

Package leaflet: Information for the user

Morphine Sulfate 10mg/ml Solution for Injection Morphine Sulfate 30mg/ml Solution for Injection Morphine Sulfate 60mg/ml 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 or pharmacist or nurse.
- If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

This product will be referred to as Morphine Sulfate Injection from here on.

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 are given Morphine Sulfate Injection
3. How Morphine Sulfate Injection is given to you
4. Possible side effects
5. How to store Morphine Sulfate Injection
6. Contents of the pack and other information

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

Morphine Sulfate Injection belongs to a group of medicines that are called opioid (narcotic) analgesics. Analgesics are medicines that relieve pain.

Morphine Sulfate Injection is used to relieve moderate to severe pain.

2. What you need to know before you are given Morphine Sulfate Injection

Do not take Morphine Sulfate Injection:

- if you are allergic to morphine sulfate or any of the other ingredients of this medicine (listed in section 6).
- if you are taking monoamine oxidase inhibitors (MAOIs) or have been taking them within the last two weeks. MAOIs, such as phenelzine or isocarboxazid, are medicines used to treat depression
- if you suffer from breathing disorders
- if you suffer from a condition causing bluish discolouration of the skin due to lack of oxygen in the blood
- if you are at a risk of having a blocked intestine
- if you have recently undergone an operation of the abdomen, suffer from severe stomach cramps or severe pain in your abdomen or a condition in which there is partial paralysis of the stomach
- if you have had a head injury or increased pressure in the brain
- if you know that you have a tumour of the adrenal glands, a condition called pheochromocytoma

- If you are prone to having fits
 - if you know that you have severe liver or kidney problems
 - if you have recently been drinking large amounts of alcohol
 - if you suffer from ulcers in the large intestine (ulcerative colitis) which may lead to swelling of the stomach causing stomach pain, fever or shock.
- Tell your doctor if this applies to you before you are given this medicine.

Warnings and precautions

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 Sulphate 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 Sulphate 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 using Morphine Sulphate 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 using Morphine Sulfate Injection).

Talk to your doctor or pharmacist or nurse before using Morphine Sulfate Injection:

- if you have problems with breathing properly (your doctor will let you know if you can still have Morphine Sulfate Injection depending on the reason for your breathing problem)
- if you have severe asthma
- if you have an under-active thyroid
- if you suffer from shock
- if you have kidney or liver problems
- if you are prone to having fits
- if you have low blood pressure and do not have enough blood in your body, which may make you feel lightheaded, faint, dizzy or have cold hands and feet
- if you have swelling of the pancreas or bile duct problems
- if you have poor adrenal gland function. 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
- if you have an enlarged prostate gland
- if you have bowel problems (inflammatory bowel disorders)
- if you have a heart problem after long-term lung disease (known as severe cor pulmonale)
- if you are about to have an operation or have had one less than 24 hours ago
- if you have an addiction to or a history of alcohol or drug abuse or you have previously suffered from withdrawal symptoms such as agitation, anxiety, shaking and sweating upon stopping taking alcohol or drugs. Also tell if you feel that you are becoming dependent on Morphine Sulfate Injection while you are using it. You may have started to think a lot about when you can take the next dose, even if you do not need it for the pain.
- if you are elderly or are in poor state of health.
- if you are taking any medicine from the group of medicines known as benzodiazepines. Taking these medicines with Morphine Sulfate Injection may result in sedation, difficulties in breathing (respiratory depression), coma and may be fatal. Even if benzodiazepines are prescribed, your doctor may need to change the dose, the duration of treatment or monitor you regularly.
- increased sensitivity to pain despite the fact that you are taking 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).
- loss of libido, impotence, cessation of menstruation. This may be because of decreased sex hormone production.
- abstinence symptoms or dependence. The most common abstinence symptoms are mentioned in section 3. If this occurs, your doctor may change the type of medicine or the times between doses.

Acute generalized exanthematous pustulosis (AGEP) has been reported in association with Morphine Sulphate 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 using Morphine Sulphate Injection or other opioids. Stop using Morphine Sulphate 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 Sulphate 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.

This product must be used with caution in newborn and premature babies.

Speak to your doctor if any of these apply to you before you are given this medicine.

