# PRODUCT MONOGRAPH

# [N]KETAMINE HYDROCHLORIDE INJECTION USP
**(ketamine hydrochloride)**
**10 mg/mL**
**50 mg/mL**

**Parenteral General Anesthetic**

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**[N]Ketamine Hydrochloride Injection USP**
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10 mg/mL
50 mg/mL

## THERAPEUTIC CLASSIFICATION

Parenteral General Anesthetic

## ACTION AND CLINICAL PHARMACOLOGY

Ketamine hydrochloride is a rapid-acting, nonbarbiturate general anesthetic. It produces an anesthetic state characterized by profound analgesia, normal pharyngeal-laryngeal reflexes and normal or slightly enhanced skeletal muscle tone. Mild cardiac stimulation and occasionally respiratory depression occur

The anesthetic state produced by ketamine hydrochloride has been termed "dissociative anesthesia" in that it appears to selectively interrupt association pathways of the brain before producing somesthetic sensory blockage. Ketamine hydrochloride decreases the activity of the neocortex and subcortical structures (thalamus) and increases the activity in the limbic system and reticular substance.

Following administration of recommended doses of ketamine hydrochloride, blood pressure and pulse rate are usually moderately and temporarily increased. In 12,283 procedures, the median systolic rise was 24% and the median diastolic rise was 22%.

Respiration is usually unaffected. Mild stimulation occasionally occurs. However, transient respiratory depression (rate and tidal volume) may occur and is generally associated with rapid (less than 60 seconds) intravenous administration. Blood gas tensions ($PO_2$ and $PCO_2$) are relatively unaffected.

A patent airway is maintained partly by virtue of unimpaired pharyngeal and laryngeal reflexes.

Ketamine undergoes N-demethylation and hydroxylation of the cyclohexanone ring, with the formation of water-soluble conjugates which are excreted in the urine. Further oxidation also occurs with the formation of a cyclohexanone derivative. The unconjugated N-demethylated metabolite was found to be less than one sixth as potent as ketamine. The unconjugated demethyl cyclohexanone derivative was found to be less than one tenth as potent as ketamine.

Studies in human subjects resulted in the mean recovery of 91% of the dose in the urine and 3% in the feces. Peak plasma levels averaged about 0.75 mcg/mL and CSF levels were about 0.2 mcg/mL, 1 hour after dosing.

## INDICATIONS AND CLINICAL USE

1. **As the sole anesthetic agent** for recommended diagnostic and surgical procedures. Although best suited to short procedures, Ketamine Hydrochloride Injection USP can be used, with additional doses, for longer procedures.

   **NOTE:** If skeletal muscle relaxation is desired, a muscle relaxant should be used. In surgical procedures involving visceral pain pathways, Ketamine Hydrochloride Injection USP should be supplemented with an agent that obtunds visceral pain.

2. **For the induction of anesthesia** prior to the administration of other general anesthetic agents.

3. **To supplement low potency agents** such as nitrous oxide.

Specific areas of application or types of procedures have included:

1. Neurodiagnostic procedures such as pneumoencephalograms, ventriculograms, myelograms, and lumbar punctures.

2. Diagnostic and operative procedures of the eye, ear, nose and mouth. Eye movements may persist during ophthalmological procedures. Before Ketamine Hydrochloride Injection USP can be recommended for intraocular surgery, more data are required.

3. Diagnostic and operative procedures of the pharynx, larynx or bronchial tree.

   **NOTE:** Adequate muscle relaxants must be used in such procedures (see CONTRAINDICATIONS and PRECAUTIONS).

4. Sigmoidoscopy and minor surgery of the anus and rectum, and circumcision.

5. Extraperitoneal procedures used in gynecology such as dilation and curettage. More data is required before Ketamine Hydrochloride Injection USP can be recommended for use in obstetrical delivery or cesarean section. (See WARNINGS and PRECAUTIONS).

6. Orthopedic procedures such as closed reductions, manipulations, femoral pinning, amputations, and biopsies.

7. Dental extractions.

8. Miscellaneous procedures of general surgery such as debridement, painful dressings, and skin grafting in burn patients.

