Package leaflet: Information for the user

Hydromorphone hydrochloride 20 mg/ml solution for injection/infusion
Hydromorphone hydrochloride 50 mg/ml solution for injection/infusion

hydromorphone hydrochloride

Read all of this leaflet carefully before you are given 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 nurse.
- 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 nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Hydromorphone hydrochloride is and what it is used for

This medicine contains the active substance hydromorphone hydrochloride, which is a potent analgesic (strong "painkiller") of the opioid group.
You have been prescribed Hydromorphone hydrochloride for the treatment of severe pain.

The medicine is intended for use in adults and adolescents over 12 years of age.

2. What you need to know before you use Hydromorphone hydrochloride

Do not use Hydromorphone hydrochloride if you:
- are allergic to hydromorphone or any of the other ingredients of this medicine (listed in section 6);
- have breathing problems (respiratory depression);
- suffer from a severe lung disease associated with obstruction of the airways (severe chronic obstructive pulmonary disease or severe COPD);
- have heart problem after long-term lung disease (cor pulmonale);
- have severe pain in your abdomen;
- have a condition where the small bowel does not work properly (paralytic ileus);
- are taking a type of medicine known as monoamine oxidase inhibitor (examples include tranylcypromide, phenelzine, isocarboxazid, moclobemide and linezolid), or you have taken this type of medicine in the last two weeks.

Hydromorphone hydrochloride must not be used if the patient is in a coma.

Warnings and precautions
Before treatment with Hydromorphone hydrochloride tell your doctor if you:
- have a head injury (due to the risk of increased brain pressure);
- suffer from seizures, fits or convulsions;
- have an addiction to alcohol;

- have previously suffered from withdrawal symptoms such as agitation, anxiety, nervousness, difficulty in sleeping, being unusually overactive, shaking and gastrointestinal problems upon stopping taking alcohol or drugs;
- suffer from a mental disorder as a result of an intoxication (toxic psychosis);
- have low blood pressure associated with low circulating blood volume (hypotension with hypovolaemia);
- are feeling light-headed or faint;
- have problems with your gall bladder;
- have inflammation of the pancreas (pancreatitis);
- have any bowel problems (such as obstructive or inflammatory bowel disease);
- have prostate problems (such as difficulties in passing urine);
- have poor adrenal gland function (e.g. Addison's disease);
- have an under-active thyroid gland (hypothyroidism);
- have a chronic obstructive airway disease (such as COPD) or reduced pulmonary function;
- suffer from a debilitated general condition or are elderly or infirm;
- suffer from severe kidney problems (including ureteric colic);
- suffer from severe liver problems;
- or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs ("addiction");
- are a smoker;
- 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 this information applies to you or formerly applied to you, please speak to your doctor.

Hydromorphone hydrochloride is not recommended for children under 12 years of age.

The major risk of opioid excess is difficulty in breathing (respiratory depression).

This medicine contains hydromorphone which is an opioid medicine. Repeated use of opioid painkillers may result in the drug being less effective (you become accustomed to it).

Repeated use of Hydromorphone hydrochloride may lead to dependence and abuse which may result in life-threatening overdose. If you have concern that you may become dependent on Hydromorphone hydrochloride, it is important that you consult your doctor.

If treatment is stopped abruptly, withdrawal symptoms such as agitation, anxiety, nervousness, difficulty in sleeping, involuntary muscle contractions, shaking, and gastro-intestinal problems may occur. If you no longer require therapy with hydromorphone, your doctor will taper the daily dose gradually to prevent these symptoms.

An increase in sensitivity to pain (hyperalgesia) that will not respond to a further dose increase of Hydromorphone hydrochloride may very rarely occur in particular in high doses. Your doctor will decide whether a dose reduction or change in analgesic (opioid) is required in such a situation.

Please tell your doctor, if you experience small bowel problems (paralytic ileus) during the treatment with Hydromorphone hydrochloride. He or she will take appropriate measures.

If you are going to have an operation, please tell your doctors at the hospital that you are using Hydromorphone hydrochloride as they may need to adjust the amount of injection you are given.

<u>Sleep-related breathing disorders</u>
Hydromorphone hydrochloride can cause sleep-related breathing disorders such as sleep apnea (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.

Other medicines and Hydromorphone hydrochloride
Tell your doctor if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription.

When taken with some other medicines or alcohol, the side effects of Hydromorphone hydrochloride (such as drowsiness, breathing problems, constipation, dry mouth, difficulty in passing urine) or the other medicine may be altered.