Other medicines and Morphine Sulfate Injection

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

A large number of drugs can interact with Morphine Sulfate Injection which can significantly alter their effects. These drugs include:

- medicines that help you to sleep e.g. tranquilisers, hypnotics or sedatives (e.g. temazepam, diazepam, haloperidol and sulpiride)
- medicines to treat schizophrenia or other serious mental illness, such as phenothiazines (which may be present in various medicines including some for treating allergic disorders e.g. prochlorperazine, chlorpromazine and pipotiazine, promethazine)
- medicines to relax your muscles (e.g. baclofen, tizanidine)
- medicines to treat high blood pressure (e.g. methyldopa, moxonidine)
- gabapentin or pregabalin to treat epilepsy or pain due to nerve problems
- a general anaesthetic that makes you sleep, usually before an operation
- cimetidine (a medicine for ulcers, indigestion, or heartburn)
- ciprofloxacin (a type of antibiotic)
- another opioid painkiller (e.g. buprenorphine, nalbuphine, pentazocine)
- rifampicin (a medicine for tuberculosis)
- some medicines used to treat blood clots (e.g. clopidogrel, prasugrel, ticagrelor) may have delayed and decreased effect when taken together with opium.
- ritonavir (a medicine to treat HIV)
- MAOIs used to treat depression (refer to “Do not take Morphine Sulfate Injection if” in section 2 above).

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.

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

If you are already taking one of these medicines, speak to your doctor before you are given Morphine Sulfate Injection.

Morphine Sulfate Injection with food, drink and alcohol

You must avoid drinking alcohol during your treatment with Morphine Sulfate Injection.

Pregnancy and breast feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. If you are given Morphine Sulfate Injection while you are in labour, your baby may have breathing problems. This medicine should not be administered to breast-feeding mothers. If Morphine Sulfate Injection is used for a long time during pregnancy, there is a risk of the new-born child having drug withdrawal (abstinence) symptoms which should be treated by a doctor.

If you have been treated with Morphine Sulfate Injection before your baby is born, the baby may experience symptoms of withdrawal after it is born (e.g. watery eyes, diarrhoea, runny nose, loss of appetite, vomiting, feeling hot then cold).

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Morphine Sulfate Injection will cause drowsiness which could interfere with your ability to drive or to use machines. Do not drive or operate machinery whilst you are taking this medicine. When your Morphine Sulfate Injection treatment has stopped, ask your doctor when it will be safe for you to drive or use machines.

Tolerance and dependence

Morphine Sulfate Injection can become less effective with repeated use. This is called tolerance and it means that the dose may need to be increased for morphine to remain as effective. If Morphine Sulfate Injection is used repeatedly, it may become habit-forming. This is called dependence and if morphine treatment is stopped suddenly unpleasant withdrawal symptoms may occur. Dependence on morphine may occur after one or two weeks of treatment with the doses required to relieve pain.

Morphine Sulfate Injection contains

- **sodium metabisulfite**

This medicine contains sodium metabisulfite, a preservative which may rarely cause severe allergic (hypersensitivity) reactions and breathing difficulties (bronchospasm) in individuals who are sensitive to sulfites.

- **sodium**

This medicine contains less than 1 mmol sodium (23 mg) per ampoule, that is to say essentially 'sodium-free'.

3. How Morphine Sulfate Injection is given to you

Morphine Sulfate Injection may be given by injection into a muscle or into the tissue just beneath the skin. It may also be diluted and given by slow injection into a vein.

It will be administered by a trained healthcare professional.

Before starting treatment and regularly during treatment, your doctor will discuss with you what you may experience from Morphine Sulphate Injection, when and how long the course will last, when to contact your doctor, and when you need to stop it (see also, If you stop being given Morphine Sulphate Injection, in this section). Your doctor will decide the most suitable dosage and route of administration for your particular case according to your age and physical circumstances.

If you are elderly and weak or infirm your doctor may reduce the dose of your medicine, because this medicine can make breathing difficult.

If you have kidney or liver problems your doctor may reduce the dose of medicine.

If you think you have been given more Morphine Sulfate Injection than you should have

This is unlikely as your injection will be administered by a doctor. If you are concerned about the dose, discuss this with your doctor. 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 think you have missed a dose of Morphine Sulfate Injection

If you think that you have missed a dose, tell your doctor immediately.

If you stop using Morphine Sulfate Injection

Do not stop treatment with Morphine Sulfate Injection unless agreed with your doctor. If you want to stop the treatment with Morphine Sulfate Injection, ask your doctor how to slowly decrease the doses so you avoid abstinence symptoms. Abstinence symptoms may include body aches, tremors, diarrhoea, stomach pain, nausea, flu-like symptoms, fast heartbeat and large pupils. Psychological symptoms include an intense feeling of dissatisfaction, anxiety and irritability.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines Morphine Sulfate Injection can cause side-effects, although not everybody gets them. Side effects grouped by frequency of occurrence

All medicines can cause allergic reactions although serious allergic reactions are uncommon.

