

PACKAGE LEAFLET: Information for the patient

MORFINE

Solution for injection – 10 mg / ml (1%)

(Morphine hydrochloride)

Read all of this leaflet carefully before you start taking this medicine.

- 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 any of the side effects gets serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Morfine is and what it is used for
2. Before you take Morfine
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4. Possible side effects
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1. WHAT MORFINE IS AND WHAT IT IS USED FOR

Morphine is a narcotic analgesic that causes analgesia mainly centrally than peripherally in the perception of pain. It also acts in the smooth muscles by increasing the tonus, especially of the sphincters of the gastrointestinal tract by reducing peristalsis. The pharmacological effects of morphine are: analgesia, drowsiness, behavioral changes (euphoria), lowering of body temperature and depending on the dose even respiratory depression.

Cough suppression is caused by the direct effect in the medullar center.

Morphine is readily absorbed after intramuscular and subcutaneous injection. Maximum plasmatic levels appear within 30 minutes of the intramuscular injection. Morphine is rapidly

distributed in the body but mainly in the parenchymatous tissue such as in the kidneys, liver and spleen. Lower concentrations are found in the skeletal muscles. Small amounts of morphine cross the hematoencephalic barrier. Morphine does not remain for a long time in the tissues and 24 hours after receiving the last dose, the concentrations are quite low. Morphine passes through the placenta and its traces are found in sweat and in breast milk. About 33% of the drug is bound with proteins, mainly with albumin. Morphine is metabolized mainly in the liver by conjugation with glucuronic acid in the 3 - hydroxyl group and in a lesser extent in the 6 - hydroxyl group. The elimination half-life is about 1.5 to 2 hours in healthy subjects and 90% of the dose is excreted through urine within 24 hours. About 7 to 10% of the dose is excreted through faeces. There is evidence that urinary excretion of morphine may be increased by lowering the pH of urine.

Morphine is used in:

- the relief of moderate to severe pain, in malignant tumors, after severe trauma, after surgeries and myocardial infarction;
- cardiac asthma;
- acute pulmonary oedema;
- peripheral vascular obstruction;
- traumatic shock;
- pulmonary embolism;
- abdominal, renal and biliary colics;
- pretreatment before general anaesthesia.

Morphine is also used in other emergencies such as in left ventricular failure, abdominal perforation and haematemesis.

Morphine alleviates the anxiety associating severe pain and it is used as hypnotic in case sleeplessness is caused by pain.

2. BEFORE YOU TAKE MORFINE

Do not take Morfine:

- if you are sensitive (allergic) to morphine hydrochloride, to opioids or to any of the other excipients of Morfine solution for injection;
- after biliary tract surgeries or surgical anastomosis;
- if you have increased intracranial pressure or head trauma (affects breathing and pupillary response that is vital in the neurological assessment);
- if you have acute abdomen or paralytic ileus;
- *if you have bronchial stasis*;
- if you have renal, hepatic, or respiratory failure;
- if you have heart failure secondary to chronic lung diseases;
- if you suffer of acute alcoholism, delirium tremens;
- if you suffer from convulsive states, such as status epilepticus, tetanus (because of the stimulating effects in the spinal medulla) or in strychnine toxicity;
- if you use or have used monoamine oxidase inhibitors (MAOIs) in the last 2 weeks;
- if you have pheochromocytoma.

Morfine should not be used in premature children or during labour.

Take special care with Morfine

Ask your doctor before taking Morfine.

- Morphine should be used with caution in patients with: hypotension, hypothyroidism, asthma and decreased respiratory reserve, adrenocortical failure, prostate hypertrophy, shock, urethral stenosis, inflammatory or obstructive bowel disorders, pancreatitis, cardiac arrhythmias, severe cor pulmonale, myasthenia gravis.
- Care should be taken during pregnancy and breastfeeding. Withdrawal syndrome may appear to children born from mothers who have continuously used morphine. Morphine appears in breast milk, so its use is not recommended during breastfeeding.
- In patients with liver impairment it may cause coma (although morphine is well tolerated in many of those patients).

- The dose of morphine should be reduced in renal disorders, in the elderly and in debilitated patients.
- Morphine and narcotic analgesics generally should be used only for a short time for the relief of pain that is not dominated by non-narcotic analgesics.
- As a result of the use of repeated doses, morphine may cause physical and psychological dependence; abrupt withdrawal of the treatment with morphine in these patients may cause the withdrawal syndrome, including seizures.
- The use in children is reserved only for the necessary cases.

Talk to your doctor or pharmacist if you experience any of the following symptoms while being given Morfine solution for injection:

- increased sensitivity to pain despite the fact that you are taking increasing doses (hyperalgesia); the doctor will decide if you need to change the dosage or the analgesic;
- 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;
- loss of libido, impotence, cessation of menstruation. This may be because of decreased sex hormone production.

Taking other medicines

Concomitant treatment with other drugs may affect or be affected by morphine.

Please contact your doctor or pharmacist if you are taking or have recently taken other drugs, including those obtained without a prescription. Do not forget to inform your doctor for the treatment with morphine if you have been given any other drug during treatment.

It is especially important to inform your doctor that you are treated or have taken:

- central nervous system depressants, like: other opioids, sedatives, hypnotics, anesthetics, tricyclic antidepressants, barbiturates and phenothiazines, sedative antihistamines, alcohol, because they may increase the depressant effects of morphine.
- The combination of morphine with monoamino-oxidase inhibitors (MAOI-s) may cause marked respiratory depression, hypotension and hyperpyrexia.

