Package leaflet: Information for the user

Ondansetron 2mg/ml Solution for Injection/Infusion in Prefilled Syringe

ondansetron

Read all of this leaflet carefully before you start using 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.
- 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.

The name of the medicinal product is Ondansetron 2mg/ml Solution for Injection/Infusion in Prefilled Syringe but will be referred to as Ondansetron throughout the package leaflet.

What is in this leaflet:

1. What Ondansetron is and what it is used for

Ondansetron contains the active substance ondansetron, which belongs to a group of medicines called anti-emetics. Ondansetron is a 5HT3 receptor antagonist. It works by inhibiting 5HT3 receptors on neurons located in the central and peripheral nervous systems.

Ondansetron is used to

- prevent nausea (feel sick) and vomiting (be sick) caused by
  - chemotherapy for cancer in adults and children from the age of 6 months.
  - radiotherapy for cancer in adults
- prevent and treatment of nausea and vomiting after surgery in adults and children from the age of 1 month.

Ask your doctor, nurse or pharmacist if you would like any further explanation about these uses.

2. What you need to know before you use Ondansetron

Do not use Ondansetron:

- If you are allergic to ondansetron or other selective $5HT_3$ receptor antagonists (e.g. granisetron, dolasetron) or any of the other ingredients of this medicine (listed in section 6).
- If you are taking apomorphine (a medicine used to treat Parkinson's disease).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Ondansetron if:

- you have had allergy to other medicines against feeling sick or being sick, such as granisetron or palonosetron.
- you have a blockage in your gut or suffer from severe constipation. This medicine can impede the mobility of the lower gut. You have liver problems or take any medicines that may be harmful to the liver (hepatotoxic chemotherapy drugs). In these cases, your liver function will be monitored closely, especially in children and adolescents;
- you have ever had heart problems, including an uneven heartbeat (arrhythmias). Ondansetron prolongs the QT interval (ECG sign of delayed repolarization of the heart following a heartbeat with the risk of life-threatening arrhythmias) in a dose-dependent manner.
- you are going to have tonsil surgery. In this case, you need to be carefully monitored as treatment with this ondansetron may hide symptoms of internal bleeding.
- you have problems with the levels of salts in your blood, such as potassium and magnesium

If you are going to perform any diagnostic test (including analysis of blood, urine, skin tests that use allergens, etc.) Tell doctor that you are taking this medicine, therefore the results may alter them.

Tell your doctor or pharmacist immediately if you notice any of these symptoms during or after treatment.

- If you notice sudden pain or tightness in the chest (myocardial ischemia)

Other medicines and Ondansetron
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

In particular, tell your doctor, nurse or pharmacist if you or your child are taking any of the following medicines:
- Phenytoin (used to treat epilepsy & heart arrhythmias) the effect of ondansetron may be weakened.
- Carbamazepine (used to treat epilepsy & neuralgic pain) the effect of ondansetron may be weakened.
- Rifampicin used to treat infections such as tuberculosis (TB) The effect of ondansetron may be weakened.
- Antibiotics such as erythromycin
- Ketokenazole (used to treat Cushing disease)
- Anti-arrhythmic medicines (used to treat an uneven heartbeat) such as amiodarone
- Beta-blocker medicines used to treat certain heart or eye problems, anxiety or prevent migraines such as atenolol or timolol
- Tramadol (used to treat pain) the pain killing effect of tramadol may be weakened.
- Medicines that affect the heart (such as haloperidol or methadone)
- Cancer medicines (especially anthracyclines such as doxorubicin, daunorubicin or 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

Ondansetron with food, drink and alcohol
You may use Ondansetron independently of food and drink

Pregnancy, breast-feeding and fertility
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 using this medicine.

If you are a woman of childbearing potential, you may be advised to use effective contraception.

Ondansetron passes into mother's milk. Therefore, mothers receiving ondansetron should NOT breast-feed.
Ask your doctor for advice before taking any medicine.

Driving and using machines
Ondansetron has no effect on the ability to drive or use machines.

