PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S6

RuTrex concentrate for oral solution

Methadone hydrochloride

Contains sugar (400 mg sucrose per 1 mL).

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

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- RuTrex has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What RuTrex is and what it is used for

RuTrex has been prescribed for you for opioid addiction. It contains methadone which belongs to a class of medicines called opioids.

RuTrex 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.

2. What you need to know before you take RuTrex

Do not take RuTrex if:

- If you are allergic to methadone hydrochloride or any of the other ingredients of RuTrex (see section 6).
- If you have any breathing difficulties or a history of asthma.
- If you are addicted to alcohol.
- If you are taking monoamine oxidase inhibitors (MAOIs) used to treat depression or if you have taken MAOI medicine in the past two weeks (See "Taking other medicines").
- If you have lower consciousness (feeling less alert or aware than normal).
- If you have a head injury.
- If you have heart problems relating to the way in which it conducts electricity (QT prolongation).
- If you have severe liver problems.

RuTrex should not be given to children.

Warnings and precautions:

Taking RuTrex for a long time, can lead to addiction.

Addiction can cause withdrawal symptoms when you stop taking RuTrex. Withdrawal symptoms can include restlessness, tearing, runny nose, 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 RuTrex 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 RuTrex 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.

Before taking RuTrex, tell your doctor:

- if you have breathing problems or asthma.
- if your liver or kidneys are not functioning properly.
- if you have low thyroid function (hypothyroidism).
- if you have prostate problems.
- if you have a head injury.
- if you are an elderly. You may be sensitive to RuTrex and may cause low blood pressure and fainting.
- if you have or have had a heart disease or irregular heartbeat.
- if you have weakness, fatigue, lack of appetite, nausea, vomiting or low blood pressure. This may be a symptom of your adrenal glands producing too little of the hormone called cortisol, and you may need to take hormone supplement.
- if you have diabetes (low blood sugar). Regular monitoring of your blood sugar levels is recommended if your dose of RuTrex changes.
- if you have a history of seizures or convulsions.
- if you have low blood pressure.
- if you are in shock.
- if you have a muscle weakness disease called myasthenia gravis.
- if you have bowel problems.
- if you have low sodium or potassium levels in your blood.
- if you are taking medicines that affects your heart rhythm.
- if you have epilepsy (fits/seizures).
- if you are extremely ill or an older person, you may be more sensitive to RuTrex and may need your dose adjusted.
- if you are pregnant or breastfeeding.

If during treatment you notice that your breathing becomes slow and shallow, stop taking RuTrex and see a doctor straight away. These may be signs of respiratory depression (see section 4) and may not be fully apparent for a week or two.

You and your caregiver must be aware of the signs of excessive dosing, as addressed below in section 3, subsection “If you take more RuTrex than you should”.

If you have been using RuTrex for a long time, it may become less effective over time and you could develop tolerance and dependence. The risks of developing dependence are increased if you have a current or past history of substance misuse disorders, e.g. alcohol use disorder, opioid (strong pain medication, e.g. morphine) use disorder or drug use disorder.

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).

Children and adolescents:

RuTrex is not intended to be used in children and adolescents under the age of 18 years.

Other medicines and RuTrex:

Always tell your health care provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

Please consult with your doctor, pharmacist or health care provider for advice if you need to take any other medicines.

Do not take RuTrex at the same time or within 2 weeks after stopping taking monoamine oxidase inhibitors (MAOIs) (used to treat depression, e.g. selegiline).

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

- medicines to help you sleep (including anaesthetics) and medicines to calm you down called tranquillisers.

  The use of RuTrex and sedative medicines such as benzodiazepines or related medicines 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. If your doctor does prescribe RuTrex 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.
- medicines used to treat mental disorders.
- medicines used to treat depression (i.e. antidepressants, such as desipramine, nefazodone, fluvoxamine, fluoxetine, paroxetine and sertraline). The risk of side effects increases, if you use RuTrex concomitantly with antidepressants. 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).
- alcohol may enhance the sedative effects of RuTrex.
- chlormethiazole, used to treat alcohol withdrawal.
- anti-inflammatory and immunosuppressants (e.g. dexamethasone and ciclosporin).
- cimetidine, used to treat stomach ulcers.
- rifampicin, used to treat tuberculosis (TB).
- antibiotics such as ciprofloxacin or macrolide antibiotics such as erythromycin.
- medicines used to treat fungal infections such as ketoconazole, voriconazole or fluconazole.
- medicines used to treat epilepsy such as phenytoin, carbamazepine, phenobarbitone and primidone.
- medicines that make your urine acidic such as ascorbic acid (vitamin C).

