Package leaflet: Information for the user

***Palladone*® 2 mg/ml and 10 mg/ml solution for injection or infusion**
Hydromorphone hydrochloride

<u>This medicine contains hydromorphone which is an opioid, which can cause addiction. You can get withdrawal symptoms if you stop taking it suddenly.</u>

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.
- 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.

What is in this leaflet:
1. What ***Palladone*** injection is and what it is used for
2. What you need to know before you use ***Palladone*** injection
3. How to use ***Palladone*** injection
4. Possible side effects
5. How to store ***Palladone*** injection
6. Contents of the pack and other information

1. What *Palladone* injection is and what it is used for
This medicine has been prescribed for you for the relief of severe pain. It contains hydromorphone, which belongs to a class of medicines called opioids, which are 'pain relievers'. This medicine has been prescribed for you and should not be given to anyone else.

Opioids can cause addiction and you may get withdrawal symptoms if you stop taking this medicine suddenly. Your prescriber should have explained how long you will be taking it for and when it is appropriate to stop, how to do this safely.

2. What you need to know before you use *Palladone* injection

Do not use *Palladone* injection if you:
- are allergic to hydromorphone or to any of the other ingredients of this medicine (listed in section 6);
- have breathing problems, such as severe chronic obstructive airways disease, respiratory depression or severe asthma. Symptoms may include breathlessness, coughing or breathing more slowly and weakly than expected;
- have a heart problem after long-term lung disease (cor pulmonale);
- have severe pain in your abdomen;
- have a condition where the small bowel does not work properly (paralytic ileus);
- are taking a type of medicine known as a monoamine oxidase inhibitor (examples include tranylcypromine, phenelzine, isocarboxazid, moclobemide and linezolid), or you have taken this type of medicine in the last two weeks.

Palladone injection must not be used if the patient is in a coma.

Warnings and precautions
Talk to your doctor or pharmacist before using ***Palladone*** injection if you:

- are or have ever been addicted to opioids, alcohol, prescription medicines, or illegal drugs;
- have previously suffered from withdrawal symptoms such as agitation, anxiety, shaking or sweating, when you have stopped taking alcohol or drugs;
- feel you need to take more of ***Palladone*** to get the same level of pain relief, this may mean you are becoming tolerant to the effects of this medicine or are becoming addicted to it. Speak to your prescriber who will discuss your treatment and may change your dose or switch you to an alternative pain reliever;
- have a head injury (due to the risk of increased brain pressure);
- suffer from seizures, fits or convulsions;
- suffer from a mental disorder as a result of an intoxication (toxic psychosis);
- have low blood pressure associated with low circulating blood volume (hypotension with hypovolaemia);
- are feeling light-headed or faint;
- have problems with your gall bladder;
- have inflammation of the pancreas (pancreatitis);
- have any bowel problems (such as obstructive or inflammatory bowel disease);
- have prostate problems (such as difficulties in passing urine);
- have poor adrenal gland function (e.g. Addison's disease).
- have an under-active thyroid gland (hypothyroidism);
- have a chronic obstructive airway disease (such as COPD) or reduced pulmonary function;
- suffer from a debilitated general condition or are elderly;
- suffer from severe kidney problems (including ureteric colic);
- suffer from severe liver problems;
- suffer from constipation.

This medicine may cause breathing problems or worsen already existing problems while sleeping. These problems may include pauses in breathing during sleep, being awoken by shortness of breath, difficulty staying asleep or excessive daytime drowsiness. If you or someone else observes these symptoms contact your doctor. Your doctor may want to lower your dose.

Using this medicine regularly, particularly for a long time, can lead to addiction. Your prescriber should have explained how long you will be using it for and when it is appropriate to stop, how to do this safely.

Rarely, increasing the dose of this medicine can make you more sensitive to pain. If this happens, you need to speak to your prescriber about your treatment.

Addiction can cause withdrawal symptoms when you stop taking this medicine. Withdrawal symptoms can include restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being sick, diarrhoea, loss of appetite, shaking, shivering or sweating. Your doctor will discuss with you how to gradually reduce your dose before stopping the medicine. It is important that you do not stop taking the medicine suddenly as you will be more likely to experience withdrawal symptoms.

