

PACKAGE LEAFLET: INFORMATION FOR THE USER

Methadone 10mg/ml Solution for Injection

Methadone Hydrochloride
(This medicine will be referred to as Methadone Solution for Injection in this leaflet)

Read all of this leaflet carefully before you are given Methadone Solution for Injection because it contains important information for you.

- Keep this leaflet. You may need to read it again
- If you have any further questions, please ask your doctor or nurse
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

This medicine contains methadone, which is an opioid, which can cause addiction. You can get withdrawal symptoms if you stop taking it suddenly.

1. What Methadone Solution for Injection is and what it is used for

This medicine has been prescribed for you for treatment of addiction in order to reduce withdrawal symptoms. It contains the methadone which belongs to a class of medicines called opioids.

This medicine has been prescribed to you and should not be given to anyone else.

Opioids can cause addiction and you may get withdrawal symptoms if you stop taking it 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.

This medicine may also be used as a painkiller if you are unable to take morphine.

2. What you need to know before Methadone Solution for Injection is given

You should not be given Methadone Solution for Injection if:

- You are allergic to methadone hydrochloride or any of the ingredients of this medicine (listed in section 6)
- You have any problem with your breathing or any chronic lung disease such as chronic obstructive pulmonary disease
- You are having an asthma attack. Do not take your dose until you have completely recovered.
- You are taking, or have stopped taking within the last two weeks, a type of medicine known as monoamine oxidase inhibitors (MAOIs) which are used to treat depression
- You have pheochromocytoma, a tumour of the adrenal glands.
- You have a bowel disorder known as paralytic ileus
- You have loss of consciousness

Methadone Solution for Injection is not suitable for children under the age of 16 years. If any of the conditions above apply to you, please consult your doctor.

Warnings and precautions

Talk to your doctor or pharmacist before taking Methadone Solution for Injection

- because it can be addictive.
- only use the dose prescribed for you by your doctor because higher doses could be fatal. Without you knowing, the levels of the drug can build up in your body and affect your breathing, causing drowsiness and possible loss of consciousness.
- if you have increased pressure on the brain or have just had a head injury.
- if you are suffering from acute alcoholism.
- if you are suffering from mental illness brought on by an infection
- if you have liver problems
- if you have kidney problems
- if you have problems with your bile duct
- if you suffer from an enlarged prostate gland (in men) or have difficulty passing urine
- if you have an under-active thyroid or adrenal gland.
- if you have low blood pressure
- if you are in a state of severe shock
- if you are very run down and feeling weak
- if you have bowel disease, such as Crohn's disease or ulcerative colitis
- if you suffer from convulsions (fits)
- if you are a child. Even at low doses methadone is a special hazard to children if taken accidentally. Children under 6 months, particularly newborns, may be more sensitive to breathing difficulties than adults
- if you are elderly
- if you have myasthenia gravis (a disorder that causes extreme muscle fatigue)
- if you suffer from certain types of heart disorders. These types of heart disorder are usually confirmed after an electrocardiogram (ECG) has been performed and may be more likely to occur with the following:
 - if you have, or have had in the past any heart disorder or disease.
 - if you have liver disease
 - if other members of your family have died suddenly from unexplained causes.
 - if you have reduced blood levels of potassium or magnesium
 - if you take particular medicines while you are taking Methadone; please read the section 'Taking/using other medicines'.
 - if you are taking high doses of Methadone (e.g. more than 100 mg per day).

Sleep-related breathing disorders

Methadone solution 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.

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 Methadone Solution can also lead to dependence, abuse, and addiction, which may result in life-threatening overdose.

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.

Your doctor may wish to monitor you by doing an ECG either before you start taking Methadone and/or during treatment.

Injections may be painful; check the site of injection regularly for swelling, reddening or itching. Always tell your doctor or nurse about any of these conditions or medicines before having your treatment

Taking this medicine regularly, particularly for a long time, can lead to addiction.

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 prescriber 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.

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 (amenorrhoea).

