Front size: 130mm x 180mm Back

Danset®

(Ondansetron) Tablet & Injection

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

Product Specs.: USP

Danset Injection 8 mg/4 ml:
Each ml contains:
Ondansetron Hydrochloride Dihydrate USP equivalent to
Ondansetron ..... 2 mg.

Product Specs.: USP

DESCRIPTION:
DANSET (ondansetron hydrochloride) is a selective antagonist of the serotonin receptor subtype, 5-HT3. 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 initiating a vomiting reflex through stimulation of 5-HT3 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 antiemetic effect of ondansetron is probably due to the selective antagonism of 5-HT3 receptors on neurons located in either the peripheral or central nervous systems, or both. The mechanisms of ondansetron's antiemetic action in post-operative nausea and vomiting are not known.

PHARMACOKINETICS:
Pharmacokinetic studies have shown peak plasma levels of 20-30 ng/ml at around 1½ hours after an 8 mg oral dose of ondansetron. An 8 mg infusion of ondansetron resulted in peak plasma levels of 80-100 ng/ml repeat dosing of an 8 mg tablet every 8 hours for 6 days increased the peak plasma value to 40 ng/ml. A continuous intravenous infusion of 1 mg/hour after the initial 8 mg loading dose of ondansetron maintained plasma levels over 30 ng/ml during the following 24 hour period. The absolute bioavailability of ondansetron in humans was approximately 60% and the plasma protein binding was approximately 73%. Following oral or IV administration, ondansetron is extensively metabolized and excreted in the urine and faeces. In humans, less than 10% of the dose is excreted unchanged in the urine. The major urinary metabolites are glucuronide conjugates (45%), sulphate conjugates (20%) and hydroxylation products (10%). The half-life of ondansetron after either an 8 mg oral dose or intravenous dose was approximately 3-4 hours and may be extended to 6-8 hours in the elderly.

USE IN SPECIFIC POPULATIONS:
Pregnancy:
Pregnancy Category B: There are no adequate and well-controlled studies in pregnant women.
Nursing Mothers: It is not known whether ondansetron is excreted in human milk or not.
Pediatric Use: Little information is available about the use of ondansetron in pediatric surgical patients younger than 1 month. Little information is available about the use of ondansetron in pediatric cancer patients younger than 6 months. The clearance of ondansetron in pediatric patients aged 1 month to 4 months is slower and the half-life is ~2.5-fold longer than patients who are aged >4 to 24 months. As a precaution, it is recommended that patients younger than 4 months receiving this drug be closely monitored.
Geriatric Use: Dosage adjustment is not needed in patients over the age of 65.
Hepatic Impairment: In patients with severe hepatic impairment (Child-Pugh score of 10 or greater), clearance is reduced and apparent volume of distribution is increased with a resultant increase in plasma half-life. In such patients, a total daily dose of 8 mg should not be exceeded.
Renal Impairment: Although plasma clearance is reduced in patients with severe renal impairment (creatinine clearance <30 ml/min), no dosage adjustment is recommended .

INDICATIONS AND USAGE:
Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Cancer Chemotherapy DANSET Injection is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin. DANSET is approved for patients aged 6 months and older. Prevention of Postoperative Nausea and/or Vomiting: DANSET 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, DANSET Injection is recommended even when the incidence of postoperative nausea and/or vomiting is low. For patients who do not receive prophylactic DANSET Injection and experience nausea and/or vomiting postoperatively, DANSET Injection may be given to prevent further episodes. DANSET is approved for patients aged 1 month and older.

DOSAGE AND ADMINISTRATION:
Prevention of Nausea and Vomiting Associated with Initial and Repeat Courses of Emetogenic Chemotherapy:
DANSET Injection should be diluted in 50 ml of 5% Dextrose Injection or 0.9% Sodium Chloride Injection before administration.
Adults: The recommended adult intravenous dosage of DANSET is three 0.15-mg/kg doses up to a maximum of 16 mg per dose. The first dose is infused over 15 minutes beginning 30 minutes before the start of emetogenic chemotherapy. Subsequent doses (0.15 mg/kg up to a maximum of 16 mg per dose) are administered 4 and 8 hours after the first dose of DANSET.
Pediatrics: For pediatric patients aged 6 months through 18 years, the intravenous dosage of DANSET is three 0.15-mg/kg doses up to a maximum of 16 mg per dose. The first dose is to be administered 30 minutes before the start of moderately to highly emetogenic chemotherapy. Subsequent doses (0.15 mg/kg up to a maximum of 16 mg per dose) are administered 4 and 8 hours after the first dose of DANSET. The drug should be infused intravenously over 15 minutes.
Prevention of Postoperative Nausea and Vomiting: DANSET Injection should not be mixed with solutions for which physical and chemical compatibility have not been established. In particular, this applies to alkaline solutions as a precipitate may form.
Adults: The recommended adult intravenous dosage of DANSET is 4 mg undiluted administered intravenously in not less than 30 seconds, preferably over 2 to 5 minutes, 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. Alternatively, 4 mg undiluted may be administered intramuscularly as a single injection for adults. While recommended as a fixed dose for patients weighing more than 40 kg, few patients above 80 kg have been studied. In patients who do not achieve adequate control of postoperative nausea and vomiting following a single, prophylactic, preinduction, intravenous dose of ondansetron 4 mg, administration of a second intravenous dose of 4 mg ondansetron postoperatively does not provide additional control of nausea and vomiting.
Pediatrics: For pediatric patients aged 1 month through 12 years, the dosage is a single 0.1-mg/kg dose for patients weighing 40 kg or less, or a single 4-mg dose for patients weighing more than 40 kg. The rate of administration should not be less than 30 seconds, preferably over 2 to 5 minutes immediately prior to or following anesthesia induction, or postoperatively if the patient did not receive prophylactic antiemetics and experiences nausea and/or vomiting occurring shortly after surgery. Prevention of further nausea and vomiting was only studied in patients who had not received prophylactic DANSET.
Stability and Handling: After dilution, do not use beyond 24 hours. Although DANSET Injection is chemically and physically stable when diluted as recommended, sterile precautions should be observed because diluents generally do not contain preservative. DANSET Injection is 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.
Note: Parenteral drug products should be inspected visually for particulate matter and discoloration before administration whenever solution and container permit.
Dosage Adjustment for Patients with Impaired Hepatic Function: 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 .

