Sandem

TABLETS
INJECTION

[Ondansetron] USP

COMPOSITION:
Sandem Tablet:
Each film coated tablet contains:
Ondansetron as HCl (USP).....8mg
Sandem Injection:
Each 4ml ampoule contains:
Ondensetron as HCl (USP).....8mg

CLINICAL PHARMACOLOGY:
Ondansetron is a selective antagonist of the serotonin receptor subtype, 5-HT_3. Its precise mode of action in the control of chemotherapy induced nausea and vomiting is not known. Cytotoxic chemotherapy and radiotherapy are associated with the release of serotonin (5-HT) from enterochromaffin cells of the small intestine, presumably irritating a vomiting reflex through stimulation of 5-HT_3, receptors located on vagal afferents. Ondansetron may block the initiation of this reflex, activation of vagal afferents may also cause a central release of serotonin from the chemoreceptor trigger zone of the area postrema located on the floor of the fourth ventricle, thus the anti-emetic effect of ondansetron is probably due to the selective antagonism of 5-HT_3 receptors on neurons located in either the peripheral or central nervous system or both. The mechanisms of ondansetron's antiemetic action in postoperative nausea and vomiting are not known.

INDICATIONS:
For the prevention of nausea and vomiting associated with emetogenic chemotherapy including high dose cisplatin and radiotherapy. Ondansetron is also indicated for the prevention and treatment of post operative nausea and vomiting.

CONTRAINDICATIONS:
It is contraindicated in patients with a history of hypersensitivity to the drug or any component of its formulations.

PRECAUTIONS:
Ondansetron is not effective in preventing motion-induced nausea and vomiting. There is no experience in patients who are clinically jaundiced. The clearance of an 8 mg intravenous dose of Ondansetron was significantly reduced and the serum half-life significantly prolonged in subjects with severe impairment of hepatic function. In patients with moderate to severe hepatic function, reduction in dosage is therefore recommended and a total daily dose of 8mg should not be exceeded. This may be given as a single I.V or oral dose.

Pregnancy: The safety of ondansetron during pregnancy has not been established. It should not be used if it outweighs the possible risk to the fetus.

Lactation: Ondansetron is excreted in the milk of lactating rats. It is not known if it is excreted in human milk, however nursing is not recommended during treatment with Ondansetron.

Children: Insufficient information is available to provide dosage recommendations for children 3 years of age or younger.

ADVERSE EFFECTS:
Ondansetron has been administered to over 2500 patients worldwide in controlled clinical trials and has been well tolerated.
The most frequent adverse events reported in controlled clinical trials were headache (11%) and constipation (4%). Other adverse events include sensations of flushing or warmth (1%).

Metabolic: There were transient increases of AST and ALT over twice the upper limit of normal in approximately 5% of patients. This increase did not appear to be related to dose or duration of therapy. There have been reports of liver failure and death in patients with cancer receiving concurrent medications including potentially hepatotoxic cytotoxic chemotherapy and antibiotics. The etiology of liver failure is unclear. There have been rare reports of hypokalemia.

CNS: There have been rare reports of seizures.

Hypersensitivity: Rare cases of immediate hypersensitivity reactions sometimes severe, including anaphylactic bronchospasm, urticaria and angioedema have been reported.

Cardiovascular: There have been rare reports of tachycardia, angina, bradycardia, hypotension, syncope and electrocardiographic alteration.

Dermatological: Rash has occurred in approximately 1% of the patients receiving Ondansetron.

Special Senses: Rare cases of transient visual disturbances (e.g. blurred vision) have been reported during or shortly after I.V administration of Ondansetron particularly at rates equal to or greater than 30mg in 15minutes.

Other Effects: Pain, redness and burning at the site of injection have been reported. There have been reports of abdominal pain, weakness and xerostomia.

DOSAGE AND ADMINISTRATION:
Chemotherapy induced nausea and vomiting: Ondansetron should be given as an initial dose prior to chemotherapy, followed by a dosage regimen to the anticipated severity of emetic response caused by different cancer treatments. The route of administration and dosage of ondansetron should be flexible in the range of 8 to 32mg a day.

Adults:
Chemotherapy (e.g. regimens containing cisplatin):
Ondansetron has been shown to be effective in the following dose schedules for the prevention of emesis during first 24 hours following chemotherapy.

Initial Dose: 8mg infused I.V. over 15 minutes given 30 minutes prior to chemotherapy followed by 1mg/h by continuous infusion for 24 hours; or 32mg diluted in 50 minutes given 30 minutes prior to chemotherapy.

