PACKAGE LEAFLET: INFORMATION FOR THE USER

Ondansetron 2 mg/ml Solution for Injection

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may want to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- 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 pharmacist. This includes any possible side effects not listed in this leaflet. See Section 4.

What is in this leaflet

1. What Ondansetron Injection is and what it is used for
2. What you need to know before you are given your Ondansetron Injection
3. How your Ondansetron Injection is given to you
4. Possible side effects
5. How to store your Ondansetron Injection
6. Contents of the pack and other information.

The name of your medicine is Ondansetron 2mg/ml Solution for Injection (referred to as Ondansetron Injection throughout this leaflet).

1. What Ondansetron Injection is and what it is used for

Your medicine comes as a solution for injection or infusion (drip). The active ingredient is ondansetron. The other ingredients are listed in section 6. Ondansetron belongs to a group of medicines called anti-emetics or anti-sickness medicine. Ondansetron can be used to prevent or treat nausea (feeling sick) or vomiting, following an operation, cancer chemotherapy or radiation treatment. Ask your doctor, nurse or pharmacist if you would like any further explanation about these uses.

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

You should not be given this injection if:
- You have ever had an allergic (hypersensitive) or unusual reaction to Ondansetron or any of the other ingredients of this medicine (listed in section 6), or to medicinal products from the same class (e.g. granisetron, dolasetron).
- You are taking apomorphine (used to treat Parkinson's disease).

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

Warnings and precautions

Talk to your doctor or pharmacist before receiving Ondansetron Injection
- if you have or have had prolonged QT interval (seen on an ECG, electrical recording of the heart),
- if you have or have had alterations in heart rhythm (including a slow or uneven heartbeat) or other heart problems (such as heart failure or conduction disorders) or,
- if you have problems with the levels of salts in your blood, such as potassium, sodium and magnesium or,
- if you have liver problems or,
- if you have gut problems such as a blockage or suffer from severe constipation or,
- if you have just had or are going to have your adenoids or tonsils removed.

- if you have depression or other conditions that are treated with antidepressants, or if you are taking painkillers such as opioids. The use of these medicines together with Ondansetron Injection can lead to serotonin syndrome, a potentially life-threatening condition (see "Other medicines and Ondansetron Injection").
- If you are allergic to medicines similar to ondansetron, such as granisetron (known as 'Kytril')

Special precautions should be taken if Ondansetron Injection is to be given to a child receiving medication for cancer treatment which might alter liver function.

Other medicines and Ondansetron Injection
Please tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines and especially any of the following 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.

* Phenytoin, carbamazepine; to treat epilepsy, as these medicines may reduce the effect of Ondansetron Injection
* Antibiotics such as rifampicin or erythromycin, as these medicines may reduce the effect of Ondansetron Injection
* Ketoconazole, a medicine used to treat a fungal infection,
* Tramadol, a strong painkiller, as Ondansetron Injection may reduce the effect of tramadol
* Medicines used to treat an uneven heartbeat (arrhythmias), as these medicines may interact with Ondansetron Injection and affect the rhythm of the heart
* Cancer medicines (e.g. anthracyclines or trastuzumab), antibiotics (e.g. erythromycin), antifungals (e.g. ketoconazole) or other medicines which might disturb your heart rhythm,
* Beta-blocker medicines used to treat certain heart or eye problems, anxiety or prevent migraines, as these medicines may interact with Ondansetron Injection and affect the rhythm of the heart
* Medicines that affect the heart (such as haloperidol or methadone)
* Medicines to treat depression such as SSRIs (selective serotonin reuptake inhibitors) including fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, escitalopram, or SNRIs (serotonin and noradrenaline reuptake inhibitors) including venlafaxine, duloxetine or medicines known as opioids/opiates, e.g. buprenorphine used in the treatment of acute or chronic pain, as these may cause serotonin syndrome, a potentially life-threatening reaction. The symptoms of serotonin syndrome may include a combination of the following: nausea (feeling sick), vomiting, agitation, confusion, diarrhoea, high temperature, increased blood pressure, excessive sweating, rapid heartbeat, hallucinations, loss of coordination, overactive reflexes and coma.

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

You should not be given this medicine if you are already taking apomorphine (used to treat Parkinson's disease); because severe hypotension (low blood pressure) and loss of consciousness have been reported in patients treated with both apomorphine and Ondansetron Injection at the same time.

