

Package Leaflet: Information for the user
Morphine Sulfate 1mg in 1mL Solution for Injection
Morphine Sulfate

Read all of this leaflet carefully before you start using 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, nurse or pharmacist.**
- **If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See Section 4.**



What is in this leaflet:

- 1. What Morphine Sulfate Injection is and what it is used for**
- 2. What you need to know before you use Morphine Sulfate Injection**
- 3. How to use Morphine Sulfate Injection**
- 4. Possible Side Effects**
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- 6. Contents of the pack and other information.**

This medicine contains morphine sulfate which is an opioid, which can cause addiction. You can get withdrawal symptoms if you stop using it suddenly.

1. What Morphine Sulfate Injection is and what it is used for

This medicine has been prescribed for you for the long term relief of moderate to severe pain, such as the pain caused by surgery, heart attacks and cancer. This medicine also helps to reduce the anxiety and sleeplessness which may be caused by the pain. It contains morphine sulfate which belongs to a class of medicines called opioids, which are 'pain relievers'. This medicine is a solution for injection that has been prepared in water so that it can be used with specially designed pumps which provide a continuous injection into the body.

This medicine 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 using it suddenly. Your doctor, pharmacist or nurse should have explained how long you will be using it for and when it is appropriate to stop, how to do this safely.

2. What you need to know before you use Morphine Sulfate Injection

Do not use Morphine Sulfate Injection if you:

- Are allergic to morphine sulfate or any other strong painkilling drugs
- Have a history of alcohol abuse
- Suffer from malfunctioning of the adrenal gland (phaeochromocytoma)
- Have suffered a head injury
- Are at risk of a paralytic ileus (reduced gut motility)
- Have acute respiratory depression (breathlessness)
- Have raised pressure inside your skull

Check with your doctor if you are concerned about any of the above.

Warnings and Precautions:

Talk to your doctor, pharmacist or nurse before using this medicine if you:

- Are or have ever been addicted to opioids, alcohol, prescription medicines, or illegal drugs.
- Have previously suffered from withdrawal symptoms such as agitation, anxiety, shaking or sweating, when you have stopped taking alcohol or drugs.
- Feel you need to take more Morphine Sulfate Injection to get the same level of pain relief, this may mean you are becoming tolerant to the effects of this medicine or are becoming addicted to it. Speak to your doctor, pharmacist or nurse who will discuss your treatment and may change your dose or switch you to an alternative pain reliever.
- Are pregnant or breast feeding
- Have taken this medicine in the last two weeks
- Suffer from asthma, chronic bronchitis or have any other illness which causes breathing difficulties
- Suffer from kidney or liver problems
- Suffer from stomach or bowel problems
- Have difficulty in passing urine due to an enlarged prostate
- Suffer from bad headaches or feel sick
- Suffer from epilepsy or other fits
- Suffer from poor blood supply to the heart or other heart problems
- Have low blood pressure (hypotension)
- Have a tumour of the adrenal gland
- Suffer from myasthenia gravis
- Suffer from pain from gallstones (biliary colic)
- Suffer from thyroid problems
- Are elderly and/or debilitated
- Have increased sensitivity to pain despite the fact that you are using increasing doses (hyperalgesia). Your doctor will decide whether you will need a change in dose or a change in strong analgesic ("painkiller"), (see section 2).
- Have 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.
- Suffer loss of libido, impotence, cessation of menstruation. This may be because of decreased sex hormone production.

Check with your doctor if you are concerned about any of the above. This medicine is only suitable for long lasting pain and is not intended for pain which only lasts for short periods.

Using this medicine regularly, particularly for a long time, can lead to addiction. Your doctor, pharmacist or nurse should have explained how long you will be using it for and when it is appropriate to stop, how to do this safely.

Rarely, increasing the dose of this medicine can make you more sensitive to pain. If this happens, you need to speak to your doctor, pharmacist or nurse about your treatment.

Addiction can cause withdrawal symptoms when you stop using this medicine. Withdrawal symptoms can include restlessness, 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 doctor, pharmacist or nurse will discuss with you how to gradually reduce your dose before stopping the medicine. It is important that you do not stop using the medicine 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 your medicine to anyone else. Using higher doses, or more frequent doses of opioid, may increase the risk of addiction. Overuse and misuse can lead to overdose and/or death.