Talk to your doctor or pharmacist if you experience any of the following symptoms while taking Methadone Solution for Injection:

- Weakness, fatigue, lack of appetite, nausea, vomiting or low blood pressure. This may be a symptom of the adrenals producing too little of the hormone cortisol, and you may need to take hormone supplement.

Other medicines and Methadone Solution for Injection

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

- Medicines used to treat addiction e.g. naltrexone, naloxone and buprenorphine
- Cimetidine (a medicine used to treat stomach ulcers)
- Metoclopramide or domperidone (medicines used to stop you feeling or being sick)
- Drugs used to treat epilepsy (e.g. phenytoin)
- Mexiletine, a drug used to treat heart irregularities
- Antibiotics (medicines used to treat bacterial infections) e.g. ciprofloxacin, rifampicin, erythromycin and rifabutin

- Antifungals (medicines used to treat fungal infections) e.g itraconazole and fluconazole
- Medicines that makes urine more acidic such as ammonium chloride
- Antiviral drugs including some medicines used to treat HIV e.g. nevirapine, zidovudine, efavirenz, nelfinavir, ritonavir and abacavir
- Medicines used to treat depression known as tricyclic antidepressants, such as amitriptyline, and selective serotonin re-uptake inhibitors, such as fluvoxamine
- Medicines used to treat severe depression known as monoamine oxidase inhibitors (MAOIs)
- CNS depressants (medicines that act on the brain and cause drowsiness or sleepiness) e.g benzodiazepines, chloral hydrate and chlormethiazole
- Other opioid type drugs e.g. morphine
- Medicines used to treat sleep disorders e.g. sodium oxybate
- Pentazocine (a pain killer)
- Medicines used to help you relax (tranquillisers)
- Cyclizine (an antihistamine used to treat nausea, vomiting and dizziness)
- Medicines used to treat pain and fever such as metamizole.
- fluconazole (used for treating infections)
- Cannabidiol (a medicine used to treat seizures)
- Gabapentin and pregabalin (medicines used to treat epilepsy, nerve pain or anxiety), can increase the risk of opioid overdose, respiratory depression (breathing difficulties) and may be life-threatening.

The risk of side effects increases, if you use methadone concomitantly with antidepressants (such as citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, venlafaxine, 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)

Other medicines you may be taking can also affect the heart.

You must tell your doctor about any other medicines that you are taking such as atomoxetine, as they may be dangerous if they are taken with methadone. In these situations your doctor may decide that it is necessary to monitor your heart with an electrocardiogram (ECG) at the start of treatment to ensure that these effects do not occur.

Concomitant use of Methadone Solution for 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 Methadone Solution for 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

Continued overleaf

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.

Methadone Solution for Injection with food drink and alcohol

You must not drink alcohol whilst you are being treated with Methadone Solution for Injection as this could cause serious side effects.

You are advised not to drink grapefruit juice whilst you are being treated with Methadone Solution for Injection as it could cause an overdose.

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 before taking this medicine.

Talk to your doctor if you are breastfeeding 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.

Pregnancy

Do not take Methadone Solution for Injection if you are pregnant or think you might be pregnant unless you have discussed this with your prescriber and the benefits of treatment are considered to outweigh the potential harm to the baby.

If you use Methadone Solution for Injection during pregnancy, your baby may become dependent and experience withdrawal symptoms after the birth which may need to be treated.

Breast-feeding

Do not take Methadone Solution for Injection while you are breastfeeding as methadone passes into breast milk and will affect your baby.

Driving and using machines

The ability to drive or use machines may be severely affected during and after treatment with Methadone. You must not drive or use machines until you are told that you can do so by your doctor.

The 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 if this medicine affects your ability to drive
- However, you would not be committing an offence if :
 - 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 or in the information provided with the machines and
 - It was not affecting your ability to drive safely

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

3. How Methadone Solution for Injection is given

Methadone Solution for Injection will be given to you by a doctor in a hospital. It will be given under the skin or

into a muscle.

Before starting treatment and regularly during treatment, your doctor will discuss with you what you may expect from using Methadone Solution, 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 Methadone Solution).

