

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS'
REGULATIONS (PREPARATIONS) – 1986**

The medicine is dispensed with a doctor's prescription only

M.I.R. 15

M.I.R. 30

Tablets

Active ingredient:

Each tablet of **M.I.R. 15** contains: Morphine sulfate 15 mg

Each tablet of **M.I.R. 30** contains: Morphine sulfate 30 mg

For the list of the additional 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 the 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 meticulous evaluation of the benefit versus 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 in 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 relief of moderate to severe pain.

Therapeutic Group: Opioid analgesics.

The 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 the 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 additional ingredients the medicine contains (for the list of the additional ingredients, see section 6).
- You suffer from breathing problems, such as an illness that blocks the respiratory tract, respiratory depression or severe asthma. The symptoms can include shortness of breath, coughing or breathing more slowly or weakly than expected.
- You suffer from a head injury. (The symptoms can include a severe headache and/or nausea). The medicine may worsen the symptoms or hide the severity of the injury.
- You suffer from a condition where the small intestine 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 currently taking a medicine from the monoamine oxidase inhibitor group (MAOIs) or have taken such a medicine within the last two weeks. See the 'Drug interactions' section.
- The medicine is not intended for children under 3 years of age.
- Do not use this medicine if you are pregnant. See the 'Pregnancy and breastfeeding' section.

Special warnings regarding the use of the medicine:

Before (and during) treatment with M.I.R. tell the doctor if:

- You suffer or have suffered in the past from addiction to opioids, alcohol, medicines or drugs.
- You have suffered in the past from withdrawal symptoms such as: agitation, anxiety, shaking or sweating as a result of stopping the use of alcohol, medicines, or drugs.
- You feel you need to take more tablets to achieve the same measure of pain relief. This phenomenon may be a sign that you are developing tolerance to the medicine or are becoming addicted to it. In this case refer to the doctor in order to see whether a change in dosage or replacement of the medicine with another pain reliever is necessary.
- You suffer from mental problems such as depression.
- You suffer from breathing problems such as impaired lung function. The symptoms can include shortness of breath and coughing.
- You suffer from a condition in which your breathing stops for a short time when you are sleeping, a condition called sleep apnea.
- You suffer from an underactive thyroid gland (hypothyroidism), kidney or liver problems: the doctor may prescribe a lower dosage for you.
- You suffer from increased pressure in the 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 spasms.
- 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 pancreas inflammation (causing severe abdominal and back pain); problems in the gallbladder or biliary tract due to gallstones; inflammatory bowel disease; constipation; prostate gland problems.
- You suffer from impaired adrenal gland function. Symptoms of weakness, tiredness, lack of appetite, nausea, vomiting or low blood pressure, may indicate impaired adrenal gland function and reduced production of the cortisol hormone.
- You suffer from loss of libido, impotence, cessation of menstruation. These symptoms can be caused by reduced production of sex hormones.

Additional warnings

- M.I.R. tablets contain morphine, an opioid substance, and have the potential for abuse. Take all precautions in order to prevent the medicine from falling into the hands of somebody who is not the patient.
- Prolonged 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 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, irritability, agitation, anxiety, feeling your heartbeat (palpitations), rise in blood pressure, nausea, vomiting, diarrhea, loss of appetite, shaking, shivering, sweating. Before discontinuing the medicine, consult the doctor who will guide you on how to gradually reduce the dosage. It is important to not stop taking the medicine suddenly since then the risk of experiencing withdrawal symptoms increases.
- Taking high or frequent doses of opioids increases the risk of developing an addiction. Overuse and abuse may lead to an overdose and even death.

- In rare cases, increasing the medicine dosage may cause you to be more sensitive to pain. In this case, refer to the doctor for consultation regarding the treatment.
- The medicine may cause and/or worsen sleep apnea. These problems can include pauses in breathing during sleep, waking up because of shortness of breath, difficulty remaining asleep or excessive daytime drowsiness. If you feel these symptoms or someone else around you observes these symptoms in you, refer to the doctor. The doctor may recommend reducing the dosage.
- Avoid sudden passage from a prone/sitting position to a standing position, in order to prevent dizziness and in extreme cases fainting.
- If you are due to undergo surgery or any other procedure involving anesthesia, please tell the doctor that you are taking this medicine. Its 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.
- Great caution is required in the elderly because of their increased sensitivity to the medicine. The doctor may recommend a reduced dosage.
- You may experience hormonal changes during the treatment with the medicine.

Children and adolescents: The medicine is not intended for children under 3 years of age.

Tests and follow-up:

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

Drug interactions

Using M.I.R. concomitantly with sedative medicines (those 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 when other treatment options are not possible. If your doctor has decided to prescribe M.I.R. for you together with sedatives, he might limit the dosage and the duration of the concomitant treatment. Inform the doctor of all the sedatives you are taking and strictly follow the doctor's dosage recommendations. It is recommended to ask friends and relatives to be on the alert for the symptoms mentioned. Refer to 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 the doctor or pharmacist if you are taking the following medicines (it should be noted that the following list indicates the active ingredients in the medicines. If you are not sure whether you are using one of these medicines, please consult with the doctor or pharmacist):

- Do not use M.I.R. concomitantly with medicines belonging to the monoamine oxidase inhibitor group (MAOIs) such as tranylcypromine, phenelzine, isocarboxazid, moclobemide, linezolid, or if you have taken a medicine from this group during the last two weeks - see the 'Do not use this medicine if' section.
- Medicines which affect the central nervous system such as: anti-anxiety medicines, sedatives, and sleeping pills such as benzodiazepines; anesthetics including barbiturates; other opioid pain relievers.
- Medicines to treat certain mental disorders (such as phenothiazines, antidepressants).
- Medicines for muscle relaxation; medicines for treating high blood pressure.
- Cimetidine (to treat digestive problems, heartburn, stomach ulcer).
- Certain medicines against nausea and vomiting.
- Other types of strong medicines for pain treatment, e.g.: buprenorphine, nalbuphine, pentazocine.
- Antihistamines for prevention or relief of allergy symptoms.
- Rifampicin (for treatment of tuberculosis); ritonavir (against the AIDS/HIV virus).