Opioids should only be used by those they are prescribed for. Do not give your medicine to anyone else. Taking higher doses or more frequent doses of opioid may increase the risk of addiction. Overuse and misuse can lead to overdose and/or death.

You may experience hormonal changes whilst using this medicine. Your doctor may want to monitor these changes.

If this information applies to you or formerly applied to you, please speak to your doctor.

Palladone injection is not recommended for children under 12 years of age.

The major risk of opioid excess is difficulty in breathing (respiratory depression).

Please tell your doctor if you experience small bowel problems (paralytic ileus) during treatment with this medicine. He or she will take appropriate measures.

If you are going to have an operation, please tell the doctor at the hospital that you are using this medicine as they may need to adjust the amount of injection you are given.

The use of this medicine may produce positive results in doping controls.

Other medicines and *Palladone* injection
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

When taken with some other medicines or alcohol, the side effects of ***Palladone*** injection (such as drowsiness, breathing problems, constipation, dry mouth, difficulty in passing urine) or the other medicine may be altered.

Tell your doctor if you:

- are taking medicines to treat anxiety (for example tranquillisers);
- have been given an anaesthetic (for example a barbiturate);
- are taking medicines to help you sleep (benzodiazepines, hypnotics or sedatives);
- are taking medicines to treat psychiatric or mental disorders (neuroleptics or psychotropics);
- are taking medicines to treat depression (antidepressants);
- are taking medicines used to stop you feeling sick or being sick (antiemetics);
- are taking medicines used to prevent or relieve the symptoms of an allergy (antihistamines);
- are taking medicines to treat Parkinson's disease;
- are taking other strong analgesics or 'painkillers', or have recently taken another painkiller from the opioid class.

Concomitant use of ***Palladone*** injection and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible.

However if your doctor does prescribe ***Palladone*** injection together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor.

Please tell your doctor about all sedative medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

Do not take this medicine if you are taking a specific type of medicine known as a monoamine oxidase inhibitor, or you have taken this type of medicine in the last two weeks.

***Palladone* injection with food, drink and alcohol**
Drinking alcohol during your treatment with this medicine may make you drowsy. If you are affected you should avoid drinking alcohol.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Pregnancy
Do not use ***Palladone*** injection if you are pregnant or think you might be pregnant unless you have discussed this with your doctor and the benefits of treatment are considered to outweigh the potential harm to the baby. If you use ***Palladone*** injection during pregnancy your baby may become dependent and experience withdrawal symptoms after the birth which may need to be treated, such as high-pitched cry, jitteriness, fits, poor feeding and diarrhoea.

If you use this medicine during labour, uterine contractility may be impaired. In addition slow and shallow breathing (respiratory depression) may occur in the newborn infant.

Breast-feeding
Do not use ***Palladone*** injection while you are breastfeeding as hydromorphone passes into breast milk and will affect your baby.

Driving and using machines
This medicine may make you drowsy and thus impair your ability to drive and use machines. This applies particularly:

- at the beginning of treatment;
- if your dose is increased;
- if you have switched to this medicine from a different opioid.
- if you drink alcohol or use medicines which influence your brain function.

You should consult your doctor before driving or using machinery.

This medicine can affect your ability to drive as it may make you sleepy or dizzy.

- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive while you have this medicine in your body over a specified limit unless you have a defence (called the 'statutory defence').
- This defence applies when:
    - The medicine has been prescribed to treat a medical or dental problem; and
    - You have taken it according to the instructions given by the prescriber and in the information provided with the medicine.
- Please note that it is still an offence to drive if you are unfit because of the medicine (i.e. your ability to drive is being affected).

Details regarding a new driving offence concerning driving after drugs have been taken in the UK may be found here: https://www.gov.uk/drug-driving-law

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

***Palladone* injection contains sodium**

This medicine contains less than 1 mmol sodium (23 mg) per ml, i.e. essentially “sodium-free”.

3. How to use *Palladone* injection
Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

A doctor or nurse will usually prepare and administer the injection for you.

Your doctor will decide how much ***Palladone*** injection you require based on:
- the severity of your pain;
- the dose of painkiller you have previously been given;
- your age and weight.

Your doctor will increase the amount of this medicine you are given until your pain is relieved. If you find that you are still in pain whilst undergoing treatment with this medicine discuss this with your doctor.

