Kalcex

Package leaflet: Information for the user

Esketamine 5 mg/ml solution for injection/infusion
Esketamine 25 mg/ml solution for injection/infusion

Esketamine

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.
- 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 Esketamine is and what it is used for

- Esketamine belongs to a group of medicines called anaesthetic agents (anaesthetics). These medicines are used to put you to sleep during an operation.
- Esketamine can be given alone or in combination with other anaesthetic agents.
- Esketamine can be given as a pain relief/anaesthesia in emergency situations.
- Esketamine can be used for supplementing regional or local anaesthesia.

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

You should not be given Esketamine:
- if you are allergic to esketamine or any of the other ingredients of this medicine (listed in section 6);
- if high blood pressure or increased pressure in the brain (intracranial pressure) is a serious risk for you;
- if you have chest pain (angina) and/or cardiac disease (in such case, Esketamine should not be given as the only anaesthetic);
- if you have a condition called eclampsia or pre-eclampsia (complication of pregnancy that causes high blood pressure);
- in combination with xanthine derivatives or ergometrine (used to induce labour).

If any of the above applies to you, you should not be given this medicine.

Warnings and precautions
Talk to your doctor or nurse before Esketamine is given to you, to help them decide if this medicine is suitable for you:
- if you have decreased blood volume or diminished body fluid, dehydration;
- if you have a heart disease (cardiac insufficiency, coronary artery disease) and untreated high blood pressure;
- if you have chest pain or have had heart attack in the last 6 months;
- if you have heart rhythm disorders;
- if you have increased pressure in the brain and disease or damage of the central nervous system. Increased pressure in the brain has been seen in patients given ketamine (a similar product) as an anaesthetic;
- if you have pulmonary or upper respiratory infection;
- if you have increased pressure in the eye (e.g. glaucoma), penetrating eye injury or if you need an eye examination or eye surgery in which pressure in the eye must not be increased;
- if you have a condition called 'acute intermittent porphyria' (a rare metabolic disorder);
- if you are under the influence of alcohol;
- if you have or have had severe psychiatric problems;
- if you have an overactive thyroid gland (insufficiently treated hyperthyroidism);
- if you have liver disease;
- if you have a history of drug abuse or addiction.

Caution should be observed in situations during childbirth which require relaxed uterus muscle (e.g. threat of a uterus rupture, prolapsed umbilical cord).

Out-patient treatment
You should be accompanied home after out-patient anaesthesia and you should not drink alcohol within the next 24 hours.

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

Tell your doctor or nurse if you are using or have recently used:
- sympathomimetics (e.g. adrenaline or noradrenaline), thyroid hormones, vasopressin (may lead to increased blood pressure, increased heart rate or heart rhythm disorders);
- xanthine derivatives (e.g. aminophylline, theophylline) which may lead to fits or convulsions and therefore these combinations should be avoided;
- sleeping pills, benzodiazepines (e.g. diazepam) or antipsychotics (used for mental disorders) as the duration of effect of Esketamine may be prolonged;
- barbiturates and opiates (such as morphine) given together with Esketamine may prolong the recovery phase after the anaesthetic;
- the anaesthetic effect of some gas anaesthetics (e.g. halothane, isoflurane, desflurane, sevoflurane) is increased by administration of Esketamine so lower doses of gas anaesthetics may be needed;
- muscle relaxants (such as pancuronium-type or suxamethonium–type drugs) as their effects may be prolonged due to the use of esketamine;
- Esketamine should not be used in combination with ergometrine (used to start labor);
- medicines that inhibit CYP3A4 enzyme activity as reduced Esketamine doses may be required when used concomitantly;
- medicines that induce CYP3A4 enzyme activity as increased Esketamine doses may be required when used concomitantly.

Esketamine with food, drink and alcohol
As with all general anaesthetics, you should fast for 4 to 6 hours before you are given Esketamine. You should not drink alcohol within 24 hours of having this anaesthetic.

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 advice before being given this medicine.

Pregnancy
This medicine will not be used during pregnancy unless your doctor comes to the conclusion that the therapeutic benefit for you outweighs any possible hazard for the child.
This medicine could cause breathing problems (decreased breathing rate) to your baby if used during delivery.

Breast-feeding
This medicine can pass into breast milk.
However, it is unlikely to affect the baby when it is used at the recommended doses.

Driving and using machines
Esketamine may reduce reaction ability, which is important in situations requiring special alertness, e.g. when driving a car. Therefore, you should not drive or operate machinery for at least 24 hours after receiving this medicine.
The medicine can affect your ability to drive as it may make you sleepy or dizzy.
- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence if:
  - The medicine has been prescribed to treat a medical or dental problem and
  - You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
  - It was not affecting your ability to drive safely.

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while

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The following information is intended for healthcare professionals only:

pH of solution is 3.0 - 5.0.
Osmolality is 270 - 310 mOsmol/kg.

Incompatibilities
Esketamine is chemically incompatible with barbiturates, diazepam and doxapram because of precipitate formation. They are not to be administered with the same syringe and needle. This medicinal product must not be mixed with other medicinal products except those mentioned in section 'Instructions for use'.