- medicine used to treat diarrhoea (e.g. loperamide, diphenoxylate).
- narcotic painkillers such as morphine, codeine and pentazocine.
- naloxone used to reverse the effects of opioid medicines.
- medicines used to stop opioid medicines working such as naltrexone and buprenorphine.
- medicines used to treat HIV such as nevirapine, efavirenz, abacavir and nelfinavir. The doctor may have to change the dose of RuTrex, if you are taking these medicines.
- cannabinoids (active components of marijuana, which may be used to reduce anxiety, reduce inflammation and pain, reduce nausea and vomiting from cancer treatment, to relax muscles in patients with multiple sclerosis, to stimulate appetite and weight gain in cancer and AIDS patients).

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

- medicines for heart problems such as verapamil, enalapril, sotalol, amiodarone, flecainide, quinidine.
- medicines which affect electrolyte balance such as diuretics (water tablets, e.g. spironolactone).

Also tell your doctor if you are taking:

- St. John’s Wort - a herbal preparation for mood disorders.
- Grapefruit juice.

RuTrex may also affect some blood and urine tests (including doping tests and pregnancy tests). Please tell your doctor if you are taking RuTrex before any test is performed.

RuTrex with drink and alcohol:

Do not drink alcohol while taking RuTrex. RuTrex can make you drowsy and drinking alcohol will make you even more drowsy.

Grapefruit juice may affect how RuTrex works. Do not drink grapefruit juice with RuTrex.

Pregnancy and breastfeeding:

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you take RuTrex.

Pregnancy:

Do not take RuTrex 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 used during pregnancy, this should be done after a careful risk-benefit assessment by a doctor, preferably under supervision in a specialised medical centre.
If you use RuTrex during pregnancy, your baby may become dependent and experience withdrawal symptoms after the birth which may need to be treated.

You should not take RuTrex whilst you are in labour.

Take care if you are taking a pregnancy test as RuTrex may interfere with the results.

Breastfeeding:

Talk to your doctor if you are breastfeeding or thinking of breastfeeding while you are taking RuTrex. RuTrex passes into the breastmilk and may affect your baby.

Mothers taking RuTrex should not breastfeed their baby.

Fertility:

RuTrex does not appear to have an effect on fertility if you are a female. Maintenance treatment of male patients with RuTrex may cause sexual dysfunction and can affect ejaculate volume and sperm mobility.

Driving and using machines:

RuTrex can severely affect your ability to drive or use machines as it may make you sleepy or dizzy.

You should only start doing these activities again with the permission of your doctor.

Do not drive while taking RuTrex until you know how it affects you.

RuTrex contains sucrose and propylene glycol:

- Sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking RuTrex.
- Propylene glycol. RuTrex contains 200 mg propylene glycol per 1 mL. If you are pregnant, breastfeeding or if you suffer from a liver or kidney disease, do not take RuTrex unless recommended by your doctor. Your doctor may require additional tests to be performed while you are taking RuTrex.

3. How to take RuTrex

Do not share medicines prescribed for you with any other person.

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

Your doctor should discuss your treatment and whether you need to continue taking RuTrex at regular intervals. If you and your doctor decide to stop treatment a plan will be put in place to gradually reduce the dose and stop taking RuTrex to minimise the risk of withdrawal effects.

RuTrex contains 10 mg of methadone in each 1 mL.

RuTrex needs to be diluted to with another liquid before it is taken orally. You should only take RuTrex by mouth. Under no circumstances should you inject RuTrex, as it may cause serious and permanent damage to your body, with the possibility of death. Your pharmacist or doctor will dilute the concentrate to provide the appropriate concentration in a 5 mL dose.

Your doctor will tell you how much RuTrex you need to take, and how often you need to take it. It is

important that you do not take more than the dose agreed with your doctor. If you have the impression that the effect of RuTrex is too strong or too weak, talk to your doctor.

