

**Package leaflet: Information for the user
Morphine Sulfate 10mg/ml, 15mg/ml and 30mg/ml
Solution for Injection**

morphine sulfate

This medicine contains morphine sulfate which is an opioid, which can cause addiction. You can get withdrawal symptoms if you stop taking it suddenly. 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 further questions, please ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Morphine Injection is and what it is used for
2. What you need to know before you are given Morphine Injection
3. How Morphine Injection should be given
4. Possible side effects
5. How to store Morphine Injection
6. Contents of the pack and other information

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

This medicine has been prescribed for you for the relief of severe pain. It is also used to treat breathlessness caused by fluid in the lungs and as a pre-medication before operations.

It contains morphine sulfate which belongs to a class of medicines called opioids, which are 'pain relievers'.

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 taking it suddenly. Your prescriber should have explained how long you will be taking it for and when it is appropriate to stop, how to do this safely.

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

Morphine Injection should not be given if you:

- are allergic to morphine sulfate or any of the other ingredients of this medicine (listed in section 6)
- have been told you have a tumour of the adrenal gland near your kidney called pheochromocytoma
- have severe problems with breathing
- have increased pressure on the brain, have just had a head injury or if you are unconscious
- are suffering from acute alcoholism
- are at risk from a blocked intestine (paralytic ileus)
- have severe stomach cramps caused by a condition known as biliary colic
- are suffering from severe diarrhea.

Warnings and precautions

Talk to your prescriber before taking this medicine if you:

- are or have ever been addicted to opioids, alcohol, prescription medicines, or illegal drugs
- have previously suffered withdrawal symptoms such as agitation, anxiety, shaking or sweating, when you have stopped taking alcohol or drugs
- feel you need to take more Morphine 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 prescriber who will discuss your treatment and may change your dose or switch you to an alternative pain reliever.

Taking this medicine regularly, particularly for a long time, can lead to addiction. Your prescriber should have explained how long you will be taking it for and when it is appropriate to stop, how to do this safely.

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 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 use of how often you need to use it.

The risk of becoming dependent or addicted varies from person to person. You may have a greater risk of becoming dependent or addicted to Morphine 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 Injection, it could be a sign that you have become dependent or addicted:

- you need to use the medicine for longer than advised by your doctor
- you need to use 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 using the medicine you feel unwell, and you feel better once using 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 treatment with Morphine Injection is stopped).

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 prescriber will discuss with you how to gradually reduce your dose before stopping

INFORMATION FOR HEALTHCARE PROFESSIONALS

4.1 Therapeutic indications

The symptomatic relief of severe pain; relief of dyspnoea of left ventricular failure and pulmonary oedema; pre-operative use.

4.2 Posology and method of administration

Morphine Sulfate may be given by the subcutaneous, intramuscular or intravenous route. The subcutaneous route is not suitable for oedematous patients. The dosage should be based on the severity of the pain and the response and tolerance of the individual patient. The epidural or intrathecal routes must not be used as the product contains a preservative.

Prior to starting treatment with opioids, a discussion should be held with patients to put in place a strategy for ending treatment with morphine sulphate in order to minimise the risk of addiction and drug withdrawal syndrome.

Adults:

Subcutaneous or intramuscular injection:

10mg every four hours if necessary (the dose may vary from 5-20mg depending on the individual patient).

Slow intravenous injection (2mg/minute):

Quarter to half of corresponding intramuscular dose not more than four hourly.

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.

Take special care with Morphine Injection:

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

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.

Sleep-related breathing disorders

Morphine 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.

Talk to your doctor if you experience any of the following symptoms when Morphine Injection is given to you:

- 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)
- 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.

Talk to your doctor before Morphine Injection is given to you if you:

- are using drugs or have used drugs in the past
- suffer from asthma (your doctor may decide to administer Morphine Injection if your asthma is controlled. However, you should not be given this medicine if you are having an acute asthma attack)
- suffer from bronchitis (an inflammation of the lining of the tubes in the lungs, resulting in coughing spells accompanied by thick phlegm and breathlessness) or emphysema (a lung condition which leaves you struggling for breath)
- suffer from cor-pulmonale (a type of heart failure)
- are severely obese
- have a severely deformed spine
- are suffering from mental illness brought on by an infection
- have liver problems
- have kidney problems
- have problems with your bile duct
- suffer from an enlarged prostate gland (in men) or have difficulty passing urine
- have an under-active thyroid or adrenal gland
- have low blood pressure
- are in a state of severe shock
- are very run down
- have bowel disease, such as Crohn's disease or ulcerative colitis
- suffer from blockages of the bowel
- suffer from convulsions (fits)
- are elderly
- are feeling weak and feeble.

If any of the above applies to you, speak to your doctor or nurse before Morphine Injection is given to you.

Children

This medicine is not recommended for use in children.

