NOVARTIS

TRADE NAME

Zofran™

DESCRIPTION AND COMPOSITION

Pharmaceutical form

A clear, colourless, sterile solution for injection or infusion. Each 1 mL of aqueous solution contains 2 mg ondansetron as hydrochloride dihydrate.

Active substance

Ondansetron

Excipients

Ampoules contain:

Sodium chloride
Citric acid monohydrate
Sodium citrate
Water for Injection

INDICATIONS

Adults

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.

Paediatric Population

Injection and oral formulations:

ZOFRAN is indicated for the management of nausea and vomiting induced by cytotoxic chemotherapy.

No studies have been conducted on the use of orally administered ondansetron in the prevention or treatment of post-operative nausea and vomiting; IV injection is recommended for this purpose.

DOSAGE REGIMEN AND ADMINISTRATION

Dosing Regimen

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.

CINV and RINV in Adults

The recommended intravenous (IV) or intramuscular (IM) dose of *ZOFRAN* is 8 mg administered immediately before treatment.

For highly emetogenic chemotherapy, a maximum initial ondansetron dose of 16 mg IV infused over 15 minutes may be used. A single IV dose greater than 16 mg should not be given due to dose-dependent increase of QT prolongation risk (see sections WARNINGS AND PRECAUTIONS, ADVERSE DRUG REACTIONS, CLINICAL PHARMACOLOGY).

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.

IV doses greater than 8 mg and up to a maximum of 16 mg must be diluted in 50 mL to 100 mL of 0.9% Sodium Chloride Injection or 5% Dextrose Injection before administration and infused over not less than 15 minutes (see section PHARMACEUTICAL INFORMATION - Instructions for Use and Handling). *ZOFRAN* doses of 8 mg or less, do not need to be diluted and may be administered as a slow IM or IV injection in not less than 30 seconds.

The initial dose of *ZOFRAN* may be followed by 2 additional IV or IM doses of 8 mg by 2 to 4 hours apart, or by a constant infusion of 1 mg/h for up to 24 hours.

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

CINV in Children and Adolescents (aged 2 years and over)

In children with a body surface area of 0.6 to 1.2 m^2 ondansetron is administered as a single IV dose of 5 mg/m^2 immediately before chemotherapy, followed by 4 mg orally 12 hours later. 4 mg orally twice daily can be continued for up to five days after a course of treatment.

CINV and RINV in Elderly

In patients 65 to 74 years of age, the initial IV dose of *ZOFRAN* 8 mg or 16 mg, infused over 15 minutes, may be followed by 2 doses of 8 mg infused over 15 minutes and given no less than 4 hours apart. All IV doses should be diluted in 50-100 mL of saline or other compatible infusion fluid and infused over 15 minutes

In patients 75 years of age or older, the initial IV dose of *ZOFRAN* should not exceed 8 mg infused over 15 minutes. The initial dose of 8 mg may be followed by 2 doses of 8 mg, infused over 15 minutes and given no less than 4 hours apart (see section CLINICAL PHARMACOLOGY - Special Patient Populations, Elderly). All IV doses should be diluted in 50-100 mL of saline or other compatible infusion fluid and infused over 15 minutes.

POST-OPERATIVE NAUSEA AND VOMITING

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 2 years and over)

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.

There is limited data on the use of *ZOFRAN* in the prevention and treatment of PONV in children under 2 years of age.

PONV in 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.

Special populations

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 is 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 (see section INTERACTIONS).

Hypersensitivity to any components of the preparation (see sections WARNINGS AND PRECAUTIONS and ADVERSE DRUG REACTIONS).

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 section 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.

Therefore, caution should be exercised in patients with cardiac rhythm or conduction disturbances, in patients treated with anti-arrhythmic agents or beta-adrenergic blocking agents and in patients with significant electrolyte disturbances.

Myocardial ischemia has been reported in patients treated with ondansetron. In some cases, predominantly during intravenous administration, the symptoms appeared immediately after administration but recovered with prompt treatment. Therefore, caution should be exercised during and after administration of ondansetron.

Hypokalemia and hypomagnesemia should be corrected prior to ondansetron administration.