Adults:

The usual starting dose is 20 mg once daily. The dose will be slowly increased over a few weeks until you show no signs of withdrawal or intoxication. Your doctor can increase the dose up to 60 to 120 mg per day. Your doctor will decide what dose you need and when to reduce the dose.

Older people and ill people:

If you are elderly, have liver or kidney problems, have an under active thyroid gland or have prostate problems, your doctor may want to monitor you more closely and may reduce your dose of RuTrex.

If you take more RuTrex than you should:

- If you take more RuTrex than you should, talk to a doctor or go to your nearest hospital straight away. Take the remaining medicine with you.
- The signs you may notice are difficulty in breathing; feeling very drowsy which may lead to a stupor or coma; very small pupils; cold and clammy skin; a very slow pulse rate; low blood pressure and muscle weakness. In extreme cases, you may stop breathing, your blood flow may stop, you may have a heart attack which could lead to death.

If you forget to take RuTrex:

- 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 RuTrex:

Do not suddenly stop taking RuTrex. If you want to stop taking RuTrex, 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 RuTrex.

4. Possible side effects

RuTrex can have side effects.

Not all side effects reported for RuTrex are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking RuTrex, please consult your doctor, pharmacist or other health care provider for advice.

If any of the following happens, stop taking RuTrex and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing.
- Rash or itching.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to RuTrex. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Heart problems. The signs of this may include changes in the way your heart beats, such as it is beating faster or missed heart beats, breathing difficulties and dizziness.
- Your breathing becomes slow and shallow.
- Worsening of the pressure inside your head if you already have this condition following an injury to your brain or brain disease.
- You have asthma and it gets worse.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- feeling sick (nausea) or being sick (vomiting)
- feeling weak, tired
- weight gain
- water retention
- constipation
- rash, that may appear and disappear
- sweating a lot more than usual
- blurred vision, dry eyes
- feeling of dizziness, spinning sensation, confusion
- changes in your mood, feeling “high” or over excited, feeling drowsy
- seeing or hearing things that are not there (hallucinations)
- lower sexual urge or desire
- headache

Less frequent side effects:

- feeling dizzy, particularly when standing up. This may be a sign that you have low blood pressure.
- feeling down (dysphoria), agitation, difficulty sleeping
- itching, rashes
- dry mouth or nose, inflammation of the tongue
- facial flushing
- difficulty in passing water (urine)
- tendency to swelling, due to retention of fluids
- effect to decrease excretion of urine
- low body heat (hypothermia)
- addiction to this medicine
- build-up of fluid in the lungs
- disorder of the biliary part of the digestive system (bile duct dyskinesis)
- small pupils

- the inappropriate production of milk (galactorrhoea), excessive pain with menstruation (dysmenorrhoea) and absence of menstrual period (amenorrhoea)

Frequency unknown:

- reduction in blood platelets, which increase the risk of bleeding or bruising
- high prolactin levels in the blood (which may cause the breasts to grow and produce breast milk)
- rapid, uncontrollable movements of the eyes
- low blood sugar
- dependence and addiction.

Withdrawal:

When you stop taking RuTrex, you may experience medicine 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.

The following side effects have also been reported:

- swollen arms and legs. This may be a sign of your body retaining more water than usual.
- low potassium and magnesium which will be found by blood tests.
- reduction in the body's normal production of adrenal and sexual hormones.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects:

If you get side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide

more information on the safety of RuTrex.

5. How to store RuTrex

- Store at or below 30 °C.
- Keep the container tightly closed.
- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use after the expiry date printed on the blister/carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What RuTrex contains:

The active substance is methadone hydrochloride.

The other ingredients are anhydrous citric acid, cherry flavour, D & C Red 33 (colourant), FD & C Red 40 (colourant), methyl hydroxybenzoate, propyl hydroxybenzoate, propylene glycol, purified water, sucrose and sodium hydroxide (pH adjuster).

What RuTrex looks like and contents of the pack:

RuTrex is a clear, red coloured liquid.

RuTrex is supplied in a 1 litre amber HDPE container with a white HDPE screw cap with an induction wad.

Holder of the certificate of registration:

LeBasi Pharmaceuticals (Pty) Ltd

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10 Church Street,

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