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

Pregnancy and breast-feeding
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 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 are being treated with Ondansetron Injection. This is because small amounts pass into the mother's breast milk. Ask your doctor or midwife for advice.

Driving and using machines
Ondansetron Injection should not affect your ability to drive or use machines. However, if any of the side effects (see Section 4) affect you (e.g. dizziness, blurred vision) caution is advisable. **Do not drive or operate if you are feeling unwell.**

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

3. How your Ondansetron Injection is given to you

Ondansetron Solution for Injection will usually be given to you by a nurse or doctor by slow injection or infusion (drip) into a vein (intravenously).

The dose you have been prescribed will depend on the treatment you are having.

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

- A single dose should not be more than 16mg.
- 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 tablet or 8 mg Ondansetron syrup.

On the following days

- The usual adult dose is one 8 mg tablet or 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 to 17 years
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 (up to 8 mg) 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 mg syrup twice a day for small children and those weighing 10 kg or less
- one 4 mg tablet or 4 mg syrup twice a day for larger children and those weighing more than 10 kg
- two 4 mg tablets or 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

Elderly

- If you are over 65 years of age, your doctor will adjust your dose as required.

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 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 have blood tests to check how your liver is working, this medicine may affect the results.

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

If you are concerned about how much medicine you have been given or how often you have been given it, please tell your doctor or nurse.

If you have more Ondansetron Injection than you should

There is limited experience of ondansetron overdose. In a few patients, the following symptoms were observed: visual disturbances, severe constipation, low blood pressure and unconsciousness. In all cases, the symptoms disappeared completely. Tell your doctor if any of these symptoms occur.

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.

Tell your doctor or a member of the medical staff straight away if you have:
- An allergic reaction. 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. If you are allergic to similar medicine you are more likely to suffer these effects.
- Fits (seizures)
- Disturbances in heart rhythm (sometimes causing a sudden loss of consciousness).

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)
- Constipation. If you are constipated tell your doctor,
- Feeling flushed or warm,
- Redness or irritation at the injection site.
- Changes to liver function test results (if you are given Ondansetron Injection with a medicine called cisplatin, otherwise this side effect is uncommon).

Uncommon side effects (may affect up to 1 in 100 people)
- Spasms in the muscles of the face and eyes, tremor, uncontrollable movements,
- Hiccups,
- Chest pain, an irregular or slow heartbeat or low blood pressure
- Low blood pressure, which can make you feel faint or dizzy,

- Fits,
- Unusual body movements or shaking

Rare side effects (may affect up to 1 in 1,000 people)
- Blurred vision,
- Dizziness when ondansetron is injected quickly into the vein,
- Disturbance in heart rhythm (sometimes causing a sudden loss of consciousness).

Very rare side effects (may affect up to 1 in 10,000 people)
- Temporary loss of eyesight, which usually comes back within 20 minutes,
- A widespread rash with blisters and skin peeling on much of the body surface (toxic epidermal necrolysis)

Unknown (cannot be estimated from the available data)
- myocardial ischemia – signs include sudden chest pain or chest tightness

Side effects in children and adolescents were comparable to that seen in adults.

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 or search for MHRA Yellow Card in the Google Play or Apple App Store.
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 store the injection above 30ºC.
- Store in the original package. Protect from light.
- Do not use this medicine after the expiry date which is stated on the ampoule and carton. The expiry date refers to the last day of that month.

6. Contents of the pack and other information

What Ondansetron Injection contains

The active substance is: ondansetron (as ondansetron hydrochloride dihydrate).
Each ml of solution contains 2 mg of ondansetron.
Each 2 ml ampoule contains 4 mg of ondansetron.
Each 4 ml ampoule contains 8 mg of ondansetron.
The other ingredients are: citric acid monohydrate, sodium citrate, sodium chloride and water for injections.

What Ondansetron Injection looks like and contents of the pack
Ondansetron Solution for Injection or Infusion is a clear solution (liquid) and is supplied in 2ml (4mg) and 4ml (8mg) amber glass ampoules.
Pack of 1, 2, 5 or 10 ampoule(s).
Not all pack size may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Mylan, Potters Bar, Hertfordshire, EN6 1TL, United Kingdom.

