

Patient Leaflet According to the Pharmacists' Regulations (Preparations) – 1986

This medicine is sold with a doctor's prescription only

MCR® 10, MCR® 30, MCR® 100 **Controlled-release tablets**

Active ingredient:

Each tablet of **MCR 10** contains: 10 mg Morphine sulfate

Each tablet of **MCR 30** contains: 30 mg Morphine sulfate

Each tablet of **MCR 100** contains: 100 mg Morphine sulfate

For the list of the other ingredients, see section 6.

See also 'Important information about some of the medicine's ingredients' in section 2.

Read the entire leaflet carefully before using the medicine.

This leaflet contains concise information about the medicine. If you have any further questions, please refer to your doctor or pharmacist.

This medicine has been prescribed to treat your condition. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours. This is particularly important when using a medicine of this kind, which was prescribed for you after careful evaluation of the benefit versus the risk of using it unnecessarily.

Medicines of the opioids group may cause addiction, especially with prolonged use and they have a potential for misuse and overdose. A reaction to an overdose may be manifested by slow breathing and may even cause death.

Make sure you know the name of the medicine, the dosage that you take, how often you take it, the duration of treatment, potential side effects and risks. Additional information regarding the risk of dependence and addiction can be found at the following link:

https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/risk/DocLib/opioids_en.pdf

Taking this medicine along with medicines from the benzodiazepines group, other medicines which depress the central nervous system (including drugs) or alcohol may cause a feeling of profound drowsiness, breathing difficulties (respiratory depression), coma and death.

1. What is the medicine intended for?

The medicine is intended for prolonged relief of severe pain.

Therapeutic group: Opioid analgesics.

This medicine has been prescribed for you only and should not be given to anyone else. Opioids may cause addiction and you may experience withdrawal symptoms if you stop taking them suddenly.

Make sure that you received an explanation from your doctor on the duration of treatment with the medicine, when it is appropriate to stop taking it and how to do so safely.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients the medicine contains (for a list of the other ingredients, see section 6).
- You suffer from breathing problems, such as obstructive airways disease, respiratory depression or severe asthma. The symptoms can include breathlessness, coughing or breathing more slowly or weakly than expected.
- You suffer from a head injury (the symptoms can include severe headache and/or nausea). The medicine may make the symptoms worse or conceal the severity of the injury.

- You suffer from a condition where the small bowel does not work properly (intestinal obstruction, suspected intestinal obstruction), slow gastric emptying or severe abdominal pain.
- You suffer from an acute liver disease.
- You are taking a medicine of the monoamine oxidase inhibitor group (MAOIs) or you have taken such a medicine within the last two weeks. See 'Drug interactions' section.
- The use is not recommended before surgery and for at least 24 hours after the surgery.
- The medicine is not intended for children under three years of age.

Special warnings regarding the use of this medicine:

Before (and during) treatment with MCR, tell your doctor if:

- You suffer or have suffered in the past from opioid, alcohol, medicines or drug addiction.
- You have suffered in the past from withdrawal symptoms such as: agitation, anxiety, shaking, sweating or psychosis due to discontinuing the use of alcohol, medicines or drugs.
- You feel you need to take more tablets to get the same level of pain relief. This may be a sign that you are developing tolerance to the medicine or are becoming addicted to it. In such a case, contact your doctor in order to evaluate whether a change in dosage or switching to another pain reliever is necessary.
- You suffer from mental problems such as depression.
- You suffer from breathing problems such as impaired lung function or asthma. The symptoms can include breathlessness and coughing. See also 'Do not use the medicine if'.
- You suffer from a condition in which your breathing stops for a short time while you are sleeping, a condition called sleep apnea.
- You suffer from underactive thyroid gland (hypothyroidism), kidney or liver problems: the doctor may prescribe a lower dosage for you.
- You suffer from increased pressure in your skull (that can be manifested in severe headaches and nausea), brain damage or a reduction in level of consciousness.
- You suffer or have suffered in the past from epilepsy, convulsions or seizures.
- You suffer from sickle-cell anemia, low blood pressure and/or low blood volume.
- You suffer from a severe heart problem after a prolonged lung disease (cor pulmonale).
- You suffer from inflammation of the pancreas (causing severe abdominal and back pain); problems in the gallbladder or biliary tract; digestive system problems, inflammatory bowel disease; constipation; prostate gland problems.
- You suffer from impaired adrenal glands function. Symptoms of weakness, tiredness, dizziness, lack of appetite, nausea, vomiting or low blood pressure may indicate impaired adrenal glands function and reduced production of the cortisol hormone.
- You suffer from decreased sexual drive, impotence, cessation of menstruation. These symptoms can be caused by reduced production of sex hormones.

