

## Patient Information Leaflet:

### ONDEMET 2mg/ml Injection (Ondansetron 2mg/ml Solution for Injection and Infusion)

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

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

#### In this leaflet:

1. What Ondemet Injection is and what it is used for
2. Before you receive Ondemet Injection
3. How Ondemet Injection will be given
4. Possible side effects
5. Storing Ondemet Injection

The name of this medicine is Ondemet 2mg/ml Injection (referred to as Ondemet Injection throughout this leaflet).

#### Marketing Authorisation Holder:

Beacon Pharmaceuticals Ltd., The Regent, The Broadway, Crowborough, East Sussex, TN6 1DA, UK.

#### Manufacturer:

This medicine is manufactured by Pharmathen S.A., 6 Dervenakion Str., Pallini 153 51, Attikis, Greece.

1. **What Ondemet Injection is and what it is used for**  
Ondemet 2mg/ml Injection is a solution for injection or infusion into a vein or injection into a muscle. It contains the active ingredient ondansetron. Each ampoule contains 4mg or 8mg ondansetron (as hydrochloride dihydrate) in a solution containing 2mg/ml of ondansetron. Other ingredients in Ondemet Injection are sodium chloride, citric acid monohydrate, sodium citrate and water for injections. Ondemet Injection is available in 2ml or 4ml glass ampoules. Each pack of Ondemet Injection contains 5 or 25 ampoules.

Ondansetron is one of a group of medicines called anti-emetics. It is used in children over 2 years, adolescents and adults (including the elderly) to treat nausea (feeling sick) and vomiting (being sick) caused by chemotherapy or radiotherapy. It is also used to prevent nausea and vomiting in patients following an operation.

#### 2. Before you receive Ondemet Injection

Ondemet Injection should NOT be used if:

- You have ever had an allergic reaction to ondansetron or to other similar anti-emetics (e.g. granisetron, dolasetron) or to any of the other ingredients.

Before receiving Ondemet Injection, tell your doctor if:

- You have a sensitivity to medicines similar to Ondemet Injection.
- You have a blockage in your gut

- You have liver problems
- You are due to have surgery to the adenoids or tonsils
- You have a heart problem or are taking medicines used to treat a heart problem
- Your child is being treated and he/she is very small or is younger than 2 years old

Consult your doctor or pharmacist if these statements were applicable to you at any time in the past.

#### Taking Ondemet Injection with other medicines

Tell your doctor if you are taking any of the following medicines:

- Phenytoin (used to treat epilepsy and heart arrhythmias), Carbamazepine (used to treat epilepsy and neuralgic pain) or Rifampicin (an antibiotic), as these medicines may reduce the effect of ondansetron
  - Tramadol (used to treat pain following surgery), as the effect of this medicine may be reduced by ondansetron
- Tell your doctor if you are taking any other medicine including those that you have bought.

#### Pregnancy and breast feeding

It is not recommended that Ondemet Injection be used during pregnancy. If it is absolutely necessary it should be given with caution especially in the first trimester. If you are receiving Ondemet Injection you should not breast-feed your baby.

#### Driving and using machines

Ondemet Injection is unlikely to affect your ability to drive or operate machinery.

#### 3. How Ondemet Injection will be given

Your doctor will have decided the correct dose of Ondemet Injection for you.

#### Treatment of nausea and vomiting in patients receiving chemotherapy or radiotherapy

For patients receiving chemotherapy or radiotherapy ondansetron can be given either orally or by injection or infusion into a vein. For most patients Ondemet Injection is given by injection into a vein immediately before treatment, followed by 8mg orally every 12 hours. The dose of Ondemet Injection will depend on the dose and combination of chemotherapy and radiotherapy given.

