Package leaflet: Information for the user

Fentanyl Kalceks 0.05 mg/ml solution for injection

fentanyl

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 nurse.
- 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 Fentanyl Kalceks is and what it is used for

Fentanyl Kalceks solution for injection contains the active substance fentanyl (as citrate). It belongs to a group of medicines known as opioid analgesics. These medicines prevent and relieve pain.

Fentanyl Kalceks is used:
- as a narcotic analgesic supplement in general or regional anaesthesia;
- in combination with a neuroleptic (e.g. droperidol) in the technique of neuroleptanalgesia;
- for the induction of anaesthesia, and as an adjuvant in the maintenance of general and regional anaesthesia;
- as an anaesthetic agent with oxygen in high-risk patients undergoing surgery.

2. What you need to know before you receive Fentanyl Kalceks

Do not use Fentanyl Kalceks:
- if you are allergic to fentanyl or any of the ingredients of this medicine (listed in section 6);
- if you are allergic to medicines called morphinomimetics.

Warnings and precautions
Talk to your doctor or nurse before using Fentanyl Kalceks.

As with all potent opioids, respiratory depression is dose related and can be reversed by the administration of a narcotic antagonist (naloxone), but it may be necessary to administer additional doses of the antagonist as respiratory depression may have a longer duration of action than the opioid antagonists. Profound analgesia is accompanied by marked respiratory depression that may persist or recur in the post-operative period. Therefore, patients should remain under appropriate surveillance. Fentanyl should be administered in an environment where the airways can be controlled, and resuscitation equipment and narcotic antagonists should be available, along with personnel who can control the airways. Hyperventilation during anaesthesia may alter the patient's response to CO_2, affecting breathing, in the post-operative period.

Muscular rigidity, which may also involve the thoracic muscles, may occur, but can be avoided by the following measures:
- slow intravenous injection (usually sufficient for lower doses);

- premedication with benzodiazepines;
- use of muscle relaxants.

Non-epileptic (myo)clonic movements may occur.

Bradycardia, and possibly cardiac arrest, can occur if the patient has received an insufficient amount of anticholinergic, or when fentanyl is combined with non-vagolytic muscle relaxants. Bradycardia can be antagonised by atropine.

Opioids may cause hypotension, especially in patients with hypovolaemia. Appropriate measures should be taken to maintain stable blood pressure.

The use of rapid bolus injection of opioids should be avoided in patients with compromised intracerebral compliance; in such patients, a transient decrease in the mean arterial pressure has occasionally been accompanied by a reduction of short duration in the cerebral perfusion pressure.

Patients on chronic opioid therapy or with a history of opioid abuse may require higher doses.

Dose reduction is recommended in the elderly and in debilitated patients.

Opioids should be titrated with caution in patients with any of the following conditions: uncontrolled hypothyroidism, pulmonary disease, decreased respiratory reserve, alcoholism, or impaired renal or hepatic function. Such patients also require prolonged post-operative monitoring.

If the fentanyl is administered with a neuroleptic, such as droperidol, there is higher incidence of hypotension. Neuroleptics can induce extrapyramidal symptoms that may be controlled with anti-Parkinson agents.

As with other opioids, administration of fentanyl may lead to increases of bile duct pressure and, in isolated cases, spasms of the sphincter of Oddi (the round muscle that controls the flow of bile) might be observed.

In patients with *myasthenia gravis*, careful consideration should be applied in the use of certain anticholinergic agents and neuromuscular-blocking pharmaceutical agents prior to, and during the administration of a general anaesthetic regimen which includes administering intravenous fentanyl.

Tell your doctor if you have ever abused or been dependent on opioids, alcohol, prescription medicines, or illegal drugs.

Repeated use of the product may result in the drug being less effective (you become accustomed to it) or becoming dependent on it.

If your treatment is stopped withdrawal symptoms may occur. Please tell your doctor or nurse if you think this is happening to you (see also section 4).

Children and adolescents
Techniques that involve analgesia in a spontaneously breathing child should only be used as part of an anaesthetic technique, or given as part of a sedation/analgesia technique, with experienced personnel in an environment that can manage sudden chest wall rigidity requiring intubation, or apnoea requiring airway support.

Other medicines and Fentanyl Kalceks
Tell your doctor or nurse if you are using, have recently used or might use any other medicines.

