Zofra®

Ondansetron USP Orally Dispersible Tablet, Ondansetron Hydrochloride
USP Oral Solution and Injection

DESCRIPTION

Zofra® ODT is a preparation of Ondansetron base, Zofra® Oral Solution and Zofra® IM/IV Injection is the preparation of Ondansetron Hydrochloride, the racemic form of ondansetron which is a selective 5HT$_3$ receptor antagonist.

INDICATIONS

Zofra® ODT, Oral Solution and IM/IV Injection is indicated for :

The management of nausea and vomiting induced by cytotoxic chemotherapy, for the prevention and treatment of post-operative nausea and vomiting and for the prevention of nausea and vomiting associated with radiotherapy, either total body irradiation or single high dose fraction or daily fractions to the abdomen.

DOSAGE AND ADMINISTRATION

Instructions for use Zofra® ODT:

With dry hands, push back the foil of 1 tablet and gently remove the tablet. Immediately place the Zofra® ODT on top of the tongue where it will dissolve in seconds, then swallow with saliva. Administration with liquid is not necessary.

Prevention of nausea and vomiting associated with emetogenic cancer chemotherapy:

Adults : The recommended adult oral dosage is one 8 mg Zofra® ODT or 10 ml of Zofra® Oral Solution given twice a day. The first dose should be administered 30 minutes before the start of emetogenic chemotherapy, with a subsequent dose 8 hours after the first dose. One 8 mg Zofra® ODT or 10 ml of Zofra® Oral Solution should be administered twice a day (every 12 hours) for 1 to 2 days after completion of chemotherapy. Zofra® IM/IV Injection - A dose of 8 mg by slow IM or IV injection immediately before chemotherapy, followed by two further IM or IV doses of 8 mg two to four hours apart, or by constant infusion of 1 mg/hour for up to 24 hours.

OR

A single dose of 32 mg diluted in 50-100 ml of saline or other compatible infusion fluid, infused over not less than 15 minutes immediately before chemotherapy.

Children : Patients 12 years of age and older, the dosage is the same as for adults. Patients 4 to 11 years of age, the dosage is one 4 mg Zofra® ODT or 5 ml of Zofra® Oral Solution given 3 times a day. The first dose should be administered 30 minutes before the start of emetogenic chemotherapy, with subsequent dose 4 and 8 hours after the first dose. One 4 mg Zofra® ODT or 5 ml of Zofra® Oral Solution should be administered 3 times a day (every 8 hours) for 1 to 2 days after the completion of chemotherapy.

Zofra® IM/IV Injection - Experience is currently limited, but Ondansetron was effective and well tolerated in children over the age of 4 years, when given intravenously at a dose of 5 mg/m^2 over 15 minutes, immediately before chemotherapy.

For prevention of post-operative nausea and vomiting in paediatric patients two years and older having surgery performed under general anesthesia, Zofra® IM/IV Injection 8 mg/4 ml, may be administered by slow intravenous injection at a dose of 0.1 mg/kg up to a maximum of 4 mg prior to, at or after induction of anesthesia. For the treatment of established post-operative nausea and vomiting in paediatric patients two years and older Zofra® IM/IV Injection 8 mg/4 ml may be administered by slow intravenous injection at a dose of 0.1 mg/kg up to a maximum of 4 mg. Repeat dosing for paediatric patients who continue to experience nausea and/or vomiting has not been studied and should not be given.

Elderly : Zofra® ODT / Zofra® Oral Solution is well tolerated by patients over 65 years and no alteration of dosage, dosing frequency or route of administration are required.

Zofra® IM/IV Injection - Efficacy and tolerance in patients over 65 years was similar to that seen in younger adults indicating no need to alter dosage or route of administration in the elderly.

Prevention of postoperative nausea and vomiting:

Adults: The recommended dosage is 16 mg given as two 8 mg Zofra® ODT or 20 ml of Zofra® Oral Solution one hour before induction of anesthesia or 8 mg Zofra® ODT or 10 ml of Zofra® Oral Solution by mouth an hour before anesthesia followed by 2 further doses of 8 mg or 10 ml of Zofra® Oral Solution at 8-hour intervals.

Zofra® IM/IV Injection - Immediately before induction of anesthesia, or post-operatively if the patient experiences nausea and/or vomiting occurring shortly after surgery, administer 4 mg undiluted intramuscularly or intravenously. If given intravenously, it must be administered in not less than 30 seconds, preferably over 2 -5 minutes. Repeat dosing for patients who continue to experience nausea and/or vomiting postoperatively has not been studied. While recommended as a fixed dose for all, few patients above 80 kg or below 40 kg have been studied.

Children: Aged 2 years and over may be given up to a maximum dose of 4 mg Zofra® ODT or 5 ml of Zofra® Oral Solution, both for prevention and treatment of post operative nausea and vomiting.