#### Treatment of severe nausea and vomiting in patients receiving chemotherapy

Adults: the usual dose is 8mg given as a slow injection or as a short infusion into a vein, lasting 15 minutes

immediately before chemotherapy. If this dose is not enough, either a further 8mg dose can be given every 4<sup>th</sup> hour (maximum of two doses), or a continuous infusion of 1mg/hour for 24 hours. In some cases the initial dose can be increased to 32mg given as an infusion lasting at least 15 minutes immediately before chemotherapy. After 24 hours treatment is changed to the oral route. The effect of Ondemet Injection may be increased by giving another



## Technical Leaflet

### Ondemet 2mg/ml Injection (Ondansetron)

**Please read this information carefully before using Ondemet 2mg/ml Injection. Further information is contained in the Summary of Product Characteristics.**

#### Presentation

Ondemet 2mg/ml Injection contains 2mg/ml ondansetron as ondansetron hydrochloride dihydrate in each ampoule. Ampoules are 2ml or 4ml amber glass ampoules in packs of 5 or 25.

#### Indications

Nausea and vomiting induced by cytotoxic chemotherapy or radiotherapy.

Prevention of post-operative nausea and vomiting (PONV).

#### Dosage and Method of Administration

Whenever solution and container permit, parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Ondemet 2mg/ml Injection should be injected either as a slow bolus injection or as a short term infusion lasting 15 minutes, directly into a large vein through a large-gauge needle or intravenous catheter.

For infusion administration Ondemet 2mg/ml Injection may be diluted with solution for infusion containing: 0.9% sodium chloride, 5% glucose, 10% mannitol, 0.3% potassium chloride + 0.9% sodium chloride and 0.3% potassium chloride + 5% glucose as well as Ringer solution for infusion. It should not be mixed with other pharmaceutical products.

#### Chemotherapy and radiotherapy induced nausea and vomiting

Adults: The emetogenic potential of cancer treatment varies according to the doses and combinations of chemotherapy and radiotherapy regimens used. The route of administration and dose of ondansetron should be flexible and selected as shown below.

#### Emetogenic chemotherapy and radiotherapy

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

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

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

To protect against delayed or prolonged emesis after the first 24 hours, oral treatment with Ondemet should be continued for up to 5 days after a course of treatment. The recommended dose for oral administration is 8 mg twice daily.

#### Highly emetogenic chemotherapy

Adults: Either 8 mg as a slow intravenous bolus injection or as a short-term infusion lasting 15 minutes immediately before chemotherapy. If this initial dose has insufficient effect it can be supplemented by either 8 mg (intravenous bolus or 15 minutes' infusion) every 4<sup>th</sup> hour, at most twice, or continuous infusion of 1 mg/hour for 24 hours. In some cases the initial dose can be increased to 32 mg diluted with a compatible infusion fluid as an infusion lasting at least 15 minutes immediately before chemotherapy.

After 24 hours treatment is changed to the oral route.

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

Children (aged 2 years and over) and adolescents (< 18 years)

Experience in paediatric patients is limited. In children older than two years, Ondemet may be administered as a single intravenous dose of 5 mg/m<sup>2</sup> over 15 minutes immediately before chemotherapy, followed by 4 mg orally twelve hours later. Oral treatment with a dose according to the body area should be continued for up to 5 days after a course of treatment. Children with a total body area between 0.6 and 1.2 m<sup>2</sup> should receive a dosage schedule of 4 mg 3 times a day, while children with a body area above 1.2 m<sup>2</sup> should receive 8 mg 3 times a day.

There is no experience in children younger than 2 years old.

Ondemet 2mg/ml Injection cannot be used in children with a total body surface below 0.6 m<sup>2</sup>.

#### Elderly

Ondansetron is well tolerated by patients over 65 years and no alteration of dosage, dosing frequency or route of administration are required.

Please refer also to "Special populations".

#### Post-operative nausea and vomiting (PONV)

##### Prevention of PONV

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

Adults: 8 mg as a slow intravenous bolus injection at induction of anaesthesia.

