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For the use of a Registered medical practitioner, Hospital or Laboratory only

KETAPIL

Ketamine Hydrochloride Injection USP
(50mg/ml,10 ml)

COMPOSITION
Each ml contains:

Ketamine Hydrochloride	USP	
Equivalent to Ketamine		50mg
Benzethonium Chloride	USP	0.01% w/v
(As Preservative)		
Water for Injection	USP	q.s.

PHARMACEUTICAL FORM
A clear, colourless liquid filled in amber colour USP Type I glass vial with rubber bung and aluminium seal having dark red flip on top.

THERAPEUTIC INDICATIONS
- As an anaesthetic agent for diagnostic and surgical procedures. When used by intravenous or intramuscular injection, Ketamine is best suited for short procedures. With additional doses, or by intravenous infusion, Ketamine can be used for longer procedures. If skeletal muscle relaxation is desired, a muscle relaxant should be used and respiration should be supported.
- For the induction of anaesthesia prior to the administration of other general anaesthetic agents.
- To supplement other anaesthetic agents. Specific areas of application or types of procedures.
- When the intramuscular route of administration is preferred.
- Debridement, painful dressings, and skin grafting in burned patients, as well as other superficial surgical procedures. Neurodiagnostic procedures such as pneumoencephalograms, ventriculograms, myelograms, and lumbar punctures.
- Diagnostic and operative procedures of the eye, ear, nose, and mouth, including dental extractions.
- Note: Eye movements may persist during ophthalmological procedures.
- Anaesthesia in poor-risk patients with depression of vital functions or where depression of vital functions must be avoided, if at all possible.
- Orthopaedic procedures such as closed reductions, manipulations, femoral pinning, amputations, and biopsies.
- Sigmoidoscopy and minor surgery of the anus and rectum, circumcision and pilonidal sinus. Cardiac catheterisation procedures.
- Caesarean section; as an induction agent in the absence of elevated blood pressure. Anaesthesia in the asthmatic patient, either to minimise the risks of an attack of bronchospasm developing, or in the presence of bronchospasm where anaesthesia cannot be delayed.

DOSAGE AND METHOD OF ADMINISTRATION
Preoperative preparations
Ketamine has been safely used alone when the stomach was not empty. However, 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
Premedication with an anticholinergic agent (e.g. atropine, hyoscine or glycopyrolate) or another drying agent should be given at an appropriate interval prior to induction to reduce Ketamine-induced hypersalivation. 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
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 2 mg/kg of bodyweight usually produces surgical anaesthesia within 30 seconds 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.

Induction
Intravenous Infusion
The use of Ketamine 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 1 mg/ml of Ketamine in dextrose 5% or sodium chloride 0.9% is suitable for administration by infusion.

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. It is recommended that Ketamine Hydrochloride injection be administered slowly (over a period of 60 seconds). More rapid administration may result in respiratory depression and enhanced pressor response.

Intramuscular Route
The initial dose of Ketamine administered intramuscularly may range from 6.5 mg/kg to 13 mg/kg (in terms of Ketamine base). 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.

Maintenance of general 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 Ketamine by either the intravenous or intramuscular route. Each additional dose is from half 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 Ketamine 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.

Ketamine as supplement to anaesthetic agents
Ketamine is clinically compatible with the commonly used general and local anaesthetic agents when an adequate respiratory exchange is maintained. The dose of Ketamine 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 Ketamine.

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.

Method of administration
For intravenous infusion, intravenous injection or intramuscular injection.
NOTE: All doses are given in terms of Ketamine base
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.
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.

CONTRAINDICATIONS
It is contra-indicated in persons in whom an elevation of blood pressure would constitute a serious hazard. Ketamine Hydrochloride is contraindicated in patients who have shown hypersensitivity to the drug or its components. Ketamine Hydrochloride should not be used in patients with eclampsia or pre-eclampsia, severe coronary or myocardial disease, cerebrovascular accident or cerebral trauma.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Ketamine Hydrochloride injection should be used by or under the direction of physicians experienced in administering general anesthetics and in maintenance of an airway and in the control of respiration.
As with any general anaesthetic agent, resuscitative equipment should be available and ready for use. Ketamine is metabolised in the liver and hepatic clearance is required for termination of clinical effects. A prolonged duration of action may occur in patients with cirrhosis or other types of liver impairment. Dose reductions should be considered in these patients. Abnormal liver function tests associated with Ketamine use have been reported,

