Ondansetron

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Package leaflet: Information for the user

Ondansetron 2 mg/ml Solution for Injection or Infusion

Ondansetron

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Ondansetron is and what it is used for

Ondansetron Injection contains the active ingredient ondansetron, which belongs to a group of medicines called anti-emetics.
Ondansetron Injection is used for
- Preventing nausea and vomiting caused by chemotherapy (in adults and children) or radiotherapy for cancer (adults only)
- Preventing nausea and vomiting after surgery. Ask your doctor, nurse or pharmacist if you would like any further explanation about this uses.

2. What you need to know before you use Ondansetron

Do not use Ondansetron:
- If you are **allergic** to ondansetron or any of the other ingredients of this medicine (listed in section 6) or to any similar medicines e.g. granisetron or dolasetron.
- If you are taking Apomorphine (medicine used to treat Parkinson's disease)

If you are not sure, talk to your doctor, nurse or pharmacist before having Ondansetron injection.

Warnings and precautions
Talk to your doctor or nurse before using Ondansetron:
- If you have liver problems
- If you have ever had heart problems (e.g. congestive heart failure which causes shortness of breath and swollen ankles)
- If you have an uneven heart beat (arrhythmias)
- If you are allergic to medicines similar to ondansetron, such as granisetron or palonosetron
- If you have a blockage in your gut
- If you have problems with the levels of salts in your blood, such as potassium, sodium and magnesium

If you are not sure if any of the above apply to you, talk to your doctor, nurse or pharmacist before having Ondansetron injection.

Other medicines and Ondansetron:
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines that you buy without a prescription and herbal medicines. This is because Ondansetron can affect the way some medicines work. Also some other medicines can affect the way ondansetron works.

In particular, tell your doctor, nurse or pharmacist if you are taking any of the following medicines:
- carbamazepine or phenytoin used to treat epilepsy.
- rifampicin used to treat infections such as tuberculosis (TB) antibiotics such as erythromycin or ketoconazole anti-arrhythmic medicines used to treat an uneven heart beat
- Beta-blocker medicines used to treat certain heart or eye problems, anxiety or prevent migraines
- Tramadol, a pain killer
- Medicines that affect the heart (such as haloperidol or methadone)
- Cancer medicines (especially anthracyclines and trastuzumab)
- SSRIs (selective serotonin reuptake inhibitors) used to treat depression and/or anxiety including fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, escitalopram
- SNRIs (serotonin noradrenaline reuptake inhibitors) used to treat depression and/or anxiety including venlafaxine, duloxetine

If you are not sure if any of the above applies to you, talk to your doctor, nurse or pharmacist before having Ondansetron injection.

Ondansetron injection should not be given in the same syringe or infusion (drip) as any other medication.

Pregnancy and breast feeding:
Pregnancy:
Only use during the first trimester of pregnancy after discussion with your doctor of the potential benefits and risks to you and your unborn baby of the different treatment options. This is because Ondansetron can slightly increase the risk of a baby being born with cleft lip and/or cleft palate (openings or splits in the upper lip and/or the roof of the mouth). If you are already pregnant, think you might be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking Ondansetron. If you are a woman of childbearing potential you may be advised to use effective contraception.

Breast –Feeding:
Do not breast-feed if you have Ondansetron. This is because small amounts pass into the mother's milk. Ask your doctor or midwife for advice.

Ondansetron contains sodium
This medicinal product contains 2.5 mmol (or 57.0 mg) sodium per maximum daily dose of 32 mg. To be taken into consideration by patients on a controlled sodium diet.

3. How to use Ondansetron

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist or nurse has told you. Check with your doctor, pharmacist or nurse if you are not sure Ondansetron is normally given by a nurse or doctor. The dose you have been prescribed will depend on the treatment you are having.

To prevent nausea and vomiting from chemotherapy or radiotherapy
On the day of chemotherapy or radiotherapy
- the usual adult dose is 8 mg given by an injection into your vein or muscle, just before your treatment, and another 8 mg twelve hours later.

On the following days
- The usual adult intravenous dose does not exceed 8 mg.
- this may be given for up to 5 days.

If your chemotherapy or radiotherapy is likely to cause severe nausea and vomiting, you may be given more than the usual dose of Ondansetron. Your doctor will decide this.

To prevent nausea and vomiting from chemotherapy in children aged over 6 months and adolescents
The doctor will decide the dose depending on the child's size (body surface area) or weight. Look at the label for more information.

On the day of chemotherapy
- The first dose is given by an injection into the vein, just before your child's treatment. After chemotherapy, your child's medicine will usually be given by mouth the usual dose is a 4 mg.

To prevent nausea and vomiting after an operation
Adult:
- The usual dose for adults is 4 mg given by a slow injection into your vein or an injection into your muscle. For prevention, this will be given just before your operation.