Serotonin syndrome has been described following the concomitant use of *ZOFRAN* and other serotonergic drugs (see section INTERACTIONS). If concomitant treatment with *ZOFRAN* and other serotonergic drugs is clinically warranted, appropriate observation of the patient is advised.

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

ADVERSE DRUG REACTIONS

Summary of the safety profile

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 predominantly 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.

Skin and subcutaneous tissue disorders

Very rare: Toxic skin eruption, including toxic epidermal necrolysis.

General disorders and administration site conditions

Common: Local IV injection site reactions.

Adverse drug reactions from spontaneous reports and literature cases (frequency not known)

The following adverse drug reactions have been derived from post-marketing experience with Zofran/Zydis via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate

their frequency which is therefore categorized as not known. Adverse drug reactions are listed according to system organ classes in MedDRA.

Cardiac disorders

Myocardial ischemia

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 P-450 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.

Use of *ZOFRAN* with QT prolonging drugs and/or drugs that cause electrolyte abnormalities may result in additional QT prolongation. Concomitant use of *ZOFRAN* with cardiotoxic drugs (e.g. anthracyclines) may increase the risk of arrhythmias. Therefore, caution should be exercised when ondansetron is co-administered with drugs that prolong the QT interval and/or cause electrolyte abnormalities and/or cardiotoxic drugs (see section 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.

Serotonergic Drugs (e.g., SSRIs and SNRIs)

Serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) has been described following the concomitant use of *ZOFRAN* and other serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs) and serotonin noradrenaline reuptake inhibitors (SNRIs) (see section WARNINGS AND PRECAUTIONS).

Tramadol

Data from small studies indicate that ondansetron may reduce the analgesic effect of tramadol.

PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL

Pregnancy

Risk Summary

In human epidemiological studies, an increase in orofacial clefts was observed in infants of women administered ondansetron during the first trimester of pregnancy(see Human data). Regarding cardiac malformations the epidemiological studies showed conflicting results.

Reproductive studies in rats and rabbits did not show evidence of harm to the fetus (see Animal data).

The use of ondansetron in pregnancy is not recommended.

Human Data

Three epidemiological studies in the US assessed the risk of specific congenital anomalies, including orofacial clefts and cardiac malformations in offspring born to mothers exposed to ondansetron during the first trimester of pregnancy.

One cohort study with 88,467 pregnancies exposed to ondansetron showed an increased risk of oral clefts (3 additional cases per 10, 000 women treated, adjusted relative risk (RR), 1.24 (95% CI 1.03-1.48)) without an apparent increase in risk of cardiac malformations. A separately published subgroup analysis of 23,877 pregnancies exposed to intravenous ondansetron did not find an increased risk of either oral clefts or cardiac malformations.

One case-control study using population-based birth defect registries with 23,200 cases across two datasets reported an increased risk of cleft palate in one dataset and no increased risk in the other dataset. There was no increased risk of cardiac malformations in this study.

The second cohort study with 3,733 pregnancies exposed to ondansetron found an increased risk of ventricular septal defect, adjusted RR 1.7 (95% CI 1.0-2.9), but no statistically significant increase in risk of cardiac malformations , adjusted RR 1.3 (95% CI 0.86-1.8).

Animal data

In embryo-fetal development studies in rats and rabbits, pregnant animals received oral doses of ondansetron up to 15 mg/kg/day and 30 mg/kg/day, respectively, during the period of organogenesis. With the exception of a slight decrease in maternal body weight gain in the rabbits, there were no significant effects of ondansetron on the maternal animals or the development of the offspring. At doses of 15 mg/kg/day in rats and 30 mg/kg/day in rabbits, the maternal dose was approximately 6 and 24 times the maximum recommended human oral dose of 24 mg/day, respectively, based on body surface area. In a pre- and postnatal developmental toxicity study, pregnant rats received oral doses of ondansetron up to 15 mg/kg/day from Day 17 of pregnancy to litter Day 21. With the exception of a slight reduction in maternal body weight gain, there were no

effects upon the pregnant rats and the pre- and postnatal development of their offspring, including reproductive performance of the mated F1 generation. At a dose of 15 mg/kg/day in rats, the maternal dose was approximately 6 times the maximum recommended human oral dose of 24 mg/day based on BSA.