Additional warnings

- MCR tablets contain morphine, an opioid substance, and have a potential for abuse. Take all precautions in order to prevent the medicine from falling into the hands of somebody other than the patient.
- Long-term use may cause dependence!
 - Taking this medicine regularly particularly for a long period, may cause addiction. Make sure you received an explanation from the doctor on the duration of the treatment with the medicine, when it is appropriate to stop taking it and how to do so safely.
 - Addiction may cause withdrawal symptoms when you stop taking the medicine. Withdrawal symptoms may include restlessness, sleeping difficulties, nervousness, agitation, anxiety, feeling the heartbeat (palpitations), increase in blood pressure, nausea, vomiting, diarrhea, loss of appetite, shaking, chills, sweating. Before discontinuing the medicine, consult with your

doctor who will guide you how to gradually reduce the dosage. It is important to not stop taking the medicine suddenly since then the risk that you will experience withdrawal symptoms rises. See also in section 3 'If you stop taking the medicine'.

- Taking high or frequent doses of opioids increases the risk of developing an addiction. Excessive use and abuse may lead to an overdose and even death.
- In rare cases, increasing the dosage of the medicine may cause you to be more sensitive to pain. In this case, contact your doctor for consultation about the treatment.
- The medicine may cause and/or worsen breathing problems while sleeping. These problems can include pauses in breathing during sleep, waking up because of shortness of breath, difficulties remaining asleep or excessive daytime drowsiness. If you experience these symptoms or someone else in your surroundings observes these symptoms in you, contact your doctor. The doctor may recommend reducing the dosage.
- **Great** caution is required in elderly patients because of their increased sensitivity to the medicine. The doctor may recommend a lower dosage.
- You may experience hormonal changes during the treatment with the medicine.
- Avoid sudden passage from a lying/sitting position to a standing position, in order to prevent dizziness and in extreme cases fainting.
- If you are due to have a surgery or any other procedure involving anesthesia, please tell the doctor that you are taking this medicine. The use is not recommended before surgery. It should be used with extreme caution for up to 24 hours after the surgery and according to the doctor's instructions.

Children and adolescents:

The medicine is not intended for children under three years of age.

The medicine is not recommended in children for post-surgery pain relief.

Tests and follow-up:

- During prolonged treatment you must undergo periodic assessments in order to evaluate the continued need for the medicine.
- Your doctor may carry out monitoring for possible hormonal changes.

Drug interactions

Taking MCR concomitantly with sedatives (medicines that cause sedation, calmness or sleep induction), such as benzodiazepines or similar medicines increases the risk of drowsiness, breathing difficulties (respiratory depression) and coma, and may be life-threatening. Therefore, concomitant use should be considered only if there are no other treatment options. If your doctor has decided to prescribe MCR for you together with sedatives, the doctor may limit the dosage and the duration of the concomitant treatment. Inform your doctor of all the sedatives you are taking and strictly follow the doctor's recommendations regarding the dosage. It is recommended to ask friends and relatives to be alert for the symptoms mentioned. Contact the doctor if you experience these symptoms.

