

PACKAGE LEAFLET: INFORMATION FOR THE USER

Gamidarin 2 mg/ml Solution for Injection/infusion ondansetron

The name of your medicine is Gamidarin 2 mg/ml Solution for Injection/infusion, which will be called Gamidarin injection or Gamidarin throughout this leaflet.

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Gamidarin injection is and what it is used for
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1. What Gamidarin injection is and what it is used for

Gamidarin injection is a clear solution containing the active ingredient ondansetron (as ondansetron hydrochloride dihydrate), which is an anti-emetic (prevents nausea [feeling sick] and vomiting).

Gamidarin injection is used to prevent and treat nausea and vomiting caused by chemotherapy or radiotherapy and for the prevention and treatment of nausea and vomiting after surgery.

2. Before you are given Gamidarin injection

You should not be given Gamidarin injection if:

You are hypersensitive to ondansetron or to other selective 5HT₃ receptor antagonists (e.g. granisetron, dolasetron) or to any of the excipients (see list of ingredients in section 6).

Take special care with Gamidarin injection if:

- you have a blockage in your gut or suffer from severe constipation. Gamidarin can enhance the blockage or constipation
- you have ever had heart problems
- you have an uneven heart beat (arrhythmias)
- you are having your tonsils out
- you have liver problems
- you have undergone surgery to remove tonsils situated at the back of the nose (adenotonsillar surgery).

Taking other medicines:

You should tell your doctor if you are taking or have taken any of the following medicines as they may interact with your Gamidarin injection:

- phenytoin, carbamazepine (treatments for epilepsy)
- rifampicin (an antibiotic)
- tramadol (a painkiller)
- beta-blockers (drugs that slow heart rate)

Please tell your doctor or pharmacist if you are taking, or have recently taken, any other medicines, including medicines obtained without a prescription.

It may still be alright for you to be given Gamidarin injection and your doctor will be able to decide what is suitable for you.

Pregnancy and lactation

Please tell your doctor if you are pregnant or planning to be pregnant. Ondansetron passes into breast milk, therefore nursing mothers should not breast-feed.

Driving and using machines

Gamidarin injection has no effect on your ability to drive or use machines.

Important information about some of the ingredients in Gamidarin injection

This medicinal product contains 2.52 mmol (57.6 mg) sodium per maximum daily dose of 32 mg. To be taken into consideration by patients on a controlled sodium diet.

3. How you are given Gamidarin injection

Method of administration

Gamidarin injection is given as intravenous injection (into a vein) or, after dilution, as intravenous infusion (for a longer time). It will usually be given by a doctor or a nurse.

To prevent nausea and vomiting from chemotherapy or radiotherapy

On the day of chemotherapy or radiotherapy

- the usual adult dose is 8 mg given by an injection into your vein, just before your treatment, and another 8 mg twelve hours later. The usual dose in adults is 8 to 32 mg ondansetron a day. 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 Gamidarin injection. Your doctor will decide this.

Children aged over 6 months and adolescents

The usual dose for children is a single intravenous dose of 5 mg/m² (body area) immediately before chemotherapy; two further intravenous doses may be given in 4-hourly intervals. 4 mg orally twice daily should be continued for up to 5 days after a course of treatment.

On the day of chemotherapy or radiotherapy

- the first dose is given by an injection into the vein, just before your child's treatment. After chemotherapy, your child's medicine will usually be given by mouth; the usual dose is a 4 mg Ondansetron tablet or 5 ml (4 mg) Ondansetron syrup twelve hours later.

On the following days

- one 4 mg tablet or 5 ml (4 mg) syrup twice a day
- this can be given for up to five days.

To prevent nausea and vomiting after an operation

- The usual dose for adults is 4 mg given by an injection into your vein. This will be given just before your operation.
- For children aged over 6 months and adolescents, the usual dose for children is a dose of 0.15 mg/kg (body weight). The maximum dose is 4 mg given as an injection into the vein. This will be given just before the operation.

To treat nausea and vomiting after an operation

- The usual adult dose is 4 mg given by an injection into your vein.
- For children aged over 6 months and adolescents, the usual dose for children is a dose of 0.1 mg/kg (body weight). The maximum dose is 4 mg given as an injection into the vein.