Adults:

For the treatment of drug addiction:

The recommended initial dose is 10-20 mg a day. The dose will be slowly increased until you show no signs of withdrawal or intoxication. The dose may need to be over 100mg daily (depending of the level of tolerance you have to Methadone) in order to prevent withdrawal symptoms. Your doctor will decide what dose you need and when to reduce the dose.

For the treatment of pain:

The recommended dose is 5-10mg every 6 to 8 hours although your doctor may decide to give you a different dose. You may be prescribed a different dose if you are elderly, have liver disease or are ill.

The elderly or ill:

If you are elderly or ill, your doctor will only prescribe repeated doses with caution.

Use in children and adolescents:

Methadone Solution for Injection should not be used in children under the age of 16 years.

If you think you have been given too much Methadone Solution for Injection

The medicine will be given to you by your doctor so it is unlikely you will receive too much. If you are concerned about your treatment, please talk to your doctor. If you are given too much Methadone Solution for Injection, you can experience the following:

- Difficulty in breathing
- Extreme sleepiness, fainting or coma
- small pupils
- Muscle weakness
- Cold and clammy skin
- Slow heartbeat, low blood pressure, heart attack or shock. In severe cases death may occur.
- Low blood sugar
- A brain disorder (known as toxic leukoencephalopathy)

In the event of overdose you should seek medical assistance immediately even if you feel well as you may be suffering methadone poisoning.

If you stop having Methadone Solution for Injection

Do not suddenly stop taking this medicine. If you want to stop taking this medicine, discuss this with your prescriber 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.

4. Possible side effects

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

medicine and see a doctor straightaway if you have any of the following:

- Heart problems. The signs of this may include changes in the way your heart beats, such as it beating faster or missed heart beats, breathing difficulties and dizziness
- If your breathing become slow and shallow.

Keep taking this medicine but tell your doctor straightaway if you get the following side effect:

- Worsening of the pressure inside your head if you already have this condition following an injury to your brain or brain disease.

Frequency not known:

You can become dependent on Methadone solution (for more information see section 2 Warnings and Precautions)

Other side effects:

- Dizziness
- Nausea (feeling sick) or vomiting (being sick)
- Headaches
- Pain and skin irritation at the site of injection
- Rashes or itching
- Sweating
- Reduced blood pressure (you may feel dizzy on standing up)
- small pupils
- Confusion, mood changes
- Fast, slow beating of the heart, a feeling of trembling in the heart
- Facial flushing
- Spasms of the tubes from the gall bladder or urinary bladder
- Difficulty passing urine
- A reduction in sex drive
- Feeling cold (fall in body temperature)
- Redness, swelling and hardening of the skin at the site of injection
- Painful menstruation cramps or absence of period
- Constipation
- High blood levels of the hormone prolactin
- Hearing or seeing things that are not there (hallucinations)
- Dependence and addiction
- Low blood sugar
- Sleep apnoea (breathing pauses during sleep)

You can become dependent on methadone Solution for Injection.

In the case of serious side effects, patients should be kept conscious wherever possible and an airway established; artificial respiration may be necessary.

Drug Withdrawal

When you stop taking Methadone Solution for 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.

Repeated intravenous administration or appropriate antidote medication (nalorphine or levallorphine) may be required if there is evidence of significant breathing difficulty. Oxygen, intravenous fluids, drugs to increase blood pressure and other supportive measures should be employed as necessary according to the severity of the side effect.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme. Website: 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 Methadone Solution for Injection

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 use this medicine after the expiry date which is stated on the ampoule. The expiry date refers to the last date of that month. Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Protect from light.

6. Contents of the pack and other information

What Methadone Solution for Injection contains:

The **active ingredient** is Methadone Hydrochloride 10 mg in 1 ml. The **other ingredient** is water for injections.

What Methadone Solution for Injection looks like and the content of the pack:

Methadone Solution for Injection is a clear colourless solution supplied in clear glass ampoules, each containing 1, 2, 3.5 or 5 ml of the solution. The 2, 3.5 and 5ml ampoules are supplied in packs of 10. The 1ml ampoules are supplied in packs of both 10 and 100 ampoules.

Marketing Authorisation Holder and Manufacturer:

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