Instructions for use
Parenteral products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit. The solution should not be used if discoloured or cloudy or if particulate matter is observed.

For single use only. The medicinal product should be used immediately after opening the ampoule. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Esketamine solution for injection/infusion can be mixed with sodium chloride 9 mg/ml (0.9%) solution for injection and glucose 50 mg/ml (5%) solution for injection.

Shelf life after dilution
Do not refrigerate. Chemical and physical in-use stability has been demonstrated for 48 hours at 25°C. From a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of user.

taking this medicine.

Esketamine contains sodium
This medicine contains 3.2 mg sodium (main component of cooking/table salt) in each millilitre of solution (Esketamine 5 mg/ml). This is equivalent to 0.16% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 1.2 mg sodium (main component of cooking/table salt) in each millilitre of solution (Esketamine 25 mg/ml). This is equivalent to 0.06% of the recommended maximum daily dietary intake of sodium for an adult.

3. How Esketamine will be given

This medicine will only be given to you in a hospital or prehospital setting by or under the supervision of an anaesthetist (a specialist in anaesthetics).

Esketamine is given as a slow injection into your vein or muscle. If necessary, the injection can be repeated or the preparation can be given as an infusion.

In patients with cirrhosis of the liver or other forms of liver function impairment dose reduction should be considered.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Side effects usually depend on the dose and speed of injection and usually get better without treatment.

Common (may affect up to 1 in 10 people)
- Recovery reactions after anaesthesia. These include vivid dreams, nightmares, dizziness and restlessness.
- Blurred vision.
- Temporary increase in heart beat, increase in blood pressure.
- Effects on breathing during anaesthesia.
- Nausea and vomiting, increased salivation.

Uncommon (may affect up to 1 in 100 people)
- Increased body movements (e.g. muscle twitching), which can resemble seizures, increased eye movements.
- Double vision, increased pressure in the eye.
- Rash.
- Pain and/or redness at the injection site.

Rare (may affect up to 1 in 1,000 people)
- Severe allergic reactions.
- Irregular heart beat, slower heart beat.
- Low blood pressure.

Not known (frequency cannot be estimated from the available data)
- Hallucinations, a feeling of depression and dissatisfaction, anxiety, disorientation.
- Abnormal liver function test results.
- Liver injury.

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 Esketamine

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

This medicinal product does not require any special storage conditions.

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.

6. Contents of the pack and other information

What Esketamine contains
- The active substance is esketamine.

Esketamine ***5 mg/ml***
1 ml of solution contains 5 mg of esketamine (corresponding to 5.77 mg of esketamine hydrochloride).
Each 5 ml ampoule contains 25 mg of esketamine (corresponding to 28.85 mg of esketamine hydrochloride).

Esketamine ***25 mg/ml***
1 ml of solution contains 25 mg of esketamine (corresponding to 28.85 mg of esketamine hydrochloride).
Each 2 ml ampoule contains 50 mg of esketamine (corresponding to 57.7 mg of esketamine hydrochloride).
Each 10 ml ampoule contains 250 mg of esketamine (corresponding to 288.5 mg of esketamine hydrochloride).

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

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

2 ml, 5 ml or 10 ml of solution in colourless glass ampoules with one point cut. Ampoules are marked with a specific colour ring code for each strength and volume.
Ampoules are packed in liners. Liners are packed into a cardboard box.

Pack sizes:

Esketamine ***5 mg/ml***
5 or 10 ampoules of 5 ml

Esketamine ***25 mg/ml***
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

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

Latvia	Esketamine Kalceks 5 mg/ml, 25 mg/ml šķīdums injekcijām/infūzijām
Austria	Esketamin Kalceks 5 mg/ml 25 mg/ml Injektions-/Infusionlösung
Belgium	Esketamine Kalceks 5 mg/ml, 25 mg/ml, solution injectable/pour perfusion Esketamine Kalceks 5 mg/ml, 25 mg/ml, oplossing voor injectie/infusie Esketamin Kalceks 5 mg/ml, 25 mg/ml, Injektions-/Infusionslösung
Finland	Esketamine Kalceks 5 mg/ml, 25 mg/ml injektio-/infuusioneste, liuos
Germany	Esketamin Ethypharm 5 mg/ml, 25 mg/ml Injektions-/Infusionlösung
The Netherlands	Esketamine Kalceks 5 mg/ml, 25 mg/ml, oplossing voor injectie/infusie
Slovenia	Esketamin Kalceks 5 mg/ml, 25 mg/ml raztopina za injiciranje/infundiranje
Sweden	Esketamine Kalceks
United Kingdom (Northern Ireland)	Esketamine 5 mg/ml, 25 mg/ml solution for injection/infusion

This leaflet was last revised in 03/2022

Place for AS Kalceks internal code
Place for manufacturer internal code

After dilution to 1 mg/ml and 2 mg/ml with the above mentioned solutions Esketamine solution for injection/infusion is chemically and physically stable when in contact with PVC and EVA infusion bags, PVC and polyethylene tubing, and polypropylene and polycarbonate syringes.

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).