9. Anesthesia in poor-risk patients where depression of vital functions precludes the use of other general anesthetics.

10. In procedures where the intramuscular route of administration is preferred.

## CONTRAINDICATIONS

Ketamine Hydrochloride Injection USP is contraindicated :

- in persons with a history of cerebrovascular accident.
- in those in whom a significant elevation of blood pressure would constitute a serious hazard, such as patients with significant hypertension.
- in persons with severe cardiac decompensation.
- in surgery of the pharynx, larynx, or bronchial tree unless adequate muscle relaxants are used.
- in those showing hypersensitivity to ketamine.

## WARNINGS

1. Ketamine hydrochloride is for use only **by or under the direction of physicians experienced in administering general anesthetics** and in the maintenance of an airway and in the control of respiration.

2. Cardiac function should be continually monitored during the procedure in patients found to have hypertension or cardiac decompensation.

3. Hepatocellular and cholestatic pattern of elevations in liver enzymes as well as biliary ductal dilatations and hepatic fibrosis have been reported following exposure to ketamine especially with repeated doses, chronic use or misuse. Regular monitoring of liver function is recommended with repeated use of ketamine. Treatment discontinuation should be considered.

4. Barbiturates and ketamine hydrochloride, being chemically incompatible because of precipitate formation, **should not** be injected from the same syringe.

5. Barbiturates and narcotics, being central nervous system depressants, may prolong recovery time if used concurrently with ketamine hydrochloride.

6. Postoperative confusional states may occur during the recovery period (see item 6 under PRECAUTIONS).

7. Respiratory depression may occur with overdosage or too rapid administration of ketamine hydrochloride, in which case supportive ventilation should be employed. Mechanical support of respiration is preferred to administration of analeptics.

8. An increase in cerebrospinal fluid pressure has been reported following the administration of ketamine hydrochloride. Special caution should be exercised when using ketamine hydrochloride in cases with pre-existing elevated intracranial pressure, and in those cases with normal intracranial pressure in which, in the opinion of the physician, a rise in such pressure would entail special risks. Use with extreme caution in patients with preanesthetic elevated cerebrospinal pressure.

9. Although animal studies of teratogenicity, fertility, and reproduction supported the safety of ketamine hydrochloride, its safe use in human pregnancy has not been established. (see PRECAUTIONS).

10. The safety of epidural administration of ketamine hydrochloride has not been established and is therefore not recommended. A case of paraplegia with sensory deficit and partial recovery in human has been reported following epidural administration of ketamine. Studies done on the neurotoxicity of ketamine on the spinal cord were inconclusive. More studies investigating the neurotoxicity and clinical effects of ketamine hydrochloride on the spinal cord must be done before epidural administration of ketamine hydrochloride can be recommended.

11. Ketamine hydrochloride should only be used after careful consideration of the benefit/risk assessment.

## PRECAUTIONS

1. Because pharyngeal and laryngeal reflexes are usually active, ketamine should not be used alone in surgery or diagnostic procedures of the pharynx, larynx, or bronchial tree. Mechanical stimulation of the pharynx should be avoided, whenever possible if ketamine is used alone. Muscle relaxants with proper attention to respiration, may be required in both of these instances.

2. Precautions should be used in patients with upper respiratory infection because of the increased danger of respiratory difficulties, such as laryngospasm, in these cases.

3. Resuscitative equipment should be available and ready for use.

4. The initial intravenous dose should be administered over a period of 60 seconds. More rapid administration may result in respiratory depression and enhanced pressor response.

5. In surgical procedures involving visceral pain pathways, ketamine hydrochloride should be supplemented with an agent that obtunds visceral pain.

6. During recovery from anesthesia, the patient may go through a phase of emergence reaction characterized by vivid dreams, dream-like states, confusion (with or without psychomotor activity), excitement, delirium, irrational behavior and occasionally hallucinations. In some cases these states have been accompanied by confusion, excitement, and irrational behavior which a few patients recall as an unpleasant experience. The duration ordinarily is no more than a few hours; in a few cases, however, recurrences have taken place up to 24 hours postoperatively. No residual psychological effects are known to have resulted from the use of ketamine.

