

PACKAGE LEAFLET: INFORMATION FOR THE USER

Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution

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

What is in this leaflet

1. What Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution is and what is it used for?
2. What you need to know before you take Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution
3. How to take Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution
4. Possible side effects
5. How to store Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution
6. Contents of the pack and other information

1. What Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution is and what is it used for?

The name of your medicine is Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution (referred to as Methadone Solution in this leaflet). It contains methadone hydrochloride. This belongs to a group of medicines called Narcotic Analgesics.

Methadone is used:

- to treat drug addiction.

2. What you need to know before you take Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution

Do not take Methadone Solution and tell your doctor if:

- you are allergic to methadone or any other ingredients of this medicine (listed in section 6). An allergic reaction can include a rash, itching or shortness of breath.
- you have severe breathing problems or a history of asthma. You must not use this medicine during an asthma attack.
- you are taking Monoamine Oxidase Inhibitors (MAOIs) used to treat depression or if you have taken a MAOI medicines in the past two weeks (see 'Other medicines and Methadone Solution')
- you are taking central nervous systems (CNS) depressants (medicines that dull the senses including tranquillisers, sedatives and antidepressants)
- you are likely to go into labour. Taking methadone while you are in labour can have serious effects on your baby.
- you have ever had an unusual reaction to methadone or any of the ingredients.

- you are dependent on any other medicines.
- you are being treated for alcoholism.
- you have raised pressure in your skull, or you have recently suffered a head injury (check this with your doctor). You might be getting bad headaches.
- you have ulcerative colitis.
- your liver or kidneys are not functioning properly, or you get spasms around your kidney and bile duct.

Children must **not** be given this medicine.

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor before taking methadone.

Warnings and precautions

Talk to your doctor before taking Methadone Solution if:

- you are pregnant
- you are breast-feeding
- take care if you are taking a pregnancy test as methadone may interfere with the results
- you have low thyroid function, an under-active adrenal gland or an under-active pituitary gland
- you have prostate problems
- you have a history of asthma or breathing difficulties
- you have liver or kidney problems
- you are suffering from shock
- you have phaeochromocytoma (a non-cancerous tumour of the adrenal gland)
- you have a history of convulsions, fits or epilepsy
- you have low blood pressure
- you have a muscle weakness disease called myasthenia gravis
- you are constipated or other bowel problems
- you are extremely ill or an older person. You may be more sensitive to the medicine.

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

- 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.

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).

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking methadone.

Methadone may affect the electrical signals which control your heart contractions, particularly at high doses.

Tell your doctor you have recognised risk factors for the heart condition 'QT prolongation' that include:

- a history of heart problems
- liver disease
- any blood abnormalities such as low levels of potassium or magnesium
- a history of sudden death in the family.

During treatment, this medicine should not be stopped suddenly, but gradually, as sudden stoppage could lead to withdrawal symptoms.

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. 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. (The following sentence is applicable where methadone has an authorised indication for treatment of pain) 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 Methadone Solution 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 Methadone Solution, 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 Methadone Solution).

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.

Other medicines and Methadone Solution

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines bought without a prescription, including herbal medicines. This is because methadone can affect the way some other medicines work. Also, some medicines can affect the way methadone works.

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).

You must **not** take Methadone Solution:

- at the same time or within 2 weeks of taking Monoamine Oxidase Inhibitors (MAOIs).

Some medicines can increase the risk of heart problems when used with methadone. Talk to your doctor before taking methadone if you are taking:

- medicines for heart problems such as verapamil and enalapril
- medicines which affect electrolyte balance such as laxatives, diuretics (water tablets) or lithium.