Other medicines and Morphine Injection

Tell your doctor if you are taking, have recently taken or might take any other medicines. In particular, tell your doctor if you are taking any of the following:

- monoamine oxidase inhibitors (MAOIs) such as moclobemide or phenelzine used in the treatment of depression
- tricyclic antidepressants, which are used in the treatment of depression
- tranquillising drugs or sleeping tablets such as diazepam, nitrazepam and temazepam
- medicines used to treat mental illnesses, including schizophrenia (e.g. chlorpromazine, haloperidol)
- medicines used for diarrhoea (e.g. loperamide, kaolin)
- medicines which are used as premedication before operations and after heart attacks such as atropine
- medicines used to treat nausea and vomiting, such as metoclopramide or domperidone
- mexiletine, used to control heart rhythm
- some antihistamines, used to treat allergies, hayfever and asthma
- certain antibiotics, used to treat infections (e.g. ciprofloxacin and linezolid)
- selegiline, used in the treatment of Parkinson's disease
- pethidine, used to treat pain
- rifampicin to treat e.g. tuberculosis
- gabapentin or pregabalin to treat epilepsy and pain due to nerve problems (neuropathic pain)
- concomitant use of Morphine 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 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

Elderly and debilitated patients: The dose should be reduced because of the depressant effect on respiration. Caution is required.

Children: Use in children is not recommended.

Hepatic impairment:

A reduction in dosage should be considered in hepatic impairment.

Renal impairment:

The dosage should be reduced in moderate to severe renal impairment.

For concomitant illnesses/conditions where dose reduction may be appropriate see 4.4 Special warnings and precautions for use.

Treatment goals and discontinuation

Before initiating treatment with Morphine Sulfate, 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, 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

helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

Morphine Injection with food, drink and alcohol

You should not drink alcohol whilst being given Morphine Injection, as it will increase its effects.

Pregnancy and breast-feeding

Do not take Morphine Injection if you are pregnant or think you might be pregnant unless you have discussed this with your prescriber and the benefits of treatment are considered to outweigh the potential harm to the baby.

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

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

Driving and using machines

If the injection makes you feel drowsy, do not drive or operate machinery.

This medicine can affect your ability to drive.

Do not drive whilst taking this medicine until you know how this medicine affects you.

It may be an offence to drive if your ability to drive safely is affected.

There is further information for patients who are intending to drive in Great Britain - go to <http://www.gov.uk/drug-driving-law>

Morphine Injection contains sodium metabisulfite

Sodium metabisulfite may rarely cause severe hypersensitivity reactions and bronchospasm.

3. How Morphine Injection should be given

The recommended adult dose for relief of pain by subcutaneous injection (an injection underneath the skin) or intramuscular injection (an injection into a muscle) is 10mg every four hours, if necessary. However, this can vary between 5mg and 20mg depending on your size and response to the drug.

For severe pain your doctor may give you a slow intravenous injection (an injection given slowly into a vein). The usual dose is quarter to half of the intramuscular dose.

- If you are elderly, severely run down including feeling weak and feeble, or have liver and kidney problems the dose will be lower. You may also be given a reduced dose if you suffer from any of the conditions listed in section 2 entitled "Talk to your doctor before Morphine Injection is given to you if you:" and "Talk to your doctor if you experience any of the following symptoms when Morphine Injection is given to you:"
- Your doctor will decide the dose that is best for you. If you do not understand what you are being given, or are in any doubt, ask your doctor or nurse.

Before starting treatment and regularly during treatment, your doctor will discuss with you what you may expect from using Morphine Injection, when and how long it will be given, when to contact your doctor, and when it needs to be stopped (see also, If treatment with Morphine Injection is stopped, in this section).

If you are given more Morphine Injection than you should be

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 miss a dose of Morphine Injection

If you think that an injection has been missed, speak to your doctor or nurse.

Do not take a double dose to make up for a forgotten dose.

If treatment with Morphine Injection is stopped

Do not suddenly stop taking this medicine. If you want to stop taking this medicine, discuss this with your prescriber 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 taking this medicine.

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

4. Possible side effects

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

Stop using Morphine Injection and seek medical attention 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 Generalised Exanthematous Pustulosis (AGEP).

Tell your doctor or nurse immediately if you experience the following serious side effect:

- A severe allergic reaction, such as dizziness, breathing difficulties, shock or low blood pressure. If you suffer such a reaction, you should not be given any more morphine. Your doctor will decide on the appropriate treatment for allergic reactions.

Difficulty in breathing and physical and psychological dependence are possible serious side effects. It is possible that you could become dependent on morphine (for symptoms see section 3: If treatment with Morphine Injection is stopped).

Common: may affect up to 1 in 10 people

- drowsiness
- feeling sick or being sick
- constipation
- dizziness.