The use of opioid premedication, barbiturates, benzodiazepines, neuroleptics, halogenic gases and other non-selective CNS depressants (e.g. alcohol) may enhance or prolong the respiratory depression

of fentanyl. When patients have received such medicines, the dose of fentanyl required to be less than usual.

Tell your doctor if you are using other CNS-depressants, such as a selective serotonin re-uptake inhibitor (SSRI) or a serotonin norepinephrine re-uptake inhibitor (SNRI).

When patients have received such medicines, the dose of fentanyl required to be less than usual.

Fentanyl, a high clearance drug, is rapidly and extensively metabolised mainly by CYP3A4. Itraconazole (a potent CYP3A4 inhibitor) administered orally at 200 mg/day for 4 days had no significant effect on the pharmacokinetics of intravenous fentanyl.

Orally administered ritonavir (one of the most potent CYP3A4 inhibitors) reduced the clearance of intravenous fentanyl by two thirds. However, peak plasma concentrations after a single dose of intravenous fentanyl were not affected.

When fentanyl is used as a single dose, the concomitant administration of potent CYP3A4 inhibitors such as ritonavir requires special patient care and observation.

Concomitant administration of fluconazole or voriconazole and fentanyl may result in increased exposure to fentanyl.
With continuous treatment a dose reduction of fentanyl may be required to avoid accumulation, which may increase the risk of prolonged or delayed respiratory depression.

It is usually recommended that the administration of monoamine oxidase inhibitors (MAOIs) should be discontinued two weeks prior to any surgical or anaesthetic procedure. However, several reports describe the use of fentanyl during surgical or anaesthetic procedures in patients on MAOIs without any interaction.

The effects of fentanyl on other medicines
Following the administration of fentanyl, the dose of other CNS depressants should be reduced.

The total plasma clearance and volume of distribution of etomidate are decreased (by a factor 2-3), with no change in half-life, when combined with fentanyl, which results in a considerable increase in the plasma concentration of etomidate. Simultaneous administration of fentanyl and intravenous midazolam results in an increase in the terminal plasma half-life and a reduction in the plasma clearance of midazolam. When these medicines are co-administered with fentanyl their dose may need to be reduced.

Fentanyl Kalceks with alcohol
Alcohol may enhance or prolong the breathing depression of fentanyl.

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 nurse for advice before using this medicine.
There are no adequate data on the use of fentanyl in pregnant women. Fentanyl can cross the placenta in early pregnancy. Studies in animals have shown some reproductive toxicity. The potential risk for humans is unknown.
Consequently, the risks and potential benefits should be considered before administering this medicine to pregnant women.
Administration (intramuscular or intravenous) during childbirth (including caesarean section) is not recommended because fentanyl crosses the placenta and affects the foetal respiratory centre that is particularly sensitive to opioids. However, if fentanyl is administered, an antidote for the newborn should always be available.

Fentanyl is excreted into human milk therefore, breast-feeding is not recommended within 24 hours following administration of this medicine. The risk/benefit of breast-feeding following administration of fentanyl should be considered.

Driving and using machines
Patient should not drive or operate machinery if sufficient time has not elapsed after the administration of fentanyl.

Fentanyl Kalceks contains sodium
This medicine contains 7.08 mg sodium per 2 ml ampoule, that is to say essentially 'sodium-free'.

3. How Fentanyl Kalceks is given to you

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

- Fentanyl Kalceks may be given as an infusion or injection into a vein, or as an injection into a muscle.
- Fentanyl Kalceks will be injected into your vein just before operation. This medicine will help to put you to sleep and will prevent you from feeling pain during your operation.
- You may be given anaesthetic and/or other medicines to prevent some side effects of fentanyl such as slower heartbeat and rigid muscles.
- Your doctor will decide how much fentanyl you need. This will depend on your age, body weight, general health condition, existing illness, other drug using, the type and length of operation you are having.

Use in children and adolescents
In children the dose given will always depend on their body weight.

If you have received more Fentanyl Kalceks than you should
As this medicine is given to you by a doctor or nurse, so it is unlikely that you will be given more fentanyl than you should. Overdose of fentanyl can cause breathing depression (see *Warnings and precautions*).
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.

