Package leaflet: Information for the patient
KETALAR® 10 mg/ml SOLUTION FOR INJECTION / INFUSION
KETALAR® 50 mg/ml SOLUTION FOR INJECTION / INFUSION
Ketamine hydrochloride

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- If you have been given Ketalar in an emergency you will not have had a chance to read this leaflet. Your doctor or anaesthetist will have considered the important safety information in this leaflet, but your urgent need for treatment may have been more important than some of the usual precautions.
- If you are discharged on the same day as the operation, you should be accompanied by another adult.
- 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 4.4.

What is in this leaflet

1. What Ketalar Injection is and what it is used for

- This medicine contains ketamine hydrochloride which belongs to a group of medicines called anaesthetic agents, which are used to put you to sleep during an operation. Ketalar may be used in both routine and emergency surgery.
- Ketalar is used in adults, the elderly and children.
- Ketalar can be given alone or in combination with other anaesthetic agents.

2. What you need to know before you are given Ketalar Injection

Do not take Ketalar:

- if you are allergic (hypersensitivity) to ketamine hydrochloride or any of the other ingredients of this medicine (listed in section 6).
- if you are suffering from any condition in which an increase in blood pressure may be harmful to you or have suffered in the past from a medical condition which may have been caused/made worse by an increase in blood pressure.
- if you have been pregnant and during your pregnancy you have suffered from a condition called eclampsia or pre-eclampsia which causes an increase in your blood pressure.
- if you have recently suffered a stroke or serious head or brain injury.
- have severe heart disease.
- if you are pregnant, trying to become pregnant or breast-feeding. However, Ketalar may be used in caesarean section surgery and vaginal delivery.
- if you have a history of or have current mental health problems.

Warnings and precautions

Talk to your doctor or nurse if any of the following apply to you, to help them decide if Ketalar is suitable for you. If you:

- regularly drink alcohol or have recently drank a large amount of alcohol.
- have a history of drug abuse or addiction.
- have a chest infection or problems breathing.
- have problems with your liver.
- have increased pressure in the eye (glaucoma).
- have an inherited disease that affects the blood (porphyria).
- have ever had seizures (i.e. fits).
- have mental health problems (e.g schizophrenia, hallucinations or psychosis).
- are receiving treatment for your thyroid gland.
- have had any injury to your head or abnormal growth on the brain.
- suffer from dehydration or have recently lost a lot of blood.
- suffer from heart failure or have had a heart attack or have any other form of heart problem.
- have mild to moderate increase in high blood pressure.
- have an irregular heartbeat.

If before your operation the pressure in your spinal cord is raised, your anaesthetist will pay special attention to this during the operation.

Long term use

Ketalar is not indicated and not recommended for long-term use.

Bladder infection sometimes accompanied by bleeding, and liver problems have been reported particularly with long-term use (> 3 days) or drug abuse. See section 4 Possible side effects.

Drug Abuse and Addiction

If used on a daily basis for a few weeks, dependence and tolerance may develop, particularly in individuals with a history of drug abuse and dependence. Other adverse effects have also been reported: see “Long-Term Use”.

Other medicines and Ketalar

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

Ketalar is usually given together with other medicines during surgery.

- When used for an operation on the chest or abdominal organs, Ketalar is usually combined with a pain-killer. This is not because you would be conscious of any pain but to stop any reflexes which might be triggered.
- Tell your doctor if you are taking barbiturates (e.g. thiopental) and narcotics (morphine-like drugs) since use with Ketalar may slow your recovery from anaesthesia, as may the use of medication given before the operation such as benzodiazepines. Otherwise, Ketalar may be used with all other general and local anaesthetics.
- Sympathomimetics (for example adrenaline or noradrenaline) and vasopressin may lead to an increase in blood pressure and in heart rate.

Ketalar must be used with particular care on anyone who is a chronic alcoholic, who is intoxicated (drunk) or who has a history of drug abuse or dependence.

The use of Ketalar with other central nervous system (CNS), blocking drugs (e.g. atracurium, tubocurarine, ethanol, phenothiazines) may stop the transmission of nerves to the muscles. This may also slow down your rate of breathing.

Tell your Doctor if you are taking Diazepam, or any other medicine in the same group (known as benzodiazepines), as it increases the effect of ketamine and the length of time it takes for Ketamine to be removed from your body. As a result the dose of Ketalar may need to be adjusted.