Ondansetron contains sodium
This medicine contains 3.60 mg sodium (main component of cooking/table salt) in each ml. This is equivalent to 0.18% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Ondansetron

This medicinal product should always be administered as an infusion or injection (in a vein or muscle) by a qualified healthcare professional, usually a doctor or a nurse, and never by yourself.

Dose
Your doctor will decide on the correct dose of ondansetron treatment for you.
The dose depends on your medical treatment (chemotherapy or surgery), how well your liver is working, and whether it is given by intravenous injection or infusion.

Nausea and vomiting from chemotherapy or radiotherapy

Adults
On the day of chemotherapy or radiotherapy the recommended adult dose is 8 mg given by a slow 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 single dose does not exceed 8 mg.

Oral dosing can commence twelve hours after chemotherapy or radiation therapy and may be continued for up to 5 days. The usual dose is 8 mg twice a day.

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

A single dose greater than 16 mg should not be administered due to the increased risk of experiencing hearth rhythm alterations (see section 2).

Nausea and vomiting from chemotherapy

Children aged over 6 months and adolescents
The doctor will decide the dose based on the child's weight or size (body surface area).

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 twelve hours later, as tablets or syrup. The usual dose is 4 mg twice a day and can continue for up to 5 days.

Nausea and vomiting after an operation

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 this will be given just before your operation.

Children older than 1 month of age and adolescents
The doctor will decide the dose. The maximum dose is 4 mg given as a slow injection into the vein, this will be given just before the operation.

To treat nausea and vomiting after an operation

Adult:
- The usual dose for adults is 4 mg given by a slow injection into your vein.

Children older than 1 month of age and adolescents
The doctor will decide the dose. The maximum dose is 4 mg given as a slow injection into the vein.

Dosage adjustments

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

Elderly, renally impaired, or sparteine / debrisoquine poor metabolizers
It is not necessary to modify the daily dose or the frequency of the dose or the route of administration.

Treatment duration
Your doctor will decide the duration of your treatment with ondansetron. Do not stop treatment earlier.

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

If you or your child take more Ondansetron than you should

Your doctor or nurse will give this medicinal product to you or your child 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.

Little is known at present about overdose with ondansetron. In a majority of patients, symptoms were similar to those already reported in patients receiving recommended doses of this medicine (see aection ‘possible side effects’). The following effects were observed after overdose: visual disturbances, severe constipation, low blood pressure and unconsciousness. In all cases, the symptoms disappeared completely.
This medicine may alter your heart rhythm especially if you had an overdose. In this case your doctor will further monitor your heart beat.
There is no specific antidote to ondansetron; for that reason, if overdose is suspected, only the symptoms should be treated.
Tell your doctor if any of these symptoms occur.

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.

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

Uncommon: may affect up to 1 in 100 people

- Chest pain, uneven heartbeat (arrhythmia which may be fatal in individual cases) and slow heartbeat (bradycardia)

Rare: may affect up to 1 in 1,000 people
- Immediate allergic reactions including life-threatening allergic reaction (anaphylaxis). These reactions may be itchy rash, swelling of the eyelids, face, lips, mouth and tongue.

Not known (frequency cannot be estimated from available data)
- Sudden chest pain or tightness (myocardial ischemia)
  If you experience any of these symptoms, stop taking the medicine immediately and contact your doctor.

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
- irritation and redness at the site of injection

Uncommon (may affect up to 1 in 100 people)
- Seizures (fits or convulsions)
- Unusual body movements or shaking
- Uneven heart beat
- Chest pain
- Low blood pressure, which can make you feel faint or dizzy
- Hiccups
- changes to liver function test results (if you have Ondansetron with a medicine called cisplatin, otherwise this side effect is uncommon)

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

Very rare (may affect up to 1 in 10,000 people)
- Poor vision or temporary loss of eyesight, which usually comes back within 20 minutes.
- Extensive eruption on the skin with blisters and scamming, which affects a great part of the body surface (toxic epidermal necrolysis).