Possible side effects may occur especially during surgery and will be resolved by your doctor. However, some may also occur shortly thereafter; therefore the observation after the operation will be carried out.

Very common (may affect more than 1 in 10 people):
- Feeling sick (nausea), being sick (vomiting)
- Muscle stiffness (which may involve your chest muscles)

Common (may affect up to 1 in 10 people):
- Involuntary, repetitive body movements
- Drowsiness, dizziness
- Visual disturbances
- Rapid or slow heartbeat
- Irregular heartbeat
- Low or high blood pressure
- Venous pain

- Choking caused by cramping (spasm) of the muscles in your throat
- Difficulty in breathing or wheezing
- Stop breathing for a short period of time (apnoea) (the doctor has the medicine to prevent it)
- Skin rash
- Confusion after surgery

Uncommon (may affect up to 1 in 100 people):
- Mood elevation
- Headache
- Swelling and clotting in a vein (phlebitis)
- Irregular changes of blood pressure
- Breathing faster than normal
- Hiccups
- Fall in body temperature below normal or chills
- Airway complication of anaesthesia
- Agitation after surgery

Not known (frequency cannot be estimated from the available data):
- Severe allergic reaction with a sudden fall in blood pressure, difficulty in breathing or skin rash (anaphylaxis)
- Hives
- Convulsions
- Loss of consciousness
- Muscle twitching
- Cardiac arrest (the doctor has the medicine to prevent it)
- Breathing depression
- Itching of the skin
- Delirium (symptoms may include a combination of agitation, restlessness, disorientation, confusion, fear, seeing or hearing things that are not really there, sleep disturbance, nightmares)
- Symptoms of withdrawal syndrome (may manifest by the occurrence of the following side effects: nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating)

If fentanyl is used together with other medicines called neuroleptics, which are given before an operation to cause drowsiness, other effects can be experienced, such as shivering and/or thrill, agitation; after surgery – hallucinations, trembling, pronounced muscle stiffness or spasm, slowness of movement and excess saliva.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Fentanyl Kalceks

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

Do not store above 30 °C.
Store in the original package in order to protect from light. Do not freeze.

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

Once ampoule has been opened, the product should be used immediately.

Chemical and physical in-use stability has been demonstrated for 48 hours at room temperature or 2-8 °C.

From a microbiological point of view, the medicine 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 2-8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

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 Fentanyl Kalceks contains

- The active substance is fentanyl (as citrate).

1 ml of solution contains 0.0785 mg of fentanyl citrate corresponding to 0.05 mg of fentanyl.
One ampoule (2 ml) contains 0.157 mg of fentanyl citrate corresponding to 0.1 mg of fentanyl.

- The other ingredients are sodium chloride, sodium hydroxide (for pH adjustment), water for injections.

What Fentanyl Kalceks looks like and contents of the pack
Fentanyl Kalceks is clear colourless liquid. pH of solution 4.0 - 7.5.

Fentanyl Kalceks is produced in Type I colourless glass ampoules of 2 ml.
Pack size: 10 ampoules.

Marketing Authorisation Holder
AS KALCEKS
Krustpils iela 71E, Rīga, LV-1057, Latvia
Tel.: +371 67083320
E-mail: kalceks@kalceks.lv

Manufacturer
HBM Pharma s.r.o.
Sklabinska 30, Martin, 036 80, Slovakia

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The following information is intended for healthcare professionals only:

Dosage
The dose of medicine should be individualised according to age, body weight, physical condition, underlying pathological condition, concomitant use of other drugs, and type of surgery and anaesthesia.

- As an analgesic supplement in general anaesthesia

In low doses for minor surgical procedures: 2 mcg/kg of fentanyl.
Moderate dose: 2-20 mcg/kg of fentanyl.
In high doses during major surgery: 20-50 mcg/kg of fentanyl. The duration of the effect depends on the dose. During major surgery the administration of 20-50 mcg/kg of fentanyl with nitrous oxide/oxygen has been shown to have an attenuating effect.
When these doses were used during surgery, it is necessary to provide post-operative ventilation and to monitor the patient, due to the extended respiratory depression in the post-operative period.
Supplements of 25-250 mcg (0.5-5 ml) of fentanyl may be administered, according to patient requirements and duration of surgery.

- As an anaesthetic agent