Children:
- For children aged over 1 month and adolescents, the doctor will decide the dose. The maximum dose is 4 mg given as a slow injection into the vein. For prevention, this will be given just before the operation.

Patients with moderate or severe liver problems
The total daily dose should not be more than 8 mg.

If you keep feeling or being sick
Ondansetron injection should start to work soon after having the injection. If you continue to be sick or feel sick, tell your doctor or nurse.

The following information is intended for medical or healthcare professionals only

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 route of administration and dose of Ondansetron should be flexible in the range of 8-32 mg a day and selected as shown below.

Emetogenic chemotherapy and radiotherapy:

For most patients receiving emetogenic chemotherapy and radiotherapy, ondansetron 8 mg should be administered as a slow intravenous injection (in not less than 30 seconds) or intramuscular injection or other routes of administration over 15 minutes immediately before treatment. However this product is for injection or infusion only.

To protect against delayed or prolonged emesis after the first 24 hours, oral treatment with ondansetron should be continued for up to 5 days after a course of treatment.

Highly emetogenic chemotherapy: For patients receiving highly emetogenic chemotherapy, e.g.. high-dose cisplatin, ondansetron can be given either by intravenous or intramuscular administration.

Ondansetron has been shown to be equally effective in the following dose schedules over the first 24 hours of chemotherapy:
- A single dose of 8 mg by slow intravenous injection (in not less than 30 seconds) or intramuscular injection over 15 minutes immediately before chemotherapy.
- A dose of 8 mg by slow intravenous injection (in not less than 30 seconds) or intramuscular injection over 15 minutes immediately before chemotherapy, followed by two further intravenous injection (in not less than 30 seconds) or intramuscular doses of 8 mg no less than four hours apart, or by a constant infusion of 1 mg/hour for up to 24 hours.
- Doses of greater than 8 mg and up to a maximum dose of 16 mg diluted in 50-100 ml of saline or other compatible infusion fluid (See Instructions for Use/Handling)and infused over not less than 15 minutes immediately before chemotherapy.
- A single dose greater than 16 mg must not be given due to dose dependent increase of QTprolongation risk (see sections 4.4, 4.8 and 5.1 of the SPC).

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, oral treatment with ondansetron should be continued for up to 5 days 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.
In paediatric clinical studies, ondansetron was given by IV infusion diluted in 25 to 50 ml of saline or other compatible infusion fluid and infused over not less than 15 minutes
Weight-based dosing results in higher total daily doses compared to BSA-based dosing – see sections 4.4 and 5.1

Ondansetron hydrochloride should be diluted in 5% dextrose or 0.9% sodium chloride or other compatible infusion fluid (see Instructions for Use/Handling) and infused intravenously over not less than 15 minutes.

There are no data from controlled clinical trials on the use of ondansetron Injection in the prevention of chemotherapy induced delayed or prolonged nausea and vomiting. There are no data from controlled clinical trials on the use of ondansetron Injection for radiotherapy-induced nausea and vomiting in children.

<u>Dosing by BSA:</u>
Ondansetron Injection should be administered immediately before chemotherapy as a single intravenous dose of 5 mg/m^2. The single intravenous dose must not exceed 8 mg. Oral dosing can commence twelve hours later and may be continued for up to 5 days (see SPC for dosing tables). The total daily dose must not exceed adult dose of 32 mg.

<u>Dosing by bodyweight:</u>
Weight-based dosing results in higher total daily doses compared to BSA-based dosing. Ondansetron Injection should be administered immediately before chemotherapy as a single intravenous dose of 0.15 mg/kg. The single intravenous dose must not exceed 8 mg. Two further intravenous doses may be given in 4-hourly intervals. Oral dosing can commence twelve hours later and may be continued for up to 5 days. The total dose over 24 hours (given as divided doses) must not exceed adult dose of 32 mg (see SPC for further details).

Elderly
In patients 65 to 74 years of age, the dose schedule for adults can be followed. All intravenous doses should be diluted in 50-100 ml of saline or other compatible infusion fluid (see Instructions for Use/Handling) and infuse over 15 minutes.

If you take more Ondansetron than you should
Your doctor or nurse will give you or your child Ondansetron injection so it is unlikely that you or your child will receive too much. If you think you or your child have been given too much or have missed a dose, tell your doctor or nurse.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Allergic Reactions
If you have an allergic reaction, tell your doctor or a member of the medical staff straight away. The signs may include:
- sudden wheezing and chest pain or chest tightness
- swelling of your eyelids, face, lips, mouth or tongue
- skin rash - red spots or lumps under your skin (hives) anywhere on your body
- collapse.

