# ZOFRAN™ INJECTION

10000000109476

## Ondansetron hydrochloride dihydrate

### QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1 ml of aqueous solution contains 2 mg ondansetron as hydrochloride dihydrate.

### PHARMACEUTICAL FORM
A clear, colourless, sterile solution for injection or infusion.

### CLINICAL PARTICULARS
**Indications**
*ZOFRAN* injection is indicated for the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy.

*ZOFRAN* is also indicated for the prevention and treatment of post-operative nausea and vomiting.

**Dosage and Administration**
*ZOFRAN* is available for oral, parenteral and rectal use to allow the route of administration and dosing to be flexible.

**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. The selection of dose regimen should be determined by the severity of the emetogenic challenge.

**Populations**
- **Adults**

**EMETOGENIC CHEMOTHERAPY AND RADIOTHERAPY**
The recommended intravenous (IV) or intramuscular (IM) dose of *ZOFRAN* is 8 mg administered as a slow injection immediately before treatment.

Oral or rectal treatment is recommended to protect against delayed or prolonged emesis after the first 24 hours.

**HIGHLY EMETOGENIC CHEMOTHERAPY e.g. high-dose cisplatin**
*ZOFRAN* can be given by oral, IV, IM or rectal administration.

*ZOFRAN* may be administered as a single 8 mg IV or IM dose immediately before chemotherapy. Doses of greater than 8 mg up to 16 mg of *ZOFRAN* may only be given by IV infusion diluted in 50 to 100 ml of saline or other compatible infusion fluid *(see Instructions for Use and Handling)* and infused over not less than 15 minutes. A single dose greater than 16 mg should not be given. (*see Warnings and Precautions*)

For management of highly emetogenic chemotherapy, a dose of 8 mg of *ZOFRAN* may be administered by slow IV in not less than 30 seconds, or IM injection immediately before chemotherapy, followed by two further IV or IM doses of 8 mg 2 to 4 hours apart, or by a constant infusion of 1 mg/h for up to 24 hours.

The efficacy of *ZOFRAN* in highly emetogenic chemotherapy may be enhanced by the addition of a single IV dose of dexamethasone sodium phosphate 20 mg, administered prior to chemotherapy.

Oral or rectal treatment is recommended to protect against delayed or prolonged emesis after the first 24 hours.

- **CINV in Children and Adolescents (aged 6 months to 17 years)**

The dose for CINV can be calculated based on body surface area (BSA) or weight. In paediatric clinical studies, *ZOFRAN* was given by IV infusion diluted in 25 to 50 ml of saline or other compatible infusion fluid (*see Instructions for Use and Handling*) and infused over not less than 15 minutes.

**Dosing by BSA**
*ZOFRAN* should be administered immediately before chemotherapy as a single IV dose of 5 mg/m². The IV dose must not exceed 8 mg. Oral dosing can commence 12 hours later and may be continued for up to 5 days (Table 1). Adult doses must not be exceeded.

**Table 1. BSA-based dosing for CINV (aged 6 months to 17 years)**

| BSA | Day 1 | Days 2 - 6 |
|---|---|---|
| < 0.6 m² | 5 mg/m² IV plus 2 mg syrup after 12 hours | 2 mg syrup every 12 hours |
| ≥ 0.6 m² to ≤ 1.2 m² | 5 mg/m² IV plus 4 mg syrup or tablet after 12 hours | 4 mg syrup or tablet every 12 hours |
| > 1.2 m² | 5 mg/m² IV or 8 mg IV plus 8 mg syrup or tablet after 12 hours | 8 mg syrup or tablet every 12 hours |

**Dosing by body weight**
*ZOFRAN* should be administered immediately before chemotherapy as a single IV dose of 0.15 mg/kg. The IV dose must not exceed 8 mg. On Day 1, two further IV doses may be given in 4-hourly intervals. Oral dosing can commence 12 hours later and may be continued for up to 5 days (Table 2). Adult doses must not be exceeded.

**Table 2. Weight-based dosing for CINV (aged 6 months to 17 years)**

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

- **Elderly**

*ZOFRAN* is well tolerated by patients over 65 years and no alteration of dosage, dosing frequency or route of administration are 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 8 mg IV or oral should not be exceeded and therefore.

- **Patients with Poor Sparteine/Debrisoquine Metabolism**

The elimination half-life of ondansetron is not altered in subjects classified as poor metabolisers of sparteine and debrisoquine. Consequently in such patients repeat dosing will give drug exposure levels no different from those of the general population. No alteration of daily dosage or frequency of dosing are required.

