Nixvom

(Ondansetron) Injection, USP

نکسووم

(اونڈینسیٹرون) انجکشن

I.M. / I.V. Injection عضلاتی یا وریدی استعمال کیلئے

COMPOSITION:
Each 2ml ampoule contains: Ondansetron (as Ondansetron HCl Dihydrate) USP ... 4mg. [USP Specs.]
Each 4ml ampoule contains: Ondansetron (as Ondansetron HCl Dihydrate) USP ... 8mg. [USP Specs.]

PHARMACOLOGY: Mechanism of action: Ondansetron is a potent, highly selective $5HT_3$ 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 $5HT_3$ receptors. Ondansetron blocks the initiation of this reflex.

PHARMACOKINETIC: The disposition of Ondansetron following oral, intramuscular (IM) and intravenous (IV) dosing is similar with a steady state volume of distribution of about 140L. Equivalent systemic exposure is achieved after IM and IV administration of Ondansetron. Ondansetron is not highly protein bound (70 to 76%). 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. The absence of the enzyme CYP2D6 (the debrisoquine polymorphism) has no effect on Ondansetron's pharmacokinetics. The pharmacokinetic properties of Ondansetron are unchanged on repeat dosing.

INDICATIONS: Nixvom: is used to treat nausea (feeling sick) and vomiting (being sick) caused by some medical treatments, such as chemotherapy or radiotherapy for cancer (in adults and children). It is also used to prevent nausea and vomiting in patients following an operation (adults only).

DOSAGE AND ADMINISTRATION:
Adults:

Indication:	Dose:
Chemotherapy and radiotherapy induced nausea and vomiting	Ondansetron 8mg should be administered as a slow intravenous injection (in not less than 30 seconds) or as a short-time intravenous infusion over 15 minutes immediately before treatment, followed by 8mg orally twelve hourly.
For patients receiving chemotherapy that causes severe nausea and vomiting	8mg given by intravenous or intramuscular injection immediately before chemotherapy, as a single dose or followed by two further intravenous or intramuscular doses of 8mg 2 to 4 hours apart, or by an intravenous infusion (drip) of 1mg per hour for up to 24 hours. 32mg given as an intravenous infusion (drip), over not less than 15 minutes, immediately before chemotherapy
	After the initial Ondansetron injection you may be given tablets or suppositories for up to 5 days to prevent any further nausea and vomiting.
Post-Operative Nausea and Vomiting (PONV): To treat nausea and vomiting after an operation:	The usual adult dose is 4mg given as an intravenous or intramuscular injection. For children aged 2 years and over the dose is 0.1mg per kilogram of body weight, up to a maximum of 4mg, given as an intravenous injection.
Paediatric population: PONV in children aged ≥ 1 month and adolescents:	a single dose of ondansetron may be administered by slow intravenous injection (not less than 30 seconds) at a dose of 0.1mg/kg up to a maximum of 4mg either prior to, at or after induction of anaesthesia.
Patients with moderate or severe liver disease	The total daily dose should not be more than 8mg

Dosing by bodyweight: Ondansetron should be administered immediately before chemotherapy as a single intravenous dose of 0.15mg/Kg. The single intravenous dose must not exceed 8mg. Two further intravenous doses may be given in 4-hourly intervals. Oral dosing can commence 12 hours later and may be continued for up to 5 days.
Weight-based dosing for Chemotherapy - Children aged ≥ 6 months and adolescents

Weight	Day 1	Days 2-6
≤10kg	Up to 3 doses of 0.15mg/kg IV every 4 hours	2mg syrup every 12 hours
≥10kg	Up to 3 doses of 0.15mg/kg IV every 4 hours	4mg syrup or tablet every 12 hours

Elderly:

In patients 65 to 74 years of age:	All intravenous doses should be diluted in 50-100ml of saline or other compatible infusion fluid and infused over 15 minutes.
In patients 75 years of age or older:	The initial intravenous dose of Ondansetron should not exceed 8mg. All intravenous doses should be diluted in 50-100ml of saline or other compatible infusion fluid and infused over 15 minutes. The initial dose of 8mg may be followed by two further intravenous doses of 8mg, infused over 15 minutes and given no less than four hours apart

Special Populations:
Patients with renal impairment: No alteration of daily dosage or frequency of dosing, or route of administration are required.