Zofra® IM/IV Injection - For prevention of post-operative nausea and vomiting in paediatric patients two years and older having surgery performed under general anaesthesia, Zofra® IM/IV Injection 8 mg/4 ml may be administered by slow intravenous injection at a dose of 0.1 mg/kg up to a maximum of 4 mg prior to, at or after induction of anaesthesia. For the treatment of established post-operative nausea and vomiting in paediatric patients two years and older, Zofra® IM/IV Injection 8 mg/4 ml may be administered by slow intravenous injection at a dose of 0.1 mg/kg up to a maximum of 4 mg. Repeat dosing for paediatric patients who continue to experience nausea and/or vomiting has not been studied, and should thus not be given.

Elderly: The dosage is the same as for the adults. Safety and efficacy have not been established with the use of Zofra® IM/IV Injection 8 mg/4 ml in the prevention and treatment of post-operative nausea and vomiting in the elderly.
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 and serum half-life significantly prolonged in subjects with moderate or severe impairment of hepatic function. In such patients a total daily dose of 8 mg should not be exceeded.
Clearance of Zofra® IM/IV Injection 8 mg/4 ml is significantly reduced and serum half-life significantly prolonged in patients with moderate or severe impairment of hepatic function. In such patients, a total daily dose of 8 mg should not be exceeded.
Prevention of nausea and vomiting associated with radiotherapy
Adults : The recommended adult oral dosage is one 8 mg Zofra® ODT or 10 ml of Zofra® Oral Solution given 3 times a day.
For total body irradiation, one 8 mg Zofra® ODT or 10 ml of Zofra® Oral Solution should be administered 1 to 2 hours before each fraction of radiotherapy administered each day.
For single high-dose fraction radiotherapy to the abdomen, one Zofra® ODT 8 mg or 10 ml of Zofra® Oral Solution should be administered 1 to 2 hours before radiotherapy, with subsequent doses every 8 hours after the first dose for 1 to 2 days after completion of radiotherapy.
For daily fractionated radiotherapy to the abdomen, one Zofra® ODT 8 mg or 10 ml of Zofra® Oral Solution should be administered 1 to 2 hours before radiotherapy, with subsequent doses every 8 hours after the first dose for each day radiotherapy is given.
For most patients receiving radiotherapy Zofra® IM/IV Injection 8 mg/4 ml, 8 mg should be administered as a slow IM or IV injection immediately before treatment.
Children : There is no experience with the use of Zofra® ODT or Zofra® Oral Solution in the prevention of radiation induced nausea and vomiting in pediatric patients of 4 years or younger.
Elderly : Efficacy and tolerance in patients over 65 years was similar to that seen in younger adults indicating no need to alter dosage or route of administration in the elderly.

CONTRAINDICATIONS
Ondansetron is contraindicated in patients known to have hypersensitivity to the drug.

PRECAUTIONS
Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5-HT_3 receptor antagonists. As Ondansetron is known to increase large bowel transit time, patients with signs of sub acute intestinal obstruction should be monitored following administration.

DRUG INTERACTION
Potent inducers (i.e. phenytoin, carbamazepine, and rifampicin) of CYP3A4 : 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.

SIDE-EFFECTS
Headache, a sensation of flushing or warmth, hiccups, constipation may occur. Blurred vision, chest pain with or without ST segment depression, cardiac arrhythmias, hypotension and bradycardia have been rarely reported.

USE IN PREGNANCY & LACTATION
Pregnancy category B. Reproduction studies at daily oral dose up to 10 and 30 mg/kg/day have been performed in animals and have revealed no evidence of impaired fertility harm to the fetus due to Ondansetron. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Tests have shown that Ondansetron passes into the milk of lactating animals. It is not known whether Ondansetron is excreted in human milk. Caution should be exercised when Ondansetron is administered to nursing women.

PHARMACEUTICAL PRECAUTION
Keep away from light, store in a cool (below 30^0 C for Zofra® ODT, 2^0 C - 30^0 C for Zofra® IM/IV Injection) and dry place. Keep out of reach of children. Do not keep Zofra® oral solution in freeze.

PACKAGING

Zofra® ODT 4	:	Box containing 2 strips of 10 tablets each. Each orally dispersible tablet contains Ondansetron USP 4 mg.
Zofra® ODT 8	:	Box containing 2 strips of 10 tablets each. Each orally dispersible tablet contains Ondansetron USP 8 mg.
Zofra® Oral Solution	:	Each amber glass bottle contains 50 ml oral solution. Each 5 ml solution contains Ondansetron Hydrochloride USP equivalent to Ondansetron 4 mg.
Zofra® IM/IV Injection	:	Box containing 1 strip of 5 ampoules. Each ampoule (4 ml) contains Ondansetron Hydrochloride USP equivalent to Ondansetron 8 mg.

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