

Package leaflet: Information for the patient

<Morphine hydrochloride trihydrate> 60 mg prolonged-release tablets

Active substance: Morphine hydrochloride trihydrate

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

What is in this leaflet

1. What <Morphine hydrochloride trihydrate> is and what it is used for
2. What you need to know before you take <Morphine hydrochloride trihydrate>
3. How to take <Morphine hydrochloride trihydrate>
4. Possible side effects
5. How to store <Morphine hydrochloride trihydrate>
6. Contents of the pack and other information

1. What <Morphine hydrochloride trihydrate> is and what it is used for

<Morphine hydrochloride trihydrate> is a very strong and efficient analgesic (painkiller), and it is used **for the prolonged relief of strong and very strong persistent pain** when other analgesics are not sufficient. It should not be used for the treatment of mild pain.

<Morphine hydrochloride trihydrate> prolonged-release tablets steadily release active substance over a long period of time. The pain-relieving effect is prolonged, thus <Morphine hydrochloride trihydrate> tablets can be taken in intervals of 12 hours.

2. What you need to know before you take <Morphine hydrochloride trihydrate>

Do not take <Morphine hydrochloride trihydrate>

- if you are **allergic** to morphine or any of the other ingredients of this medicine (listed in section 6).
- if you suffer from an **airway disease** or have breathing disorders due to other reasons.
- if the **mucus secretion** of your airways is impaired.
- if you suffer from **seizures** or if you have a **head injury**.
- if you have a **bowel obstruction**.
- if **stomach pain** occurs suddenly or if you suffer from **indigestion** (delayed gastric emptying).
- if you have a **liver disease**.
- if you have drunk **alcohol** or if you have taken **sleeping pills** earlier on.

<Morphine hydrochloride trihydrate> must not be given to children below 1 year.

Warnings and precautions

Talk to your doctor or pharmacist before taking <Morphine hydrochloride trihydrate>.

<Morphine hydrochloride trihydrate> must be used with caution

- if you have **impaired respiratory function**.
- if you have **impaired liver and/or kidney function**.

- if you have **heart problems**.
- if you are concomitantly taking so-called **MAO inhibitors** (certain medicines used to treat depression) or have taken them **within the last 2 weeks**.
- if you are or have been **dependent on opiates**.
- if you have high **intracranial pressure** or low **blood pressure**.
- if you suffer from **impaired consciousness**.
- if you have a disorder of the **bile ducts** or if you have **spasms of the bile or the ureter**.
- if you suffer from inflammation of the **pancreas** or the **bowel**.
- if your **prostate** is enlarged.
- if your **adrenal cortex** does not work properly (e.g. Addison's disease).
- if you have a **pheochromocytoma** (a tumour of the adrenal medulla).
- if you are an elderly patient.

Inform your doctor that you are using <Morphine hydrochloride trihydrate> if you are having a surgery.

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 hydrochloride trihydrate> 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 hydrochloride trihydrate> 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 hydrochloride trihydrate>, 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 hydrochloride trihydrate>).

Talk to your doctor or pharmacist if you experience any of the following symptoms while taking <Morphine hydrochloride trihydrate>:

- 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.

Acute generalised exanthematous pustulosis (AGEP) has been reported in association with <Morphine hydrochloride trihydrate> 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 hydrochloride trihydrate> or other opioids. Stop using <Morphine hydrochloride trihydrate> 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 hydrochloride trihydrate> 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.

In case of suspected or manifest **intestinal paralysis** (paralytic ileus) <Morphine hydrochloride trihydrate> must be discontinued immediately.

Drinking alcohol whilst taking <Morphine hydrochloride trihydrate> may make you feel more sleepy or increase the risk of serious side effects such as shallow breathing with a risk of stopping breathing, and loss of consciousness. It is recommended not to drink alcohol while you're taking <Morphine hydrochloride trihydrate>.