Post-chemotherapy: After first 24 hours, 8mg orally after every 8 hours for up to 5 days.
No significant difference in terms of emesis control or grade of nausea has been demonstrated between 32mg single dose, 8 mg single dose or the 8mg dose followed by 24 hours 1mg/hour continuous infusion.
However, in some studies conducted in patients receiving medium or high doses of cisplatin chemotherapy, the 32mg single dose has demonstrated a statistically significant superiority over 8mg single dose with regard to control or emesis. The efficacy of Ondansetron in highly emetogenic chemotherapy may be enhanced by the addition of single I.V. dose of dexamethasone sodium phosphate, 20mg administered prior to chemotherapy.

Post-chemotherapy: 8mg tablet orally twice daily for up to 5 days.
Children: Clinical experience of Ondansetron in children is currently limited, however, Ondansetron was effective and well tolerated when given to children 4 to 12 years of age. Ondansetron injection should be given I.V at a dose of 3 to 5mg/m^2 over 15 minutes immediately before chemotherapy. After therapy, one tablet of Ondansetron (4mg) should be given orally every 8 hours for up to 5 days.

Geriatrics: Efficacy and tolerance in patients aged over 65 years were similar to that seen in younger adults indicating no need to alter dosage schedules in the population.

Radiotherapy induced nausea and vomiting:
Adults:
Initial dose: 8mg tablet orally 1 to 2 hours before radiotherapy.
Post-radiotherapy: 8mg tablet every 8 hours for up to 5 days after course of treatment.

Geriatrics: Efficacy and tolerance in patients aged over 65 years were similar to that seen in younger adults indicating no need to alter dosage schedules in this population.

Note: The efficacy of twice daily dosage regimens for the treatment of post-chemotherapy emesis has been established only in adult patients receiving less emetogenic chemotherapy. The appropriate of twice versus 3 times daily dosage regimens for other patient groups should be based on an assessment of the needs and responsiveness of the individual patients. Infusion of 32mg Ondansetron injection should take place over a period or not less than 15 minutes, because of increased risk of blurred vision.

Post-operative nausea and vomiting:
Adults:
For the prevention of post-operative nausea and vomiting Ondansetron may be given 16mg orally 1 hour prior to anesthesia. Approximately a single dose of 4mg may be given by slow I.V. injection at induction of anesthesia. For the treatment of established post-operative nausea and vomiting, a single dose of 4mg given by slow I.V injection is recommended.

Children: There is no experience in the use of Ondansetron in the prevention and treatment of post-operative nausea and vomiting in the children.

Geriatrics: There is limited experience in the use of Ondansetron in the prevention and treatment of post-operative nausea and vomiting in the elderly.

Impaired renal function: No alteration of daily dosage, frequency of dosing, and route of administration is required.

Impaired hepatic function: The clearance of an 8mg I.V. dose was significantly reduced and the serum half-life was significantly prolonged in subjects with severe impairment of hepatic function. In patients with moderate or severe hepatic function, reduction in the dosage is therefore recommended and a total daily dose of 8mg should not be exceeded. This may be given as a single I.V. or oral dose. No studies have been conducted to indicate in patients with jaundice.

OVERDOSE:
Symptoms and Treatment: At present there is little information concerning over dosage with Ondansetron and total daily dose as large as 252mg has been administered with only mild side effects. There is no specific antidote for Ondansetron, therefore in cases of suspected over dosage, symptomatic and supportive therapy should be given as. "Sudden blindness" (amaurosis) of 2 to 3 minutes duration plus severe constipation occurred in patients who were administered 72mg of Ondansetron I.V. as a single dose. (Hypotension and fainting occurred in another patient who took 48mg of oral Ondansetron following infusion of 32mg over only a 4 minutes period, a vasovagal episode with transient second degree heart block was observed. In all instances, the events resolved instantly.)

STABILITY:
Sandem injection is stable at room temperature under normal light for 48 hours after dilution with the following I.V 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.

Although Sandem injection is chemically and physically stable when diluted as recommended. However, precautions should be taken because diluents generally do not contain preservatives. After dilution do not use beyond 24 hours.

PRESENTATION:
SANDEM INJECTION is supplied as 8mg/4ml Ondansetron in a transparent glass ampoule.
SANDEM TABLET contains 8mg Ondansetron packed in blister of 10's.

Instructions:
Store at 15-30°C.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Physician sample is not for sale.
For Tablets:
Protect from heat, light and moisture.
For Injection:
Protect from heat and light.
Avoid freezing.
Injection should not be used if ampoule is leaking, solution is cloudy or contain undissolved particles.

سینڈم

(اونڈنسٹرون) یو ایس پی

گولیاں

انجیکشن

خوراک: دواڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات: دوا کو 15-30° سینٹی گریڈ پر رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

برائے گولیاں: گرمی، روشنی اور نمی سے محفوظ رکھیں۔

برائے انجیکشن: گرمی اور روشنی سے محفوظ رکھیں۔ منجمد ہونے سے بچائیں۔ انجیکشن کے لیک ہونے، دھندلا ہونے یا اس میں کوئی غیر حل پذیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

STANDPHARM

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