PACKAGE LEAFLET: INFORMATION FOR THE USER

Ondansetron 2 mg / mL Solution for Injection

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, 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.

The name of your medicine is Ondansetron 2 mg / mL Solution for Injection
In the rest of this leaflet Ondansetron 2 mg / mL Solution for Injection is called Ondansetron Injection.

What is in this leaflet:

1. WHAT ONDANSETRON INJECTION IS AND WHAT IT IS USED FOR

Ondansetron injection contains a medicine called ondansetron. This 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 these uses.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ONDANSETRON INJECTION

Do not take Ondansetron Injection if:
- you are taking apomorphine (used to treat Parkinson's disease)
- you are allergic (hypersensitive) to ondansetron or any of the other ingredients of this medicine (listed in section 6).

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

Warnings and precautions
Talk to your doctor, nurse or pharmacist before taking Ondansetron injection if:
- you have ever had heart problems (e.g. congestive heart failure which causes shortness of breath and swollen ankles)
- you have an uneven heart beat (arrhythmias)
- you are allergic to medicines similar to ondansetron, such as granisetron or palonosetron (known as 'Kytril')
- you have liver problems
- you have a blockage in your gut
- 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 Injection
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 Injection can affect the way some medicines work. Also some other medicines can affect the way Ondansetron Injection 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 breastfeeding
Only use Ondansetron Injection 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 Injection 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 Injection. If you are a woman of childbearing potential you may be advised to use effective contraception.
Do not breast-feed if you have Ondansetron Injection. This is because small amounts pass into the mother's milk. Ask your doctor or midwife for advice.

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

3. HOW TO TAKE ONDANSETRON INJECTION

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

To prevent nausea and vomiting from chemotherapy or radiotherapy in adults
On the day of chemotherapy or radiotherapy

- the usual 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. After chemotherapy, your medicine will usually be given by mouth as an 8 mg Ondansetron tablet or 10 mL (8 mg) Ondansetron syrup.

On the following days

- the usual adult dose is one 8 mg tablet or 10 mL (8 mg) syrup taken twice a day
- 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.

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 ondansetron syrup or an ondansetron tablet.

On the following days

- 2.5 mL (2 mg) syrup twice a day for small children and those weighing 10 kg or less
- one 4 mg tablet or 5 mL (4 mg) syrup twice a day for larger children and those weighing more than 10 kg
- two 4 mg tablets or 10 mL (8 mg) syrup twice a day for teenagers (or those with a large body surface area)
- these doses can be given for up to five days.

To prevent and treat 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.

If you take more Ondansetron Injection 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.

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)

- a feeling of warmth or flushing

- 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)
- hiccups
- low blood pressure, which can make you feel faint or dizzy
- uneven heart beat
- chest pain
- fits
- unusual body movements or shaking.

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.

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
For UK: Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard.
For IE: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971, Fax: +353 1 6762517, Website: www. hpra.ie, E-mail: medsafety@hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE ONDANSETRON INJECTION

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 label, and carton after EXP. The expiry date refers to the last day of that month. Do not use this medicine if you notice signs of deterioration such as discolouration.
Store below 25oC.
Keep the ampoules in the outer carton, in order to protect from light.
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 to protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Ondansetron Injection contains
The active substance is ondansetron (as Hydrochloride Dihydrate).
Each 1 mL (millilitre) will contain 2 mg (milligram) of Ondansetron.
Each 2 mL ampoule (container) will contain 4 mg of Ondansetron.
Each 4 mL ampoule will contain 8 mg of Ondansetron.
The other ingredients are citric acid monohydrate, sodium citrate dihydrate, sodium chloride and water for injections.

What Ondansetron Injection looks like and contents of the pack
Ondansetron Injection is a clear, colourless solution for injection which can be diluted before use.
Each plastic or glass ampoule (container) will contain 2 mL (millilitres) or 4 mL of your medicine. These are packed in cartons of 5 ampoules. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder: Noridem Enterprises Limited, Evagorou & Makariou, Mitsi Building 3, Office 115, 1065 Nicosia, Cyprus.
Manufacturer: DEMO S.A. PHARMACEUTICAL INDUSTRY, 21st Km National Road Athens–Lamia, 14568 Krioneri, Attiki, Greece, T: +30 210 8161802, F: +30 2108161587.

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

United Kingdom:	Ondansetron 2 mg / mL Solution for injection
Ireland:	Ondansetron 2 mg / mL Solution for injection
Germany:	Ondansetron Noridem 2 mg/ml Injektionslösung
Austria:	Ondansetron Noridem 2 mg/ml Injektionslösung
Greece:	ONDANSETRON/NORIDEM Ενέσιμο διάλυμα 2 mg / mL

This leaflet was last revised in October 2019.