Tell your doctor if you:
- are taking medicines to treat anxiety (for example tranquillisers);
- have been given an anaesthetic (for example a barbiturate);
- are taking medicines to help you sleep (hypnotics or sedatives);
- are taking medicines to treat psychiatric or mental disorders (neuroleptics or psychotropics);
- are taking medicines to treat depression (antidepressants);
- are taking medicines used to stop you feeling sick or being sick (antiemetics);
- are taking medicines used to prevent or relieve the symptoms of an allergy (antihistamines);
- are taking medicines to treat Parkinson's disease;
- are taking other strong analgesics or 'painkillers', or have recently taken another painkiller from the opioid class.

Do not take Hydromorphone hydrochloride if you are taking a specific type of medicine known as monoamine oxidase inhibitor, or you have taken this type of medicine in the last two weeks.

Concomitant use of Hydromorphone hydrochloride 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. The concomitant use of opioids and drugs used to treat epilepsy, nerve pain or anxiety (gabapentin and pregabalin) increases the risk of opioid overdose, respiratory depression and may be life-threatening. However if your doctor does prescribe Hydromorphone hydrochloride 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.

Hydromorphone hydrochloride with alcohol
Drinking alcohol during your treatment with Hydromorphone hydrochloride may make you drowsy. If you are affected you should avoid drinking alcohol.

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 for advise before using this medicine.

<u>Pregnancy</u>
Hydromorphone crosses placenta. You should not use Hydromorphone hydrochloride during pregnancy and labour unless you have been specifically told by your doctor. If you use Hydromorphone hydrochloride during labour uterine contractility may be impaired. In addition slow and shallow breathing (respiratory depression) may occur in the newborn infant.
Newborn babies may suffer withdrawal effects (such as high-pitched cry, jitteriness, fits, poor feeding and diarrhoea) if their mothers have taken hydromorphone for a long time during pregnancy.

<u>Breast-feeding</u>
Hydromorphone hydrochloride should not be used while breast-feeding because the active substance can get into breast milk.

Driving and using machines

Hydromorphone hydrochloride may make you drowsy and thus impair your ability to drive and use machines. This applies particularly:
- at the beginning of treatment;
- if your dose is increased;
- if you have switched to Hydromorphone hydrochloride from a different opioid;
- if you drink alcohol or use medicines which influence your brain function.

You should consult your doctor before driving or using machinery.

Hydromorphone hydrochloride contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per 1 ml, that is to say essentially "sodium-free".

3. How to use Hydromorphone hydrochloride

A doctor or nurse will usually prepare and administer the injection for you. Your doctor will decide how much Hydromorphone hydrochloride you require based on:
- the severity of your pain;
- the dose of painkiller you have previously been given;
- your age and weight.

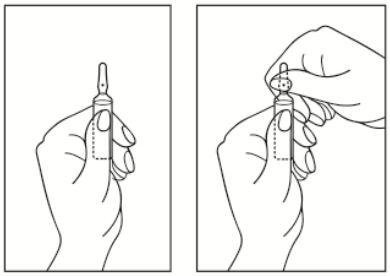
Your doctor will increase the amount of Hydromorphone hydrochloride you are given until your pain is relieved. If you find that you are still in pain whilst undergoing treatment with Hydromorphone hydrochloride, discuss this with your doctor.

You should not use Hydromorphone hydrochloride 20 mg, 50 mg as initial opioid therapy. This higher dosage form may only be used as individual doses if you have no longer sufficiently responded to lower doses of hydromorphone preparations (2 mg) or comparably strong analgesics as part of long term pain therapy.

The usual starting doses of Hydromorphone hydrochloride are as follows:

<u>Adults and Adolescents (older than 12 years of age)</u>
- As a single injection into a vein, the usual dose is 1 to 1.5 mg given slowly over 2 to 3 minutes. This can be repeated every 3 to 4 hours.
- As a single injection through a fine needle into the tissue under the skin, the usual dose is 1 to 2 mg. This can be repeated every 3 to 4 hours.
- As an infusion into a vein or through a fine needle into the tissue under the skin, the usual starting dose is 0.15 to 0.45 mg/hour (or 0.004 mg/kg bodyweight/hour).
- If given by patient controlled analgesia (PCA), the usual recommended bolus dose is 0.2 mg with a stop interval of 5 to 10 minutes.

Instruction of ampoule opening:
1) Turn the ampoule with coloured point up. If there is any solution in the upper part of the ampoule, gently tap with your finger to get all the solution to the lower part of the ampoule.
2) Use both hands to open; while holding the lower part of the ampoule in one hand, use the other hand to break off the upper part of the ampoule in the direction away from the coloured point (see the pictures below).



Use in children (under 12 years of age)
Hydromorphone hydrochloride is not recommended for children under 12 years of age.