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

- medicines used to treat irregular heartbeat (arrhythmia) such as amiodarone, diltiazem, disopyramide, procainamide, sotalol and verapamil
- medicines that dull your senses such as:
 - medicines for depression (for example SSRIs such as fluvoxamine and fluoxetine, SNRIs such as venlafaxine, TCAs such as desipramine), or MAOIs including moclobemide
 - medicines to help you sleep (including anaesthetics) and barbiturates
 - medicines to calm you down called tranquillisers (e.g. phenothiazines) and other psychotropic drugs
- serotonergic medicines used to treat migraine, such as sumatriptan
- serotonergic anti-emetics medicines used to treat nausea and vomiting, such as ondansetron
- medicines known as neuromuscular blocking agents, usually used when you are having an operation
- certain hormones (mineralocorticoid hormones) such as aldosterone
- cimetidine, used to treat stomach ulcers
- rifampicin, used to treat tuberculosis (TB)
- medicines used to treat epilepsy such as phenytoin, phenobarbital, carbamazepine and primidone
- medicines that make your urine acidic such as ascorbic acid (vitamin C)
- narcotic painkillers such as codeine and pentazocine
- naloxone, used to reverse the effects of opioid drugs
- medicines used to stop opioid drugs working such as naltrexone and buprenorphine
- medicines used to treat HIV such as nevirapine, efavirenz, nelfinavir, zidovudine, abacavir, amprenavir and some protease inhibitors. The doctor may have to change the amount of methadone you take while on these medicines
- antibiotics such as ciprofloxacin or macrolide antibiotics for example erythromycin
- medicines used to treat fungal infections such as ketoconazole or fluconazole

- St. John's Wort - a herbal preparation for depression
- lofexidine or clonidine, used to treat withdrawal effects
- medicines used to treat pain and fever such as metamizole
- 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.

If any of the above apply to you, talk to your doctor before taking Methadone Solution.

The use of Methadone Oral Solution at the same time as 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, taking Methadone Solution and sedative medicines at the same time should only be considered when other treatment options are not possible.

However, if your doctor does prescribe Methadone Oral Solution together with sedative medicines the dose and duration of taking both treatments together 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 if you experience such symptoms.

Other medicines you may be taking can also affect the heart. You must tell your doctor about any other medicines that you are taking 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.

Methadone Solution with alcohol

Do not drink alcohol whilst taking Methadone Solution. This is because Methadone Solution can make you feel sleepy and drinking alcohol will make you even more sleepy.

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 for advice before taking this medicine.

- taking methadone while you are in labour can have serious effects on your baby.
- take care if you are taking a pregnancy test as the methadone may interfere with the results.
- you should not take this medicine whilst you are in labour.
- if you breast-feed whilst taking this medicine, small amounts can pass to the baby in the breast milk.
- if used during pregnancy, your baby may suffer from withdrawal syndromes.
- 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.

Driving and using machines

Methadone Solution will severely affect your ability to drive or use machines, whilst taking it and afterwards. You should only start doing these activities again with the permission of your doctor.

Methadone Solution contains methyl and propyl parahydroxybenzoates, liquid maltitol and propylene glycol:

- methyl (E218) and propyl parahydroxybenzoates (E216). These may cause allergic reactions (possibly delayed).
- liquid maltitol (E965) (0.55g/ml). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product. May have a mild laxative effect and has a calorific value of 2.3kcal/g.
- propylene glycol (E1520). This medicine contains 20.7mg propylene glycol in each ml.

3. How to take Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution

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

Under no circumstances should you inject this product as injection may cause serious and permanent damage to your body with possibly fatal consequences.

Taking this medicine

- this medicine contains 1mg of methadone in each 1ml.
- take this medicine by mouth.

Dose

Adults

For addiction

- the starting dose is 10mg to 20mg (10ml to 20ml) each day.
- the doctor can increase this to 40mg to 60mg (40ml to 60ml) each day.
- if you have problems with your liver or kidney your doctor may adjust your dose.

Elderly or ill

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

Use in children

Children must not take this medicine.

If you take more Methadone Solution than you should

If you take more of this medicine than you should, talk to a doctor or go to your nearest hospital **straight away**. Take the medicine pack with you.

You must contact your doctor immediately if any of the following symptoms occur as it may be a sign of overdose:

- difficulty in breathing, which may lead to a collapse in circulation, heart attack and death.
- extreme drowsiness or even a stupor or coma
- very small pupils
- cold and clammy skin
- a very slow pulse rate
- lack of muscle control

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

If you forget to take Methadone Solution

- if you forget a dose do not take it. Wait until the next dose is due and take only that amount.
- do not take a double dose (two doses at the same time) to make up for a forgotten dose.