You should not use ***Palladone*** 10 mg, injection as initial opioid therapy. This higher strength may only be used as individual doses if you have no longer sufficiently responded to lower doses of hydromorphone preparations (***Palladone*** 2 mg) or comparably strong analgesics as part of long term pain therapy.

The usual starting doses of ***Palladone*** injection are as follows:

Use in adults and adolescents (older than 12 years of age)
- As a single injection into a vein, the usual dose is 1 to 1.5 mg given slowly over 2 to 3 minutes. This can be repeated every 3 to 4 hours.
- As a single injection through a fine needle into the tissue under the skin, the usual dose is 1 to 2 mg. This can be repeated every 3 to 4 hours.
- As an infusion into a vein or through a fine needle into the tissue under the skin, the usual starting dose is 0.15 to 0.45 mg/hour (or 0.004 mg/kg bodyweight/hour).
- If given by patient controlled analgesia (PCA), the usual recommended bolus dose is 0.2 mg with a stop interval of 5 to 10 minutes.

Use in children (under 12 years of age)
Palladone injection is not recommended for children under 12 years of age.

Use in elderly patients (over 75 years of age)
A lower dosage might be enough for adequate pain relief in elderly patients.

Use in patients with liver and kidney problems
If you suffer from liver or kidney problems, you may require less of this medicine in order to relieve your pain.

Route of administration
A doctor or nurse will usually administer ***Palladone*** injection for you.

This medicine is intended for injection or infusion into a vein (intravenous = IV) or through a fine needle under the skin (subcutaneous = SC).

Duration of treatment
This medicine should only be used as long as necessary. Your doctor should have discussed with you how long your treatment with ***Palladone*** will last. They will arrange a plan for stopping treatment. This will outline how to gradually reduce the dose and stop taking the medicine.
If you get long term treatment, your doctor should verify regularly whether you still need this medicine. Do not stop the treatment without talking to your doctor (see "If you stop using ***Palladone*** injection").

If you use more *Palladone* injection than you should
Call your doctor, hospital or an ambulance **straight away** as the patient may need emergency treatment in hospital. In severe cases an overdose may lead to unconsciousness, pneumonia caused by inhaling vomit or foreign matter (symptoms may include breathlessness, cough and fever) or even death. The following symptoms may occur after an overdose:

- pin point pupils;
- slowing of heartbeat;
- respiratory problems;
- low blood pressure;
- unconsciousness leading to coma.
- breathlessness, cough and fever

If you have used too much ***Palladone*** injection under no circumstances should you put yourself in a situation that requires you to be alert e.g. driving a car. When seeking medical attention make sure that you take this leaflet and any remaining ampoules with you to show to the doctor.

If you forget to use *Palladone* injection
Please use ***Palladone*** injection as soon as you notice that you forgot a dose. Never double the dose. If you forget to use ***Palladone*** injection or use a smaller dose than prescribed, this will lead to unsatisfactory and/or insufficient pain relief.

If you stop using *Palladone* injection
Do not suddenly stop taking this medicine. If you want to stop taking this medicine discuss this with your doctor first. They will tell you how to do this, usually by reducing the dose gradually so that any unpleasant withdrawal effects are kept to a minimum. Withdrawal symptoms such as restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being sick, diarrhoea, shaking, shivering or sweating may occur if you suddenly stop taking this medicine.

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

4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.

This medicine can cause allergic reactions (hypersensitivity reactions). The incidence of serious allergic reactions (anaphylactic reactions) is not known. **Tell your doctor immediately** if you get any sudden wheeziness, difficulties in breathing, swelling of the eyelids, face, lips, mouth or throat, or any rash or itching especially those covering your whole body.

Difficulty in breathing (respiratory depression) is the chief hazard of an opioid overdose.

Drug withdrawal

When you stop using ***Palladone*** injection you may experience drug withdrawal symptoms, which include restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being sick, diarrhoea, shaking, shivering or sweating.

How do I know if I am addicted?

If you notice any of the following signs whilst using ***Palladone*** injection it could be a sign that you have become addicted.

- You need to use the medicine for longer than advised by your prescriber;
- You feel you need to use more than the recommended dose;
- You are using the medicine for reasons other than prescribed;
- When you stop using the medicine you feel unwell, and you feel better once using the medicine again.