Apart from constipation, these side effects tend to disappear with time.

Other side effects

- sweating
- feeling faint on standing up
- small pupils (in the eye)
- blurred vision
- double vision or other changes in vision
- mental clouding or confusion
- mood changes, feeling extremely happy for no particular reason, or a feeling of emotional and mental unease (dysphoria)
- imagining things (hallucinations)

(see section 4.4).

Duration of treatment

Morphine Sulfate should not be used longer than necessary.

4.3 Contraindications

Acute respiratory depression, known morphine sensitivity, biliary colic (see also biliary tract disorders 4.4 Special Warnings and Precautions), acute alcoholism. Conditions in which intracranial pressure is raised, comatose patients, head injuries, as there is an increased risk of respiratory depression that may lead to elevation of CSF pressure. The sedation and pupillary changes produced may interfere with accurate monitoring of the patient. Morphine is also contraindicated where there is a risk of paralytic ileus, or in acute diarrhoeal conditions associated with antibiotic-induced pseudomembranous colitis or diarrhoea caused by poisoning (until the toxic material has been eliminated).

Phaeochromocytoma (due to the risk of pressor response to histamine release).

6.1 List of excipients

Water for injections
Sodium metabisulfite (E223)
Sodium hydroxide
Hydrochloric acid

- headache
- vertigo
- facial flushing
- dry mouth
- difficulty or pain in passing urine
- passing less urine than usual
- biliary spasm (causing pain in the right side of your abdomen, particularly after eating a meal, which may spread towards your right shoulder)
- palpitations (being aware of your heart beat)
- slower or faster pulse
- skin rash
- wheals (lumpy, red rash) or itching
- red, itchy, scaly skin at the injection site
- pain and irritation at the injection site
- reduced sexual drive or impotence after long term use
- muscle twitching
- an increased sensitivity to pain
- unknown frequency: 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 taking Morphine 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 taking Morphine Injection, it could be a sign that you have become addicted.

- you need to take the medicine for longer than advised by your prescriber
- you feel you need to use more than the recommended dose
- you are using the medicine for reasons other than prescribed
- when you stop taking the medicine you feel unwell, and you feel better once taking the medicine again.

If you notice any of these signs, it is important you talk to your prescriber.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. 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 Injection

Keep out of the sight and reach of children.

Store below 25°C. Keep the ampoule in its outer carton, in order to protect it from light.

Do not use this medicine if you notice signs of discolouration.

Do not use this medicine after the expiry date, which is stated on the carton. The expiry date refers to the last day of that month.

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

6. Contents of the pack and other information

What Morphine Injection contains

The active substance is morphine sulfate. The injection is available in three strengths, 10mg/ml (10mg of active ingredient in 1ml of solution), 15mg/ml (15mg of active ingredient in 1ml of solution) and 30mg/ml (30mg of active ingredient in 1ml of solution).

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

What Morphine Injection looks like and contents of the pack

Morphine Injection is a colourless or almost colourless solution, practically free from particles.

Morphine Sulfate 10mg/ml Solution for Injection is available in cartons containing 5 × 1ml glass ampoules and 10 × 1ml glass ampoules.

Morphine Sulfate 15mg/ml Solution for Injection is available in cartons containing 5 × 1ml glass ampoules and 10 × 1ml glass ampoules.

Morphine Sulfate 30mg/ml Solution for Injection is available in cartons containing 5 × 1ml glass ampoules and 10 × 1ml glass ampoules. It is also available in cartons containing 5 x 2ml ampoules.

Not all strengths and pack sizes may be marketed.

Marketing Authorisation Holder: Wockhardt UK Ltd, Ash Road North, Wrexham, LL13 9UF, UK

Manufacturer: CP Pharmaceuticals Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

Other sources of information:

To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge:

0800 198 5000 (UK Only)

Please be ready to give the following information:

Product Name	Reference Number
Morphine Sulfate 10mg/ml Solution for Injection	29831/0146
Morphine Sulfate 15mg/ml Solution for Injection	29831/0145
Morphine Sulfate 30mg/ml Solution for Injection	29831/0147

This is a service provided by the Royal National Institute of Blind People.

This leaflet was last revised in 09/2023.

106963/6

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6.2 Incompatibilities

Morphine salts are sensitive to changes in pH and morphine is liable to be precipitated out of solution in an alkaline environment. Compounds incompatible with morphine salts include aminophylline and sodium salts of barbiturates and phenytoin. Other incompatibilities (sometimes attributed to particular formulations) have included aciclovir sodium, doxorubicin, fluorouracil, furosemide, heparin sodium, pethidine hydrochloride, promethazine hydrochloride and tetracyclines. Specialised references should be consulted for specific compatibility information.

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

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 25°C. Keep container in the outer carton.

6.6 Special precautions for disposal

None

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