

Package leaflet: Information for the patient
PINADONE 1 mg/ml Oral Solution
methadone hydrochloride

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.
- 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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Pinadone is and what it is used for

Pinadone 1 mg/ml Oral Solution contains the active substance methadone hydrochloride and belongs to a group of medicines called opioid analgesics. The opioid class of drugs includes the commonly known morphine and codeine which are obtained by a doctor's prescription. The opioid class of drugs also includes illegal drugs such as heroin. Pinadone works like other opioid drugs, but tends to have a longer life in the body, stopping the withdrawal symptoms that can occur during your treatment.

Pinadone is used for:

- Relief of pain in adults with conditions where morphine may be reasonable alternative, such as severe cancer pain.
- Treatment of adults with opioid dependency.

If you have any questions about why you are taking Pinadone, ask your doctor or pharmacist.

2. What you need to know before you take Pinadone

Do NOT take Pinadone:

- if you are allergic to methadone hydrochloride or any of the other ingredients of this medicine (*listed in section 6*)
- if you are suffering from breathing difficulties, in particular asthma
- if you are suffering from alcoholism
- if you have suffered a recent head injury or increased pressure in the head
- if you are taking monoamine oxidase inhibitors (MAOIs) or if you have taken them within the last 2 weeks
- if you are suffering from a bowel condition such as ulcerative colitis
- if you are suffering from an abnormal reduction in liver function
- if you are suffering from a kidney condition such as a renal tract spasm

- if you are suffering from pain under the right rib cage, usually after a meal
- if you are pregnant or breast-feeding, or in labour.

Warnings and precautions

Please tell your doctor or pharmacist immediately if you notice:

- your breathing is slower or shallower than normal
- your heart beat is slower or is irregular.

Talk to your doctor or pharmacist before taking Pinadone:

- if you have heart disease
- if you have liver disease
- if you have a low level of potassium in your blood (hypokalaemia)
- if you have imbalances in your body salts (electrolytes)
- if you have a family history of sudden death
- if you have hypothyroidism – a condition in which the body lacks sufficient thyroid hormone
- if you have adrenocortical insufficiency – a condition in which the adrenal glands do not produce adequate amounts of steroid hormones
- if you have hypopituitarism – a condition in which there is a decline in the level of hormones produced by the pituitary gland
- if you have an enlarged prostate gland
- if you suffer from shock – a condition in which there is a dramatic reduction in blood flow
- if you have low blood pressure
- if you have inflammatory or obstructive bowel disorders
- if you have muscle weakness (myasthenia gravis)
- if you have a tumour of the adrenal gland known as pheochromocytoma
- if you have renal dysfunction – also known as kidney disease
- if you have an intolerance to some sugars.

You should contact your doctor or pharmacist immediately if you experience symptoms such as fatigue, weakness, lack of appetite, nausea, vomiting and low blood pressure (see section 4). This may be a symptom of the adrenals producing too little of the hormone cortisol, and you may need to take hormone supplement.

It is important that your doctor knows if you suffer from any other medical conditions.

Long-term use may cause decreased sex hormone levels and increased levels of the hormone prolactin. Contact your doctor if you experience symptoms such as decreased libido, impotence or absence of menstruation (amenorrhea).

Tolerance, dependence, and addiction

This medicine contains methadone which is an opioid medicine. Repeated use of opioids can result in the drug being less effective (you become accustomed to it, known as tolerance). Repeated use of Pinadone can also lead to dependence, abuse, and addiction, which may result in life-threatening overdose. The risk of these side effects can increase with a higher dose and longer duration of use.

Dependence or addiction can make you feel that you are no longer in control of how much

medicine you need to take or how often you need to take it. When used for the treatment of pain, you might feel that you need to carry on taking your medicine, even when it doesn't help to relieve your pain.

The risk of becoming dependent or addicted varies from person to person. You may have a greater risk of becoming dependent or addicted on Pinadone if:

- You or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs (“addiction”).
- You are a smoker.
- You have ever had problems with your mood (depression, anxiety, or a personality disorder) or have been treated by a psychiatrist for other mental illnesses.

If you notice any of the following signs whilst taking Pinadone, it could be a sign that you have become dependent or addicted.

- You need to take the medicine for longer than advised by your doctor
- You need to take more than the recommended dose
- You are using the medicine for reasons other than prescribed, for instance, ‘to stay calm’ or ‘help you sleep’
- You have made repeated, unsuccessful attempts to quit or control the use of the medicine
- When you stop taking the medicine you feel unwell, and you feel better once taking the medicine again (‘withdrawal effects’)

If you notice any of these signs, speak to your doctor to discuss the best treatment pathway for you, including when it is appropriate to stop and how to stop safely (See section 3, If you stop taking Pinadone).

Sleep-related breathing disorders

Pinadone can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.

Children

Pinadone is not recommended for use in children.