If before your operation the pressure inside your spinal cord is raised, your anaesthetist will pay special attention to this during the operation.

Ketalar should be given with care to patients taking thyroid hormones, as they have a high risk of developing high blood pressure.

Using Ketalar with anti-hypertensive agents also increases the risk of developing low blood pressure and changes in the heart's rhythm.

Using Ketalar with ergometrine may lead to an increase in blood pressure.

Using Ketalar with theophylline or aminophylline may cause unpredicted seizures.

Ketalar with food and drink
It is normal not to eat or drink for at least six hours before an operation; therefore Ketalar is usually given when your stomach is empty. If in an emergency, this is not possible, Ketalar may still be used.

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.

Driving and using machines
Caution should be taken when driving or operating machines following treatment with Ketalar. You should not drive or operate machines in the first 24 hours after your operation.

Ketalar contains sodium
Ketalar 10 mg/ml Injection contains 53 mg of sodium (main component of cooking/table salt) in each vial. This is equivalent to 2.65% of the recommended maximum daily dietary intake of sodium for an adult.

3. How Ketalar Injection is given

- Ketalar is not indicated nor recommended for long term use.
- Except in an emergency, Ketalar should only be used in hospitals by experienced anaesthetists with resuscitation equipment available.
- Before your operation you will usually be given a medicine such as atropine or hyoscine to dry up your secretions (body fluids like saliva and tears) and another medicine called a benzodiazepine. The benzodiazepine will help you to relax and help to prevent a side effect known as "emergence reaction".
- The dose of Ketalar depends on its use and varies from person to person. When injected directly into a vein at a dose of 2 mg for every kg of your bodyweight, Ketalar produces unconsciousness within 30 seconds and this lasts for 5 to 10 minutes. Because it works so quickly, it is important to be lying down, or supported in some other way when the drug is given. When Ketalar is injected into a

muscle, at a dose of 10 mg for every kg of bodyweight, it takes longer to work (3 to 4 minutes) but lasts 12 to 25 minutes.

- Your anaesthetist will then keep you anaesthetised with either:
  - another anaesthetic
  - more Ketalar given by injection into a muscle or vein, or in a drip (infusion)
  - Ketalar together with another anaesthetic.
- When it is injected directly into a vein, Ketalar is given over at least a minute so that it does not slow your breathing too much. If breathing is slowed, it can be helped mechanically.
- While you are anaesthetised, your anaesthetist will watch over you constantly, paying particular attention to your breathing, airways, reflexes, the degree of anaesthesia and the condition of your heart.
- You should not be released from hospital until you have completely recovered from the anaesthetic. If you are discharged on the same day as the operation, you should be accompanied by another adult (see also the section on 'Driving and using machines').

- **If you are given more Ketalar than you should** you may experience breathing difficulties. Your doctor or nurse may provide you with equipment to help you breath.

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 everyone gets them.

Tell your doctor **immediately** if you notice pain, inflammation of the skin or rash at the injection site. Ketalar can sometimes cause allergic symptoms ('anaphylaxis') such as breathing problems, swelling and rash. Some people have hallucinations, vivid dreams, nightmares, feel ill at ease, confused, anxious or behave irrationally while recovering from anaesthesia with Ketalar. These side effects are collectively known as an 'emergence reaction'. You will be allowed to recover from the anaesthetic in a quiet place and this helps to prevent the reaction (see Section 3 under 'How Ketalar Injection is given').

Common: may affect up to 1 in 10 people

- the following, while recovering from anaesthesia (these are collectively known as an 'emergence reaction'): hallucinations (which may include flashbacks or floating sensation), vivid dreams, nightmares, feeling ill at ease, confused, anxious and irrational behaviour.
- unusual eye movements, increased muscle tone and muscle twitches (which may resemble 'fits' or convulsions).
- double vision.
- increased blood pressure and increased pulse rate.
- breathing more quickly.
- nausea, vomiting.
- skin inflammation/rash.

Uncommon: may affect up to 1 in 100 people

- loss of appetite.
- feeling anxious.
- slowing of heart rate, changes in heart rhythm.
- lowering of blood pressure.
- breathing more slowly, narrowing of the voice-box leading to difficulty in breathing.
- pain, inflammation of the skin or rash at the injection site.

Rare: may affect up to 1 in 1,000 people

- allergic symptoms ('anaphylaxis') such as breathing problems, swelling and rash.

