Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ondansetron 2 mg/ml solution for injection or infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution for injection contains:
Ondansetron hydrochloride dihydrate equivalent to 2 mg ondansetron.
Each ampoule with 2 ml contains 4 mg ondansetron.
Each ampoule with 4 ml contains 8 mg ondansetron.

1 ml solution for injection contains 3.34 mg of sodium as sodium citrate dihydrate and sodium chloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection

A clear colourless solution in a clear glass ampoule (Type I) containing either 2ml or 4ml of solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ondansetron is indicated for the prevention and treatment of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy, and for the prevention and treatment of post-operative nausea and vomiting (PONV).

Paediatric Population:
Ondansetron is indicated for the management of chemotherapy-induced nausea and vomiting (CINV) in children aged ≥ 6 months, and for the prevention and treatment of PONV in children aged ≥1 month.

4.2 Posology and method of administration

For intravenous injection or for intravenous infusion after dilution.
For instructions on dilution of the product before administration, see section 6.6.

Prescribers intending to use ondansetron in the prevention of delayed nausea and vomiting associated with chemotherapy or radiotherapy in adults, adolescents or children should take into consideration current practice and appropriate guidelines.

Chemotherapy and radiotherapy induced nausea and vomiting

Adults
The emetogenic potential of cancer treatment varies according to the doses and combinations of chemotherapy and radiotherapy regimens used. The dose range of ondansetron solution for injection or infusion is 8-32 mg a day and selected as shown below.

Emetogenic chemotherapy and radiotherapy
For patients receiving emetogenic chemotherapy or radiotherapy ondansetron can be given either by intravenous or other routes of administration, however this product is for intravenous use only.

The recommended intravenous dose of ondansetron is 8 mg administered as a slow injection or as a short-time infusion over 15 minutes immediately before treatment, followed by treatment with other dosage forms than intravenous.

Treatment with other dosage forms than intravenous is recommended to protect against delayed or prolonged emesis after the first 24 hours.

Highly emetogenic chemotherapy
For patients receiving highly emetogenic chemotherapy, e.g. high-dose cisplatin, ondansetron can be given by intravenous or other routes of administration, however this product is for intravenous use only.

Ondansetron has been shown to be equally effective in the following intravenous dose schedules over the first 24 hours of chemotherapy:

- A single dose of 8 mg by slow intravenous injection immediately before chemotherapy.
- A dose of 8 mg by slow intravenous injection or as a short-time intravenous infusion over 15 minutes immediately before chemotherapy, followed by two further intravenous doses of 8 mg two to four hours apart, or by a constant infusion of 1 mg/hour for up to 24 hours.
- A single dose of 32 mg diluted in 50-100 ml of sodium chloride 9 mg/ml (0.9 % w/v) solution or other compatible infusion fluid (see compatibility with solutions for infusion under section 6.6) and infused over not less than 15 minutes immediately before chemotherapy.

Doses of greater than 8 mg and up to 32 mg of ondansetron may only be given by intravenous infusion over not less than 15 minutes.

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

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

To protect against delayed or prolonged emesis after the first 24 hours, ondansetron treatment with other dosage forms than intravenous should be continued after a course of treatment.

Paediatric Population:
CINV in children aged ≥ 6 months and adolescents

The dose for CINV can be calculated based on body surface area (BSA) or weight – see below. Weight-based dosing results in higher total daily doses compared to BSA-based dosing (sections 4.4.and 5.1).

Ondansetron injection should be diluted in 5% glucose or 0.9% sodium chloride or other compatible infusion fluid (see section 6.6) and infused intravenously over not less than 15 minutes. There are no data from controlled clinical trials on the use of Ondansetron in the prevention of delayed or prolonged CINV. There are no data from controlled clinical trials on the use of Ondansetron for radiotherapy-induced nausea and vomiting in children.

Dosing by BSA:
Ondansetron should be administered immediately before chemotherapy as a single intravenous dose of 5 mg/m2. The intravenous dose must not exceed 8 mg.
Oral dosing can commence twelve hours later and may be continued for up to 5 days (Table 1).

