

Package leaflet: Information for the user

Ondansetron 2 mg/mL solution for injection/infusion

ondansetron

Read all of this leaflet carefully before you are given 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, pharmacist 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, pharmacist 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
2. What you need to know before you are given Ondansetron
3. How Ondansetron is given
4. Possible side effects
5. How to store Ondansetron
6. Contents of the pack and other information

1. What Ondansetron is and what it is used for

Ondansetron belongs to a group of medicines called anti-emetics. Ondansetron inhibits the effect of the neuron-transmitter serotonin in the brain. Serotonin causes nausea and vomiting.

Ondansetron is used for

- preventing and treating nausea and vomiting induced by cytotoxic chemotherapy (CINV) and radiotherapy (adults and children aged ≥ 6 months)
- preventing and treating nausea and vomiting in patients following an operation (PONV) (in adults and children aged ≥ 1 month)

Your doctor may have prescribed Ondansetron for another use. Always follow your doctor's advice.

2. What you need to know before you are given Ondansetron

Do not use Ondansetron:

- if you are allergic to ondansetron or any of the other ingredients of this medicine (listed in section 6)
- if you are taking apomorphine (used to treat Parkinson's disease)
- if you have previously experienced allergy to other medicines belonging to the group of serotonin antagonists (e.g. granisetron, dolasetron). If this is the case it is possible that you are also allergic to Ondansetron.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Ondansetron;

- if you have a blockage of your intestines or constipation, as you will need to be closely monitored by your doctor.
- if you are going to have or recently had your tonsils removed, as treatment with Ondansetron may hide symptoms of internal bleeding.
- if you have heart problems (with arrhythmias or conduction disorders) and are being treated with other medicines such as anaesthetics, anti-arrhythmics or beta-blockers at the same time.

- if you need to pay attention to your sodium intake. However, Ondansetron has a low sodium content (less than 1 mmol per ampoule).
- if it is for children below the age of 6 months or with a body surface of less than 0.6 m².
- if you have liver problems.
- if children or adolescents receive ondansetron together with medicines, that may have a harmful effect on the liver. Careful monitoring of the liver function is recommended.
- if you have problems with the levels of salts in your blood, such as potassium and magnesium.

Always tell the laboratory if you are having blood or urine tests, that you are being treated with Ondansetron.

Other medicines and Ondansetron

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Ondansetron may have an effect on other medicines or other medicines may have an effect on Ondansetron.

You must tell your doctor that you are being given Ondansetron, if he/she starts treating you with any of the following medicine:

- Medicines for epilepsy (phenytoin, carbamazepine)
- Antibiotics and antifungal medicines (e.g. rifampicin, erythromycin or ketoconazole)
- Pain-relieving medicine (tramadol)
- Medicines inducing heart damage (e.g. anthracyclines or trastuzumab)
- Anti-arrhythmic medicines used to treat an uneven heart beat (e.g. amiodarone)
- Drugs which may result in QT prolongation (heart rhythm disorder)
- Beta-blocker medicines used to treat certain heart or eye problems, anxiety or prevent migraines (e.g. atenolol or timolol)
- Serotonergic medicines (medicines of the type SSRI or SNRI used in the treatment of depressions)
- Apomorphine (used to treat Parkinson's disease)

Contact your doctor. It may be necessary to adjust the dose.

Ondansetron with food and drink

Ondansetron may be given independently of food and drink.

Pregnancy, breast-feeding and fertility

Pregnancy:

You should not use Ondansetron during the first trimester of pregnancy. 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 take Ondansetron if you are breast-feeding, because it is excreted into the milk.

Driving and using machines

Ondansetron does not affect the ability to use any tools or machines or the ability to drive safely in traffic.

Ondansetron contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per ampoule, that is to say essentially 'sodium-free'.

3. How Ondansetron is given

Always use this medicine exactly as your doctor or nurse has told you. Check with your doctor or nurse if you are not sure.

Adults

Your doctor or hospital may give you ondansetron as an injection, an infusion (drip) or tablets. The dose is individual to each patient.

