Kalcex

Package leaflet: Information for the user

Alfentanil 500 micrograms/ml solution for injection/infusion

Alfentanil

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 Alfentanil is and what it is used for

Alfentanil contains the active substance alfentanil hydrochloride (hereinafter referred to as alfentanil). It belongs to a group of medicines called 'opioid anaesthetics'. Alfentanil is a strong painkiller (analgesic) used in hospitals. It has a fast onset and short duration of action, and is therefore used for anaesthesia in surgical procedures and investigations.

This medicine is used in adults:
- as analgesic for initiating and/or maintaining general anaesthesia.

This medicine is used in newborns, infants, children and adolescents:
- as analgesic together with a sleeping medicine (hypnotic) to induce anaesthesia;
- as analgesic in connection with general anaesthesia during surgical procedures of both short and long duration.

2. What you need to know before you are given Alfentanil

You should not be given Alfentanil
- if you are allergic to alfentanil hydrochloride, other opioids or any of the other ingredients of this medicine (listed in section 6).

If you are not sure if any of the above applies to you, talk to your doctor or nurse before you are given this medicine.

Warnings and precautions
Talk to your doctor or nurse before being given Alfentanil if you:
- have muscle weakness (myasthenia gravis);
- have problems with your heart or blood circulation;
- have a head injury or increased pressure in the brain;
- are on a low-sodium diet;
- have uncontrolled reduced thyroid gland function;
- have lung disease, breathing difficulties called 'obstructive airway disease' or 'respiratory depression', or other breathing difficulties. You may only be able to have this medicine if your breathing is helped by a machine called a ventilator;
- have impaired liver or kidney function;
- have alcoholism;
- take a medicine called 'monoamine oxidase (MAO) inhibitor' or have taken them in the last 2 weeks;
- 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.

This medicine contains alfentanil which is an opioid medicine. Repeated use of opioid painkillers may result in the drug being less effective (you become accustomed to it). It may also lead to dependence and abuse which may result in life-threatening overdose. If you have concern that you may become dependent on Alfentanil, it is important that you consult your doctor.

Muscular stiffness, which may also involve thoracic muscles, can occur. This can be avoided by slow i.v. injection (normally sufficient in small doses), premedication with benzodiazepines and the use of muscle relaxants.

Newborns, children and adolescents
Alfentanil can cause breathing difficulties, especially in infants and newborns. If infants or newborns are given Alfentanil:
- their breathing will be monitored closely during the operation and for some time afterwards;
- the doctor can give a medicine that causes the muscles to relax and prevent them from becoming stiff.

Other medicines and Alfentanil
Tell your doctor or nurse if you are using, have recently used or might use any other medicines. Some medicines may enhance, weaken or modify the effect of Alfentanil. In some cases, it may be necessary to adjust the dose of Alfentanil or other concomitantly used medicines.

It is especially important to tell your doctor or nurse if you are using or have recently used any of the following medicines:
- medicines to treat depression called 'monoamine oxidase (MAO) inhibitors' (must not be taken during the last two weeks before or at the same time as you are given Alfentanil);
- medicines to treat depression called 'selective serotonin reuptake inhibitors (SSRI)' or 'serotonin and noradrenaline reuptake inhibitors (SNRI)'.
  MAO, SSRI and SNRI can increase the risk of a potentially life threatening condition called serotonin syndrome and **must not be given** concomitantly with Alfentanil. Symptoms for serotonin syndrome may include confusion, restlessness, nausea, vomiting or diarrhoea, sweating, fever, tremor, muscle contractions, fast or irregular heartrate, seizures (fits);
- antifungal medicines (fluconazole, ketoconazole, itraconazole, voriconazole);
- erythromycin (an antibiotic);
- ritonavir (an antiviral);
- diltiazem (for lowering blood pressure);
- cimetidine (medicine to treat stomach ulcers);
- medicines affecting the central nervous system (CNS depressants):
  - sedative medicines such as benzodiazepines or related medicines (tranquillizers, sleeping pills, medicines for treating mental disorders);
  - other strong painkillers over a long period of time;
  - certain illegal substances;
  - alcohol.

  Concomitant use of Alfentanil and CNS depressants increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. In these cases, it may be necessary to reduce dose of Alfentanil or other medications in order to decrease the risk of these side effects. 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.

Alfentanil with alcohol
Simultaneous alcohol consumption may influence Alfentanil activity.

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 for advice before being given this drug.

Pregnancy
It is likely that the foetus can be affected. Your doctor will assess whether you can be given Alfentanil. If you are given this medicine anyway, artificial respiration equipment will be readily available for mother and infant, as needed. Alfentanil is not recommended during childbirth.