The total daily dose must not exceed adult dose of 32 mg.
Table 1: BSA-based dosing for Chemotherapy - Children aged ≥ 6 months and adolescents

BSA	Day 1(a,b)	Days 2-6(b)
< 0.6 m2	5 mg/m2 i.v. plus 2 mg oral liquid after 12 hrs	2 mg oral liquid every 12 hrs
≥ 0.6 m2	5 mg/m2 i.v. plus 4 mg oral liquid or tablet after 12 hrs	4 mg oral liquid or tablet every 12 hrs

a The intravenous dose must not exceed 8 mg.
b The total daily dose must not exceed adult dose of 32 mg

Dosing by bodyweight:
Weight-based dosing results in higher total daily doses compared to BSA-based dosing (sections 4.4. and 5.1).

Ondansetron should be administered immediately before chemotherapy as a single intravenous dose of 0.15 mg/kg. The intravenous dose must not exceed 8 mg. Two further intravenous doses may be given in 4-hourly intervals. The total daily dose must not exceed adult dose of 32 mg.
Oral dosing can commence twelve hours later and may be continued for up to 5 days (Table 2).

Table 2: Weight-based dosing for Chemotherapy - Children aged ≥ 6 months and adolescents

Weight	Day 1 (a,b)	Days 2-6(b)
≤ 10 kg	Up to 3 doses of 0.15 mg/kg every 4 hours	2 mg oral liquid every 12 hours
> 10 kg	Up to 3 doses of 0.15 mg/kg every 4 hrs	4 mg oral liquid or tablet every 12 hrs

a The intravenous dose must not exceed 8 mg.
b The total daily dose must not exceed adult dose of 32 mg.

Elderly
Ondansetron is well tolerated by patients over 65 years and no alteration of dosage, dosing frequency or route of administration is required.

Please refer also to “Special Populations”.

Post-operative nausea and vomiting (PONV)

Prevention of PONV
Adults: For the prevention of PONV ondansetron can be administered by intravenous injection or other dosage forms.

Ondansetron may be administered as a single dose of 4 mg given by slow intravenous injection at induction of anaesthesia.

Treatment of established PONV
For treatment of established PONV a single dose of 4 mg given by slow intravenous injection is recommended.

Paediatric population
PONV in children aged ≥ 1 month and adolescents

For prevention of PONV in paediatric patients having surgery performed under general anaesthesia, a single dose of ondansetron may be administered by slow intravenous 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.
For the treatment of PONV after surgery in paediatric patients having surgery performed under general anaesthesia, a single dose of Ondansetron may be administered by slow intravenous injection (not less than 30 seconds) at a dose of 0.1mg/kg up to a maximum of 4 mg. There are no data on the use of Ondansetron in the treatment of PONV in children below 2 years of age.

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

Please refer also to “Special Populations”.

Special Populations

Patients with renal impairment
No alteration of daily dosage or frequency of dosing, or route of administration is 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.

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.

4.3 Contraindications

Hypersensitivity to ondansetron or to other selective 5-HT_3-receptor antagonists (e.g. granisetron, dolasetron) or to any of the excipients.

4.4 Special warnings and precautions for use

Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5-HT3 receptor antagonists.

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

As there is little experience to date of the use of ondanstron in cardiac patients, caution should be exercised if ondansetron is coadministered with anaesthetics to patients with arrhythmias or cardiac conduction disorders or to patients who are being treated with antiarrhythmic agents or beta-blockers.

Very rarely and predominantly with intravenous Ondansetron, transient ECG changes including QT interval prolongation have been reported. Caution is advised if patients have received cardiotoxic agents and in patients with a history or family history of prolonged QT syndrome.

In patients with adenotonsillar surgery prevention of nausea and vomiting with ondansetron may mask occult bleeding. Therefore, such patients should be followed carefully after ondansetron.

Paediatric Population:
Paediatric patients receiving ondansetron with hepatotoxic chemotherapeutic agents should be monitored closely for impaired hepatic function.