Manufacturer
Viatris Santé, 1 rue de Turin, 69007 Lyon - France
Pharmathen S.A., 6 Dervenakion, 153 51 Pallini, Attikis, Athens – Greece
Mylan B.V., Dieselweg 25, 3752 LB Bunschoten – The Netherlands
Demo S.A., 21st Km National Road Athens-Lamia, 145 68 Athens – Greece

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The following information is intended for healthcare professionals only:

Posology and method of administration

- Patients with moderate to severe liver problems will not be given more than 8 mg of Ondansetron in a day.
- No alteration of daily dosage or frequency of dosing, or route of administration are required.
- Ondansetron is also available as a tablet.

FOR MOST PATIENTS HAVING EMOTOGENIC CHEMOTHERAPY OR RADIATION TREATMENT

Adults (including the elderly)
8 mg of Ondansetron –should be administered as a slow intravenous injection (in not less than 30 seconds) or intramuscular injection, immediately before treatment, followed by an 8 mg tablet 12 hours after treatment. To prevent further sickness after treatment an 8 mg tablet twice a day may be taken for up to 5 days. The selection of dose regimen should be determined by the severity of the emetogenic challenge.

FOR PATIENTS HAVING CHEMOTHERAPY THAT CAUSES SEVERE NAUSEA AND VOMITING

Adults (including the elderly)

The dose range of Ondansetron Solution for Injection or Infusion is 8 to 32 mg a day and selected as shown below.
During the first day of treatment, any of the following doses may be given:
- 8 mg injected, by slow intravenous injection (in not less than 30 seconds) or intramuscular injection, immediately before treatment, followed by 8 mg orally twelve hourly
- 8 mg injected, by slow intravenous injection (in not less than 30 seconds) or intramuscular injection, immediately before chemotherapy, followed by two more 8 mg doses injected 4 hours apart or by intravenous infusion (drip) of 1 mg per hour for up to 24 hours

Patients age 75 years or older:
- A single dose of 8 mg given as an intravenous infusion (drip), over not less than 15 minutes, immediately before chemotherapy. A single dose greater than 8 mg must not be given.

Adult patients younger than 75 years:
- A single dose of 16 mg given as an intravenous infusion (drip), over not less than 15 minutes, immediately before chemotherapy. A single dose greater than 16 mg must not be given.

All intravenous doses should be diluted in 50-100 mL of saline or other compatible fluid and infused over at least 15 minutes in patients age 65 years or older.

Repeat intravenous doses should be given no less than 4 hours apart.

To prevent sickness after treatment an 8 mg tablet twice a day may be taken for up to 5 days.

Children (aged 6 months and above) and adolescents
- For chemotherapy, the usual dosage is either a single intravenous dose of 5 mg/m^2 body surface area or up to 3 doses of 0.15 mg/kg body weight at 4-hourly interval (section 4.4 and 5.1 of the prescribing information). The intravenous dose must not exceed 8 mg. The total daily dose must not exceed adult dose of 32 mg.
- There is no recommendation for the use of ondansetron either for the prevention of delayed or prolonged nausea and vomiting induced by chemotherapy or nausea and vomiting caused by radiotherapy.

Table 1: BSA-based dosing for Chemotherapy - Children aged ≥ 6 months to 17 years

BSA	Day 1 [a,b]	Days 2-6 [b]
< 0.6 m^2	5 mg/m^2 IV plus 2 mg syrup after 12 hours	2 mg syrup every 12 hours
≥ 0.6 m^2 to ≤ 1.2 m^2	5 mg/m^2 IV plus 4 mg syrup or tablet after 12 hours	4 mg syrup or tablet every 12 hours
> 1.2 m^2	5 mg/m^2 or 8 mg IV plus 8 mg syrup or tablet after 12 hours	8 mg syrup or tablet every 12 hours

a The intravenous dose must not exceed 8 mg.
b 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 (see sections 4.4 and 5.1).

Ondansetron should be administered immediately before chemotherapy as a single IV dose of 0.15 mg/Kg. The single intravenous dose must not exceed 8 mg.

On Day 1, 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).
The total dose over 24 hours (given as divided doses) must not exceed adult dose of 32 mg.