Elderly patients (over 75 years of age)
A lower dosage might be enough for adequate pain relief in elderly patients.

Patients with liver and kidney problems
If you suffer from liver or kidney problems, you may require less Hydromorphone hydrochloride in order to relieve your pain.

Route of administration
A doctor or nurse will usually administer Hydromorphone hydrochloride for you.
Hydromorphone hydrochloride is intended for injection or infusion into a vein (intravenous = IV) or through a fine needle under the skin (subcutaneous = SC).

Duration of treatment
Hydromorphone hydrochloride should only be used as long as necessary. Your doctor will decide when and how the treatment will be stopped. If you get a long term treatment, your doctor should verify regularly whether you still need Hydromorphone hydrochloride. Do not stop the treatment without talking to your doctor (see "If you stop using Hydromorphone hydrochloride").

If you use more Hydromorphone hydrochloride than you should
Call your doctor or hospital straight away. In severe cases an overdose may lead to unconsciousness or even death. The following symptoms may occur after an overdose:
- pin point pupils;
- slowing of heartbeat;
- respiratory problems;
- low blood pressure;
- unconsciousness leading to coma;
- pneumonia caused by inhaling vomit or foreign matter (symptoms may include breathlessness, cough and fever).

If you have used too much Hydromorphone hydrochloride injection under no circumstances should you put yourself in a situation that requires you to be alert e.g. driving a car.

The patient may need emergency treatment in hospital. When seeking medical attention make sure that you take this leaflet and any remaining ampoules with you to show to the doctor.

If you forget to use Hydromorphone hydrochloride
Please use Hydromorphone hydrochloride as soon as you noticed that you forgot it. Never use the double dose.

If you forgot to use Hydromorphone hydrochloride or used a smaller dose than prescribed, this will lead to unsatisfactory and/or insufficient pain relief.

If you stop using Hydromorphone hydrochloride
You should not suddenly stop using Hydromorphone hydrochloride unless your doctor tells you to. If you want to stop using Hydromorphone hydrochloride, discuss this with your doctor first. If you do

stop using Hydromorphone hydrochloride suddenly after longer treatment, you may experience withdrawal symptoms such as agitation, anxiety, nervousness, difficulty in sleeping, involuntary muscle contractions, shaking, and gastro-intestinal problems. Your doctor will tell you how to stop treatment, usually by reducing the dose gradually so you do not experience unpleasant effects.

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.

This medicine can very rarely cause allergic reactions (hypersensitivity reactions). The incidence of serious allergic reactions (anaphylactic reactions) is not known. Tell your doctor immediately if you get any sudden wheeziness, difficulties in breathing, swelling of the eyelids, face, lips, mouth or throat, or any rash or itching especially those covering your whole body.

Difficulty in breathing (respiratory depression) is the chief hazard of an opioid overdose.

Most people will have constipation when using Hydromorphone hydrochloride. Increasing the amount of fibre (fruit, vegetables, wholemeal bread, pasta, brown rice) and fluids you eat and drink may help reduce the problem, but if necessary your doctor may prescribe a laxative.

You may feel sick or vomit (be sick) when you use Hydromorphone hydrochloride, this should normally wear off after a few days however your doctor can prescribe an anti-vomiting medicine if it continues to be a problem.

Very common side effects (may affect more than 1 in 10 people)
- dizziness, feel more sleepy than normal
- constipation
- feel sick, vomiting (be sick)
- itchy skin
- a feeling of unusual weakness

Common side effects (may affect up to 1 in 10 people)
- confusional state
- low blood pressure
- dry mouth
- sweating
- rash
- difficulty in passing urine, urgency in passing urine
- loss of appetite
- anxiety, sleeplessness
- hallucinations
- abdominal pain or discomfort
- skin reactions at the injection site

Uncommon side effects (may affect up to 1 in 100 people)
- unpleasant or uncomfortable mood, feeling of extreme happiness
- headache, shaking, muscle spasms, tingling in the hands or feet
- reduction in size of the pupils in the eye, blurred vision
- fast heartbeat
- indigestion
- itching rash
- decreased sexual drive, impotence
- drug tolerance
- withdrawal symptoms such as agitation, anxiety, nervousness, difficulty in sleeping, being

unusually overactive, shaking and gastrointestinal problems
- malaise and fatigue
- depression, nightmares
- shortness of breath
- diarrhoea, changes in taste
- may affect the results of blood tests to check that your liver is working properly

Rare side effects (may affect up to 1 in 1,000 people)
- drug dependence, agitation
- seizures, fits or convulsions, sedation
- slow heartbeat, irregular heartbeat
- difficulty in breathing or wheezing
- may affect the results of blood tests to check that your pancreas is working properly
- facial flushing (redness of the face)