Patients with hepatic impairment: Clearance of Ondansetron is significantly reduced, in such patients a total daily dose of 8mg should not be exceeded and therefore parenteral or oral administration is recommended.

Patients with poor sparteine/Debrisoquine metabolism: No alteration of daily dosage or frequency of dosing is required.

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CONTRAINDICATIONS: Co-administration with apomorphine; combination reported to cause profound hypotension and loss of consciousness 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. **Serotonergic Drugs (e.g. SSRIs and SNRIs):** 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). Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

OVERDOSAGE: Symptoms and Signs: Ondansetron prolongs the QT interval in a dose-dependent manner. ECG monitoring is recommended in cases of overdose. **Paediatric population:** Paediatric cases consistent with serotonin syndrome have been reported after inadvertent oral overdoses of ondansetron (exceeded estimated ingestion of 4mg/kg) in infants and children aged 12 months to 2 years.

WARNINGS & PRECAUTIONS: Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5HT3 receptor antagonists. Avoid Ondansetron in patients with congenital long QT syndrome. Ondansetron should be administered with caution to patients who have or may develop prolongation of QT, including patients with electrolyte abnormalities, congestive heart failure, Brady arrhythmias or patients taking other medicinal products that lead to QT prolongation or electrolyte abnormalities. Hypokalemia and hypomagnesaemia should be corrected prior to Ondansetron administration. 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.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-hour intervals, the total daily dose will be higher than if one single dose of 5mg/m2 followed by an oral dose is given. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

DRUG INTERACTIONS: There have been interactions reported when the Ondansetron is used concomitantly with the following drugs; drugs that prolong the QT interval and/or cause electrolyte abnormalities; 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; SSRIs and SNRIs; profound hypotension and loss of consciousness have been reported when Ondansetron was administered with apomorphine hydrochloride, thus concomitant use with apomorphine is contraindicated; phenytoin, carbamazepine and rifampicin may increase the clearance of Ondansetron and Ondansetron blood concentrations were decreased. Ondansetron may reduce the analgesic effect of tramadol.

FERTILITY, PREGNANCY AND LACTATION:
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: There is no information on the effects of Ondansetron on human fertility.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: There was no effect on psychomotor system nor does it impair performance or cause sedation.

ADVERSE REACTIONS: Immediate hypersensitivity reactions sometimes severe, including anaphylaxis, headache, seizures, movement disorders including extrapyramidal reactions such as dystonic reactions, oculogyric crisis and dyskinesia have been observed, dizziness predominantly during rapid IV administration, which in most cases is prevented or resolved by lengthening the infusion period, transient visual disturbances (e.g. blurred vision) predominantly during IV administration, Transient blindness predominantly during IV administration, some cases of transient blindness were reported as cortical in origin, arrhythmias, chest pain with or without ST segment depression, bradycardia, QTC prolongation (including Torsade de Pointes), sensation of warmth or flushing, hypotension, hiccups, constipation, asymptomatic increases in liver function tests. Paediatric population: The adverse event profile in children and adolescents was comparable to that seen in adults.

INSTRUCTIONS: Store below 30° C. Do not freeze. **For single use only.** Any unused solution should be discarded. Protect from heat & light. Keep out of the reach of children. Do not use if container is leaking, solution is cloudy or it contains undissolved particles.

PRESENTATION:
Nixvom Injection (Ondansetron 4mg/2ml solution for injection) is available in pack size of 1's.
Nixvom Injection (Ondansetron 8mg/4ml solution for injection) is available in pack size of 5's.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ منجمد ہونے سے بچائیں۔ صرف ایک دفعہ استعمال کریں۔ غیر استعمال شدہ محلول کو ضائع کر دیں۔ روشنی اور گرمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔ بوتل کے لیک ہونے، دھندلا ہونے یا اس میں کوئی غیر حل پزیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

PHARMA

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