Breast-feeding
It is possible that breast-fed children can be affected. Breast-feeding should be avoided until the drug is out of the body (approximately 24 hours). Do not use breast milk that has been expressed within 24 hours after having Alfentanil.

Fertility
There are limited human data available on the effects of alfentanil on male or female fertility. Animal studies do not indicate direct harmful effects with respect to fertility.

Driving and using machines
This medicine may make you sleepy or dizzy. Therefore, depending on the dose, you must wait at least 24 hours after having Alfentanil before driving a vehicle or operating machinery. Talk to your doctor or nurse if you are not sure whether it is safe for you to drive or operate machinery.

Alfentanil contains sodium
If large amounts of the solution are administered (e.g. more than 6.5 ml, equivalent to more than 1 mmol sodium) the following should be taken into account: This medicine contains 3.54 mg sodium (main component of cooking/table salt) in each ml of solution. This is equivalent to 0.18% of the recommended maximum daily dietary intake of sodium for an adult.

3. How Alfentanil will be given

Your doctor will decide what dose you/your child will be given. This depends on your age, body weight, physical status, diseases you have, what other medication you are taking, and type of surgery and anaesthesia you are having. Check with your doctor or nurse if you are not sure.

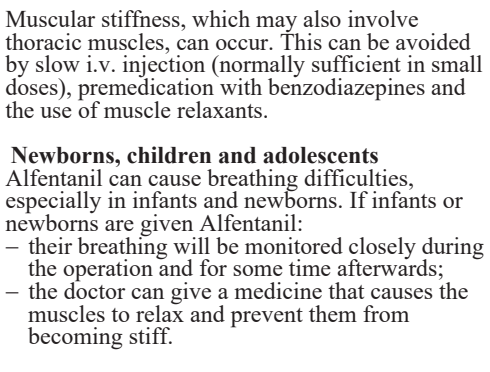
Alfentanil will be given to you by specifically trained health care professionals as an injection or as a drip (infusion) into a vein. The medicine may be given just before or during the operation.

Alfentanil is a strong painkiller that can inhibit breathing. You will therefore be monitored both during and for some time after the surgery.

The following information is intended for healthcare professionals only:

Instructions for use and other handling
For single use only.
Instructions on preparation of diluted solution:
- Inspect the ampoule visually prior to use. Only clear solutions free from particles should be used.
- Wear gloves while opening the ampoule.
- Open the ampoule:

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 medicinal product immediately after opening the ampoule.
- Dilute the content of ampoule to a concentration of 25-80 mcg/ml with:
  - 0.9% sodium chloride solution or
  - 5% glucose solution or
  - Ringer lactate solution.
- Discard any unused portion.
- If the skin is accidentally exposed, treat by flushing the affected area with water. Avoid using soap, alcohol and other detergents, which may cause chemical or physical damage to the skin.

Such diluted solutions are chemically and physically stable when in contact with widely used intravenous administration devices.

Shelf life after dilution
Chemical and physical in-use stability has been demonstrated for 48 hours at 25°C and 2 to 8°C. From a microbiological point of view, the diluted 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.

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

Method of administration
For intravenous use.
Alfentanil should be given as bolus injections (short procedures) or bolus supplemented by repeat administration of alfentanil, or by infusion (long painful procedures).
Alfentanil should only be given by individuals trained in the administration of general anaesthetics and the management of the respiratory effects of potent opioids.

Posology
The dosage of alfentanil should be individualised according to patient's age, body weight, physical status, underlying pathological conditions, use of other drugs and type of surgery and anaesthesia.

Adult patients

The usual recommended dosage regimen is as follows:

Adults	*Initial*	*Supplemental*
Spontaneous respiration	500 mcg (1 ml)	250 mcg (0.5 ml)
Assisted ventilation	30-50 mcg/kg	15 mcg/kg

- *Short procedures and outpatient surgery*

In spontaneously breathing patients, the initial bolus dose should be given slowly over about 30 seconds (dilution may be helpful).

After intravenous administration in unpremedicated adult patients, 500 mcg (1 ml) alfentanil may be expected to have a peak effect in 90 seconds and to provide analgesia for 5-10 minutes.

- *Procedures of medium and long duration*

Periods of more painful stimuli may be overcome by repeat administration of 250 mcg (0.5 ml) alfentanil. For procedures of longer duration, additional administrations will be required.

In ventilated patients, the last dose of alfentanil should not be given later than about 10 minutes before the end of surgery to avoid the continuation of respiratory depression after surgery is complete.