- When morphine is simultaneously taken with cimetidine, the patient should be carefully monitored for the increased depressant effect of the respiration and of the central nervous system; on the other side, this combination may cause apnea and confusion.
- The effects of morphine may be inhibited by the partial antagonistic activity of pentazocine.
- The neuromuscular blocking effects of tubocurarine are enhanced by morphine.
- Ritonavir may reduce the plasmatic concentrations of morphine.
- Morphine increases the biodisponibility of gabapentin.
- Morphine may reduce the effect of diuretics.
- Rifampicin markedly increases the metabolism of morphine, and reduces its effects.
- The use of nalmeffen with opioid analgesics should be avoided.
- Opioid analgesics enhance the effects of sodium oxibate, hence concomitant use should be avoided.
- The action of morphine in the gastrointestinal peristalsis may affect the absorption of other drugs.

Taking Morfine with food and drinks

It should not be taken with alcohol because the hypotensive and sedative effects and the respiratory disorders are enhanced.

Pregnancy

Ask your doctor or pharmacist for advice before taking this drug.

Morfine 1% should not be taken during pregnancy. Withdrawal syndrome may appear to babies born from mothers who have continuously used morphine.

Breastfeeding

Morfine passes into breast milk, thus its use is not recommended during breastfeeding.

It is absolutely necessary for the mother to consult the doctor before taking Morfine.

Driving and using machines

You should not drive and use machines during treatment with morphine because some of its side effects are: euphoria, dizziness, drowsiness, orientation disorders.

Important information about some of the excipients of Morfine

Morfine solution for injection contains sodium metabisulphite, which may rarely cause severe hypersensitivity reactions and bronchospasm.

3. HOW TO TAKE MORFINE

Always take Morfine exactly as your doctor has told you. If you are not sure, contact your doctor or pharmacist. If you feel that the effects of Morfine are too strong or too weak, talk to your doctor or pharmacist.

The dosage of Morfine is as follows:

- In acute pain, by subcutaneous or intramuscular injection: 10 mg, repeated if necessary every 4 hours (15 mg in burly and high weight patients).
- Children up to 1 month: 0.15 mg/kg body weight; 1 – 12 months: 0.2 mg/kg body weight; 1 – 5 years old: 2.5 – 5 mg; 6 – 12 years old: 5 – 10 mg.
- By slow intravenous injection: 1/4 - 1/2 of the corresponding subcutaneous or intramuscular dose.
- In myocardial infarction, by slow intravenous injection (2 mg/min.): 10 mg and if necessary may be followed by a further 5 to 10 mg; for elderly or debilitated patients the dose is halved.
- In acute pulmonary oedema, by slow intravenous injection (2 mg/min.): 5 to 10 mg.
- In chronic pain, by subcutaneous or intramuscular injection: 5 – 20 mg, every 4 hours; the dose may be increased as needed.

If you take more Morfine than you should

This drug will be administered to you in a hospital, therefore there is not much possibility to occur any overdose, although you should immediately inform your doctor if you think you have taken a higher dose.

If you forget to take Morfine

This drug will be administered to you in a hospital, therefore there are not many possibilities of any forgetfulness, although a double dose (or higher) should not be taken to compensate the forgotten dose.

If you stop taking Morfine

The treatment should not be withdrawn abruptly. Abrupt withdrawal causes the withdrawal syndrome.

If you have any further question on the use of this medicinal product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all other drugs, morphine may cause side effects, although not everybody manifests them. Most of the side effects are dose-related and disappear when dosage is reduced or treatment is stopped. Some side effects may occur at the beginning of treatment and disappear spontaneously with treatment continuance.

Morfine may cause:

- serious allergic reactions which cause: difficulty in breathing or dizziness;
- gastrointestinal disorders (nausea, vomiting, constipation, abdominal pain, anorexia, dyspepsia, biliary spasms, dry mouth, exacerbation of pancreatitis);
- cardiovascular disorders (hypotension, orthostatic hypotension, bradycardia, tachycardia, palpitations);
- central nervous system disorders (dizziness, drowsiness, euphoria, dysphoria, hallucinations, delirium, orientation disorders, raised intracranial pressure);
- skin disorders (sweating, itching, urticaria);
- respiratory disorders (respiratory depression, apnea, respiratory arrest, laryngospasms, suppression of cough reflex);
- urogenital disorders (urethral spasms, urine retention, antidiuretic effect, reduced libido and / or sexual potency);
- musculoskeletal disorders (rigidity, paraesthesia, rhabdomyolysis);
- visual disorders (blurred vision, myosis, nystagmus).

Taste disturbances, behavior changes, psychic and physical dependence, pain at the site of injection, local irritation and induration of the site of injection have also been reported.

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.

5. HOW TO STORE MORFINE

Keep out of the reach and sight of children!

Do not use Morfine after the expiry date which is stated on the package.

Do not store above 25°C!

Keep in the original package to protect it from light.

6. OTHER INFORMATION

What Morfine contains

The active substance is morphine hydrochloride.

Each 1 ml ampoule contains 10 mg of morphine hydrochloride.

The excipients are: sodium chloride, sodium metabisulphite, hydrochloric acid, water for injections.

Content of the pack

Carton box with 10 ampoules.

Marketing Authorisation Holder (MAH) and Manufacturer:

PROFARMA sh.a.,

St. “Skënder Vila”,

Tirana, Albania.

Tel.: +355 4 23 89 602

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