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particularly with extended use (>3 days) or drug abuse.
Since an increase in cerebrospinal fluid (CSF) pressure has been reported during Ketamine anaesthesia, Ketamine should be used with special caution in patients with preanaesthetic elevated cerebrospinal fluid pressure. Because of the substantial increase in myocardial oxygen consumption, Ketamine should be used in caution in patients with hypovolemia, dehydration or cardiac disease, especially coronary artery disease (e.g. congestive heart failure, myocardial ischemia and myocardial infarction). In addition Ketamine should be used with caution in patients with mild-to-moderate hypertension and tachyarrhythmias.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION FERTILITY, PREGNANCY AND LACTATION
Ketamine Hydrochloride Injection crosses the placenta. This should be borne in mind during operative obstetric procedures in pregnancy. With the exception of administration during surgery for abdominal delivery or vaginal delivery, no controlled clinical studies in pregnancy have been conducted. The safe use in pregnancy, and in lactation, has not been established and such use is not recommended.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Patients should be cautioned that driving a car, operating hazardous machinery or engaging in hazardous activities should not be undertaken for 24 hours or more after anaesthesia.
This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:
The medicine is likely to affect your ability to drive
Do not drive until you know how the medicine affects you
It is an offence to drive while under the influence of this medicine

UNDESIRABLE 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.
It can sometimes cause allergic symptoms ('anaphylaxis') such as breathing problems, swelling and rash. Some people have hallucinations, vivid dreams, and nightmares, feel ill at ease, confused, anxious or behave irrationally while recovering from anaesthesia. These side effects are collectively known as an 'emergence reaction'.
Common side effects may affect up to 1 in 10 people.
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 side effects may affect up to 1 in 100 people.
Loss of appetite, feeling anxious.
Rare side effects may affect up to 1 in 1000 people.
- Allergic symptoms ('anaphylaxis') such as breathing problems, swelling and rash.
- Drifting in and out of consciousness (with feeling of confusion and hallucinations).
- 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.

OVERDOSE
Respiratory depression can result from an overdosage of Ketamine Hydrochloride. Supportive ventilation should be employed. Mechanical support of respiration that will maintain adequate blood oxygen saturation and carbon dioxide elimination is preferred to administration of analeptics.
Ketamine Hydrochloride Injection has a wide margin of safety; several instances of unintentional administration of overdoses of Ketamine Hydrochloride Injection (up to 10 times that usually required) have been followed by prolonged but complete recovery.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Ketamine induces sedation, immobility, amnesia and marked analgesia. The anesthetic state produced by Ketamine has been termed “dissociative anesthesia” in that it appears to selectively interrupt association pathways of the brain before producing somesthetic sensory blockade. It may selectively depress the thalamoneocortical system before significantly obtunding the more ancient cerebral centers and pathways (reticular-activating and limbic systems). Numerous theories have been proposed to explain the effects of Ketamine, including binding to N-methyl-D-aspartate (NMDA) receptors in the CNS, interactions with opiate receptors at central and spinal sites and interaction with norepinephrine, serotonin and muscarinic cholinergic receptors. The activity on NMDA receptors may be responsible for the analgesic as well as psychiatric (psychosis) effects of Ketamine. Ketamine has sympathomimetic activity resulting in tachycardia, hypertension, increased myocardial and cerebral oxygen consumption, increased cerebral blood flow and increased intracranial and intraocular pressure. Ketamine is also a potent bronchodilator. Clinical effects observed following Ketamine administration include increased blood pressure, increased muscle tone (may resemble catatonia), opening of eyes (usually accompanied by nystagmus) and increased myocardial oxygen consumption.
Pharmacokinetic properties
Ketamine is rapidly distributed into perfused tissues including brain and placenta. Animal studies have shown ketamine to be highly concentrated in body fat, liver and lung. Biotransformation takes place in liver. Termination of anaesthetic is partly by redistribution from brain to other tissues and partly by metabolism. Elimination half-life is approximately 2-3 hours, and excretion renal, mostly as conjugated metabolites.

LIST OF EXCIPIENTS
Disodium Edetate BP, Sodium Chloride BP, Hydrochloric Acid BP

INCOMPATIBILITIES
Not Applicable

SHELF LIFE
36 Months

STORAGE
Store below 30°C in a dry place away from light.

NATURE AND CONTENTS OF CONTAINER
10ml Amber colour USP Type-I Glass Vial with rubber bung aluminum seal having flip-on-top.

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING
Keep out of reach and sight of children.

Manufactured by:

Psychotropics India Limited
Plot No. 12 & 12A, Industrial Park-2,
Phase-1, Salempur, Mehdood-2,
Haridwar-249403 (Uttarakhand) India
www.pilindia.in

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