**POST-OPERATIVE NAUSEA AND VOMITING (PONV)**
- **PONV in Adults**

For prevention of post-operative nausea and vomiting, the recommended dose of *ZOFRAN* injection is a single dose of 4 mg by IM or slow IV injection administered at the induction of anaesthesia.

For treatment of established post-operative nausea and vomiting, a single dose of 4 mg given by IM or slow IV injection is recommended.

- **PONV in Children and Adolescents (aged 1 month to 17 years)**

For prevention and treatment of PONV in paediatric patients having surgery performed under general anaesthesia, *ZOFRAN* may be administered by slow IV injection (not less than 30 seconds) at a dose of 0.1 mg/kg up to a maximum of 4 mg either prior to, at or after induction of anaesthesia, or after surgery.

- **Elderly**

There is limited experience in the use of *ZOFRAN* in the prevention and treatment of post-operative nausea and vomiting in the elderly, however *ZOFRAN* is well tolerated in patients over 65 years receiving chemotherapy.

- **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 8 mg IV or oral should not be exceeded.

- **Patients with Poor Sparteine/Debrisoquine Metabolism**

The elimination half-life of ondansetron is not altered in subjects classified as poor metabolisers of sparteine and debrisoquine. Consequently in such patients repeat dosing will give drug exposure levels no different from those of the general population. No alteration of daily dosage or frequency of dosing are required.

**Contraindications**
Based on reports of profound hypotension and loss of consciousness when ondansetron was administered with apomorphine hydrochloride, concomitant use with apomorphine is contraindicated.

Hypersensitivity to any component of the preparation.

**Warnings and Precautions**
Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective $5HT_3$ receptor antagonists.

Ondansetron prolongs the QT interval in a dose-dependent manner (*see Clinical Pharmacology*). 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, bradyarrhythmias or patients taking other medicinal products that lead to QT prolongation or electrolyte abnormalities.

Hypokalemia and hypomagnesemia should be corrected prior to ondansetron administration.

As *ZOFRAN* is known to increase large bowel transit time, patients with signs of subacute intestinal obstruction should be monitored following administration.

**Interactions**
There is no evidence that *ZOFRAN* either induces or inhibits the metabolism of other drugs commonly co-administered with it. Specific studies have shown that there are no pharmacokinetic interactions when *ZOFRAN* is administered with alcohol, temazepam, furosemide, tramadol or propofol.

Ondansetron is metabolised by multiple hepatic cytochrome P450 enzymes: CYP3A4, CYP2D6 and CYP1A2. 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. (*see Warnings and Precautions*)

**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.

**Pregnancy and Lactation**
**Pregnancy**
The safety of *ZOFRAN* for use in human pregnancy has not been established. Evaluation of experimental animal studies does not indicate direct or indirect harmful effects with respect to the development of the embryo, or foetus, the course of gestation and peri- and post-natal development. However as animal studies are not always predictive of human response, the use of *ZOFRAN* in pregnancy is not recommended.

**Lactation**
Tests have shown that ondansetron passes into the milk of lactating animals. It is therefore recommended that mothers receiving *ZOFRAN* should not breast-feed their babies.

**Effects on Ability to Drive and Use Machines**
In psychomotor testing *ZOFRAN* does not impair performance nor cause sedation. No detrimental effects on such activities are predicted from the pharmacology of *ZOFRAN*.

**Adverse Reactions**
Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10,000 to <1/1000); and very rare (<1/10,000), including isolated reports. Very common, common and uncommon events were generally determined from clinical trial data. The incidence in placebo was taken into account. Rare and very rare events were generally determined from post-marketing spontaneous data.

The following frequencies are estimated at the standard recommended doses of *ZOFRAN*. The adverse event profiles in children and adolescents were comparable to that seen in adults.

**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) have been observed without definitive evidence of persistent clinical sequelae.
Rare: Dizziness 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.

The majority of the blindness cases reported resolved within 20 minutes. Most patients had received chemotherapeutic agents, which included cisplatin. Some cases of transient blindness were reported as cortical in origin.

**Cardiac disorders**
Uncommon: Arrhythmias, chest pain with or without ST segment depression, bradycardia.
Rare: QTc prolongation (including Torsade de Pointes)

**Vascular disorders**
Common: Sensation of warmth or flushing.
Uncommon: Hypotension.

**Respiratory, thoracic and mediastinal disorders**
Uncommon: Hiccups.

**Gastrointestinal disorders**
Common: Constipation
Local burning sensation following insertion of suppositories.

**Hepatobiliary disorders**
Uncommon: Asymptomatic increases in liver function tests#.
#These events were observed commonly in patients receiving chemotherapy with cisplatin.