If morphine treatment is **suddenly discontinued, withdrawal symptoms** may develop (see section 3 "If you stop taking <Morphine hydrochloride trihydrate>").

If you are **older than 65 years**, if your **thyroid** does not work properly (hypofunction), or if you suffer from a severe **liver or kidney** impairment, your doctor will prescribe you a lower dose.

If you are a **man of procreating or a woman of childbearing age**, you should take <Morphine hydrochloride trihydrate> only if the use of **effective contraceptive measures** is ensured (see "Pregnancy and breast-feeding").

The film-coated tablets must not be dissolved and injected. The ingredients may otherwise cause local tissue necrosis and granuloma in the lungs. Misuse may also lead to other adverse events with possible lethal outcome.

Other medicines and <Morphine hydrochloride trihydrate>

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

This is especially important if you are taking rifampicin to treat e.g. tuberculosis.

The concomitant use of <Morphine hydrochloride trihydrate> and other medicines may lead to mutual increase or decrease in efficacy.

Avoid concomitant treatment with <Morphine hydrochloride trihydrate> and MAOIs, such as selegiline and rasagiline (used in Parkinson's disease) and moclobemide (used in depression). If you have been treated with MAOIs, two weeks must pass before treatment with <Morphine hydrochloride trihydrate> can be started.

A large number of drugs can interact with <Morphine hydrochloride trihydrate> which can significantly alter their effects. These drugs include:

- anaesthetics (in dental and general surgery),
- sleeping pills and tranquilizers,
- certain medicines for mental disorders (e.g. for depression or psychoses),
- muscle-relaxing medicines,
- antihypertensives,
- certain medicines for nausea and vomiting,
- certain medicines for allergies,
- other strong pain killers (opioids),
- gabapentin or pregabalin to treat epilepsy and pain due to nerve problems (neuropathic pain)
- alcohol.

Concomitant use of <Morphine hydrochloride trihydrate> and sedative medicines such as benzodiazepines or related drugs (for example sleeping pills, tranquillizers, or certain medicines for mental disorders) increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Therefore you must talk to your doctor before you take <Morphine hydrochloride trihydrate> with sedative medicines. Concomitant use should only be considered when other treatment options are not possible.

However, if your doctor does prescribe <Morphine hydrochloride trihydrate> 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.

Some medicines used to treat blood clots (e.g. clopidogrel, prasugrel, ticagrelor) may have delayed and decreased effect when taken together with morphine.

The following medicines may affect the action of <Morphine hydrochloride trihydrate>

- medicines used to neutralize gastric acid (antacids). After taking one of these medicines, an interval of at least 2 hours should be observed before taking the other.
- Cimetidine (a drug which inhibits the secretion of gastric acid).
- monoamine oxidase (MAO) inhibitors (certain medicines used to treat depression).
- Rifampicin (for the treatment of tuberculosis).
- Clomipramine and amitriptyline (certain medicines used to treat depression).
- anticholinergics (certain medicines used to treat a variety of conditions, including chronic obstructive pulmonary disease (COPD), bladder conditions, gastrointestinal disorders, and symptoms of Parkinson's disease).

<Morphine hydrochloride trihydrate> must not be combined with other morphine-like analgesics (e.g. buprenorphine, nalbuphine, pentacocine).

<Morphine hydrochloride trihydrate> with food and drink and alcohol

<Morphine hydrochloride trihydrate> may be taken with or without food.

During the treatment with <Morphine hydrochloride trihydrate> you should avoid to drink **alcohol** as this may **increase its effects**. Taking higher doses of <Morphine hydrochloride trihydrate> with alcohol may lead to adverse events with lethal outcome.

Pregnancy, breast-feeding and fertility

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.

<Morphine hydrochloride trihydrate> **should not be used during pregnancy.**

If <Morphine hydrochloride trihydrate> 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.

The administration for pain-relief **during labour** is **not recommended** due to the risk of neonatal respiratory depression.