Very rare side effects (may affect up to 1 in 10,000 people)
- an increase in sensitivity to pain (hyperalgesia; see "Warnings and precautions" in section 2)
- a condition where the small bowel (part of your gut) does not work properly (paralytic ileus)
- swelling of hands, ankles or feet, irritation and hardening of the skin at the injection site (particularly after repeated subcutaneous administration)
- aggression

Not known (frequency cannot be estimated from the available data)
- hot flush
- withdrawal symptoms in newborn babies born to mothers who have used Hydromorphone hydrochloride during pregnancy (see section 2 "Pregnancy and breast-feeding")
- 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 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 Hydromorphone hydrochloride

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

This medicinal product does not require any special temperature storage conditions. Keep the ampoules in the outer carton in order to protect from light. Do not freeze.

Shelf life after first opening:
After opening, this medicinal product should be used immediately.

Shelf life after dilution:
Chemical and physical in-use stability has been demonstrated for 7 days at 25°C and 2-8°C.
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

The medicinal product is to be visually inspected prior to use. Only clear solutions free from particles should be used. For single use only.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. 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 Hydromorphone hydrochloride contains
Hydromorphone hydrochloride ***20 mg/ml***:
- The active substance is hydromorphone hydrochloride.

Each 1 ml ampoule contains 20 mg hydromorphone hydrochloride (corresponding to 17.73 mg hydromorphone).

Hydromorphone hydrochloride ***50 mg/ml***:
- The active substance is hydromorphone hydrochloride.

Each 1 ml ampoule contains 50 mg hydromorphone hydrochloride (corresponding to 44.33 mg hydromorphone).

- The other ingredients are citric acid; sodium citrate; sodium chloride; sodium hydroxide (for pH adjustment); hydrochloric acid, concentrated (for pH adjustment); water for injections.

What Hydromorphone hydrochloride looks like and contents of the pack
Clear colourless or yellowish solution for injection/infusion, free from visible particles.

Hydromorphone hydrochloride is produced in 1 ml amber glass ampoules. Ampoules are marked with a specific colour ring code for each strength.

Pack size:
5 or 10 ampoules of 1 ml

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
AS KALCEKS
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This medicine is authorised in the Member States of the European Economic Area under the following names:

Austria	Hydromorphon Kalceks 2 mg/ml, 10 mg/ml, 20 mg/ml, 50 mg/ml Injektions-/Infusionslösung
Estonia	Hydromorphone Kalceks
Denmark	Hydromorphonhydrochlorid Kalceks
Finland	Hydromorphone Kalceks
Germany	Hydromorphon Ethypharm Kalceks 2 mg/ml, 10 mg/ml, 20 mg/ml, 50 mg/ml Injektions-/Infusionslösung
Ireland	Hydromorphone hydrochloride 20 mg/ml, 50 mg/ml solution for injection/infusion
Latvia	Hydromorphone Kalceks 2 mg/ml, 10 mg/ml, 20 mg/ml, 50 mg/ml šķīdums injekcijām/infūzijām
The Netherlands	Hydromorfonhydrochloride Kalceks 2 mg/ml, 10 mg/ml, 20 mg/ml, 50 mg/ml oplossing voor injectie/infusie
Norway	Hydromorfonhydroklorid Kalceks
Sweden	Hydromorphone Kalceks

This leaflet was last revised in 10/2022

The following information is intended for healthcare professionals only:

pH of solution is 3.5-4.5.
Osmolality of solution is approximately 280 mOsm/kg.

Hydromorphone hydrochloride solution for injection/infusion undiluted or diluted with sodium chloride 9 mg/ml solution for infusion, glucose 50 mg/ml solution for infusion or water for injections, is physically and chemically stable when in contact with representative brands of polypropylene syringes, polyethylene or PVC tubing, and PVC or EVA infusion bags.

As well as product is compatible with following medicinal products: hyoscine butylbromide, hyoscine hydrobromide, dexamethasone sodium phosphate, haloperidol, midazolam hydrochloride, metoclopramide hydrochloride, levomepromazine hydrochloride, glycopyrronium bromide, ketamine hydrochloride.

This medicinal product must not be mixed with other medicinal products except those mentioned above.

The medicinal product is to be visually inspected prior to use. Only clear solutions free from particles should be used.

For single use only. Discard any remaining contents after use.

Use immediately after first opening.

Inappropriate handling of the undiluted solution after opening of the original ampoule, or of the diluted solutions may compromise the sterility of the product.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.