**General disorders and administration site conditions**
Common: Local IV injection site reactions.

**Overdose**
**Symptoms and Signs**
There is limited experience of *ZOFRAN* overdose. In the majority of cases, symptoms were similar to those already reported in patients receiving recommended doses *(see Adverse Reactions)*.

Ondansetron prolongs QT interval in a dose-dependent fashion. ECG monitoring is recommended in cases of overdose.

**Treatment**
There is no specific antidote for *ZOFRAN*, therefore in cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate.

The use of ipecacuanha to treat overdose with *ZOFRAN* is not recommended as patients are unlikely to respond due to the anti-emetic action of ondansetron itself.

**PHARMACOLOGICAL PROPERTIES**
**Pharmacodynamics**
**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.

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 $5HT_3$ 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.

**Pharmacodynamic Effects**
Ondansetron does not alter plasma prolactin concentrations.

**QT Prolongation**
The effect of ondansetron on the QTc interval was evaluated in a double blind, randomized, placebo and positive (moxifloxacin) controlled, crossover study in 58 healthy adult men and women. Ondansetron doses included 8 mg and 32 mg infused intravenously over 15 minutes. At the highest tested dose of 32 mg, the maximum mean (upper limit of 90% CI) difference in QTcF from placebo after baseline-correction was 19.6 (21.5) msec. At the lower tested dose of 8 mg, the maximum mean (upper limit of 90% CI) difference in QTcF from placebo after baseline-correction was 5.8 (7.8) msec. In this study, there were no QTcF measurements greater than 480 msec and no QTcF prolongation was greater than 60 msec.

**Pharmacokinetics**
The pharmacokinetic properties of ondansetron are unchanged on repeat dosing.

**Absorption**
Equivalent systemic exposure is achieved after IM and IV administration of ondansetron.

**Distribution**
Ondansetron is not highly protein bound (70 to 76%).

The disposition of ondansetron following oral, IM or IV dosing in adults is similar with a steady state volume of distribution of about 140 L.

**Metabolism**
Ondansetron is cleared from the systemic circulation predominantly by hepatic metabolism through multiple enzymatic pathways. The absence of the enzyme CYP2D6 (the debrisoquine polymorphism) has no effect on ondansetron's pharmacokinetics.

**Elimination**
Ondansetron is cleared from the systemic circulation predominantly by hepatic metabolism. Less than 5% of the absorbed dose is excreted unchanged in the urine.

The disposition of ondansetron following oral, IM or IV dosing is similar with a terminal elimination half-life of about 3 hours.

***Special Patient Populations***
- **Gender**

Gender differences were shown in the disposition of ondansetron, with females having a greater rate and extent of absorption following an oral dose and reduced systemic clearance and volume of distribution (adjusted for weight).

- **Children and Adolescents (aged 1 month to 17 years)**

In paediatric patients aged 1 to 4 months (n=19) undergoing surgery, weight-normalised clearance was approximately 30% slower than in patients aged 5 to 24 months (n=22) but comparable to the patients aged 3 to 12 years. The half-life in the 1 to 4 month patient population was reported to average 6.7 hours compared to 2.9 hours for patients in the 5 to 24 month and 3 to 12 year age range. The differences in pharmacokinetic parameters in the 1 to 4 month patient population can be explained in part by the higher percentage of total body water in neonates and infants and a higher volume of distribution for water soluble drugs like ondansetron.

In paediatric patients aged 3 to 12 years undergoing elective surgery with general anaesthesia, the absolute values for both the clearance and volume of distribution of ondansetron were reduced in comparison to values with adult patients. Both parameters increased in a linear fashion with weight and by 12 years of age, the values were approaching those of young adults. When clearance and volume of distribution values were normalised by body weight, the values for these parameters were similar between the different age group populations. Use of weight-based dosing compensates for age-related changes and is effective in normalising systemic exposure in paediatric patients.

Population pharmacokinetic analysis was performed on 428 subjects (cancer patients, surgery patients and healthy volunteers) aged 1 month to 44 years following IV administration of ondansetron. Based on this analysis, systemic exposure (AUC) of ondansetron following oral or IV dosing in children and adolescents was comparable to adults, with the exception of infants aged 1 to 4 months. Volume of distribution was related to age and was lower in adults than in infants and children. Clearance was related to weight but not to age with the exception of infants aged 1 to 4 months. It is difficult to conclude whether there was an additional reduction in clearance related to age in infants 1 to 4 months or simply inherent variability due to the low number of subjects studied in this age group. Since patients less than 6 months of age will only receive a single dose in PONV a decreased clearance is not likely to be clinically relevant.