- drifting in and out of consciousness (with feeling of confusion and hallucinations), flashbacks, feeling ill at ease, sleeplessness, feeling disorientated.
- affect on the reflexes which keep your airways clear, resulting in temporary inability to breathe.
- increase in salivation.
- inflammation of the bladder and/or pain when urinating ('cystitis'). The appearance of blood in the urine may also occur.

Not known: frequency cannot be estimated from the available data
- raised pressure in the eyes.
- abnormal results to liver function tests.
- drug-induced liver injury (when taken for more than 3 days).

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. 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 Ketalar Injection

- 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 label and carton after EXP. The expiry dates refers to the last day of that month. Your pharmacist will check this before the injection is given.
- This medicinal product does not require any special temperature storage conditions.
- Store in the original container. Keep the vial in the outer carton in order to protect from light. Do not freeze.

6. Contents of the pack and other information

What Ketalar contains
- The active ingredient is ketamine hydrochloride

Each 20 ml solution contains 10 mg of ketamine base per ml
Each 10 ml solution contains 50 mg of ketamine base per ml

- The other ingredients are:

10 mg/ml: sodium chloride (salt) (see section 2 "Ketalar contains Sodium"), water for injections and a preservative (benzethonium chloride).
50 mg/ml: water for injections and a preservative (benzethonium chloride).

What Ketalar looks like and contents of the pack

Ketalar is a clear solution for injection or infusion available in single glass vials and comes in two strengths. Each carton contains 1 vial.

Marketing Authorisation Holder:
Pfizer Healthcare Ireland, 9 Riverwalk, National Digital Park, Citywest Business Campus, Dublin 24, Ireland.

Manufacturer:
Siegfried Hameln GmbH, Langes Feld 13, 31789 Hameln, Germany.

Company contact address:
For further information on this medicine please contact Medical Information at Pfizer Healthcare Ireland, 9 Riverwalk, National Digital Park, Citywest Business Campus, Dublin 24, Ireland.

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The following information is intended for healthcare professional only. For full prescribing information please refer to the SmPC.

Posology and method of administration

For intravenous infusion, intravenous injection or intramuscular injection.

Note: All doses are given in terms of ketamine base

Ketalar is not indicated nor recommended for long term use (see sections 4.1 and 4.4).

Adults, elderly (over 65 years) and children
For surgery in elderly patients ketamine has been shown to be suitable either alone or supplemented with other anaesthetic agents.

Preoperative preparations

1. Ketalar has been safely used alone when the stomach was not empty. However, since it may also cause vomiting and since the need for supplemental agents and muscle relaxants cannot be predicted, when preparing for elective surgery it is advisable that nothing be given by mouth for at least six hours prior to anaesthesia.

2. Ketamine increases salivation. Premedication with an anticholinergic agent (e.g. atropine, hyoscine, glycopyrrolate) or another drying agent should be given at an appropriate interval prior to induction to reduce ketamine-induced hypersalivation (see section 4.8).

3. Midazolam, diazepam, lorazepam, or flunitrazepam used as a premedicant or as an adjunct to ketamine, have been effective in reducing the incidence of emergence reactions.

Onset and duration

As with other general anaesthetic agents, the individual response to Ketalar is somewhat varied depending on the dose, route of administration, age of patient, and concomitant use of other agents, so that dosage recommendation cannot be absolutely fixed. The dose should be titrated against the patient's requirements.

Because of rapid induction following intravenous injection, the patient should be in a supported position during administration. An intravenous dose of 1 – 2 mg/kg of bodyweight usually produces surgical anaesthesia within 30 seconds – 1 minute after injection and the anaesthetic effect usually lasts 5 to 10 minutes. An intramuscular dose of 10 mg/kg of bodyweight usually produces surgical anaesthesia within 3 to 4 minutes following injection and the anaesthetic effect usually lasts 12 to 25 minutes. Return to consciousness is gradual.

A. Ketalar as the sole anaesthetic agent

Intravenous Infusion

The use of Ketalar by continuous infusion enables the dose to be titrated more closely, thereby reducing the amount of drug administered compared with intermittent administration. This results in a shorter recovery time and better stability of vital signs.

A solution containing 1mg/ml of ketamine in dextrose 5% or sodium chloride 0.9% is suitable for administration by infusion.

If fluid restriction is required, ketamine can be added to 250 ml infusion fluid to provide a ketamine concentration of 2 mg/ml. Ketamine vials in the 10 mg/ml concentration are not recommended for dilution.