If you are taking, or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, please tell your doctor or pharmacist. Especially inform your doctor or pharmacist if you are taking the following medicines:

- Do not use MCR concomitantly with medicines of the monoamine oxidase inhibitor group (MAOIs) such as tranylcypromine, phenelzine, isocarboxazid, moclobemide, linezolid or if you have taken a medicine from this group within the last two weeks - see section 'Do not use this medicine if'.
- Medicines which affect the central nervous system such as: anti-anxiety medicines, sedatives and sleep inducing medicines such as benzodiazepines; anesthetics including barbiturates, other opioid analgesics.
- Medicines to treat certain mental disorders (such as phenothiazines, antidepressants).
- Muscle relaxants.

- Medicines for the treatment of high blood pressure.
- Cimetidine (to treat digestive problems such as heartburn, stomach ulcer).
- Certain medicines against nausea and vomiting.
- Antihistamines for prevention or relief of allergy symptoms.
- Medicines with anticholinergic activity (such as medicines to treat Parkinson's disease).
- Rifampicin (antibiotic for treatment of tuberculosis).
- Ritonavir (against the AIDS/HIV virus).
- Medicines for treatment of epilepsy or neuropathic pain including gabapentinoids (gabapentin, pregabalin).
- Certain medicines for treatment of blood clots such as clopidogrel, prasugrel, ticagrelor: their effect may be impaired (delayed or reduced) if they are taken together with MCR.

Use of this medicine and food:

The medicine can be taken regardless of mealtimes.

Use of the medicine and alcohol consumption:

Do not drink alcohol during the treatment period with this medicine.

Drinking alcohol while taking the medicine may cause you to feel more sleepy or increase the risk of serious side effects, such as shallow breathing with a risk of cessation of breathing and loss of consciousness.

Pregnancy and breastfeeding:

- **Pregnancy:** do not use the medicine during pregnancy or if you think you are pregnant, unless your doctor decided that the benefit of using of the medicine outweighs the possible risk. If the medicine is taken during pregnancy the baby may develop dependence on the medicine and experience withdrawal symptoms after the birth, which may need to be treated. The symptoms may include: high-pitched crying, irritability/restlessness, tremor, feeding difficulties, sweating.
- **Childbirth:** use during childbirth may cause respiratory depression in the newborn that will require appropriate treatment after the birth.
- **Breastfeeding:** do not use the medicine during the breastfeeding period, since the active substance (morphine) passes into breastmilk and can affect the baby (may cause respiratory depression).

Driving and use of machinery:

The use of this medicine may cause a number of side effects that could impair your ability to drive or operate machinery (for instance drowsiness, dizziness). See section 4 for the complete list of side effects. Usually, these side effects are felt more at the beginning of the treatment and/or when the dosage is increased. If you feel these effects and/or any other effect which might affect driving ability, do not drive or operate machinery. Do not drive until you know how the medicine affects you. As for children, they should be warned against riding a bicycle or playing near roads, etc.

Important information about some of the medicine's ingredients:

- MCR 10 and MCR 30 contain lactose (a type of sugar). If you have intolerance to certain sugars, inform your doctor before taking this medicine (see section 6).
- MCR 30 contains the colorant sunset yellow, which may cause allergic reactions.

3. How to use this medicine?

Always use according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

The dosage, treatment manner and duration of treatment will be determined by the doctor only.

Make sure that your prescribing doctor discussed with you the duration of the treatment with the medicine, a plan for discontinuing the treatment and how to gradually stop taking the medicine. The tablets are intended to be taken by mouth only.

The standard dosage is usually:

- The tablets are usually intended to be taken twice daily (every 12 hours, for instance at 8 o'clock in the morning and 8 o'clock in the evening).
- The dosage will be determined by the doctor according to your age, weight, your condition and the severity of your pain.
- The medicine is not intended for children under three years of age, nor for patients (adults and children) with difficulty swallowing whole tablets.
- Elderly patients: a reduced starting dosage may be recommended.

