 32mg.
Dosing by body weight:
Oral dosing can commence 12 hours later and may be continued for up to 5 days.
Elderly:
No alteration of oral dose or frequency of administration is required.
Renal impairment:
No alteration of daily dosage or frequency of dosing, or route of administration are required.
Hepatic impairment:
Clearance of ondansetron 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 8mg should not be exceeded.
Patients with poor sparteine/debrisoquine metabolism:
No alteration of daily dosage or frequency of dosing is required.
Post-operative nausea and vomiting (PONV) :
In adults for the prevention of PONV, the recommended oral dose is 16mg taken one hour prior to anaesthesia.
In paediatric population, no studies have been conducted on the use of orally administered ondansetron in the prevention or treatment of post-operative nausea and vomiting;
Elderly:
There is limited experience in the use of ondansetron in the prevention and treatment of postoperative nausea and vomiting in the elderly, however, ondansetron is well tolerated in patients over 65 years receiving chemotherapy.

CONTRAINDICATIONS:
- Concomitant use with apomorphine is contraindicated.
- Hypersensitivity to the active substance.

SPECIAL WARNINGS:
- Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5HT3 receptor antagonists.
- Respiratory events should be treated symptomatically and clinicians should pay attention. In addition, post-marketing cases of Torsade de Pointes have been reported in patients using ondansetron. Avoid ondansetron in patients with congenital long QT syndrome.
- Ondansetron should be administered with caution to patients who have or may develop prolongation of QTc, including patients with electrolyte abnormalities, congestive heart failure, bradyarrhythmia's or patients taking other medicinal products that lead to QT prolongation or electrolyte abnormalities.
- Cases of myocardial ischemia have been reported in patients treated with ondansetron.
- 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 the concomitant use of ondansetron and other serotonergic drugs (including selective serotonin reuptake inhibitors (SSRI) and serotonin noradrenaline reuptake inhibitors (SNRIs). If concomitant treatment with ondansetron and other serotonergic drugs 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 with adenotonsillar surgery prevention of nausea and vomiting with ondansetron may mask occult bleeding. Therefore, such patients should be followed carefully after ondansetron.
- Patients receiving ondansetron with hepatotoxic chemotherapeutic agents should be monitored closely for impaired hepatic function.

Lactose:
Patients with rare hereditary problems of galactose intolerance, lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS:
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 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 as erythromycin), antifungals (such as ketoconazole), antiarrhythmics (such as amiodarone) and beta blockers (such as atenolol or timolol) may increase the risk of arrhythmias.
There have been post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the concomitant use of ondansetron and other serotonergic drugs (including SSRIs and SNRIs).
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 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.

FERTILITY, PREGNANCY AND LACTATION:
Women of childbearing potential:
Women of childbearing potential should consider the use of contraception.

120mm

210mm

Pregnancy:
Ondansetron should not be used during the first trimester of pregnancy.
Breast-feeding:
It is recommended that mothers receiving ondansetron should not breast-feed their babies.
Fertility:
No information on the effects of ondansetron on human fertility.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINE:
Ondansetron has no or negligible influence on the ability to drive and use 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.

UNDESIRABLE EFFECTS:
Immune system disorders:
Rare: Immediate hypersensitivity reactions sometimes severe, including anaphylaxis.
Nervous system disorders:
Very common: Headache
Uncommon: Seizures, movement disorders (including extrapyramidal reactions such as dystonic reactions, oculogyric crisis and dyskinesia).
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
Cardiac disorders:
Uncommon: Arrhythmias, chest pain with or without ST segment depression, bradycardia.
Rare: QT prolongation (including Torsade de Pointes).
Not known: Myocardial ischemia.
Vascular disorders:
Common: Vascular disorders.
Uncommon: Hypotension.
Respiratory, thoracic and mediastinal disorders:
Uncommon: Hiccups.
Gastrointestinal disorders:
Common: Constipation.
Hepatobiliary disorders:
Uncommon: Asymptomatic increases in liver function tests.

OVERDOSE:
Manifestations that have been reported include visual disturbances, severe constipation, hypotension and a vasovagal episode with transient second-degree AV block. Ondansetron prolongs QT interval in a dose-dependent fashion. ECG monitoring is recommended in cases of overdose.
There is no specific antidote for ondansetron, therefore, in cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES:
Pharmacotherapeutic group: Serotonin (5HT3) antagonist. **ATC code:** A04AA01.
Mechanism of action:
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. Ondansetron does not alter plasma prolactin concentrations.

PHARMACOKINETIC PROPERTIES:
Absorption:
Following oral administration, ondansetron is passively and completely absorbed from the gastrointestinal tract and undergoes first pass metabolism. Peak plasma concentrations of about 30ng/ml are attained approximately 1.5 hours after an 8mg dose.
Mean bioavailability in healthy male following the oral administration of a single 8mg tablet, is approximately 55 to 60%. Bioavailability, following oral administration, is slightly enhanced by the presence of food but unaffected by antacids.
Distribution:
Ondansetron is not highly protein bound (70-76%).
Biotransformation and Elimination:
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.

SHELF LIFE
See expiry on the pack.

AVAILABILITY
ONTIV™ 8mg tablet in a pack of 10's.

INSTRUCTIONS
Dosage: As directed by the physician.
To be sold on prescription of a registered medical practitioner only.
Keep out of reach of children.
Do not store over 30°C, and protect from heat, light and moisture.
Improper storage may deteriorate the medicine.

اونٹیو™ ٹیبلٹ

(اونڈینسِٹرون ہائیڈروکلورائیڈ)

ہدایات:
خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،
گرمی، روشنی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, Off Hub River Road, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com
Mfg. Lic. No. 000072

2000006635 R.N-01/NA/04/2023

120mm