Other side effects include:
Very common (may affect more than 1 in 10 people)
- Headache

Common (may affect up to 1 in 10 people)
- Sensations of flushing or warmth
- Constipation
- Changes to liver function test results (if you have Ondansetron injection with a medicine called cisplatin, otherwise this side effect is uncommon)
- Irritation and redness at the site of injection

Uncommon(may affect up to 1 in 100 people)
- fits, Unusual body movements or shaking
- Uneven heart beat
- Chest pain
- Low blood pressure, which can make you feel faint or dizzy
- Hiccups
- Hypersensitivity reactions around the administration site (e.g. skin rash, urticaria, itching) that sometimes extend along the vien in which drug is administered

Rare (may affect up to 1 in 1,000 people)
- Feeling dizzy or light headed
- Poor vision or temporary loss of eyesight
- Disturbance in heart rhythm (sometimes causing a sudden loss of consciousness)

Very rare (may affect up to 1 in 10,000 people), including isolated reports
- Poor vision or temporary loss of eyesight, which usually comes back within 20 minutes
- Depression

Not known (cannot be estimated from the available data)
Myocardial ischemia
Signs include:
- sudden chest pain or
- chest tightness

Reporting of side effects
If you get any side effects, talk to your doctor , pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Ondansetron

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special temperature storage conditions.

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

Do not use this medicine if you notice any particulate matter or discoloration.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Ondansetron contains:
The active substance is ondansetron (as hydrochloride dihydrate).

Each ml solution for injection or infusion contains 2 mg ondansetron (as ondansetron hydrochloride dihydrate).

Each ampoule of 2 ml contains 4 mg of ondansetron (as ondansetron hydrochloride dihydrate).
Each ampoule of 4 ml contains 8 mg of ondansetron (as ondansetron hydrochloride dihydrate).

The other ingredients are Citric acid monohydrate, sodium citrate, sodium chloride, water for injection

What Ondansetron looks like and contents of the pack:
Solution for injection or infusion.
Clear and colorless solution free from visible particles.
Ondansetron is a clear colourless solution for injection or infusion filled in type-I clear glass ampoules. For ease of breaking, the ampoules may bear a “One-Point cut (OPC)” or may be “Scored”.

Ondansetron 2 mg/ml is available in fill volumes of 2 ml and 4 ml ampoules packed in boxes of 1, 5 or 10 ampoules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Milpharm Limited
Ares Block, Odyssey Business Park
West End Road
Ruislip HA4 6QD
United Kingdom

Manufacturer
APL Swift Services (Malta) Limited
HF26, Hal Far Industrial Estate, Hal Far
Birzebbugia, BBG 3000
Malta

or

Milpharm Limited
Ares Block, Odyssey Business Park
West End Road
Ruislip HA4 6QD
United Kingdom

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In patients 75 years of age or older, the initial intravenous dose of ondansetron should not exceed 8 mg. All intravenous doses should be diluted in 50-100 ml of saline or other compatible infusion fluid (see Instructions for Use/Handling) and infused over 15 minutes. The initial dose of 8 mg may be followed by two further intravenous doses of 8 mg, infused over 15 minutes and given no less than four hours apart (see SPC).

Post-operative nausea and vomiting (PONV):
Adults: For the prevention of PONV ondansetron can be administered orally or by intravenous or intramuscular injection.

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

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

Children (aged over 1 month and adolescents)
Injection:
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 0.1mg/kg up to a maximum of 4mg 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 injection 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 PONV in the elderly, however ondansetron is well tolerated in patients over 65 years receiving chemotherapy.
For all indications:
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.
Ondansetron Injection/infusion should not be autoclaved.

Incompatibilities:
Ondansetron solution for injection/infusion is physically compatible and chemically stable when mixed with the following solutions for infusion over the concentration range of 0.016 mg/ml to 0.64 mg/ml.
- 0.9%w/v Sodium Chloride
- 5%w/v Dextrose
- 10%w/v Mannitol
- Ringers solution
- 0.3%w/v Potassium Chloride and 0.9%w/v Sodium Chloride
- 0.3%w/v Potassium Chloride and 5%w/v Dextrose

Compatibility studies with above diluents have been undertaken in polyvinyl chloride infusion bags and polyvinyl chloride administration sets. It is considered that adequate stability would also be conferred by the use of polyethylene infusion bags or Type 1 glass bottles. Dilutions of Ondansetron solution for injection/infusion in 0.9%w/v Sodium Chloride Intravenous Infusion or in 5%w/v Dextrose Intravenous Infusion for infusion have been demonstrated to be stable in polypropylene syringes. It is considered that Ondansetron solution for injection/infusion diluted with other compatible infusion fluids would be stable in polypropylene syringes.

Shelf-life and storage

Unopened: 3 years

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

Infusion: Chemical and physical in-use stability has been demonstrated for 7 days at 15-25^{o}C and 28^{o}C.
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^{o}C, unless dilution has taken place in controlled and validated aseptic conditions.