   In 12,283 procedures, post anesthetic emergence responses were broken down in the following parameters and the incidence of reaction was:

| **Reaction** | **Number** | **Percent** | **Percent In 15 to 35 Yrs. Age Group** |
|---|---|---|---|
| Dreams, pleasant or not specified | 679 | 5.44 | 9.6 |
| Dreams, unpleasant | 199 | 1.62 | 3.1 |
| Hallucinations | 152 | 1.23 | 1.6 |
| Confusion, with and without vocalization | 327 | 2.66 | 4.7 |
| Excitement or irrational behavior | 111 | 0.89 | 1.8 |
| Psychic abnormalities | 62 | 0.51 | 0.8 |
| **Overall Rate**[†] | | **11.0** | **19.4** |

[†]Some procedures have multiple emergence reactions, therefore the overall rate is less than the sum of the reactions.

As this table shows, the emergence reactions are more common in the 15 to 35 years group.

The reactions tabled above occurred in the majority of instances in patients in whom droperidol or diazepam had not been used as premedications (see DOSAGE AND ADMINISTRATION).

The incidence of these emergence phenomena is least in the young (15 years of age or less) and elderly (over 65 years of age) patient. Also, they are less frequent when the drug is given intramusculary and the incidence is reduced as experience with the drug is gained.

The incidence of psychological manifestations during emergence, particularly dream-like observations and emergence delirium, may be reduced by using lower recommended dosages of ketamine in conjunction with intravenous diazepam during induction and maintenance of anesthesia.

The incidence of emergence reactions may be reduced if verbal, tactile and visual stimulation of the patient is avoided during the recovery period; and certainly until the patient is fully conscious and able to be returned to the ward. These precautions do not preclude the monitoring of vital signs.

The use of hypnotic doses of ultrashort-acting thiobarbiturates (50-100 mg IV) can be used to terminate severe emergence reactions. Diazepam, 5 mg IV has also been used to terminate emergence reactions.

Long-term follow-up observations of 221 patients (140 with ketamine hydrochloride, 81 with other anesthetic agents) have not revealed any residual psychological effects.

7. During anesthesia, the eyelids may remain retracted. During recovery, they close. Premature stimulation during recovery in the presence of nystagmus and diplopia may precipitate retching, nausea, or frank vomiting.

8. Purposeless movements of extremities may occur during the course of anesthesia. These movements do not imply a light plane and are not indicative of the need for additional doses of the anesthetic.

9. When ketamine is used on an outpatient basis, the patient should not be released until recovery from anesthesia is completed and then should be accompanied by a responsible adult.

10. Illicit use of ketamine has been reported; dependence and tolerance to ketamine can also develop (see ADVERSE REACTIONS, Drug Abuse and Dependence). Ketamine should be prescribed and administered with caution.

11. Severe irritative and inflammatory urinary tract and bladder symptoms including cystitis have been reported in individuals with a history of chronic ketamine use or abuse. Cases of damage to and/or destruction of the urinary tract have also been reported. Caution is warranted when long-term use of ketamine hydrochloride is prescribed.

12. Animal studies show that ketamine is associated with significant neuronal loss in the developing brain. Because of the lack of information on pediatric safety, the risks of ketamine use in the pediatric population must be carefully considered against its potential benefits.

**Pregnancy**

The safe use in pregnancy has not been established, and such use is not recommended (see INDICATIONS AND CLINICAL USE).

**Drug Interactions**
Prolonged recovery time may occur if barbiturates and/or narcotics are used concurrently with ketamine.

Ketamine is clinically compatible with the commonly used general and local anesthetic agents when an adequate respiratory exchange is maintained.

Use with caution in the chronic alcoholic and the acutely alcohol-intoxicated patient.

## ADVERSE REACTIONS

One of the most characteristic physiologic effects of ketamine hydrochloride is temporary augmentation of the pulse rate and blood pressure. Elevation of blood pressure begins shortly after injection, reaches a maximum within a few minutes and usually returns to preanesthetic values within 15 minutes of injection. The median peak rise has ranged from 20 to 25% of preanesthetic values for both systolic and diastolic readings. Depending on the condition of the patient, this elevation of blood pressure may be considered a beneficial effect, or in others, an adverse reaction. If elevation of blood pressure would be considered adverse to the patient, the benefit to risk ratio should be carefully determined (see CONTRAINDICATIONS). Maintaining or moderately increasing blood pressure may be beneficial to some patients, as those in shock or those in whom reduction in blood pressure is contraindicated (see WARNINGS).