The use of <Morphine hydrochloride trihydrate> **during breast-feeding is not recommended**, as the active substance morphine is excreted in breast milk.

Driving and using machines

This medicine may impair your reactivity and your ability to drive.

Discuss with your doctor, whether you are able to drive and use machines.

<Morphine hydrochloride trihydrate> contains lactose and Sunset Yellow

This medicine contains **lactose (milk sugar)**. If you have been told that you have an intolerance to certain sugars, please inform your doctor before taking this medicine.

<Morphine hydrochloride trihydrate> 60 mg prolonged-release tablets contain the colouring agent Sunset Yellow (E 110): May cause allergic reactions including asthma.

3. How to take <Morphine hydrochloride trihydrate>

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

Take the tablets **as a whole with a sufficient amount of liquid** (e.g. a glass of water).

Dividing, crushing or dissolving of the tablets will destroy the prolonged-release system which may lead to **severe side effects up to a fatal dose of morphine.**

Before starting treatment and regularly during treatment, your doctor will discuss with you what you may expect from using <Morphine hydrochloride trihydrate>, 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 hydrochloride trihydrate>, in this section).

DOSAGE

The dosage of <Morphine hydrochloride trihydrate> depends on pain intensity, your age and your medical history. **Your doctor will adjust the dosage according to your requirements.** The appropriate dose will control your pain for 12 hours causing no or tolerable side effects. Your doctor will decide on the duration of treatment.

For the optimal dosage, <Morphine hydrochloride trihydrate> is available in strengths of 10 mg, 30 mg, 60 mg, 100 mg, and 200 mg.

Do not change the prescribed dose yourself. If you think that the effect of <Morphine hydrochloride trihydrate> is too strong or too weak, talk to your doctor.

Use in children

The use of <Morphine hydrochloride trihydrate> in children under 12 years is not recommended due to insufficient experience.

<Morphine hydrochloride trihydrate> must not be given to children below 1 year.

Adults and adolescents over 12 years

Initially, **1 to 3 <Morphine hydrochloride trihydrate> 10 mg prolonged-release tablets** (equivalent to 10-30 mg morphine hydrochloride trihydrate) **twice a day** (in the morning and evening). Keep strictly to the time schedule (dosage intervals of 12 hours).

If pain intensity increases or tolerance to the morphine dose develops, your doctor will increase the dose.

<Morphine hydrochloride trihydrate> 60 / 100 / 200 mg prolonged-release tablets are not suitable for initial dosing.

Elderly patients and patients with impaired renal or hepatic function

Your doctor will prescribe you a lower initial dose.

If you take more <Morphine hydrochloride trihydrate> than you should

The **major risk** of a <Morphine hydrochloride trihydrate> overdose is **respiratory depression**.

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

Immediately contact a doctor if you have taken too many tablets. In case of overdose, the following symptoms may occur: contraction of the pupils, poor breathing that may result in apnoea, decrease of blood pressure, circulatory disorders, shock, and unconsciousness. People who have taken an overdose may get pneumonia from inhaling vomit or foreign matter, symptoms may include breathlessness, cough and fever.

Immediately contact a doctor if you assume that a child may have ingested <Morphine hydrochloride trihydrate> accidentally - do not wait until you notice symptoms.

If you forget to take <Morphine hydrochloride trihydrate>

Do **not** take a **double dose** to make up for a forgotten dose. Take your **usual dose** as soon as you notice that you have forgotten to take it. Take the next dose **after 12 hours**.

If you stop taking <Morphine hydrochloride trihydrate>

Do not stop treatment with <Morphine hydrochloride trihydrate> unless agreed with your doctor. If you want to stop the treatment with <Morphine hydrochloride trihydrate>, ask your doctor how to slowly decrease the dose 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 unsatisfaction, anxiety and irritability. If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

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

Stop using <Morphine hydrochloride trihydrate> 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 Generalized Exanthematous Pustulosis (AGEP).
- Serious allergic reaction which causes difficulty in breathing or dizziness.