- **Any sudden wheeziness, difficulties in breathing, swelling of the eyelids, face or lips, rash or itching especially those covering your whole body and paralytic Ileus (characterized by swollen belly, fullness, gas, abdominal spasms, constipation, diarrhea, nausea with or without vomiting, and foul-smelling breath)_should be reported to a doctor immediately.**

Important side effects or symptoms to look out for and what to do if you are affected:
The most serious side effect of Morphine Sulfate Injection is slowing of breathing or shallow Breathing.

Tell your doctor immediately if you notice any of the following symptoms: 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).

Common: may affect more than 1 in 10 people

- confusion, abnormal thoughts, difficulty in sleeping
- headache, dizziness, muscle twitching or spasms, drowsiness
- slowing of breathing or shallow breathing, decreased cough
- pain or discomfort in the stomach or back, loss of appetite, stomach upset or indigestion, feeling sick (nausea) or being sick (vomiting), constipation, dry mouth
- rash, sweating
- a feeling of unusual weakness, itching (pruritus)
- severe upper abdominal pain radiating to the back, nausea and vomiting which is worsened with eating (pancreatitis).
- inappropriate eating habits, abnormal physical weakness or lack of energy

Uncommon: may affect less than 1 in 100 people

- mood changes, a feeling of extreme happiness or sadness, agitation, seeing or hearing things that are not there (hallucinations)
- morphine when used repeatedly becomes habit forming (dependence on the drug)
- a feeling of dizziness or 'spinning' (vertigo), fits or convulsions, tingling in the hands and feet, fainting or loss of consciousness, stiff muscles

- constriction of pupils of the eyes, blurred vision
 - an unusually slow, fast or irregular heart beat
 - high blood pressure, low blood pressure, redness of the face
 - accumulation of fluid in the lungs, slowing of breathing or shallow breathing
 - problems with your stomach, such as upset stomach, stomach cramps, constipation or not passing wind, a life-threatening condition of the intestine (colon) known as “Toxic Megacolon” which may be accompanied by a larger stomach area than normal, pain and fever or changes in taste
 - increase in liver enzymes
 - skin rash notable for pale red, raised, itchy bumps (urticaria)
- difficulty in passing water or a severe, sharp pain on one or both sides of your lower back
 - absence of menstrual periods, decreased sexual drive, problems with erection
 - repeated use of the drug causes the drug to be less effective. When stopped suddenly causes withdrawal symptoms such as agitation, anxiety, shaking or sweating, feeling of discomfort or uneasiness, swelling of tissues due to accumulation of fluid.

Not Known: frequency cannot be estimated from the available data

- low body temperature
- narcotic bowel syndrome (chronic or frequently recurring abdominal pain)
- allodynia (pain due to stimulus which does not normally provoke pain)
- hyperaesthesia (abnormal increase in sensitivity to stimuli such as touch, heat, cold)
- abstinence symptoms or dependence (for symptoms see section 3: If you stop taking Morphine Sulfate injection)
- 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.

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.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance Website: www.hpra.ie

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.

Do not use this medicine after the expiry date which is stated on the carton and ampoule label after “Exp”. The expiry date refers to the last day of that month.

Do not store above 25°C. Keep the ampoule in the outer carton in order to protect from light.

For single use only.

Once the ampoule has been opened it should be used immediately. Do not use this medicine if you notice the ampoule is damaged or if the contents are discoloured or deteriorated. If only part of the contents of an ampoule is used, the remaining solution should be discarded.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Morphine Sulfate Injection contains

The active substance is morphine sulfate.

Morphine 10mg/ml: Each 1ml of the solution contains 10mg of morphine sulfate.

Morphine 30mg/ml: Each 1ml of the solution contains 30mg of morphine sulfate.

Morphine 60mg/ml: Each 1ml of the solution contains 60mg of morphine sulfate.

The other ingredients are sodium metabisulfite(E223) and sodium hydroxide or dilute hydrochloric acid and water for injections.

What Morphine Sulfate Injection looks like and contents of pack

Morphine Sulfate Injection is a clear, colourless or almost colourless sterile solution for injection in 1ml clear glass ampoules.

Pack size: 10 ampoules may be packaged together in cardboard cartons.

Marketing Authorisation Holder and Manufacturer

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