In ventilated patients undergoing longer procedures, alfentanil may be infused at a rate of 0.5-1 mcg/kg/minute. Adequate plasma concentrations of alfentanil will only be achieved rapidly if this infusion is preceded by a loading dose of 50-100 mcg/kg given as a bolus or fast infusion over 10 minutes.

Lower doses may be adequate, for example where anaesthesia is being supplemented by other agents.

The infusion should be discontinued up to 30 minutes before the anticipated end of surgery.

Increasing the infusion rate may prolong recovery. Supplementation of the anaesthetic, if required, for periods of painful stimuli, is best managed by extra bolus doses of alfentanil (500 mcg to 1 mg corresponding to 1-2 ml) or low concentrations of a volatile agent for brief periods.

Patients with severe burns presenting for dressing, etc., have received a loading dose of 18-28 mcg/kg/min for up to 30 minutes without requiring mechanical ventilation.

Hepatic impairment
Reduced doses may be required.

Renal impairment
Reduced doses may be required.

Elderly and debilitated patients
The dosage should be reduced in elderly and debilitated patients.

Patients with impaired thyroid function, liver, kidney or lung disorders or alcoholism may need a dose adjustment.

Dosage in neonates, infants and children
Your child will be given this medicine by a specifically trained health care professionals. In neonates a lower dose of alfentanil may be required. Your doctor will decide the correct dose for your child and how and when the injection will be given. All children will be closely monitored during administration of alfentanil. If you have any further questions or concerns on the use of this medicine for your child ask the doctor or nurse giving the injection.

If you have been given too much Alfentanil
As this medicine will be given to you by a doctor or nurse, it is unlikely that you will be given too much. However, if you feel unwell, have breathing difficulties (varies from unusually slow breathing to failure to breathe), muscle stiffness, feeling faint due to low blood pressure or slow heart rate, tell your doctor or nurse. In this case, you will receive appropriate treatment (oxygen, artificial respiration and antidote naloxone).

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Some side effects can occur during the surgery, and your doctor will deal with them, while others may arise straight after.

Severe side effects
Tell your doctor or nurse **immediately** if you experience any of the following side effects as these may require immediate medical treatment:

Uncommon (may affect up to 1 in 100 people)
- Weaker breathing, bluish discoloration of lips and nails
- Spasms in the throat with breathing difficulties

Rare (may affect up to 1 in 1,000 people)
- Shortness of breath, difficulties to breath (respiratory distress), asthma-like attacks

Not known (frequency cannot be estimated from the available data)
- Sudden skin rash, breathing difficulties and fainting (within minutes to hours) due to hypersensitivity (can be potentially fatal)

Other side effects
Very common (may affect more than 1 in 10 people)
- Nausea, vomiting

Common (may affect up to 1 in 10 people)
- Irregular breathing with respiratory pauses (apnoea)
- Elevated mood (euphoria)
- Movement disorders, involuntary movements, dizziness, drowsiness
- Visual disturbances
- Slow or fast pulse (may be serious)
- High or low blood pressure (high blood pressure must be treated, extremely high blood pressure is serious)
- Muscle stiffness
- Chills, injection site pain, fatigue
- Pain associated with the treatment

Uncommon (may affect up to 1 in 100 people)
- Headache, somnolence, unresponsive to stimuli
- Irregular heartbeats, decreased heart rate (can be or become serious)
- Hiccups, excess carbon dioxide in the blood
- Allergic eczema or irritation of the skin/rash (allergic dermatitis), intense sweating
- Pain
- Confusion or agitation after an operation, problems with the airways as a result of the anaesthesia

Rare (may affect up to 1 in 1,000 people)
- Agitation, crying
- Pain in the veins
- Bleeding from the nose
- Itching
- Anaesthesia complications of the nervous system
- Complications related to the treatment (procedural complications)
- Intubation complications (related to insertion of a tube into windpipe).

Not known (frequency cannot be estimated from the available data)
- Confusion or disorientation
- Loss of consciousness (after the operation), convulsions, attacks of involuntary muscular movements
- Narrowed pupils
- Coughing
- Reddening of the skin, rash
- Fever
- Cardiac arrest (when the heart stops)
- Respiratory arrest (when the breathing stops)

Side effects in newborns, children and adolescents
The frequency and type of side effects in children and adolescents are similar to those described above. Muscle twitching and stiffness can occur more commonly in newborn babies than in older children being treated with Alfentanil.

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 Yellow Card Scheme Website: 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 Alfentanil

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

Do not use this medicine after the expiry date stated on the ampoule label and cardboard box after EXP.
The expiry date refers to the last day of that month.

Your doctor or nurse is responsible for the correct storage, use and disposal of this medicine/diluted product.