Children aged 2 years and over: 0.1 mg/kg up to a maximum of 4 mg as a slow intravenous bolus injection either before, at or after induction of anaesthesia.

##### Treatment of established PONV

For the treatment of established PONV intravenous administration is recommended.

Up to 8 mg as a slow bolus injection intravenously or intramuscularly.

Children (aged 2 years and over) and adolescents (< 18 years)

For the prevention and treatment of PONV slow intravenous injection is recommended.

0.1 mg/kg up to a maximum of 4 mg as a slow intravenous bolus injection

type of anti-emetic (e.g. dexamethasone) as an injection into a vein at the same time.

Children (aged 2 years and over) and adolescents (under 18 years old): Ondansetron may be given as a slow injection into a vein over 15 minutes immediately before chemotherapy, followed by a 4mg dose taken orally 12 hours later. Oral treatment should be continued for up to 5 days after a course of treatment. The dose given will depend on the size of the child and will be worked out by the doctor.

Ondemet Injection should not be given to children under 2 years or children who are very small.

The elderly (over 65 years): Ondansetron is well tolerated in this patient group and no special dosing instructions are required.

**Prevention of nausea and vomiting after an operation**  
Ondansetron can be given orally or as an injection into a vein.

Adults: 8mg given as a slow injection at the same time as anaesthesia.

Children aged 2 years and over: 0.1mg/kg up to a maximum of 4mg as a slow injection into a vein either before, at or after anaesthesia.

**Treatment of established nausea and vomiting in patients after an operation**

Adults: For the treatment of established nausea and vomiting following an operation Ondemet Injection given into a vein is recommended. The usual dose is up to 8mg as a slow injection into a vein or into a muscle.

Children (aged 2 years and over) and adolescents (under 18 years): For the prevention and treatment of nausea and vomiting after an operation slow injection into a vein of 0.1 mg/kg (up to a maximum of 4mg) is recommended

The elderly (over 65 years): There is little experience in the use of ondansetron in the prevention and treatment of nausea and vomiting following an operation, however ondansetron is well tolerated in this group of patients receiving chemotherapy.

**Patients with moderate or severe liver problems**

The total daily dose should not be more than 8mg.

If you have the impression that the effect of Ondemet Injection is too strong or too weak, talk to your doctor.

#### 4. Possible side effects

Like all medicines, Ondemet Injection may cause side effects.

A few people can be allergic to some medicines. If any of the following happen, stop taking Ondemet Injection and tell your doctor immediately or go to the casualty department of the nearest hospital:

- Severe itching of the skin, rash
- Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulties in swallowing or breathing.

#### • Collapse

You may have had a serious allergic reaction to Ondemet Injection.

All of these are very serious side effects and are rare. Tell your doctor if you notice any of the following:

Side effects that are very common:

#### • Headache

Side effects that are common:

- Constipation
- Local burning sensation following insertion of suppositories
- Sensation of flushing and warmth
- Local reaction at the injection site

Side effects that are uncommon:

- Hiccups
- Low blood pressure
- Chest pains or palpitations
- Slowing of the heart rate
- Seizures
- Upward movement of the eyes
- Abnormal body movements or shaking
- An increase in liver function tests (commonly seen in patients receiving chemotherapy with cisplatin)

Side effects that are rare:

- Dizziness (during rapid injection into a vein)
- Muscle cramps
- Visual disturbances e.g. blurred vision (mainly during rapid injection into a vein)

Side effects that are very rare:

- Temporary blindness (mainly during injection into a vein and in patients receiving chemotherapy e.g. cisplatin)

If you do experience side effects these usually disappear after a few days of treatment. If they are troublesome or persistent, or if you have side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

#### 5. Storing Ondemet Injection

There are no special storage instructions. Ondemet Injection should be used immediately. Any unused solution should be discarded. Do not use if the solution is not clear.

Keep out of the reach and sight of children.