Reporting of side effects
If you or your child 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
HPRA 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.

Expiry

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

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

Do not use this medicine if you notice container is damaged or particles / crystals are visible.
Do not throw away any medicine 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 ingredient is ondansetron (as hydrochloride dihydrate).

Each ml of solution for injection/infusion in pre-filled syringe contains 2 mg ondansetron (as ondansetron hydrochloride dihydrate).

Each pre-filled syringe of 2 ml contains 4 mg ondansetron (as ondansetron hydrochloride dihydrate).
Each pre-filled syringe of 4 ml contains 8 mg ondansetron (as ondansetron hydrochloride dihydrate).

The other ingredients are citric acid monohydrate, sodium citrate, sodium chloride, sodium hydroxide and/or hydrochloric acid for pH adjustment and water for Injections.

What Ondansetron looks like and contents of the pack

Clear, colourless solution filled in amber glass prefilled syringe.

Available in pack containing 1, 5 & 10 pre-filled syringes.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:

Marketing Authorisation Holder
Accord Healthcare Ireland Limited
Euro House
Euro Business Park
Little Island
Cork
T45 K857
Ireland

Manufacturer:

Accord Healthcare Polska Sp.z o.o.
ul. Lutomierska 50,
95-200 Pabianice
Poland

Or
Pharmadox Healthcare Ltd.
KW20A
Kordin Industrial Park,
Paola, PLA3000, Malta

Or
Laboratori Fundació Dau
C/ C, 12-14 Pol. Ind.
Zona Franca, Barcelona, 08040,
Spain

This medicine is authorised in the Member States of the European Economic Area under the following names:

Name of the Member State	**Name of the medicine**
Austria	Ondansetron Accord 4 mg Injektions-/Infusionslösung in einer Fertigspritze Ondansetron Accord 8 mg Injektions-/Infusionslösung in einer Fertigspritze
Belgium	Ondansetron Accord 4 mg oplossing voor injectie/infusie in een voorgevulde spuit Ondansetron Accord 8 mg oplossing voor injectie/infusie in een voorgevulde spuit
Denmark	Ondansetron Accordpharma 4 mg Ondansetron Accordpharma 8 mg
Finland	Ondansetron Accordpharma 4 mg injektionestettä / infuusiota varten esitäytetyssä ruiskussa Ondansetron Accordpharma 8 mg injektionestettä / infuusiota varten esitäytetyssä ruiskussa
Germany	Ondansetron 4 mg Lösung zur Injektion/Infusion in einer Fertigspritze Ondansetron 8 mg Lösung zur Injektion/Infusion in einer Fertigspritze
Ireland	Ondansetron 2mg/ml Solution for Injection/Infusion in Prefilled Syringe
Italy	Ondansetron Accord
Norway	Ondansetron Accordpharma
The Netherlands	Ondansetron Accord 4 mg oplossing voor injectie/infusie in een voorgevulde spuit Ondansetron Accord 8 mg oplossing voor injectie/infusie in een voorgevulde spuit
Poland	Ondansetron Accord
Portugal	Ondansetron Accord
Spain	Ondansetron Accord 4 mg solución para inyección/infusión en jeringa precargada Ondansetron Accord 8 mg solución para inyección/infusión en jeringa precargada
Sweden	Ondansetron Accordpharma 4 mg lösning för injektion/infusion i förfylld spruta Ondansetron Accordpharma 8 mg lösning för injektion/infusion i förfylld spruta

The leaflet was last revised in July 2024

Detailed information on this medicine is available on the HPRA website.

The following information is intended for healthcare professionals only:

Instructions for use
For intravenous injection or intramuscular injection or intravenous infusion after dilution.
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.