CINV
When calculating the dose on an mg/kg basis and administering three doses at 4-hourly intervals, the total daily dose will be higher than if one single dose of 5 mg/m2 followed by an oral dose is given. The comparative efficacy of these two different dosing regimens has not been investigated in clinical trials. Cross-trial comparison indicates similar efficacy for both regimens (section 5.1).

This medicinal product contains 2.3 mmol (or 53.5 mg) sodium per 32 mg dose. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of ondansetron on other medicinal products
There is no evidence that ondansetron either induces or inhibits the metabolism of other drugs commonly coadministered with it. Specific studies have shown that ondansetron does not interact with alcohol, temazepam, furosemide, alfentanil, propofol and thiopental.

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

Effects of other medicinal products on ondansetron
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.

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.

4.6 Fertility, pregnancy and lactation

Pregnancy:
To date, the safe use of Ondansetron during 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 animal studies are not always predictive of human response. The use of Ondansetron in pregnancy is not recommended.

Lactation:
Tests have shown that ondansetron passes into the milk of lactating animals (see section 5.3). It is therefore recommended that mothers receiving ondansetron should not breast-feed their babies.

4.7 Effects on ability to drive and use machines

Ondansetron 2 mg/ml has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following frequency terminology is used:
very common: ≥1/10;
common: ≥1/100, <1/10;
uncommon: ≥1/1,000, <1/100;
rare: ≥1/10,000, <1/1,000;
very rare: <1/10,000 and isolated reports.

Immune system disorders
Rare: Immediate hypersensitivity reactions, sometimes severe including anaphylaxis. Anaphylaxis may be fatal. Hypersensitivity reactions were also observed in patients, which were sensitive towards other selective 5-HT3-antagonists.

Nervous system disorders
Very common: Headache
Uncommon: There have been reports suggestive of involuntary movement disorders such as extrapyramidal reactions, e.g. oculogyric crisis/dystonic reactions and dyskinesia without definitive evidence of persistent clinical sequelae and seizures (e.g. epilectic spasms) have been observed although no known pharmacological mechanism can account for ondansetron causing these effects.
Rare: Dizziness during rapid intravenous administration
Very rare: Depression

Eye disorders
Rare: Transient visual disturbances (e.g. blurred vision) during rapid intravenous administration.
Very rare: In individual cases transitory blindness was reported in patients receiving chemotherapeutic agents included cisplatin. Most of reported cases were resolved in 20 minutes.

Cardiac disorders
Uncommon: Chest pain with or without ST segment depression, cardiac arrhythmias and bradycardia. Chest pain and cardiac arrhythmias may be fatal in individual cases.
Very rare: Transitory changes in the electrocardiogram, including prolongation of the QT interval have been observed predominantly after intravenous application of ondansetron.

Vascular disorders
Common: Sensations of flushing or warmth.
Uncommon: Hypotension.

Respiratory, thorax and mediastinum disorders
Uncommon: Hiccups.

Gastrointestinal disorders
Common: Ondansetron is known to increase the large bowel transit time and may cause constipation in some patients.

Hepato-biliary disorders
Uncommon: Asymptomatic increases in liver function tests were observed. These reactions were frequently observed in patients under chemotherapy with cisplatin.

Skin and subcutaneous tissue disorders
Uncommon: Hypersensitivity reactions around the injection site (e.g. rash, urticaria, itching) may occur, sometimes extending along the drug administration vein.

General disorders and administration site conditions
Common: Local reactions at the I.V. injection site.

Paediatric population

The adverse event profile in children and adolescents was comparable to that seen in adults.

4.9 Overdose

Little is known at present about overdosage with ondansetron, however, a limited number of patients received overdoses. 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. There is no specific antidote for ondansetron, therefore in all cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiemetics and antinauseants, Serotonin (5HT3) antagonists
ATC Code: A04AA01

Ondansetron is a potent, highly selective 5HT3 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 5HT3 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 5HT3 receptors on neurons located both in the peripheral and central nervous system. The mechanisms of action in postoperative nausea and vomiting are not known but there may be common pathways with cytotoxic induced nausea and vomiting.