If you notice any of these signs it is important you talk to your doctor.

Most people will have constipation when using this medicine. Increasing the amount of fibre (fruit, vegetables, wholemeal bread, pasta, brown rice) and fluids you eat and drink may help reduce the problem, but if necessary your doctor may prescribe a laxative.

You may feel sick or vomit (be sick) when you use this medicine, this should normally wear off after a few days however your doctor can prescribe an anti-vomiting medicine if it continues to be a problem.

Very common side effects (may affect more than 1 in 10 people)

- dizziness, feel more sleepy than normal
- constipation, feel sick

Common side effects (may affect up to 1 in 10 people)

- confusion, anxiety, sleeplessness
- headache
- dry mouth, vomiting (be sick)
- itchy skin, sweating
- urgency in passing urine
- a feeling of unusual weakness
- loss of appetite
- abdominal pain or discomfort
- skin reactions at the injection site

Uncommon side effects (may affect up to 1 in 100 people)

- feeling of extreme happiness, hallucinations
- shaking, muscle spasms, tingling in the hands or feet
- blurred vision
- low blood pressure
- indigestion
- rash
- decreased sexual drive, impotence
- withdrawal symptoms such as agitation, anxiety, nervousness, difficulty in sleeping, being unusually overactive, shaking and gastrointestinal problems
- tiredness, generally feeling unwell
- swelling of hands, ankles or feet

- agitation, depression, nightmares
- shortness of breath
- diarrhoea, changes in taste
- difficulty in passing urine
- a worsening in liver function tests (seen in a blood test)

Rare side effects (may affect up to 1 in 1,000 people)
- sedation, lack of energy
- slow, fast or irregular heartbeat
- difficulty in breathing or wheezing
- a worsening in pancreas function tests (seen in a blood test)

Very rare side effects (may affect up to 1 in 10,000 people)
- irritation and hardening of the skin at the injection site (particularly after repeated subcutaneous administration)

Side effects with unknown frequency (frequency cannot be estimated from the available data)
- problems with breathing during sleep (sleep apnoea syndrome)
- dependence and addiction (see section 'How do I know if I am addicted?')
- drug tolerance
- unpleasant or uncomfortable mood
- reduction in size of the pupils in the eye
- an increase in sensitivity to pain (hyperalgesia; see "Warnings and precautions" in section 2)
- seizures, fits or convulsions
- uncontrolled muscle movements
- facial flushing (redness of the face)
- a condition where the small bowel (part of your gut) does not work properly (paralytic ileus)
- itching rash (hives)
- withdrawal symptoms in babies born to mothers who have used hydromorphone (see "Pregnancy and breastfeeding" in section 2)

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 *Palladone* injection

Keep this medicine out of the sight and reach of children.

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

Do not use this medicine after the expiry date which is stated on the carton and the ampoule label after "EXP". The expiry date refers to the last day of that month.

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 2-8°C, unless opening/ dilution has taken place in controlled and validated aseptic conditions.

The medicine is to be visually inspected prior to use. Only clear solutions free from particles should be used.

Do not throw away any medicines via wastewater or household waste. Ask you 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 *Palladone* injection contains:
***Palladone* 2 mg/ml injection:**

- The active substance is hydromorphone hydrochloride. Each ampoule contains 2 mg hydromorphone hydrochloride (corresponding to 1.77 mg hydromorphone) in 1 ml solution.

***Palladone* 10 mg/ml injection:**

- The active substance is hydromorphone hydrochloride. Each ampoule contains 10 mg hydromorphone hydrochloride (corresponding to 8.87 mg hydromorphone) in 1 ml solution.

The other ingredients are:

- Citric acid anhydrous
- Sodium citrate
- Sodium chloride
- Sodium hydroxide
- Hydrochloric acid
- Water for injections

What *Palladone* injection looks like and contents of the pack
Palladone injection is a clear, colourless to pale yellow, pH 4.0 solution for injection or infusion supplied in clear glass ampoules, available in packs of 5 x 1 ml ampoules.

Marketing Authorisation Holder
Napp Pharmaceuticals Limited, Cambridge Science
Park, Milton Road, Cambridge CB4 0GW, UK.