Lactation

Risk Summary

It is not known whether ondansetron is transferred into human milk. There are no data on the effects of ondansetron on the breastfed child or the effects of ondansetron on milk production. However, it has been demonstrated that ondansetron passes into the milk of lactating animals. It is therefore recommended that mothers receiving *ZOFRAN* should not breast-feed their babies.

Females and males of reproductive potential

Pregnancy testing

Pregnancy status should be verified for females of reproductive potential prior to starting the treatment with Zofran.

Contraception

Females of reproductive potential should be advised that it is possible that Zofran can cause harm to the developing fetus. Sexually active females of reproductive potential are recommended to use effective contraception (methods that result in less than 1 % pregnancy rates) when using Zofran during the treatment and for two days after stopping treatment with Zofran.

Infertility

There is no effect of Zofran on fertility.

OVERDOSAGE

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 section ADVERSE DRUG REACTIONS). Manifestations that have been reported include visual disturbances, severe constipation, hypotension and a vasovagal episode with transient second degree AV block. In all instances, the events resolved completely.

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

Cases consistent with serotonin syndrome have been reported in young children following oral 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.

CLINICAL PHARMACOLOGY

Pharmacotherapeutic group, ATC Code

Serotonin ($5HT_3$) antagonist, A04AA01

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.

Pharmacodynamics (PD)

Ondansetron does not alter plasma prolactin concentrations.

QT Prolongation

The effect of ondansetron on the QTc interval was evaluated in a double blind, randomised, 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. No significant changes were seen in the measured electrocardiographic PR or QRS intervals.

Pharmacokinetics (PK)

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 2 years and over)

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.

Elderly

Early Phase I studies in healthy elderly volunteers showed a slight age-related decrease in clearance, and an increase in half-life of ondansetron. However, wide inter-subject variability resulted in considerable overlap in pharmacokinetic parameters between young (< 65 years of age) and elderly subjects (≥ 65 years of age) and there were no overall differences in safety or efficacy observed between young and elderly cancer patients enrolled in CINV clinical trials to support a different dosing recommendation for the elderly.

Based on more recent ondansetron plasma concentrations and exposure-response modelling, a greater effect on QTcF is predicted in patients ≥ 75 years of age compared to young adults. Specific dosing information is provided for patients over 65 years of age and over 75 years of age for intravenous dosing (see DOSAGE REGIMEN AND ADMINISTRATION– CINV and RINV in Elderly).

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.

NON-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 section CLINICAL PHARMACOLOGY – QT prolongation).

Reproductive toxicity

See section PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL

PHARMACEUTICAL INFORMATION

Incompatibilities

Compatibility with IV fluids

In keeping with good pharmaceutical practice IV solutions should be prepared at the time of infusion or stored at 2-8°C for no more than 24 hours before the start of administration.

Dilutions of *ZOFRAN* injection are stable under normal room lighting conditions or daylight for at least 24 hours, thus no protection from light is necessary while infusion takes place 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

ZOFRAN 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/500 mL and 8 mg/50 mL 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 per hour (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 1 L), administered over 30 minutes to one 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 5 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 5 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.

Storage

Store below 30°C.

Protect from light.

Nature and Contents of Container

ZOFRAN injection is available in glass ampoules.

Glass ampoules containing ondansetron 4 mg in 2 mL.
Glass ampoules containing ondansetron 8 mg in 4 mL.

Pack Sizes:
5 and 10 ampoules for 4 mg in 2 mL
5 and 8 ampoules for 8 mg in 4 mL

Not all presentations may be available locally

Instructions for Use/Handling

ZOFRAN injection should not be administered in the same syringe or infusion as any other medication (see section PHARMACEUTICAL INFORMATION – INCOMPATIBILITIES).

ZOFRAN injection should only be admixed with those infusion solutions which are recommended (see section PHARMACEUTICAL INFORMATION – INCOMPATIBILITIES).

Injection (unpreserved) ampoules:

The solution for injection formulation is unpreserved, should only be used once and injected or diluted immediately after opening. Any remaining solution should be discarded.

ZOFRAN 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.

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