Do not exceed the recommended dosage.

If during treatment with the medicine you continue to experience pain - contact your doctor. Do not change the dosage, without your doctor's instruction.

Swallow the tablet with water. Do not retain the medicine in your mouth beyond the time necessary to swallow it.

Swallow the tablet whole, in order to not impair the prolonged release mechanism of the active ingredient from the tablet. Do not chew, break, halve, dissolve or crush the tablets! Taking tablets that are not whole may lead to faster absorption of the entire dose into your body; this could cause serious problems such as overdose and can be life-threatening (see section 'If you have accidentally taken a higher dosage or if a person other than the patient has accidentally swallowed the medicine').

Do not crush the tablets and inject since this may lead to serious side effects **and even death**.

If you have accidentally taken a higher dosage or if a person other than the patient accidentally swallowed the medicine,

proceed immediately to a doctor or a hospital emergency room and bring the medicine package. Symptoms of an overdose may include extreme drowsiness, nausea, vomiting, dizziness, constricted pupils, muscle problems (including muscle breakdown), slow heartbeat (bradycardia), low blood pressure, pneumonia (symptoms of this may include breathlessness, coughing and fever); in addition, breathing difficulties may also appear (to the point of respiratory depression) that may cause unconsciousness, coma and even death. It is recommended to ask your surroundings to also be alert to the appearance of these symptoms, since overdose symptoms require urgent medical attention.

If you forgot to take the medicine:

If you remember within 4 hours from the time when you should have taken the medicine, take it immediately. Take the next dose at the regular time. If more than 4 hours have elapsed from the time when you should have taken the medicine, consult your doctor.

Never take a double dose to make up for a forgotten dose.

Adhere to the treatment as recommended by your doctor.

Even if your state of health improves, do not stop the treatment with the medicine without consulting your doctor and even then usually only gradually.

If you stop taking the medicine: do not stop taking the medicine suddenly. If you want to stop taking the medicine, consult your doctor who will guide you how to do this. Your doctor will usually recommend that you gradually reduce the dosage in order to decrease the risk of the appearance of withdrawal symptoms such as: restlessness, sleeping difficulties, weakness, irritability, agitation, anxiety, feeling the heartbeat (palpitations), increase in blood pressure, nausea, vomiting, diarrhea, shaking, chills, sweating, loss of appetite, tearing, runny nose,

yawning, dilated pupils, muscle pain, body aches, flulike symptoms, abdominal cramps; increased heart and/or breathing rate.
Do not take medicines in the dark! Check the label and the dose each time you take a medicine.
Wear glasses if you need them.
If you have further questions concerning the use of the medicine, consult your doctor or pharmacist.

4. Side effects

Like any medicine, the use of MCR may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Refer immediately to a doctor or a hospital emergency room if the following side effects appear:

Allergic or anaphylactic reaction. Any medicine can cause allergic reactions, although a serious allergic reaction is uncommon. Symptoms of an allergic reaction can include sudden wheezing, breathing difficulties, swelling of the face, eyelids or lips, rash and/or itching (particularly in extensive areas of the body).

Respiratory depression. This side effect is extremely serious (is not common) and is manifested in breathing that is slower or weaker than normal.

Withdrawal symptoms: when you stop taking the medicine, you may experience withdrawal symptoms. See section 'If you stop taking the medicine'.

Addiction: How to identify a state of addiction?

Symptoms of addiction can include: a feeling that you need to take the medicine for a longer period than recommended by the doctor and/or take a higher dose than that recommended by the doctor; use of the medicine for reasons other than those for which it was prescribed for you; when you stop taking the medicine you feel unwell, and you start feeling well again when you take the medicine again. If you experience any of these symptoms refer to your doctor.

Additional side effects:

Very common side effects (appear in more than one user out of ten): nausea, constipation (the doctor may prescribe a laxative for you in order to overcome this problem).