6. Contents of the pack and other information

What Alfentanil contains
– The active substance is alfentanil hydrochloride.
Each 1 ml of solution contains alfentanil hydrochloride equivalent to 500 micrograms alfentanil.
Each 2 ml ampoule contains alfentanil hydrochloride equivalent to 1 mg alfentanil.
Each 10 ml ampoule contains alfentanil hydrochloride equivalent to 5 mg alfentanil.

– The other ingredients are sodium chloride, sodium hydroxide (for pH adjustment), water for injections. See section 2 (sodium).

What Alfentanil looks like and contents of the pack
Clear, colourless solution free from visible particles.

2 ml and 10 ml colourless glass ampoules with one point cut. Ampoules are packed in liners. Liners are packed into a cardboard box.

Pack sizes:
5 or 10 ampoules of 2 ml
5 or 10 ampoules of 10 ml

Not all pack sizes may be marketed.

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

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Denmark	Alfentanil Kalceks
Belgium	Alfentanil Kalceks 0,5 mg/ml, solution injectable/pour perfusion Alfentanil Kalceks 0,5 mg/ml, oplossing voor injectie/infusie Alfentanil Kalceks 0,5 mg/ml, Injektions-/Infusionslösung
Finland	Alfentanil Kalceks 0,5 mg/ml injektio-/infuusioneste, liuos
France	ALFENTANIL KALCEKS 0,5 mg/mL, solution injectable/pour perfusion
Germany	Alfentanil Kalceks 500 Mikrogramm/ml Injektions-/Infusionlösung
Ireland	Alfentanil 500 micrograms/ml solution for injection/infusion
Latvia	Alfentanil Kalceks 0,5 mg/ml šķīdums injekcijām/infūzijām
The Netherlands	Alfentanil Kalceks 0,5 mg/ml oplossing voor injectie/infusie
Norway	Alfentanil Kalceks
Portugal	Alfentanilo Kalceks
Sweden	Alfentanil Kalceks
United Kingdom (Northern Ireland)	Alfentanil 500 micrograms/ml solution for injection/infusion

This leaflet was last revised in 08/2022

Place for AS Kalceks internal code
Place for manufacturer internal code

In heart surgery, when used as a sole anaesthetic, doses in the range of 12-50 mg/hour have been used.

Paediatric population
Assisted ventilation equipment should be available for use in children of all ages, even for short procedures in spontaneously breathing children.

Data in children, particularly those aged 1 month to 1 year are limited.

- Neonates (0 to 27 days): The pharmacokinetics are very variable in neonates, particularly in those born preterm. Clearance and protein binding are lower, and a lower dose of alfentanil may be required. Neonates should be closely monitored and the dose of alfentanil titrated according to the response.

- Infants and toddlers (28 days to 23 months): Clearance may be higher in infants and toddlers compared to that in adults. For maintenance of analgesia, the rate of infusion of alfentanil may need to be increased.

- Children (2 to 11 years): Clearance may be slightly higher in children and the rate of infusion may need to be increased.

- Adolescents: The pharmacokinetics of alfentanil in adolescents are similar to those in adults and no specific dosing recommendations are required.

Dosing recommendations for paediatric patients
The wide variability in response to alfentanil makes it difficult to provide dosing recommendations for younger children. For older children a bolus dose of 10-20 mcg/kg alfentanil for induction of anaesthesia (i.e. to supplement to propofol or inhalation anaesthesia) or as an analgesic is considered appropriate. Supplemental boluses of 5-10 mcg/kg alfentanil at appropriate intervals can be administered.

To maintain analgesia in children during surgery, alfentanil infusion rate of 0.5 to 2 mcg/kg/min may be administered. The dose must be titrated up or down according to the needs of the individual patient. When combined with an intravenous anaesthetic agent, the recommended dose is approximately 1 mcg/kg/min.

There may be a higher risk of respiratory complications and muscle rigidity when alfentanil is administered to neonates and very young children.

Hepatic impairment
Reduced doses may be required.

Renal impairment
Clearance of alfentanil is unaltered in renal failure. However, there is an increased free fraction and hence lower doses may be required.

Elderly and debilitated patients
The initial dose must be reduced in elderly (>65 years) and debilitated patients. The effect of the initial dose must be borne in mind when determining supplementary doses.

Patients with concurrent comorbidity
Alfentanil must be titrated with care in patients with the following conditions:
- uncontrolled hypothyroidism;
- lung disease, particularly in the case of reduced respiratory capacity;
- alcoholism or impaired liver and kidney function.

These patients require prolonged postoperative monitoring.