Induction

An infusion corresponding to 0.5- 2 mg/kg as total induction dose.

Maintenance of anaesthesia

Anaesthesia may be maintained using a microdrip infusion of 10 - 40 microgram/kg/min (approximately 1 - 3 mg/min).

The rate of infusion will depend on the patient's reaction and response to anaesthesia. The dosage required may be reduced when a long acting neuromuscular blocking agent is used.

Intermittent Injection

Induction

Intravenous Route

The initial dose of Ketalar administered intravenously may range from 1mg/kg to 4.5 mg/kg. The average amount required to produce 5 to 10 minutes of surgical anaesthesia has been 2.0 mg/kg. It is recommended that intravenous administration be accomplished slowly (over a period of 60 – 120 seconds). More rapid administration may result in respiratory depression and enhanced pressor response.

Dosage in Obstetrics

In obstetrics, for vaginal delivery or in caesarean section, intravenous doses ranging from 0.2 to 1.0 mg/kg are recommended (see section 4.6 Fertility, pregnancy and lactation). However, data are lacking for maintenance infusion of ketamine in the parturient population and dosing recommendations cannot be made.

Intramuscular Route

The initial dose of Ketalar administered intramuscularly may range from 6.5 mg/kg to 13 mg/kg, usually 10 mg/kg. A low initial intramuscular dose of 4 mg/kg has been used in diagnostic manoeuvres and procedures not involving intensely painful stimuli. A dose of 10 mg/kg will usually produce 12 to 25 minutes of surgical anaesthesia.

Hepatic Insufficiency

Dose reductions should be considered in patients with cirrhosis or other types of liver impairment (see section 4.4).

Dosage in Obstetrics

Data are lacking for intramuscular injection in the parturient population, and dosing recommendations cannot be made. Available pharmacokinetic data are presented in section 5.2.

Maintenance of anaesthesia

Lightening of anaesthesia may be indicated by nystagmus, movements in response to stimulation, and vocalization. Anaesthesia is maintained by the administration of additional doses of Ketalar by either the

intravenous or intramuscular route. However, data are lacking regarding the maintenance dosage of ketamine in the parturient population and dosing recommendations cannot be made.

Each additional dose is from ½ to the full induction dose recommended above for the route selected for maintenance, regardless of the route used for induction.

The larger the total amount of Ketalar administered, the longer will be the time to complete recovery.

Purposeless and tonic-clonic movements of extremities may occur during the course of anaesthesia. These movements do not imply a light plane and are not indicative of the need for additional doses of the anaesthetic.

B. Ketalar as induction agent prior to the use of other general anaesthetics

Induction is accomplished by a full intravenous or intramuscular dose of Ketalar as defined above. If Ketalar has been administered intravenously and the principal anaesthetic is slow-acting, a second dose of Ketalar may be required 5 to 8 minutes following the initial dose. If Ketalar has been administered intramuscularly and the principal anaesthetic is rapid-acting, administration of the principal anaesthetic may be delayed up to 15 minutes following the injection of Ketalar.

C. Ketalar as supplement to anaesthetic agents

Ketalar is clinically compatible with the commonly used general and local anaesthetic agents when an adequate respiratory exchange is maintained. The dose of Ketalar for use in conjunction with other anaesthetic agents is usually in the same range as the dosage stated above; however, the use of another anaesthetic agent may allow a reduction in the dose of Ketalar.

Management of patients in recovery

Following the procedure the patient should be observed but left undisturbed. This does not preclude the monitoring of vital signs. If, during the recovery, the patient shows any indication of emergence delirium, consideration may be given to the use of diazepam (5 to 10 mg I.V. in an adult). A hypnotic dose of a thiobarbiturate (50 to 100 mg I.V.) may be used to terminate severe emergence reactions. If any one of these agents is employed, the patient may experience a longer recovery period.

Incompatibilities
Ketalar is chemically incompatible with barbiturates and diazepam because of precipitate formation. Therefore, these should not be mixed in the same syringe or infusion fluid.
This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

Shelf life

Unopened: 5 years.
After opening: From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately.
After dilution: Use immediately after dilution.
This product should be diluted immediately after opening.
For single use only. Discard any unused product at the end of each operating session.

Special precautions for storage

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

Special precautions for disposal and other handling

For single use only. Discard any unused product at the end of each operating session.

After opening: From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. Discard unused product after dosing.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

This product has been shown to be compatible with dextrose 5% and sodium chloride 0.9%. See section 4.2.