Tolerance, dependence, and addiction

This medicine contains morphine 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 Morphine Sulfate Injection 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 risk of becoming dependent or addicted varies from person to person. You may have a greater risk of becoming dependent on or addicted to Morphine Sulfate Injection 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 Morphine Sulfate Injection, 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 Morphine Sulfate Injection).

Take special care with Morphine Sulfate Injection:

Acute generalized exanthematous pustulosis (AGEP) has been reported in association with Morphine Sulfate Injection treatment. Symptoms usually occur within the first 10 days of treatment. Tell your doctor if you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking Morphine Sulfate Injection or other opioids. Stop using Morphine Sulfate Injection and seek medical attention immediately, if you notice any of the following symptoms: blistering, widespread scaly skin or pus-filled spots together with fever.

Sleep-related breathing disorders

Morphine Sulfate Injection 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. Contact your doctor if you experience severe upper abdominal pain possibly radiating to the back, nausea, vomiting or fever as this could be symptoms associated with inflammation of the pancreas (pancreatitis) and the biliary tract system.

Other medicines and Morphine Sulfate Injection

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. This is especially important if you are taking any of the medicines mentioned below or medicines for:

- Rifampicin to treat e.g. tuberculosis
- Concomitant use of Morphine Sulfate Injection and 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, concomitant use should only be considered when other treatment options are not possible. However, if your doctor does prescribe Morphine Sulfate Injection 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.
- Are taking gabapentin or pregabalin to treat epilepsy and pain due to nerve problems (neuropathic pain)
- Are taking medicines to treat depression
- Are taking medicines for sickness (phenothiazines), for drying secretions (anticholinergics e.g. hyoscine) or other pain killers
- Have taken one of a group of drugs called monoamine oxidase inhibitors (used to treat depression) within the last two weeks
- Are taking anti-psychotics, cimetidine, domperidone or metoclopramide
- Are taking esmolol, mexiletine or ritonavir
- Some medicines used to treat blood clots (e.g. clopidogrel, prasugrel, ticagrelor) may have delayed and decreased effect when taken together with morphine.

Pregnancy

Do not use Morphine Sulfate Injection if you are pregnant or think you might be pregnant unless you have discussed this with your doctor, pharmacist or nurse and the benefits of treatment are considered to outweigh the potential harm to the baby.

Continue overleaf

**Additional information for Healthcare Professionals
(as stated on the Summary of Product Characteristics)**

Therapeutic Indications

Morphine Sulfate Solution for Injection is indicated for the relief of moderate to severe pain. Morphine is used especially in pain associated with cancer, myocardial infarction and surgery. Morphine also helps to relieve the anxiety and insomnia which may be associated with severe pain.

Posology and Method of Administration

Prior to ending treatment with opioids, a discussion should be held with patients to put in place a strategy for ending treatment with morphine sulfate in order to minimise the risk of addiction and drug withdrawal syndrome (see section 4.4 of the SmPC).

Adults and children over 12 years:

Morphine Sulfate Solution for Injection is formulated for use by the intravenous route in Patient Controlled Analgesia (PCA) systems. PCA, which permits adjustments of dosage according to the patient's individual needs, must only be carried out in departments and by staff who are trained and have experience of the system. Patient selection for the use of PCA must ensure that the patient is capable of understanding and following the instructions of the medical/nursing staff. The specific department or unit protocols must be covered to ensure aseptic transfer of the contents of the ampoule or vial to the PCA system.

There is a considerable variation in analgesic requirements among patients and therefore individualised treatment strategies are required. Dosage should be based on the severity of the pain and the response and opiate tolerance of the patient.

Loading Dose

Loading doses of typically between 1mg and 10mg (maximum 15mg) of Morphine Sulfate Solution for Injection may be given by intravenous infusion over four or five minutes. The loading dose used will depend upon the patient's diagnosis and conditions.

Continue overleaf

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If you use Morphine Sulfate Injection during pregnancy, your baby may become dependent and experience withdrawal symptoms after the birth which may need to be treated.

Do not use Morphine Sulfate Injection while you are breastfeeding as morphine sulfate passes into breast milk and will affect your baby.

Driving and using machines

You must not use machinery whilst using this medicine.