Paediatric Population

CINV in children aged ≥ 6 months and adolescents:

Ondansetron injection should be mixed with 5% dextrose or 0.9% sodium chloride or other compatible infusion fluid and infused into a vein over not less than 15 minutes. Ondansetron should be administered immediately before chemotherapy as a single dose of 5 mg/m² or 0.15 mg/kg given into a vein. Oral dosing can commence 12 hours later and may be continued for up to 5 days. The maximum daily dose is 32 mg.

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 given by slow injection into a vein (not less than 30 seconds) at a dose of 0.1 mg/kg up to a maximum of 4 mg either before or after the anaesthesia.

For the treatment of PONV in paediatric patients having surgery performed under general anaesthesia, a single dose of ondansetron may be given by slow injection into a vein (not less than 30 seconds) at a dose of 0.1 mg/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.

If you receive more Ondansetron than you should

Your doctor or nurse will give you or your child Ondansetron 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. The symptoms of overdose are disturbances of vision, severe constipation, low blood pressure and disturbances in heart beat rhythm.

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

4. Possible side effects

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

Myocardial ischemia

Signs include:

- sudden chest pain or
- chest tightness

Serious, rare side effects (may affect up to 1 in 1,000 people):

Tell your doctor or nurse immediately if you experience any of the following:

- Swollen tongue and throat
- Difficulty breathing
- Collapse

Other side effects include:

Very common side effects (may affect more than 1 in 10 people):

- Headache

Common side effects (may affect up to 1 in 10 people):

- A sensation of reddening and warmth
- Constipation
- Hypersensitivity reactions at the injection site (local swelling, pain, redness, tissue hardening).

Uncommon side effects (may affect up to 1 in 100 people):

- Hiccups
- Low blood pressure
- Irregular heart beats, heart pain and slow pulse
- Seizures
- Involuntary movements
- Changes in liver function
- Upward rolling of the eye

Rare side effects (may affect up to 1 in 1,000 people):

- Dizziness during injection
- Temporary blurred vision
- Abnormally rapid heart rhythm called “Torsade des pointes”.

Very rare side effects (may affect up to 1 in 10,000 people):

- Temporary blindness. Most of these blindness cases were resolved within 20 minutes.

If any of these side effects occur, immediately seek medical attention.

Other less severe side effects may occur rarely or very rarely. If you need more information on these side effects ask your doctor or nurse for advice.

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 HPRC Pharmacovigilance Website: www.hpra.ie. 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 ampoule and the carton after “EXP”. The expiry date refers to the last day of that month.
- Before opening: This medicine does not require any special storage conditions.
- After opening/dilution: Use within 24 hours and store in a refrigerator (2 °C -8 °C).
- 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
- Each mL of solution contains 2 mg ondansetron (as hydrochloride dihydrate).
Each 2 mL ampoule contains 4 mg ondansetron (as hydrochloride dihydrate).
Each 4 mL ampoule contains 8 mg ondansetron (as hydrochloride dihydrate).

- The other ingredients are Sodium chloride; Citric acid monohydrate; Sodium citrate; Water for injections.

What Ondansetron looks like and contents of the pack

Ondansetron 2 mg/mL solution for injection/infusion is a clear liquid in brown glass ampoules. Every ampoule contains 2 mL or 4 mL solution. They are marketed in packs of 5 ampoules or 25 (5 packs of 5) ampoules. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Pinewood Laboratories Ltd., Ballymacarbry, Clonmel, Co. Tipperary, Ireland.

Manufacturer

Pharmathen S.A., 6 Dervenakion str., 15351 Pallini Attikis, Greece

This medicinal product is authorised in the Member States of the EEA under the following names:

- Denmark, Ondansetron 'Pharmathen' inj. væske, 2mg/ml.
- Greece, Trondamet solution for injection.
- Germany, Sigondan 2mg/ml Injektionslösung.
- United Kingdom, Ondemet 2mg/ml solution for injection
- Ireland, Ondansetron 2 mg/ml Solution for injection and infusion

PA number: 281/126/1

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The following information is intended for medical or healthcare professionals only:

Special precautions for disposal and other handling

For injection:

For single use only. Any unused solution should be discarded.