CONTRAINDICATIONS:
DANSET Injection is contraindicated for patients known to have hypersensitivity (e.g., anaphylaxis) to this product or any of its components. Anaphylactic reactions may be observed 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 was administered with ondansetron.

WARNINGS AND PRECAUTIONS:
Hypersensitivity Reactions: Hypersensitivity reactions, including anaphylaxis and bronchospasm, have been reported 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 . Avoid DANSET 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.
Serotonin Syndrome: The development of serotonin syndrome has been reported with 5-HT3 receptor antagonists. Most reports have been 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 reported cases were fatal. Serotonin syndrome occurring with overdose of DANSET alone has also been reported. The majority of reports of serotonin syndrome related to 5-HT3 receptor antagonist use occurred in a post-anesthesia care unit or an infusion center. 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). Patients should be monitored for the emergence of serotonin syndrome, especially with concomitant use of DANSET and other serotonergic drugs. If symptoms of serotonin syndrome occur, discontinue DANSET and initiate supportive treatment. Patients should be informed of the increased risk of serotonin syndrome, especially if DANSET is used concomitantly with other serotonergic drugs.
Masking of Progressive Ileus and Gastric Distension: The use of DANSET 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: DANSET is not a drug that stimulates gastric or intestinal peristalsis. It should not be used instead of nasogastric suction.

ADVERSE REACTIONS:
The following adverse reactions may be observed in adult patients treated with ondansetron. Adverse reactions observed when ondansetron is used for Chemotherapy-induced Nausea and Vomiting Diarrhea, Headache, Fever, Constipation, Rash.
Cardiovascular. Rare cases of angina (chest pain), electrocardiographic alterations, hypotension, and tachycardia, QT prolongation, ST segment depression, bradycardia.
Hepatic: In comparative trials in cisplatin chemotherapy patients with normal baseline values of aspartate transaminase (AST) and alanine transaminase (ALT), these enzymes have been reported to exceed twice the upper limit of normal in approximately 5% of patients. The increases were transient and did not appear to be related to dose or duration of therapy. On repeat exposure, similar transient elevations in transaminase values occurred in some courses, but symptomatic hepatic disease did not occur.
Neurological: There have been rare reports consistent with, but not diagnostic of, extrapyramidal reactions in patients receiving DANSET Injection and rare cases of grand mal seizure.
Other. Rare cases of hypokalemia.
Adverse reactions observed when ondansetron is used for Postoperative Nausea and Vomiting Headache, Drowsiness/sedation, Injection site reaction, Fever, Cold sensation, Pruritus and Paresthesia.

OTHER ADVERSE REACTIONS:
Local reactions: Pain, redness, burning at site of injection
Lower respiratory: Hiccups
Skin: Urticaria, Stenvens-Johnson syndrome, toxic epidermal necrolysis.
Eye disorders: Transient blindness
Neurological: Oculogyric crisis, appearing alone,as well as with other dystonic reactions.Transient dizziness during or shortly after intervenous administration.

DRUG INTERACTIONS:
Drugs Affecting Cytochrome P-450 Enzymes: Ondansetron does not 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 . On the basis of limited available data, no dosage adjustment is recommended for patients on these drugs.
Apomorphine: Based on reports of profound hypotension and loss of consciousness when apomorphine was 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 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.
Tramadol: Although there are no data on pharmacokinetic drug interactions between ondansetron and tramadol, data from two small trials indicate that concomitant use of ondansetron may result in reduced analgesic activity of tramadol. Patients on concomitant ondansetron self administered tramadol more frequently in these trials, leading to an increased cumulative dose in patient-controlled administration (PCA) of tramadol
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 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 have not been studied.

DRUG ABUSE AND DEPENDENCE:
Animal studies have shown that ondansetron is not discriminated as a benzodiazepine nor does it substitute for benzodiazepines in direct addiction studies.

OVERDOSAGE:
There is no specific antidote for ondansetron overdose. Patients should be managed with appropriate supportive therapy. Pediatric cases consistent with serotonin syndrome have been reported after inadvertent oral overdoses of ondansetron (exceeding estimated ingestion of 5 mg/kg) in young children. Reported symptoms included somnolence, agitation, tachycardia, tachypnea, hypertension, flushing, mydriasis, diaphoresis, myoclonic movements, horizontal nystagmus, hyperreflexia and seizure. Patients required supportive care, including intubation in some cases, with complete recovery without sequelae within 1 to 2 days.

INSTRUCTIONS:
Store below 30ºC. Protect from heat, sunlight & moisture. Keep out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Danset Tablet 8 mg	:	Pack of 2 x 6 tablets.
Danset Injection 8 mg/4 ml	:	Pack of 1 x 5 ampoules.

FOR FURTHER INFORMATIONS PLEASE CONTACT:

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۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

CCL
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