The medicine can affect your ability to drive as it may make you sleepy or dizzy.

- Do not drive while using this medicine until you know how it affects you.
- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence if:
 - The medicine has been prescribed to treat a medical or dental problem and
 - You have taken it according to the instruction given by the doctor, pharmacist or nurse or in the information provided with the medicine and
 - It was not affecting your ability to drive safely

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while using this medicine.

Morphine Sulfate Injection contains Sodium Chloride

This medicine contains 3.6mg sodium (main component of cooking/table salt) in each mL. This is equivalent to 0.2% of the WHO recommended daily intake of 2g sodium for an adult.

3. How to use Morphine Sulfate Injection

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

Before starting treatment and regularly during treatment, your doctor will discuss with you what you may expect from using Morphine Sulfate Injection, when and how long you need to take it, when to contact your doctor, and when you need to stop it (see also, If you stop taking Morphine Sulfate Injection, in this section).

The doctor will decide what dose of this medicine you should be given. It will need to be given by a nurse or doctor using a syringe and needle to draw up the injection for administration.

The syringe may be put into a small machine which allows a slow continuous injection of this medicine to be given.

There is a procedure called Patient Controlled Analgesia (PCA) where you will be provided with a button to press when you are in pain and the machine will then give you a small amount of this medicine. There will be a safety device on the machine so that you cannot exceed the maximum number of doses.

Let your doctor or nurse know if your pain gets worse while you are using this medicine. Your doctor may want to increase your dose of the medicine and/or give you some extra medicines for the pain.

If you use more Morphine Sulfate Injection than you should:

Tell your doctor as soon as possible. If you are a medical practitioner administering this medicine please refer to the Summary of Product Characteristics.

People who have taken an overdose may get pneumonia from inhaling vomit or foreign matter, symptoms may include breathlessness, cough and fever.

People who have taken an overdose may also have breathing difficulties leading to unconsciousness or even death.

If you forget to use Morphine Sulfate Injection.

The dose should be given as soon as it is remembered. The next dose should be given at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop using Morphine Sulfate Injection

Do not suddenly stop using this medicine. If you want to stop using this medicine, discuss this with your doctor, pharmacist or nurse 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 using this medicine.

4. Possible Side Effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Stop using Morphine Sulfate Injection and seek medical attention immediately if you notice any of the following symptoms:

- Serious allergic reaction which causes difficulty in breathing or dizziness.
- Severe skin reaction with blistering, widespread scaly skin, pus-filled spots together with fever.

This could be a condition called Acute Generalized Exanthematous Pustulosis (AGEP).

If you are affected by these important side effects contact a doctor immediately.

The most common side effects are respiratory depression (slow or shallow breathing), nausea, vomiting, constipation, feeling more sleepy than normal and feeling confused.

Other common side effects are:

- Muscle rigidity
- Inability to concentrate
- Itchiness
- Decreased effectiveness
- Hypothermia
- Disorientation
- Agitation
- Feeling of sadness
- Affected eye sight
- Upset stomach or indigestion
- Pain and irritation at the injection site
- Increased pressure inside the skull
- Rashes
- Affects normal sleep
- Sweating
- Dry mouth
- Tachycardia (fast heartbeat)
- Postural hypotension (low blood pressure on sitting or standing)
- Spasm of the tubes of the kidney, bladder or gallbladder
- Vertigo
- Rash due to an allergic reaction in the skin
- Excitation
- Feeling of well being
- Dizziness
- Transient loss of consciousness
- Abdominal pain
- Feeling unwell
- Itchy rash of skin with raised bumps
- An increased sensitivity to pain

Side Effects of Unknown Frequency are:

- Dependence and addiction (see section “How do I know if I am addicted?”),
- Sleep apnoea (breathing pauses during sleep),
- Symptoms associated with inflammation of the pancreas (pancreatitis) and the biliary tract system, e.g. severe upper abdominal pain possibly radiating to the back, nausea, vomiting or fever.

Drug Withdrawal

When you stop using Morphine Sulfate Injection, you may experience drug 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.

How do I know if I am addicted?

If you notice any of the following signs whilst using Morphine Sulfate Injection, it could be a sign that you have become addicted.