**Use by date:**

Do not use Ondemet Injection after the expiry/use before date on the ampoule and carton.

**Further information:**

This leaflet does not include all the information about this medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

**Date of preparation of the leaflet:**

January 2006



#### Elderly

There is limited experience in the use of ondansetron in the prevention and treatment of post-operative nausea and vomiting (PONV) in the elderly, however ondansetron is well tolerated in patients over 65 years receiving chemotherapy.

Please refer also to "Special populations".

#### Special populations

##### *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 8 mg should not be exceeded.

##### *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 medicinal product exposure levels no different from those of the general population. No alteration of daily dosage or frequency of dosing are required.

#### Contraindications

Ondemet 2mg/ml Infusion is contraindicated in patients who are hypersensitive to ondansetron or to other selective 5-HT<sub>3</sub>-receptor antagonists (e.g. granisetron, dolasetron) or to any of the excipients.

#### Special warnings and precautions for use

Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5-HT<sub>3</sub> receptor antagonists.

As ondansetron is known to increase large bowel transit time, patients with signs of subacute intestinal obstruction should be monitored following administration.

In patients with adenotonsillar surgery prevention of nausea and vomiting with ondansetron may mask occult bleeding. Therefore, such patients should be followed carefully after Ondemet.

Since there is little experience to date of the use of ondansetron in cardiac patients, caution should be exercised if Ondemet is coadministered with anaesthetics to patients with arrhythmias or cardiac conduction disorders or to patients who are being treated with antiarrhythmic agents or beta-blockers.

The solution for injection contains less than 1 mmol sodium (23 mg) per ampoule, i.e. essentially 'sodium-free'.

Ondemet 2mg/ml Injection should not be used in children with a total body surface below 0.6 m<sup>2</sup>.

The medicinal product should not be used for children younger than two years, as for these patients the experience is limited.

#### Pregnancy and lactation

Use in human pregnancy has not been established and is not recommended. If it is absolutely essential that

ondansetron be given caution should be exercised when prescribing to pregnant women especially in the first trimester.

It is recommended that mothers receiving ondansetron should not breast-feed.

**Interactions with other medicinal products and other forms of interaction**

There is no evidence that ondansetron either induces or inhibits the metabolism of other medicinal products commonly coadministered with it. Specific studies have shown that ondansetron does not interact with alcohol, temazepam, furosemide, alfentanil, propofol and thiopental.

Ondansetron is metabolised by multiple hepatic cytochrome P-450 enzymes: CYP3A4, CYP2D6 and CYP1A2. Due to the multiplicity of metabolic enzymes capable of metabolising ondansetron, enzyme inhibition or reduced activity of one enzyme (e.g. CYP2D6 genetic deficiency) is normally compensated by other enzymes and should result in little or no significant change in overall ondansetron clearance or dose requirement.

*Phenytoin, Carbamazepine and Rifampicin:* In patients treated with potent inducers of CYP3A4 (i.e. phenytoin, carbamazepine, and rifampicin), the clearance of ondansetron was increased and ondansetron blood concentrations were decreased.

*Tramadol:* Data from small studies indicate that ondansetron may reduce the analgesic effect of tramadol.

#### Pharmaceutical Information

##### Excipients

Sodium chloride, Citric acid monohydrate, Sodium citrate, Water for injections.

##### Incompatibilities

Ondemet 2mg/ml Injection should not be mixed with other pharmaceutical products.

##### Shelf-life 3 years

After opening: 24 hours stored in a refrigerator (2-8°C)

##### Storage Precautions No special precautions

Chemical and physical in-use stability has been demonstrated for 24 hours at 2-8°C.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product should be used immediately. If not, in-house storage times and conditions are the responsibility of the user.

Keep out of sight and reach of children

##### Nature of Container

Amber, type I glass ampoules.

##### Instructions for Use and Handling.

Please refer to 'Dosage and method of administration'. Discard any unused solution.