Ondansetron does not alter plasma prolactin concentrations.

The role of ondansetron in opiate-induced emesis is not yet established.

Paediatric population
CINV
The efficacy of ondansetron in the control of emesis and nausea induced by cancer chemotherapy was assessed in a double-blind randomised trial in 415 patients aged 1 to 18 years (S3AB3006). On the days of chemotherapy, patients received either Ondansetron 5 mg/m2 intravenous + ondansetron 4 mg orally after 8-12 hrs or ondansetron 0.45 mg/kg intravenous + placebo orally after 8-12 hrs. Complete control of emesis on worst day of chemotherapy was 49% (5 mg/m2 intravenous + ondansetron 4 mg orally) and 41% (0.45 mg/kg intravenous + placebo orally). Post-chemotherapy both groups received 4 mg ondansetron oral liquid twice daily for 3 days.
A double-blind randomised placebo-controlled trial (S3AB4003) in 438 patients aged 1 to 17 years demonstrated complete control of emesis on worst day of chemotherapy in:
• 73% of patients when ondansetron was administered intravenously at a dose of 5 mg/m2 intravenous together with 2-4 mg dexamethasone orally
• 71% of patients when ondansetron was administered as oral liquid at a dose of 8 mg + 2-4 mg dexamethasone orally on the days of chemotherapy.

Post-chemotherapy both groups received 4 mg ondansetron oral liquid twice daily for 2 days.

The efficacy of ondansetron in 75 children aged 6 to 48 months was investigated in an openlabel, non-comparative, single-arm study (S3A40320). All children received three 0.15 mg/kg doses of intravenous ondansetron, administered 30 minutes before the start of chemotherapy and then at four and eight hours after the first dose. Complete control of emesis was achieved in 56% of patients.
Another open-label, non-comparative, single-arm study (S3A239) investigated the efficacy of one intravenous dose of 0.15 mg/kg ondansetron followed by two oral ondansetron doses of 4 mg for children aged < 12 yrs and 8 mg for children aged ≥ 12 yrs (total no. of children n= 28). Complete control of emesis was achieved in 42% of patients.

PONV
The efficacy of a single dose of ondansetron in the prevention of post-operative nausea and vomiting was investigated in a randomised, double-blind, placebo-controlled study in 670 children aged 1 to 24 months (post-conceptual age ≥ 44 weeks, weight ≥ 3 kg). Included subjects were scheduled to undergo elective surgery under general anaesthesia and had an ASA status ≤ III. A single dose of ondansetron 0.1 mg/kg was administered within five minutes following induction of anaesthesia. The proportion of subjects who experienced at least one emetic episode during the 24-hour assessment period (ITT) was greater for patients on placebo than those receiving ondansetron ((28% vs. 11%, p <0.0001).

Four double-blind, placebo-controlled studies have been performed in 1469 male and female patients (2 to 12 years of age) undergoing general anaesthesia. Patients were randomised to either single intravenous doses of ondansetron (0.1 mg/kg for paediatric patients weighing 40 kg or less, 4 mg for paediatric patients weighing more than 40 kg; number of patients = 735)) or placebo (number of patients = 734). Study drug was administered over at least 30 seconds, immediately prior to or following anaesthesia induction. Ondansetron was significantly more effective than placebo in preventing nausea and vomiting. The results of these studies are summarised in Table 3.

Table 3 Prevention and treatment of PONV in Paediatric Patients – Treatment response over

Study	Endpoint	Ondansetron %	Placebo %	p value
S3A380	CR	68	39	≤ 0.001
S3GT09	CR	61	35	≤ 0.001
S3A381	CR	53	17	≤ 0.001
S3GT11	no nausea	64	51	0.004
S3GT11	no emesis	60	47	0.004

CR = no emetic episodes, rescue or withdrawal

5.2 Pharmacokinetic properties

The pharmacokinetic properties of ondansetron are unchanged on repeat dosing.
A direct correlation of plasma concentration and anti-emetic effect has not been established.