Common side effects (appear in 1-10 users out of 100): drowsiness (usually appears at the beginning of the treatment or when the dosage is increased, but passes generally after a few days); dry mouth, loss of appetite, abdominal pain or discomfort; vomiting (this effect usually disappears after a few days; however the doctor may prescribe an anti-vomiting medicine if the problem continues); dizziness, headache, confusion, difficulty sleeping; unusual weakness; generally feeling unwell, tiredness; involuntary muscle contractions, skin rash or itching; sweating (including excessive sweating).

Uncommon side effects (appear in 1-10 users out of 1,000): withdrawal symptoms (see section 3 'If you stop taking the medicine'); breathing difficulties (that might be a result of fluid in the lungs), pulmonary edema, wheezing, bronchospasm; intestinal obstruction; changes in taste, indigestion, spinning sensation (vertigo), fainting, convulsions/seizures, agitation, mood changes, hallucinations, a feeling of extreme happiness (euphoria); unusual muscle stiffness; numbness or tingling; difficulty in passing urine (urinary retention, spasm); low blood pressure, reddening of the face (flushing), feeling the heart beat (palpitations), swelling of the hands, ankles or feet (peripheral edema); urticaria (hives - raised, itchy rash); adverse changes in liver functions (seen in blood tests, for instance: increase in liver enzymes); visual disturbances (such as blurred vision); muscle spasms.

Side effects of unknown frequency (effects whose frequency has not yet been determined): breathing problems during sleep (sleep apnea syndrome), dependence and addiction; drug tolerance, dejected mood; abnormal thoughts; increased sensitivity to pain; reduction in size of the pupils; rapid or slow heartbeats; high blood pressure; decreased cough reflex; colicky abdominal pain and/or abdominal discomfort (that may derive from bile problems); worsening of pancreas inflammation (may be manifested in severe abdominal and back pain); impotence, decreased sex drive, absence of menstrual periods; withdrawal symptoms in babies whose mothers used the medicine during pregnancy (see section 2 'Pregnancy and breastfeeding').

If a side effect appears, if any of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult your doctor.

Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads to an online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il/>

5. How to store the medicine?

- **Avoid poisoning! This medicine in particular must be stored in a closed place out of the reach and sight of children and/or infants, to avoid poisoning that might cause life-threatening harm.** See section 'If you have accidentally taken a higher dosage or if a person other than the patient has accidentally swallowed the medicine'. Do not induce vomiting unless explicitly instructed to do so by the doctor. When you no longer need the tablets, consult the pharmacist on how to dispose of them.
- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- Storage conditions: store below 25°C.

6. Additional information:

- **In addition to the active ingredient, the tablets also contain:**

Hydroxyethylcellulose, cetostearyl alcohol, magnesium stearate, talc, titanium dioxide (E171).

MCR 10 tablet also contains: 90 mg lactose and iron oxide red, yellow and black (E172), polyvinyl alcohol, macrogol/PEG

MCR 30 tablet also contains: 70 mg lactose and indigo carmine (E132), erythrosine (E127), sunset yellow (E110), hypromellose, polyethylene glycol 400

MCR 100 tablet also contains: iron oxide yellow and black (E172), indigo carmine (E132), hypromellose, polyethylene glycol 400

- **What does the medicine look like and what does the package contain?**

MCR 10: round brown tablets, packed in blisters in packages of 50 tablets.

MCR 30: round purple tablets, packed in blisters in packages of 50 tablets.

MCR 100: round gray tablets, '100mg' is imprinted on one side; packed in blisters in packages of 20 tablets.

Registration holder: Rafa Laboratories Ltd., PO Box 405, Jerusalem 9100301.

Medicine registration number in the National Medicines Registry of the Ministry of Health:

MCR 10: 0664722515

MCR 30: 0580122516

MCR 100: 0316525386

Revised in April 2021 in accordance with the Ministry of Health guidelines.

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