- Medicines with anticholinergic activity (such as medicines to treat Parkinson).
- 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 decreased) if taken together with M.I.R.

Use of the 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 using this medicine may make you feel sleepy.

Pregnancy, childbirth and breastfeeding:

- **Pregnancy:** do not use the medicine if you are pregnant or if you think you are pregnant, unless the doctor decided that the benefit of using 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, shaking, feeding difficulties, sweating.
- **Childbirth:** use during childbirth may cause respiratory depression in the newborn.
- **Breastfeeding:** do not use the medicine during the breastfeeding period, since the active substance (morphine) passes into the breastmilk and may affect the baby (may cause respiratory depression in the baby).

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 treatment and/or with a dosage increase. If you feel these effects and/or any other effect which might affect driving 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:

- The tablets contain lactose (a type of sugar). If you have intolerance to certain sugars, inform the doctor before taking this medicine. (See section 6).
- M.I.R. 30 tablets contain azorubine (E122) that may cause allergic reactions.

3. How to use this medicine?

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

The dosage and manner 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 to be taken orally only. Swallow the medicine with water.

The standard dosage is usually:

- The dosage will be determined by the doctor according to your age, your weight, the severity of your pain and your response to the treatment. Usually, a dose should be taken every 4 to 6 hours.
- The medicine is not intended for children under the age of three.

Do not exceed the recommended dose.

If during the treatment with the medicine you continue to experience pain - refer to the doctor.

Do not change the dosage, without the doctor's instruction.
The tablet may be halved according to the scored line.
There is no information regarding crushing/chewing.
Do not crush and inject the tablets 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 package of the medicine with you. Symptoms of an overdose may include nausea, vomiting, dizziness, constricted pupils, muscle problems (e.g. muscle breakdown), slow heartbeat (bradycardia), low blood pressure, extreme sleepiness, pneumonia (symptoms of this may include shortness of breath, coughing and fever). Breathing difficulties may also appear (to the point of respiratory depression) that may cause loss of consciousness, coma and even death. It is recommended to ask people around you to also be alert to the occurrence of these symptoms, since overdose symptoms require urgent medical attention.

If you forgot to take the medicine: if you forgot to take this medicine at the set time, take a dose as soon as you remember, but make sure that there is an interval of no less than four hours between doses. Do not take a double dose to make up for a forgotten dose.

Adhere to the treatment as recommended by the doctor.
Even if your state of health improves, do not stop the treatment with the medicine without consulting the doctor and even then, usually only in a gradual manner.

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 instruct you how to do this. The 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, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increase in blood pressure, nausea, vomiting, diarrhea, loss of appetite, shaking, shivering, sweating.

Do not take medicines in the dark! Check the label and 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

As with any medicine, the use of M.I.R. 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 hospital emergency room if the following side effects appear (uncommon):

- **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, dizziness, swelling of the face, eyelids or lips, rash and/or itching (particularly in large areas of the body).
- **Respiratory depression.** This side effect is extremely serious and is manifested in breathing that is slower and/or weaker than normal.

Additional side effects:

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

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

Uncommon side effects (appear in 1-10 users out of 1,000): withdrawal symptoms (see section 3 'If you stop taking the medicine'); digestive disturbances, changes in taste; intestinal obstruction; vertigo (spinning sensation), fainting, fits/seizures; agitation, mood changes, hallucinations, euphoria (extreme sense of happiness); muscle stiffness; breathing difficulties (that might be as a result of fluid in the lungs), pulmonary edema, wheezing, bronchospasm; numbness or tingling; pain or difficulty in passing urine, urinary retention; low blood pressure, reddening of the face (flushing); feeling your heart beat (palpitations); swelling of the hands, ankles or feet (peripheral edema); urticaria (raised itchy rash); increase in liver enzymes (seen in blood tests and may indicate a liver function problem); 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), dejected mood; abnormal thoughts; increased sensitivity to pain; reduction in size of the eye pupils ; rapid or slow heartbeats; high blood pressure; decrease in cough reflex; colicky abdominal pain and/or abdominal discomfort (that may derive from bile problems); worsening of pancreas inflammation symptoms; absence of menstrual periods, decreased sex drive, impotence; drug tolerance; dependence and addiction (see details further in this paragraph); withdrawal symptoms in babies whose mothers used the medicine during pregnancy (see in section 2 'Pregnancy and breastfeeding').

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 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 anew. If you experience these symptoms refer to your doctor.

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

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 the following ingredients:**
M.I.R. 15: Lactose, corn starch, talc, povidone K25, magnesium stearate, indigotine blue (E132)
Each tablet contains approximately 168 mg lactose.

M.I.R. 30: Lactose, corn starch, talc, povidone K25, magnesium stearate, azorubine (E122)
Each tablet contains approximately 153 mg lactose.

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

M.I.R. 15: Round light blue tablets with a scored line, in blister packs of 20 tablets.

M.I.R. 30: Round pink tablets with a scored line, in blister packs of 20 tablets.

Manufacturer and registration holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301

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

M.I.R. 15: 0338325309

M.I.R. 30: 0338425310

Revised in September 2023 according to MOH's guidelines.

0770011