Manufacturer
Bard Pharmaceuticals Limited, Cambridge Science Park,
Milton Road, Cambridge CB4 0GW, UK.

This leaflet is also available in large print, Braille or as an audio CD. To request a copy, please call the RNIB Medicine Information line (free of charge) on: 0800 198 5000
You will need to give details of the product name and reference number. These are as follows:
Product name: ***Palladone*** solution for injection or infusion
Reference number: 16950/0163

This leaflet was last revised in July 2020.

Information for Health Professionals

***Palladone*® 2 mg/ml and 10 mg/ml solution for injection or infusion**
Hydromorphone hydrochloride

This leaflet provides technical information for the healthcare professional about ***Palladone*** 2 mg/ml and 10 mg/ml, solutions for injection or infusion.

Posology and method of administration
Method of administration
Intravenous injection or infusion
Subcutaneous injection or infusion

The medicinal product is to be visually inspected prior to use. Only clear solutions free from particles should be used.

After opening, this medicinal product should be used immediately.

Posology
The dosing of ***Palladone*** injection has to be adjusted to the patients' severity of pain and to their individual response.

The dose should be titrated until optimum analgesic effect is achieved. While the dose to be administered should be sufficient to achieve appropriate analgesia, the aim should also be to keep the dose as small as possible in the individual case.

Palladone injection should not be administered for longer than absolutely necessary. If long-term treatment is required careful and regular monitoring should control whether and to what degree further treatment is necessary. When a patient no longer requires therapy with hydromorphone, it may be advisable to taper the daily dose gradually to prevent withdrawal symptoms.

Age	**Bolus**	**Infusion**
Adults and adolescents (>12 years)		
subcutaneous (s.c.) use	1-2 mg s.c. every 3-4 hours	0.15-0.45 mg/h 0.004 mg/kg bodyweight/h
intravenous (i.v.) use	1-1.5 mg i.v. every 3-4 hours to be injected slowly over at least 2-3 minutes	0.15-0.45 mg/h 0.004 mg/kg bodyweight/h
PCA (s.c. and i.v.)	0.2 mg bolus, stop interval 5-10 min.	
Paediatric population (<12 years)	Not recommended	

Paediatric population
Palladone injection is not recommended for use in children under 12 years of age as the safety and efficacy has not yet been established. No data are available.

Elderly patients
Elderly patients (as a rule over 75 years) may require a lower dosage than other adults to achieve adequate analgesia.

Patients with hepatic and/or renal impairment
These patients may require lower doses than other patient groups to achieve adequate analgesia. They should be carefully titrated to clinical effect.

Cessation of therapy
When a patient no longer requires therapy with hydromorphone, it may be advisable to taper the daily dose gradually to prevent withdrawal symptoms.

Special precautions for disposal and other handling
Chemical and physical in-use stability has been demonstrated for 7 days at 4°C, 25°C and 37°C except for diluted solutions in polycarbonate syringes which should not be stored beyond 24 hours.
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 2-8 C, unless dilution has taken place in controlled and validated aseptic conditions.

No evidence of incompatibility was observed between ***Palladone*** injection and representative brands of injectable forms of the following drugs, when stored in high and low dose combinations in polypropylene syringes over a 24 hour period at ambient temperature (25°C).
Hyoscine butylbromide
Hyoscine hydrobromide
Dexamethasone sodium phosphate
Haloperidol
Midazolam hydrochloride
Metoclopramide hydrochloride
Levomepromazine hydrochloride
Glycopyrronium bromide
Ketamine hydrochloride

No evidence of incompatibility was observed between ***Palladone*** injection, undiluted or diluted with sodium chloride 9 mg/ml (0.9%) solution for infusion, glucose 50 mg/ml (5%) solution for infusion or water for injections, and representative brands of polypropylene syringes, polyethylene and PVC tubing and PVC or EVA infusion bags.

Incompatibilities were observed with diluted solutions of 50 mg/ml when stored in polycarbonate syringes beyond 24 hours at 25°C. Whereas no evidence of incompatibility was found when the same preparations were stored at 4°C up to 7 days.

The ampoules should be stored in the outer carton in order to protect from light.

Inappropriate handling of the undiluted solution after opening of the original ampoule, or of the diluted solutions may compromise the sterility of the product.

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

This leaflet was last revised in June 2018.