Hypotension, arrhythmias, and bradycardia have been occasionally observed.

Although respiration is frequently stimulated, severe depression of respiration or apnea may occur following rapid intravenous administration of high doses of ketamine. Respiratory depression, mild or moderate and transient, occurred in a small percentage of patients with normal doses. In the majority of these patients, it is not a serious problem. Laryngospasm and other forms of airway obstruction have occurred during ketamine hydrochloride anesthesia.

Hepatobiliary toxicity has been reported with acute and chronic use of ketamine. Clinically important elevations in liver enzymes, suggestive of both hepatocellular and cholestatic changes are a potential risk of acute use of ketamine. Liver enzyme elevations and biliary ductal dilatations are potential risks of repeated, chronic use or misuse of ketamine. Both the biochemical and structural hepatobiliary changes may be reversible.

Increased salivation may occur unless an antisialagogue is used.

In some patients, enhanced skeletal muscle tone may be manifested by tonic and clonic movements, sometimes resembling seizures. These movements do not imply a light plane and are not indicative of the need for additional doses of the anesthetic.

EEG recordings were made in 14 patients receiving ketamine hydrochloride. Although one of these patients exhibited slight twitching of the arms and legs, none showed EEG changes to suggest seizure reactions. Epileptiform attacks have been observed in a few patients following ketamine hydrochloride administration. However, ketamine hydrochloride has been used successfully in patients known to be suffering from epilepsy.

Blurred vision, nystagmus and diplopia are not uncommon findings during the recovery period.

Anorexia, nausea or vomiting are minimal, allowing the great majority of patients to take liquids by mouth shortly after regaining consciousness.

Except for occasional reports of local pain and exanthema at the injection site, ketamine hydrochloride is well tolerated by the patient when administered either by the intravenous or intramuscular route. Transient erythema, morbilliform rash and anaphylaxis have been reported.

Ketamine hydrochloride causes a small transient increase in intraocular pressure. However, it has been used in patients with glaucoma without causing any deterioration in this condition.

Severe irritative and inflammatory urinary tract and bladder symptoms including cystitis have been reported in individuals with history of chronic ketamine use or abuse. Cases of damage to and/or destruction of the urinary tract have also been reported in this population.

**Drug Abuse and Dependence**
Ketamine has been reported as being used as a drug of abuse. Reports suggest that ketamine produces a variety of symptoms including, but not limited to, flashbacks, hallucinations, dysphoria, anxiety, insomnia, or disorientation. Ketamine dependence and tolerance may develop in individuals with a history of drug abuse or dependence. A withdrawal syndrome with psychotic features has been described following discontinuation of long-term ketamine use.

## OVERDOSAGE

Respiratory depression can result from an overdosage or too rapid a rate of administration 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 has a wide margin of safety; several instances of unintentional administration of overdoses of ketamine hydrochloride (up to ten times of the usually required dose) have been followed by prolonged but complete recovery.

| For management of a suspected drug overdose, contact your regional Poison Control Centre. |
|---|

## PHARMACOLOGY

Ketamine hydrochloride is a cataleptic, analgesic and anesthetic agent devoid of sedative or hypnotic properties, distinguishing it from the commonly used barbiturates. The depth of analgesia and anesthesia induced by ketamine hydrochloride varies with the animal species, being more pronounced in monkeys, cats, rats and mice than in pigeons, guinea pigs, dogs and rabbits.

**Metabolism:** Ketamine hydrochloride is rapidly absorbed following parenteral administration. Animal experiments indicated that ketamine hydrochloride was rapidly distributed into body tissues, with relatively high concentrations appearing in body fat, liver, lung and brain; lower concentrations were found in the heart, skeletal muscle and blood plasma. Placental transfer of the drug was found to occur in pregnant dogs and monkeys. No significant degree of binding to serum albumin was found with ketamine hydrochloride.