- **Elderly**

Studies in healthy elderly volunteers show slight age-related increases in both oral bioavailability and half-life of ondansetron.

- **Renal Impairment**

In patients with moderate renal impairment (creatinine clearance 15 to 60 ml/min), both systemic clearance and volume of distribution are reduced following IV administration of ondansetron, resulting in a slight, but clinically insignificant, increase in elimination half-life (5.4 hours). A study in patients with severe renal impairment who required regular haemodialysis (studied between dialyses) showed ondansetron's pharmacokinetics to be essentially unchanged following IV administration.

- **Hepatic Impairment**

In patients with severe hepatic impairment, ondansetron's systemic clearance is markedly reduced with prolonged elimination half-lives (15 to 32 hours) and an oral bioavailability approaching 100% due to reduced pre-systemic metabolism.

**Pre-Clinical Safety Data**
A study in cloned human cardiac ion channels has shown ondansetron has the potential to affect cardiac repolarisation via blockade of hERG potassium channels at clinically relevant concentrations. Dose-dependent QT prolongation has been observed in a thorough QT study in human volunteers (*see Clinical Pharmacology – QT prolongation*).

**PHARMACEUTICAL PARTICULARS**
**List of Excipients**
Ampoules/pre-filled syringes contain:
Sodium chloride
Citric acid monohydrate
Sodium citrate
Water for Injection

In addition the multidose vials also contain the following antimicrobial preservatives:
Methyl hydroxybenzoate
Propyl hydroxybenzoate

**Incompatibilities**
*ZOFRAN* injection should not be administered in the same syringe or infusion as any other medication *(see Instructions for Use and Handling)*.

*ZOFRAN* injection should only be mixed with those infusion solutions which are recommended *(see Instructions for Use and Handling)*.

**Shelf-Life**
The expiry date is indicated on the packaging.

**Special Precautions for Storage**
Store below 30°C.

Protect from light.

**Nature and Contents of Container**
*ZOFRAN* injection is available in glass or plastic ampoules, multidose vials and as a pre-filled syringe.

Glass or plastic ampoules containing ondansetron 4 mg in 2 ml.
Glass or plastic ampoules containing ondansetron 8 mg in 4 ml.
Multidose vials containing ondansetron 40 mg in 20 ml.
Pre-filled syringe containing ondansetron 4 mg in 2 ml.

**Instructions for Use/Handling**
***Injection (unpreserved) ampoules/pre-filled syringe:***
The solution for injection and pre-filled syringe formulations are **unpreserved,** should only be used once and injected or diluted immediately after opening. Any remaining solution should be discarded.

Ondansetron injection ampoules should not be autoclaved.

Compatibility studies have been carried out in polyvinyl chloride infusion bags and polyvinyl chloride administration sets. Stability is conferred by the use of polyethylene infusion bags or Type 1 glass bottles.

Dilutions of unpreserved ondansetron injection in sodium chloride 0.9% w/v or in dextrose 5% w/v have been demonstrated to be stable in polypropylene syringes. Therefore, it is considered that unpreserved ondansetron injection diluted with compatible infusion fluids recommended below would also be stable in polypropylene syringes.

In keeping with good pharmaceutical practice, IV solutions should be prepared at the time of infusion, under appropriate aseptic conditions.

**Compatibility with IV fluids**
Compatibility studies have shown that unpreserved ondansetron injection is stable for seven days at room temperature (below 25 °C) under fluorescent lighting or in a refrigerator with the following IV infusion fluids:
- Sodium Chloride IV Infusion BP 0.9% w/v.
- Glucose IV Infusion BP 5% w/v.
- Mannitol IV Infusion BP 10% w/v.
- Ringers IV Infusion.
- Potassium Chloride 0.3% w/v and Sodium Chloride 0.9% w/v IV Infusion BP.
- Potassium Chloride 0.3% w/v and Glucose 5% w/v IV Infusion BP.