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

For infusion:

May be diluted with solution for infusion containing: Sodium chloride 9 mg/mL (0.9%), Glucose 50 mg/mL (5 %), Mannitol 100 mg/mL (10 %), Potassium chloride 3 mg/mL (0.3%) + Sodium chloride 9 mg/mL (0.9 %) and Potassium chloride 3 mg/mL (0.3%) + Glucose 50 mg/mL (5 %) as well as Ringer's solution for infusion.

Must not be mixed with other medicines.

From a microbiological point of view, unless the method of opening /dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user, and these should, if dilution has not been, performed controlled and under validated aseptic conditions, normally not exceed 24 hours at 2°C-8°C.

Posology and method of administration

Posology

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 and selected as shown below.

Emetogenic chemotherapy and radiotherapy

For patients receiving emetogenic chemotherapy or radiotherapy ondansetron can be given either by oral or intravenous administration.

For most patients receiving emetogenic chemotherapy or radiotherapy, ondansetron should initially be administered intravenously immediately before treatment, followed by 8 mg orally twelve hourly.

For oral administration: 8 mg 1-2 hours before treatment, followed by 8 mg 12 hours later.

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. The recommended dose for oral administration is 8 mg twice daily.

Highly emetogenic chemotherapy

Either 8 mg as a slow intravenous bolus injection or as a short-term infusion lasting 15 minutes immediately before chemotherapy. If this initial dose has insufficient effect it can be supplemented by either 8 mg (intravenous bolus or 15 minutes infusion) every 4th hour, at most twice, or continuous infusion of 1 mg/hour for 24 hours.

A single intravenous dose of 16 mg diluted in 50 – 100 mL of sodium chloride 9 mg/mL (0.9 %) solution for injection or other compatible infusion fluid 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 QT-prolongation risk (see sections 4.4, 4.8 and 5.1 of the SPC).

After 24 hours treatment is changed to the oral route.

The effect of ondansetron may be enhanced by the simultaneous administration of 20 mg dexamethasone intravenously or an equally potent dose of other glucocorticoids for intravenous use.

Paediatric Population

Chemotherapy-induced nausea and vomiting in children aged ≥ 6 months and adolescents:

The dose for chemotherapy-induced nausea and vomiting (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 – see sections 4.4 and 5.1.

There are no data from controlled clinical trials on the use of ondansetron 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 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 (see Table 1 below).

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 m ²	5 mg/m ² i.v. 2 mg syrup after 12 hours	2 mg syrup or tablet every 12 hours
≥ 0.6 m ²	5 mg/m ² i.v. 4 mg syrup or tablet after 12 hours	4 mg syrup or tablet every 12 hours

^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 (see 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 (see Table 2 below).

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 at 4 hourly intervals	2 mg syrup or tablet every 12 hours
> 10 kg	Up to 3 doses of 0.15 mg/kg at 4 hourly intervals	4 mg syrup or tablet every 12 hours

^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 dose, dosing frequency or route of administration is required.

Patients with renal impairment

No alteration of daily dose 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 and therefore parenteral or oral administration is recommended.

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 medicine exposure levels no different from those of the general population. No alteration of daily dose or frequency of dosing is required.

Post-operative nausea and vomiting (PONV)

Adults

For the prevention of PONV ondansetron can be administered orally or by intravenous injection.

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

For the treatment of established PONV a single dose of 4 mg given by intramuscular or 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 0.1 mg/kg up to a maximum of 4 mg.

There are no data on the use of ondansetron in the treatment of PONV in children under 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.

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 and therefore parenteral or oral administration is recommended.

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 medicine exposure levels no different from those of the general population. No alteration of daily dose or frequency of dosing is required.

Method of administration

For intravenous or intramuscular use.