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

Gamidarin 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 have been given more Gamidarin injection than you should

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

If you forget to take Gamidarin injection

If you think you have missed a dose, please tell your doctor or nurse.

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

4. Possible side effects

Like all medicines, Gamidarin injection 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.

Side effects can be listed according to how often they occur:

Very common:	affects more than 1 user in 10
Common:	affects 1 to 10 users in 100
Uncommon:	affects 1 to 10 users in 1,000
Rare:	affects 1 to 10 users in 10,000
Very rare:	affects less than 1 user in 10,0000
Not known:	frequency cannot be estimated from the available data

The following side effects have been reported:

Very common

- headache

Common

- constipation
- sensation of warmth or flushing
- interference with liver function tests
- irritation and redness at the site of injection
- local burning sensation following insertion of suppositories

Uncommon

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

Rare

- feeling dizzy or light headed
- blurred vision
- disturbance in heart rhythm (sometimes causing a sudden loss of consciousness)

Very rare

- temporary blindness (most resolved within 20 minutes)

If any of the side effects gets serious, or if you notice any side effect not listed in the leaflet, please tell your doctor or pharmacist.

5. How to store Gamidarin injection

Keep out of the reach and sight of children.

Your doctor or pharmacist knows how to store Gamidarin injection.

Do not use Gamidarin injection after the expiry date, which is stated on the packaging after "Exp". The expiry date refers to the last day of that month.

This medicinal product does not require any special storage temperature. Keep ampoules in the outer carton, in order to protect from light.

Shelf life after opening

After first opening the medicinal product should be used immediately.

Shelf life after dilution of the solution

Chemical and physical in-use stability has been demonstrated for 36 hours at 2-8°C with the solutions given in section 6.6.

The diluted solutions should be stored protected from light.

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.

Only clear solutions practically free from particles should be used. Do not use if container is damaged.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Further information

What Gamidarin injection contains:

The active ingredient is ondansetron (as ondansetron hydrochloride dihydrate). Each ml of solution for injection contains 2 mg ondansetron (as ondansetron hydrochloride dihydrate). Each 2 ml ampoule contains 4 mg ondansetron (as ondansetron hydrochloride dihydrate) Each 4 ml ampoule contains 8 mg ondansetron (as ondansetron hydrochloride dihydrate)

The other ingredients are:

citric acid monohydrate, sodium citrate, sodium chloride, water for injections

What Gamidarin injection looks like and contents of the pack

Gamidarin injection is a clear colourless solution for injection/infusion filled in clear glass ampoule.

2 ml type I clear glass ampoules containing 2 ml of solution: pack size of 5 or 25 ampoules.

5 ml type I clear glass ampoules containing 4 ml of solution: pack size of 5 or 25 ampoules.

Not all pack sizes may be marketed

Marketing Authorization Holder:

Amneal Pharma Europe Limited
70 Sir John Rogerson's Quay
Dublin 2
Ireland

Manufacturer:

Pfizer Service Company BVBA
Hoge Wei 10 – B-1930
Zaventem
Belgium

Pfizer PGM
Zone Industrielle 29, route des Industries
37530 POCE-SUR-CISSE
France

This leaflet was last revised in 03/2014**Information for Healthcare professionals,****The following information is intended for medical or healthcare professionals only:****1. Administration****Chemotherapy and Radiotherapy:****Adults:**

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

Emetogenic chemotherapy and radiotherapy: Ondansetron can be given either by rectal, oral (tablets or syrup), or intravenous administration.

For most patients receiving emetogenic chemotherapy or radiotherapy, ondansetron 8mg should be administered as a slow intravenous injection immediately before treatment, followed by 8mg 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 rectal or intravenous 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 8mg by slow intravenous injection immediately before chemotherapy.

A dose of 8mg by slow intravenous injection immediately before chemotherapy, followed by two further intravenous doses of 8mg two to four hours apart, or by a constant infusion of 1mg/hour for up to 24 hours.

A single dose of 16 mg diluted in 50-100ml of saline or other compatible infusion fluid (see Pharmaceutical Precautions) 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 dependant increase of QT prolongation risk (see sections 4.4, 4.8 and 5.1 of 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, 20mg 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.