- You need to take the medicine for longer than advised by your doctor, pharmacist or nurse
- You feel you need to use more than the recommended dose
- You are using the medicine for reasons other than prescribed
- When you stop using the medicine you feel unwell, and you feel better once using the medicine again

If you notice any of these signs, it is important you talk to your doctor, pharmacist or nurse.

Tell your doctor, nurse or pharmacist immediately if you think you have any of these, or other problems.

LONG-TERM TREATMENT WITH THIS MEDICINE

Further side effects can occur during long-term treatment with this medicine. These side effects include:

- Difficulty in urinating or unable to pass urine
- Hallucinations
- Colic
- Contractions of the pupils
- Dry mouth
- Restlessness
- Sweating/ facial flushing
- Mood changes
- Headache
- Decreased libido
- Palpitations
- Disruption of the menstrual cycle
- Slowed heartbeat
- Reduced blood pressure
- Spasm of the airways
- Changes in taste
- Fitting
- Recurrence of pancreatitis
- Uncontrolled movement of the eyes
- Fluid retention
- Increased blood pressure
- Loss of weight due to poor eating
- Total or partial bowel blockage
- Muscle jerk
- Muscle twitch
- Infertility
- Severe muscle pain
- Difficulty in coughing
- Depression
- Lack of strength in muscles
- Inability to obtain or sustain an erection of the penis
- Decreased effectiveness
- Increased sensitivity to the pain
- Reduced adrenal gland function

Reporting of Side Effects

If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Morphine Sulfate Injection

Keep this medicine out of the sight and reach of children.

This medicine has an expiry date printed on the ampoule or bottle (vial) and carton label. Before use the doctor or nurse will check the medicine has not passed this date and that the medicine does not show any sign of deterioration. The expiry date refers to the last day of the month.

After the expiry date return any unused medicine to a pharmacy.

Store this medicine away from sunlight and below 25°C.

6. Contents of the pack and other information

What Morphine Sulfate Injection contains:

- The active substance is morphine sulfate at a strength of 1mg in 1mL.
- The other ingredients are Sodium Chloride and Water for Injections.

What Morphine Sulfate Injection looks like and contents of the pack:

This medicine is a clear and colourless or almost colourless solution. This medicine is available in 1mL, 5mL and 10mL ampoules, and 50mL single use vials. The medicine is packed into cartons containing 10 ampoules, 1 vial or 10 vials. Both pack sizes of vials may not be available at the same time.

Marketing Authorisation Holder and Manufacturer:

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PCA demand dose

An initial demand dose of 1mg Morphine Sulfate Solution for Injection with a lockout period of 5 to 10 minutes is recommended. Dosages may vary depending on the loading dose, the tolerance and condition of the patient, and whether a background infusion of morphine sulfate is being given.

The patient should be specifically monitored for pain, sedation and respiratory rate during the first few hours of treatment to ensure that the dosage regimen is suitable.

The duration of treatment should be kept to a minimum, although dependence and tolerance are not generally a problem when morphine is used legitimately in patients with opioid-sensitive pain.

Use in children:

Not recommended for children under 12 years.

Use in the elderly:

Morphine doses need to be reduced in elderly patients.

Treatment goals and discontinuation

Before initiating treatment with Morphine Sulfate Solution for Injection, a treatment strategy including treatment duration and treatment goals, and a plan for end of the treatment, should be agreed together with the patient, in accordance with pain management guidelines. During treatment, there should be frequent contact between the physician and the patient to evaluate the need for continued treatment, consider discontinuation and to adjust dosages if needed. When a patient no longer requires therapy with Morphine Sulfate Solution for Injection, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal. In absence of adequate pain control, the possibility of hyperalgesia, tolerance and progression of underlying disease should be considered (see section 4.4 of the SmPC).

Duration of treatment

Morphine Sulfate Solution for Injection should not be used longer than necessary.

Incompatibilities

Morphine Sulfate Solution for Injection should not be mixed with other preparations.

Morphine salts, are compatible with aminophylline, sodium salts of barbiturates and phenytoin, aciclovir sodium, furosemide, heparin sodium, pethidine HCl, prochlorperazine edisylate and promethazine HCl.

Physicochemical incompatibility (formation of precipitates) has been demonstrated between solutions of morphine sulfate and 5- fluorouracil.

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