If you stop taking Methadone Solution

Do not stop taking this medicine unless your doctor tells you to as you may suffer withdrawal effects. Signs include:

- muscle aches, tremors, shivering or goose bumps.
- feeling sick (nausea), diarrhoea or stomach cramps
- weight loss
- runny nose or sneezing
- having trouble sleeping because you are feeling nervous, restless or yawning a lot.
- feeling weak
- fever
- fast heartbeat.

Your doctor will tell you how to lower the dose gradually.

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

4. Possible side effects

Like all medicines, Methadone Solution can cause side effects although not everybody gets them.

Serious side effects

Stop taking this medicine and see a doctor straight away if you have an allergic reaction to Methadone Solution.

An allergic reaction may include:

- swelling of your face, lips, tongue or throat or difficulty breathing or swallowing
- severe itching of your skin with raised lumps.

Stop taking this medicine and see a doctor straight away 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 slower or missed heart beats, breathing difficulties and dizziness
- if your breathing becomes slow and shallow.

Keep taking the medicine but tell your doctor straight away if you get any of the following side effects:

- if you have asthma and it gets worse
- worsening of the pressure inside your head particularly if you already have this condition following an injury to your brain or brain disease.

Other side effects

Tell your doctor if you get any of these side effects:

- feeling sick (nausea) or being sick (vomiting)
- constipation
- sweating a lot more than usual
- feeling dizzy, particularly when standing up. This may be sign that you have low blood pressure

- small pupils
- eye and eyesight problems, including jerky eye movements (nystagmus), in babies and young children born to mothers who used methadone during pregnancy
- breast growth and production of breast milk
- difficulty in passing water (urine), pain in lower back or abdomen caused by muscle spasms.
- dry mouth, eyes or nose, facial flushing
- feeling drowsy, confused or restless
- change in your mood, feeling 'high' or over excited
- seeing or hearing things that are not there (hallucinations)
- headache, rashes
- low body heat (hypothermia)
- lower sexual urge or desire
- reduced fertility in men
- painful periods or lack of periods
- there have been a very small number of cases where patients have had a sudden loss of blood flow or a change in the activity of their heart in the first days of methadone treatment which has led to death
- under activity of the adrenal gland
- twitching of the arms and upper body
- reduction in the body's normal production of sexual hormones
- low blood sugar (frequency not known)
- you can become dependent on Methadone Solution (for more information see section 2 Warnings and Precautions)
- sleep apnoea (breathing pauses during sleep) (for more information see section 2 Sleep-related breathing disorders).

You may notice that some of the side effects become less severe with time as you get used to the methadone.

You may develop tolerance to the effects of methadone; this means you may notice that your medicine is less effective at relieving your symptoms.

When taken for a long period of time, it is possible that you may become dependent on methadone solution.

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.

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 HPRA 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 Methadone Hydrochloride Sugar Free 1mg/1ml Oral Solution

- keep 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.
- store below 25°C. Store in original packaging (to protect from light)
- do not use after the expiry date (month, year) stated on the label and carton. The expiry date refers to the last day of that month.
- do not use Methadone Solution if you notice anything wrong with the medicine. Talk to your pharmacist.
- 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.

6. Contents of the pack and other information

What Methadone Solution contains

- The active ingredient is methadone hydrochloride.
- The other ingredients are methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), propylene glycol (E1520), caramel (E150), liquid maltitol (E965) (equivalent to 1.23g glucose), patent blue (E131) and purified water.

What Methadone Solution looks like and contents of the pack

A green solution. It comes in a brown glass bottle holding 500ml of solution.

Marketing Authorisation Holder:

Taw Pharma (Ireland) Ltd, 104 Lower Baggot Street, Dublin 2, D02 Y940, Ireland.

Manufacturer

Jenson R+ (Ireland) Ltd, Unit 15, Daingean Hall, N4 Axis Centre, Longford, N39 W6K0, Ireland.

Marketed by: Rowex Ltd, Newtown, Bantry, co cork, Ireland.

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