Compatibility with other medicinal products
The following active substances may be administered via the Y-site of the ondansetron giving set for ondansetron concentrations of 16 to 160 micrograms/ml (8 mg/500 ml and 8 mg/50 ml):

Cisplatin	Concentrations up to 0.48 mg / ml (240 mg in 500 ml) administered over 1 to 8 hours.
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 10-60 minutes.
Etoposide	Concentrations of 0.14 mg / ml - 0.25 mg / ml (72 mg in 500 ml to 250 mg in 1 l). Administered over 30-60 minutes
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 intravenous 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 intravenous bolus injection over approximately 5 minutes.
Doxorubicin	Doses in the range 10-100 mg reconstituted with Water for Injections BP, 5 ml per 10 mg doxorubicin, as recommended by the manufacturer and given as an intravenous bolus injection over approximately 5 minutes.
Dexamethasone	Dexamethasone sodium phosphate 20 mg may be administered as a slow intravenous injection over 2-5 minutes via the Y-site of an infusion set delivering 8 or 16 mg of ondansetron diluted in 50-100 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 microgram - 2.5 mg/ml for dexamethasone sodium phosphate and 8 microgram – 0.75 mg/ml for ondansetron.

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: Ondansetron 8 mg should be administered as a slow intravenous injection (in not less than 30 seconds) or intramuscular injection, immediately before treatment followed by 8 mg orally twelve hourly.

To protect against delayed or prolonged emesis after the first 24 hours, oral or rectal 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 oral, rectal, 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 immediately before chemotherapy.
- A dose of 8 mg by slow intravenous injection (in not less than 30 seconds) or intramuscular injection immediately before chemotherapy, followed by two further intravenous injection (in not less than 30 seconds) or intramuscular doses of 8 mg four hours apart, or by a constant infusion of 1 mg/hour for up to 24 hours.
- A maximum initial intravenous dose of 16 mg diluted in 50-100 ml of saline or other compatible infusion fluid (see section 6.6 of the SPC) and infused over not less than 15 minutes immediately before chemotherapy. The initial dose of Ondansetron may be followed by two additional 8 mg intravenous doses (in not less than 30 seconds) or intramuscular doses four hours apart.
- A single dose greater than 16mg 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).

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 or rectal 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.

Dosing by BSA: Ondansetron Injection should be administered immediately before chemotherapy as a single intravenous dose of 5 mg/m^2.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 dose over 24 hours (given as divided doses) 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. Ondansetron 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 12 hours later and may be continued for up to 5 days (see SPC for further details).

Ondansetron should be diluted in 5% dextrose or 9 mg/ml (0.9%) sodium chloride or other compatible infusion fluid (see section 6.6 of the SPC) 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.

Post-operative nausea and vomiting (PONV)
Adults: For the prevention of PONV ondansetron may be administered as a single dose of 4 mg given by intramuscular or slow intravenous injection before surgery.

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)
Oral formulation:
No studies have been conducted on the use of orally administered ondansetron in the prevention or treatment of post-operative nausea and vomiting; slow i.v. injection is recommended for this purpose.

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 0.1 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 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.

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 parental 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 drug exposure levels no different from those of the general population. No alteration of daily dosage or frequency of dosing is required.

Incompatibilities

The solution must not be sterilised in an autoclave.

Ondansetron should only be admixed with those infusion solutions, which are recommended:
Sodium Chloride Intravenous Infusion BP 9 mg/ml (0.9%)
Glucose Intravenous Infusion BP 5%w/v
Mannitol Intravenous Infusion BP 10%w/v
Ringers Intravenous Infusion
Potassium Chloride 0.3%w/v and Sodium Chloride 9 mg/ml (0.9%) Intravenous Infusion BP
Potassium Chloride 0.3%w/v and Glucose 5%w/v Intravenous Infusion BP

The stability of Ondansetron after dilution with the recommended infusion fluids have been demonstrated in concentrations 0.016 mg/ml and 0.64 mg/ml.

Use only clear and colourless solutions.
The diluted solutions should be stored protected from light.

Shelf-life and storage

3 years

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

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

Infusion
After dilution with recommended diluents chemical and physical in-use stability has been demonstrated for 7 days at 25°C and 2-8°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°C, unless dilution has taken place in controlled and validated aseptic conditions.