Other medicines and Pinadone

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Tell your doctor if you are taking:

- strong painkillers commonly referred to as opioids
- medication to reduce the acid in your stomach (Histamine H2 agonists)
- medicine to treat tuberculosis (rifampicin)
- medication to treat HIV infection (particularly nevirapine, efavirenz and some protease inhibitors)
- medication to control seizures (phenytoin, carbamazepine)
- medication to treat depressive illness (tricyclic antidepressants) or obsessive compulsive disorder (fluvoxamine)
- medications to treat heart arrhythmia such as amiodarone, diltiazem, disopyramide, procainamide, sotalol, verapamil

- medication known as monoamine oxidase inhibitors, such as linezolid, moclobemide, phenelzine, tranylcypromine (or have taken them in the last 14 days)
- certain hormones (mineralocorticoid hormones)
- certain antibiotics (macrolides antibiotics, ciprofloxacin)
- certain antifungals (azole antifungals)
- certain psychotropic drugs
- neuromuscular blocking agents
- any medicine that may be affected by reduced gastric mobility
- any substance that may affect the acidity of your urine
- St. John's Wort, tranquilisers (e.g. benzodiazepines), barbiturates, phenothiazines, diuretics, laxatives, cimetidine, nelfinavir, zidovudine, fluconazole and desipramine, abacavir or amprenavir, grapefruit juice
- cannabidiol (a medicine used to treat seizures)
- gabapentin or pregabalin (used to treat epilepsy, nerve pain or anxiety), can increase the risk of opioid overdose, respiratory depression (breathing difficulties) and may be life-threatening.

Concomitant use of Pinadone 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 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.

Some patients may develop a condition called serotonin syndrome, particularly if they are also taking other antidepressant medicines such as SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline), SNRIs (duloxetine, venlafaxine, sibutramine) or tricyclic antidepressants (amitriptyline, clomipramine, imipramine, nortriptyline).

Contact your doctor if you experience symptoms such as:

- mental-status changes (e.g. agitation, hallucinations, coma)
- fast heartbeat, unstable blood pressure, fever
- exaggeration of reflexes, impaired coordination, muscle stiffness
- gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea).

People sensitive to aspirin may develop allergic reactions to the food colourings used in this medicine.

Pinadone with food and drink

If you intend to drink alcohol while you are taking Pinadone, speak to your doctor.

Vegetarian diets – you should take special care if you are on a vegetarian diet. Speak to your doctor regarding the dose of this medicine.

Pregnancy, breast-feeding and fertility

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 taking this medicine.

Do not take Pinadone during pregnancy.

Use during labour is not recommended.

Talk to your doctor if you are breast-feeding or thinking of breast-feeding while you are taking methadone as it may affect your baby. Monitor your baby for abnormal signs and symptoms such as increased drowsiness (more than usual), breathing difficulties or limpness. Consult your doctor immediately if you notice any of these symptoms.

Long-term use may decrease sex hormone levels, which could cause fertility problems.

Driving and using machines

Pinadone may cause drowsiness. It is recommended that you don't drive, use machinery or undertake any activities where alertness is required. The time after which it is safe to do so depends on each individual. Discuss your own situation with your doctor.

Pinadone contains maltitol liquid, sunset yellow, benzoic acid, propylene glycol and sodium

- **maltitol liquid** (E965) if you have been told that you have an intolerance to some sugars, contact your doctor before taking this product. Pinadone contains 2.75 g maltitol/5 ml, and may have a mild laxative effect. Maltitol has a calorific value of 2.3 kcal/g. This product does not contain sugar.
- **sunset yellow** (E110) which may cause allergic reactions.
- **benzoic acid** (E210) this medicine contains 5.0 mg benzoic acid in each 5 ml which is equivalent to 1 mg/ml.
- **propylene glycol** this medicine contains 100 mg propylene glycol in 5 ml which is equivalent to 20 mg/ml.

If you are pregnant or breast-feeding, do not take this medicine unless recommended by your doctor. Your doctor may carry out extra checks while you are taking this medicine.

If you suffer from a liver or kidney disease, do not take this medicine unless recommended by your doctor. Your doctor may carry out extra checks while you are taking this medicine.

- **sodium** this medicine contains less than 1 mmol sodium (23 mg) per 5 ml, that is to say essentially 'sodium-free'.

3. How to take Pinadone

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Before starting treatment and regularly during treatment, your doctor will discuss with you what you may expect from using Pinadone, when and how long you need to take it, when to contact your doctor, and when you need to stop it (see also 'if you stop taking Pinadone').

The dose is specifically worked out for you by your doctor to stop you experiencing any withdrawal symptoms. Your dose is usually taken at the clinic or pharmacy under the guidance of a pharmacist or dispenser. Take Pinadone as directed by your doctor or pharmacist. They will tell you how much to take at each dose and when to take your dose each day. For take-home doses, the label on your bottle will give you the same information. Pinadone is only effective if you take the treatment daily, since withdrawal symptoms can still occur.

The recommended dose is:

Pain Management

The usual initial dose is 5 to 10 mg methadone (daily). However, the dose is adjusted personally for each patient.

Opioid Addiction

Adults: Pinadone is usually taken by mouth as a single daily dose. The dose is adjusted personally for each patient – your doctor will advise you.