Table 2: Weight-based dosing for Chemotherapy - Children aged ≥ 6 months to 17 years

Weight	Day 1 [a,b]	Days 2-6 [b]
≤10 kg	Up to 3 doses of 0.15 mg/kg IV every 4 hours	2 mg syrup every 12 hours
> 10 kg	Up to 3 doses of 0.15 mg/kg IV every 4 hours	4 mg syrup or tablet every 12 hours

a The intravenous dose must not exceed 8 mg.
b The total dose over 24 hours (given as divided doses) must not exceed adult dose of 32 mg.

FOR PATIENTS HAVING AN OPERATION

Adults (including the elderly)
To prevent nausea and vomiting – 4 mg injected by intramuscular or slow intravenous injection before the operation.
To treat established PONV nausea and vomiting – 4 mg given by intramuscular or slow intravenous injection.

Children (aged 1 month and above) and adolescents

- For prevention and treatment of post-operative nausea and vomiting after a surgery under general anaesthesia, a single dose of ondansetron at 0.1 mg/kg up to a maximum of 4 mg is administered into a vein during not less than 30 seconds.
- There is no recommendation for the use of ondansetron in the treatment of post-operative nausea and vomiting in children under 2 years of age.

Patients with kidney problems or who cannot metabolise sparteine/debrisoquine well can take the recommended doses of ondansetron, as detailed above.

Instructions for use/handling

- Once opened use immediately.
- In keeping with good pharmaceutical practice, dilutions of Ondansetron injection in intravenous fluids should be prepared at the time of infusion. Once diluted the solution for infusion should be stored in the original plastic container of the infusion fluid. Chemical and physical in-use stability has been demonstrated for 7 days at 5°C and 25°C when the product is diluted to a concentration of 0.32 or 0.64 mg/ml. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to the 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.
- Do not use the injection if the ampoule is damaged or the solution is cloudy or contains particles.
- Single use only. Any unused solution should be discarded.
- Ondansetron solution for injection should not be autoclaved.
- Compatibility with solutions for infusion

  Ondansetron injection should not be administered in the same syringe or infusion as any other medication.

  Ondansetron solution for injection should only be admixed with those infusion solutions which are recommended:
  - Sodium Chloride 9 mg/ml (0.9%) solution for infusion
  - Glucose 50 mg/ml (5%) solution for infusion
  - Mannitol 100 mg/ml (10%) solution for infusion
  - Ringers solution for infusion
  - Potassium Chloride 3 mg/ml (0.3%) and Sodium Chloride 9 mg/ml (0.9%) solution for infusion
  - Potassium Chloride 3 mg/ml (0.3%) and Glucose 50 mg/ml (5%) solution for infusion

  Compatibility studies 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 I glass bottles. Dilutions of Ondansetron in sodium chloride 0.9% w/v or in glucose 5% w/v have been demonstrated to be stable in polypropylene syringes. It is considered that Ondansetron injection diluted with other compatible infusion fluids would be stable in polypropylene syringes.

- Compatibility with other medicinal products

  Dexamethasone-21-dihydrogenphosphate disodium: 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.

  Ondansetron may be administered by intravenous infusion by 1 mg/hour. The following medicinal products may be administered only via a Y-site of an infusion set in concentrations of ondansetron 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.

Carboplatin:
Concentrations not exceeding the range of 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.

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.

Etoposide:
Concentrations not exceeding the range of 0.144 mg/ml to 0.250 mg/ml (e.g. 72 mg in 500 ml to 250 mg in 1 litre), administered over thirty minutes to one hour.

Ceftazidime:
Doses in the range of 250 mg to 2000 mg reconstituted with water for injections 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 of 100 mg to 1 g, reconstituted with water for injections, 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 of 10 mg to 100 mg reconstituted with water for injections, 5 ml per 10 mg doxorubicin, as recommended by the manufacturer and given as an intravenous bolus injection over approximately 5 minutes.

Overdose

Symptoms and Signs: There is limited experience of Ondansetron overdose. In the majority of cases symptoms were similar to those already reported in patients receiving recommended doses (see section 4.8 of the prescribing information). Manifestations that have been reported include visual disturbances, severe constipation, hypotension and a vasovagal episode with transient second-degree AV block. Ondansetron prolongs QT interval in a dose-dependent fashion. ECG monitoring is recommended in cases of overdose. Cases consistent with serotonin syndrome have been reported in young children following oral overdose.

There is no specific antidote to ondansetron; for that reason, if overdose is suspected, only the symptoms should be treated. Using a drug inducing vomiting (ipecacuanha) is not recommended.
ECG monitoring is recommended.