If this leaflet is difficult to see or read please contact the following address for help:
Athlone Laboratories, Ballymurray, Co. Roscommon, Ireland.
Tel +353-9066-61109. Email medical@athlone-laboratories.com

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The following information is intended for healthcare professionals only:

Please refer to the Summary of Product Characteristics (SmPC) for further details on this product.

Each 1 mL contains ondansetron hydrochloride dihydrate equivalent to 2 mg of ondansetron.
Each 2-mL ampoule contains 4 mg of ondansetron.
Each 4-mL ampoule contains 8 mg of ondansetron.

Posology and method of administration
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 can be given either by rectal, oral (tablets or syrup), intravenous or intramuscular administration.
For most patients receiving emetogenic chemotherapy or 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 injections (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 SmPC) 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 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 SmPC).
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. Ondansetron injection should be diluted in 5% dextrose or 0.9% sodium chloride or other compatible infusion fluid (see section 6.6 of the SmPC) 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/m^2. The single intravenous dose must not exceed 8 mg.
Oral dosing can commence 12 hours later and may be continued for up to 5 days (see Table 1 in SPC section 4.2 for BSA-based dosing).
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 (sections 4.4 and 5.1 of the SmPC).
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 Table 2 in SPC section 4.2 for weight-based dosing).
The total dose over 24 hours (given as divided doses) must not exceed adult dose of 32 mg.

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 section 6.6 of the SmPC) and infused over 15 minutes.
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 section 6.6 of the SmPC) 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 section 5.4 of the SmPC)

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 0.1 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.

For all indications:
Renal impairment
No alteration of daily dosage or frequency of dosing, or route of administration are required.
Hepatic impairment
Clearance of ondansetron is significantly reduced and serum half-life significantly prolonged in subjects with moderate or severe impairment of hepatic function. In such patients a total daily dose of 8 mg should not be exceeded and therefore parenteral or oral administration is recommended..
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 are required.

Special precautions for disposal and other handling
Ondansetron should not be autoclaved.

Compatibility with intravenous fluids
Ondansetron injection should only be mixed with those infusion solutions which are recommended:

Diluent
Sodium Chloride Intravenous Infusion BP 0.9%w/v
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 0.9%w/v Intravenous Infusion BP
Potassium Chloride 0.3%w/v and Glucose 5%w/v Intravenous Infusion BP

In complying with good pharmaceutical practice, dilutions of ondansetron injection in intravenous fluids should be prepared at the time of infusion. However, it has been demonstrated that dilutions of ondansetron in polyethylene bottles with the following intravenous infusion fluids remain stable for 24 hours at room temperature (25 ± 2 °C) or for 36 hours in the refrigerator (2 – 8°C).

Compatibility with other drugs
Ondansetron may be administered by intravenous infusion at 1 mg / hour, e.g. from an infusion bag or syringe pump. The following drugs may be administered via the Y-site of an infusion set for ondansetron concentrations of 16 to 160 micrograms / mL (e.g. 8 mg / 500 mL and 8 mg / 50 mL respectively):
Cisplatin:
Concentrations up to 0.48 mg / mL (e.g. 240 mg in 500 mL) administered over one to eight hours.
5-Fluorouracil:
Concentrations up to 0.8 mg / mL (e.g. 2.4 g in 3 litres or 400 mg in 500 mL) administered at a rate of at least 20 mL per hour (500 mL per 24 hours). Higher concentrations of 5-fluorouracil may cause precipitation of ondansetron. The 5-fluorouracil infusion may contain up to 0.045%w/v magnesium chloride in addition to other excipients shown to be compatible.
Carboplatin:
Concentrations in the range 0.18 mg / mL to 9.9 mg / mL (e.g. 90 mg in 500 mL to 990 mg in 100 mL), administered over ten minutes to one hour.
Etoposide:
Concentrations in the range 0.14 mg / mL to 0.25 mg / mL (e.g. 72 mg in 500 mL to 250 mg in 1L), administered over thirty minutes to one hour.
Ceftazidime:
Doses in the range 250 mg to 2000 mg reconstituted with Water for Injections BP as recommended by the manufacturer (e.g. 2.5 mL for 250 mg and 10 mL for 2 g ceftazidime) and given as an intravenous bolus injection over approximately five 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 five 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 – 1 mg / mL for ondansetron.
Any unused product or waste material should be disposed of in accordance with local requirements.

Special Precautions for Storage
Store below 25ºC. Store in the original package in order to protect from light.
Dilutions of Ondansetron injection in compatible intravenous infusion fluids are stable under normal room lighting conditions or daylight for

at least 24 hours, thus no protection from light is necessary while infusion takes place.