- **starting dose:** 10-20 mg daily. The dose is increased by 10-20 mg (two to four 5 ml spoonfuls) daily until the correct level for each patient is reached.
- **usual dose** is 40-60 mg (eight to twelve 5 ml spoonfuls) per day, which will be gradually reduced by the doctor.

Patients with heart, kidney or liver problems: your dose will be reduced and you will be monitored carefully. If your condition is severe you should not be given this medicine.

Pregnant women: you will need to stop taking this medicine at least 4 – 6 weeks before giving birth – your doctor will advise you.

Use in children: this medicine is NOT recommended for children.

If you take more Pinadone than you should

If you take too much methadone you can experience the following:

- low blood sugar
- a brain disorder (known as toxic leukoencephalopathy).

Your dose is usually taken at the clinic or pharmacy under the guidance of a pharmacist or dispenser. So it is unlikely that you will take too much. For take-home doses, the dosage is specifically worked out for you. If you think that you have taken too much, or if anyone else has taken your medicine by mistake, immediately contact your doctor or go to your nearest hospital casualty department. You are likely to need urgent medical attention even though you may feel well. Take this leaflet or your medicine with you so that the hospital will know what you have taken.

If you forget to take Pinadone

If you have forgotten to take one or more doses of your take-home doses, contact your doctor or pharmacist for advice.

Do not take a double dose to make up for a forgotten dose.

If you stop taking Pinadone

Do not stop taking this medicine suddenly. Your dose needs to be gradually reduced. Your doctor will advise you. If you stop taking the medicine suddenly you may suffer withdrawal symptoms.

Withdrawal symptoms, usually mild, may be observed after discontinuation and include: body aches, diarrhoea, erection of the hair on the skin, eating disorders, nervousness or restlessness, sneezing, runny nose, tremors or shivering, abdominal cramps, nausea, sleep disturbance, increase in sweating and yawning, weakness and unexplained fever. Some people may notice that their heart is beating a little faster or more forcefully. With appropriate dose adjustments and gradual withdrawal, these symptoms are usually mild.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Seek medical advice immediately if you notice breathing difficulty or any other signs of an overdose. Some people can be allergic to medicines. If you have any of the following symptoms soon after taking Pinadone, **STOP** taking this medicine and **seek medical help immediately**.

- sudden wheezing and chest pain or tightness
- swelling of the eyelids, face or lips
- lumpy skin rash or 'hives' anywhere on the body.

Seek medical attention immediately if you develop any symptoms of serotonin syndrome such as: Agitation, hallucinations, rapid heart rate, fever, excessive sweating, shivering or shaking, muscle twitching or stiffness, trouble with coordinating, nausea, vomiting or diarrhoea.

Also seek medical attention if you experience symptoms of adrenal insufficiency such as: Nausea or vomiting, loss of appetite, fatigue, weakness, dizziness, low blood pressure.

Inform your health care professional if you experience signs or symptoms of decreased sex hormone levels such as low libido, impotence, erectile dysfunction, lack of menstruation or infertility.

Other side effects are listed below:

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

- dizziness
- drowsiness
- light-headedness
- nausea, vomiting
- dry mouth
- constipation
- sweating.

Common (may affect up to 1 in 10 people)

- confusion
- difficulty with or inability to urinate
- an exaggerated sense of well-being has been reported at higher doses.

Rare (may affect up to 1 in 1,000 people)

- low blood pressure and collapse
- slow or irregular heartbeat.

Frequency not known:

- low blood sugar
- you can become dependent on Pinadone (for more information see section 2 Warnings and Precautions)
- sleep apnoea (breathing pauses during sleep).

Other side effects include:

- spasms in the kidney and liver
- breast enlargement in males
- palpitations
- irregular heart beat or affect of your breathing
- fainting
- contraction of pupils
- sexual dysfunction.

Studies in men on methadone have shown that methadone reduces testosterone levels, ejaculate volume and sperm motility.

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRRA Pharmacovigilance, Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Pinadone

Keep this medicine out of the sight and reach of children. Store this medicine in a safe and secure storage space, where other people cannot access it. It can cause serious harm and be fatal to people when it has not been prescribed for them.

Do not store above 25°C.

Do not use Pinadone after the expiry date which is stated on the label. The expiry date refers to the last day of that month. The amber glass bottles should be used within 3 months of first opening. Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Pinadone contains

- The **active substance** is 1 mg methadone hydrochloride in each ml.
- The **other ingredients** are: maltitol liquid (E965), benzoic acid (E210), propylene glycol, sodium hydroxide, hydroxyethylcellulose, purified water and the colours sunset yellow (E110) and green S (E142). (*For further information on some ingredients see end of Section 2*).

What Pinadone looks like and contents of the pack

Pinadone is a clear green oral solution, available in plastic bottles, pack sizes: 20 ml, 25 ml, 30 ml, 35 ml, 40 ml, 45 ml, 50 ml, 55 ml, 60 ml, 500 ml, or 5 litre and amber glass bottles of 100 ml, 500 ml and 1 litre. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Pinewood Laboratories Ltd., Ballymacarbry, Clonmel, Co. Tipperary, Ireland.

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