The following side effects may occur:

Very common (may affect more than 1 in 10 people)

- nausea
- constipation

Common (may affect up to 1 in 10 people)

- confusion
- sleeping disorders
- dizziness
- drowsiness
- somnolence
- asthenia, fatigue, malaise
- muscle spasms
- headache
- flush
- abdominal pain
- anorexia
- dry mouth
- vomiting

If nausea, vomiting and/or constipation occur, inform your doctor. He will prescribe you an appropriate medicine.

Uncommon (may affect up to 1 in 100 people)

- hypersensitivity
- agitation
- euphoria
- convulsions
- paraesthesia
- syncope
- increased muscle tone
- palpitations
- mood changes
- Overdose may lead to respiratory depression
- spasms of the airways, breathing disorders
- problems passing urine, urinary tract spasms
- bile tract spasms
- hallucinations
- vertigo
- visual disturbances
- blurred or double vision, involuntary eye movements
- increased or decreased heart rate
- increase or decrease of blood pressure
- fluid accumulation in the lung
- ileus
- dysgeusia
- dyspepsia
- colic
- increased hepatic enzymes
- hives, itching

- fluid accumulation in the tissues (oedema)
- general feeling of weakness up to fainting

Rare (may affect up to 1 in 1,000 people)

- asthma attacks in predisposed patients
- insomnia
- increased pancreatic enzymes
- 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
- renal colic

Very rare (may affect up to 1 in 10,000 people)

- syndrome of inappropriate antidiuretic hormone secretion (SIADH) (symptoms: nausea, malaise, headache, exhaustion and in severe cases may progress to seizures and coma)
- tremor
- exanthema
- chills

Not known (frequency cannot be estimated from the available data)

- anaphylactic/anaphylactoid reactions
- cognitive disorders
- dysphoria
- impotence, decreased sexual drive, absence of menstrual periods
- tolerance development
- abstinence symptoms or dependence (for symptoms see section 3: If you stop taking <Morphine hydrochloride trihydrate>)
- increased sensitivity to pain (hyperalgesia), see section “Warnings and precautions”
- sweating
- contraction of the pupil
- neonatal withdrawal syndrome
- sleep apnoea (breathing pauses during sleep)

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system: [according to Appendix V – to be completed nationally].

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store <Morphine hydrochloride trihydrate>

Do not store above 25°C.

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. The expiry date refers to the last day of that month.

Do not throw away 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 hydrochloride trihydrate> contains

- The active substance is morphine hydrochloride trihydrate. 1 film-coated tablet contains 60 mg morphine hydrochloride trihydrate equivalent to 45.55 mg morphine.
- The other ingredients are lactose monohydrate, polyacrylate dispersion 30 per cent, methacrylic acid-ethyl acrylate copolymer (1:1), ammonio methacrylate copolymerisate type B, hypromellose 4000, magnesium stearate, macrogol 6000, talc, titanium dioxide (E 171), hypromellose 5, quinoline yellow aluminium lake (E 104), Sunset yellow aluminium lake (E 110) .

What <Morphine hydrochloride trihydrate> looks like and contents of the pack

<Morphine hydrochloride trihydrate> 60 mg prolonged-release tablets are yellow, round and biconvex.

<Morphine hydrochloride trihydrate> are available in blisterpacks of 10, 14, 20, 30, 50, 60, 100, 100x1 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

G.L. Pharma GmbH, 8502 Lannach

MANr.: 1-19833

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria: Vendal retard 60 mg-Filmdabletten

Germany: M-Stada 60 mg Retardtabletten

Denmark: Depolan depottabletter 60 mg

Netherlands: Morfine HCl retard CF 60 mg

Sweden: Depolan depottabletter 60 mg

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