**Compatibility with other drugs**
Ondansetron may be administered by IV infusion at 1 mg/h, from an infusion bag or syringe pump. The following drugs may be administered via the Y-site of the ondansetron giving set for ondansetron concentrations of 16 to 160 micrograms/mL (e.g. 8 mg/500mL and 8 mg/50mL respectively):

| | |
|---|---|
| Cisplatin | Concentrations up to 0.48 mg/mL (e.g. 240 mg in 500 mL) administered over one to eight hours. |
| 5-fluorouracil | Concentrations up to 0.8 mg/mL (e.g. 2.4 g in 3 litres or 400 mg in 500 mL) administered at a rate of at least 20 mL/h (500 mL per 24 hours). Higher concentrations of 5-fluorouracil may cause precipitation of ondansetron. The 5-fluorouracil infusion may contain up to 0.045 % w/v magnesium chloride in addition to other excipients shown to be compatible. |
| Carboplatin | Concentrations in the range 0.18 mg/mL to 9.9 mg/mL (e.g. 90 mg in 500 mL to 990 mg in 100 mL), administered over 10 minutes to 1 hour. |
| Etoposide | Concentrations in the range 0.144 mg/mL to 0.25 mg/mL (e.g.. 72 mg in 500 mL to 250 mg in 1L), administered over 30 minutes to 1 hour. |
| Ceftazidime | Doses in the range 250 mg to 2000 mg reconstituted with Water for Injections BP as recommended by the manufacturer (e.g. 2.5 mL for 250 mg and 10 mL for 2 g ceftazidime) and given as an IV bolus injection over approximately five minutes. |
| Cyclophosphamide | Doses in the range 100 mg to 1 g, reconstituted with Water for Injections BP, 5 mL per 100 mg cyclophosphamide, as recommended by the manufacturer, and given as an IV bolus injection over approximately 5 minutes. |
| Doxorubicin | Doses in the range 10 to 100 mg reconstituted with Water for Injections BP, 5 mL per 10 mg doxorubicin, as recommended by the manufacturer and given as an IV bolus injection over approximately five minutes. |
| Dexamethasone | Dexamethasone sodium phosphate 20 mg may be administered as a slow IV injection over 2 to 5 minutes via the Y-site of an infusion set delivering 8 to 16 mg of ondansetron diluted in 50 to 100 mL of a compatible infusion fluid over approximately 15 minutes. Compatibility between dexamethasone sodium phosphate and ondansetron has been demonstrated supporting administration of these drugs through the same giving set resulting in concentrations in line of 32 micrograms to 2.5 mg/mL for dexamethasone sodium phosphate and 8 micrograms to 1 mg/mL for ondansetron. |

***Injection (preserved) multidose vials:***
Compatibility studies have been carried out in polyvinyl chloride infusion bags and polyvinyl chloride administration sets. Stability is conferred by the use of polyethylene infusion bags or Type 1 glass bottles.

Dilutions of unpreserved ondansetron injection in sodium chloride 0.9% w/v or in dextrose 5% w/v have been demonstrated to be stable in polypropylene syringes. Therefore, it is considered that preserved ondansetron injection diluted with compatible infusion fluids below would also be stable in polypropylene syringes.

In keeping with good pharmaceutical practice, IV solutions should be prepared at the time of infusion, under appropriate aseptic conditions.

**Compatibility with IV fluids**
Compatibility studies have shown that preserved ondansetron injection is stable for 48 hours at room temperature (below 25 °C) with the following IV infusion fluids:
- Sodium Chloride IV Infusion BP 0.9% w/v.
- Sodium Chloride IV Infusion BP 3% w/v.
- Glucose IV Infusion BP 5% w/v.
- Sodium Chloride 0.9% w/v and Glucose 5% w/v IV Infusion BP.
- Sodium Chloride 0.45% w/v and Glucose 5% w/v IV Infusion BP.

Although compatibility studies have not been undertaken, in-line with the unpreserved ampoule formulation, it is considered that stability would also be maintained with the following IV infusion fluids:
- Mannitol IV Infusion BP 10% w/v.
- Ringers IV Infusion.
- Potassium Chloride 0.3% w/v and Sodium Chloride 0.9% w/v IV Infusion BP.
- Potassium Chloride 0.3% w/v and Glucose 5% w/v IV Infusion BP.

**Compatibility with other drugs**
*ZOFRAN* diluted in a compatible infusion fluid may be infused at a rate of 1mg per hour from an infusion bag or syringe pump. The following drugs may be administered via the Y-site of the giving set:

| | |
|---|---|
| Cisplatin | Concentrations up to 0.5 mg/mL (e.g. 250 mg in 500 mL) given over 1 to 8 hours via the Y-site of an infusion set delivering ondansetron concentrations of 3 to 150 micrograms/mL (e.g. 1.5 mg/500 mL and 7.5 mg/50 mL respectively). |
| Dexamethasone sodium phosphate | 20 mg given as a slow IV injection over 2 to 5 mins via the Y-site of an infusion set delivering ondansetron 8 mg/50 mL. |

Not all presentations are available in every country.

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