Absorption
Following oral administration, ondansetron is passively and completely absorbed from the gastrointestinal tract and undergoes first pass metabolism (Bioavailability is about 60%.). Peak plasma concentrations of about 30 ng/ml are attained approximately 1.5 hours after an 8 mg dose. For doses above 8 mg the increase in ondansetron systemic exposure with dose is greater than proportional; this may reflect some reduction in first pass metabolism at higher oral doses. Bioavailability, following oral administration, is slightly enhanced by the presence of food but unaffected by antacids.
A 4 mg intravenous infusion of ondansetron given over 5 minutes results in peak plasma concentrations of about 65 ng/ml. Following intramuscular administration of ondansetron, peak plasma concentrations of about 25 ng/ml are attained within 10 minutes of injection.

Distribution
The disposition of ondansetron following oral, intramuscular (IM) and intravenous (IV) dosing is similar with a steady state volume of distribution of about 140 L. Equivalent systemic exposure is achieved after IM and IV administration of ondansetron.
Ondansetron is not highly protein bound (70-76%).

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.

Excretion
Less than 5% of the absorbed dose is excreted unchanged in the urine. Terminal half life is about 3 hours.

Special Patient Populations
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 patient population aged 1 to 4 month 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.
Based on the population pharmacokinetic parameters for subjects aged 1 month to 48 months, administration of a 0.15 mg/kg i.v. dose of ondansetron every 4 hours for 3 doses would result in a systematic exposure (AUC) comparable to that observed in paediatric surgery subjects aged 5 to 24 months and previous paediatric studies in cancer (aged 4 to 18 ears) and surgical (aged 3 to 12 years) subjects, at similar doses.

Population pharmacokinetic analysis was performed on 428 subjects (cancer patients, surgery patients and healthy volunteers) aged 1 month to 44 years following intravenous 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 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 persons
Studies in healthy elderly volunteers have shown slight age-related increases in both oral bioavailability (65%) and half-life (5 hours).

Renal impairment
In patients with renal impairment (creatinine clearance 15-60 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 h). 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
Following oral, intravenous or intramuscular dosing in patients with severe hepatic impairment, ondansetron’s systemic clearance is markedly reduced with prolonged elimination half-lives (15-32 h) and an oral bioavailability approaching 100% due to reduced pre-systemic metabolism.

Gender differences
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).

5.3 Preclinical safety data

Preclinical data revealed no special hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

Ondansetron and its metabolites accumulate in the milk of rats, milk/plasma-ratio was 5.2.

A study in cloned human cardiac ion channels has shown ondansetron has the potential to affect cardiac repolarisation via blockade of HERG potassium channels. The clinical relevance of this finding is uncertain.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium citrate dihydrate
Citric acid monohydrate
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf Life

Unopened:
2 years

Injection:
After first opening the medicinal product should be used immediately.

Infusion:
Chemical and physical in-use stability has been demonstrated for 48 hours at 25°C with the solutions given in section 6.6.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

The diluted solutions should be stored protected from light.

6.4 Special precautions for storage

Keep the ampoules in the outer carton in order to protect from light.

For storage conditions of the diluted medicinal product, see section 6.3.

6.5 Nature and contents of container

Type I clear glass ampoules

2 ml:
Pack sizes: Carton containing 5 or 10 ampoules.

4 ml:
Pack sizes: Carton containing 5 or 10 ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The solution is to be visually inspected prior to use (also after dilution). Only clear solutions practically free from particles should be used.

Any unused product or waste material should be disposed of in accordance with local requirements.

Ondansetron 2 mg/ml may be diluted with the following solutions for infusion to concentrations of ondansetron as stated in section 4.2:
Sodium chloride 9 mg/ml (0.9 % w/v) solution
Glucose 50 mg/ml (5 % w/v) solution
Mannitol 100 mg/ml (10 % w/v) solution
Ringer's lactate solution

The diluted solutions should be stored protected from light.

Note:
The solution for injection must not be sterilized in an autoclave!

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA 736/27/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30th January 2009

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March 2011