BSA-based dosing for Chemotherapy - Children aged > 6 months and adolescents

BSA	Day 1 ^(a,b)	Days 2-6 ^(c)
< 0.6 m ²	5 mg/m ² i.v. plus 2 mg syrup after 12 hrs	2 mg syrup every 12 hrs
≥ 0,6 m ² < 1,2 m ²	5 mg/m ² i.v. plus 4 mg syrup or tablet after 12 hrs	4 mg syrup or tablet every 12 hrs

^a The intravenous dose must not exceed 8mg.

^b The total daily dose must not exceed adult dose of 32 mg.

For children with a body surface area of greater than 1.2 m² an initial i.v. dose of 8 mg is administered immediately before chemotherapy, followed by 8 mg orally 12 hours later. 8mg ondansetron, orally twice daily can be continued for up to five days after a course of treatment.

Weight-based dosing for Chemotherapy - Children aged > 6 months and adolescents

Weight	Day 1 ^(a,b)	Days 2-6 ^(c)
≤ 10 kg	Up to 3 doses of 0.15 mg/kg every 4 hrs	2 mg syrup every 12 hrs
> 10 kg	Up to 3 doses of 0.15 mg/kg every 4 hrs	4 mg syrup or tablet every 12 hrs

^a The intravenous dose must not exceed 8mg.

^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 dosage, dosing frequency or route of administration are required.

Patients with Renal Impairment:

No alteration of daily dosage or frequency of dosing, or route of administration are 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 8mg should not be exceeded.

Post-Operative Nausea and Vomiting (PONV):**Adults:**

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

Paediatric population**PONV in children aged >1 month and adolescents**

For prevention and treatment of PONV in paediatric patients having surgery performed under general anaesthesia, a single dose of ondansetron may be administered by slow intravenous injection (not less than 30 seconds) at a dose of 0.1mg/kg up to a maximum of 4mg either prior to, at or after induction of anaesthesia.

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 are 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 8mg should not be exceeded.

Patients with poor Sparteine/Debrisoquine Metabolism:

No alteration of daily dosage or frequency of dosing is required.

2. Handling Instructions**Compatibility with intravenous fluids:**

0.08mg/ml concentration of Ondansetron with each diluents at the storage of 2-8 °C for 36 hours. The solution must not be sterilised in an autoclave.

The solution is to be visually inspected prior to use (also after dilution). Only clear solutions practically free from particles should be used. Do not use if container is damaged.

Any unused product or waste material should be disposed of in accordance with local requirements.

Gamidarin 2mg/ml Solution for Injection should only be mixed with those infusion solutions, which are recommended:

Sodium Chloride Intravenous Infusion 0.9%w/v

Glucose Intravenous Infusion 5%w/v

Mannitol Intravenous Infusion 10%w/v

Ringers Intravenous Infusion

Potassium Chloride 0.3%w/v and Sodium Chloride 0.9%w/v Intravenous Infusion

Potassium Chloride 0.3%w/v and Glucose 5%w/v Intravenous Infusion

Dilutions of Gamidarin in the above mentioned diluents have been demonstrated to be stable in polyvinyl chloride (PVC) infusion bags, Non polyvinyl chloride (Non-PVC) infusion bags, Ph. Eur. Type I glass bottles and polyvinyl chloride (PVC) administration sets.

Dilutions of Gamidarin in sodium chloride 0.9%w/v or in glucose 5%w/v have been demonstrated to be stable in polypropylene syringes.

Compatibility with other drugs:

Gamidarin 2mg/ml Solution for Injection may be administered by intravenous infusion at 1mg/hour, e.g. from an infusion bag or syringe pump. The following drugs may be administered via the Y-site of the Gamidarin 2mg/ml Solution for Injection giving 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.

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 1 litres), 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 2g ceftazidime) and given as an intravenous bolus injection over approximately five minutes.

3. Storage information

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

Shelf life after opening:

After first opening the medicinal product should be used immediately.

Shelf life after dilution of the solution:

Chemical and physical in-use stability has been demonstrated for 36 hours at 2-8°C.

The diluted solutions should be stored protected from light.

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.