Balance studies in rats, dogs, and monkeys resulting in the recovery of 85 to 95% of the dose in the urine, mainly in the form of degradation products. Small amounts of drug were also excreted in the bile and feces. Balance studies with tritium-labelled ketamine hydrochloride in human subjects (1 mg/lb given intravenously) resulted in the mean recovery of 91% of the dose in the urine and 3% in the feces. Peak plasma levels averaged about 0.75 mcg/mL, and CSF levels were about 0.2 mcg/mL, one hour after dosing.

Ketamine hydrochloride undergoes N-demethylation and hydroxylation of the cyclohexanone ring, with the formation of water-soluble conjugates which are excreted in the urine. Further oxidation also occurs with formation of a cyclohexanone derivative. The unconjugated N-demethylated metabolite was found to be less than one-sixth as potent as ketamine hydrochloride. The unconjugated demethyl cyclohexanone derivative was found to be less than one-tenth as potent as ketamine. Repeated doses of ketamine hydrochloride administered to animals did not produce any detectable increase in microsomal enzyme activity.

Doses of 0.5 to 2.0 mg/kg of ketamine hydrochloride produce consistent and marked changes of EEG in man. The abolition of alpha waves and induction of theta activity were the most typical effects of ketamine hydrochloride.

## TOXICOLOGY

### Acute Toxicity

The intraperitoneal $LD_{50}$ values were 275 mg/kg in neonatal mice, 209 mg/kg in preweaning mice, and 224 mg/kg in adult mice. In rats, the intraperitoneal $LD_{50}$ values were 146 mg/kg for the neonates, 170 mg/kg for the preweaning groups, and 224 mg/kg for adult rats**.**

### Local Irritation

There was no evidence of drug related local damage when ketamine hydrochloride was given by intravenous or intra-arterial routes to rats or dogs.

**Chronic Toxicity**
Rats given daily IV injections of 2.5 to 10 mg/kg of ketamine hydrochloride for six weeks had only slight food intake depression and moderate weight gain depression, which was dose related in males but not in females. Regular monitoring of laboratory data and final autopsy studies failed to demonstrate drug-related toxic effects. Weight loss in dogs given daily IM injections of ketamine hydrochloride up to 40 mg/kg for six weeks presumably was due to general depression of physical activity produced by the drug. There were no consistent hematologic or hematopoietic alterations. There were elevations in serum cholesterol, urea, alkaline phosphatase and transaminase values which were most prominent in animals receiving high doses. These values returned to normal levels at the termination of the dosing period. These altered values may be associated with temporary anorexia and weight loss. Histologic changes were not significant. When monkeys were anesthetized for three to six hours, twice weekly for four to six weeks, there were minor elevations in the sedimentation rate and variable changes in the total leukocyte and neutrophil differential values.

**Reproduction Studies**
There were no apparent adverse effects on the dam or the pups when three groups of pregnant bitches were given 25 mg/kg of ketamine hydrochloride IM twice a week over a three week period during first, second, and third trimester of pregnancy respectively.

When rats were given ketamine hydrochloride during the premating period, the period of organogenesis, and the perinatal period in doses from 10 mg to 20 mg/kg IV or IM, the breeding performance and condition of the litters were not significantly different from the control animals injected with saline.

Of inseminated rabbits given 20 mg/kg of ketamine hydrochloride IM, there were no drug induced effects on the litters during the period of organogenesis.

## DOSAGE AND ADMINISTRATION

**Preoperative Preparations**
1. Ketamine Hydrochloride Injection USP has been safely used alone when the stomach was not empty. However, since the need to use supplementary anesthetic or muscle relaxant agents cannot always be predicted, it is preferable not to give anything by mouth for at least six hours before elective surgery. Ketamine Hydrochloride Injection USP is recommended for use in patients whose stomach is not empty when in the judgment of the physician the benefits of the drug outweigh the possible hazards.

2. Atropine, scopolamine, or other drying agents should be given at an appropriate interval prior to induction.

3. Certain drugs such as droperidol or diazepam intramuscularly have been used in an attempt to reduce the incidence of emergence reactions: sufficient data have not yet been

accumulated to constitute thorough documentation. The incidence of emergence reactions is reduced as experience with the drug is gained.

**Dosage**
As with other general anesthetic agents, the individual response to Ketamine Hydrochloride Injection USP is somewhat varied depending on the dose, route of administration, and age of patient, so that dosage recommendation cannot be absolutely fixed. The drug should be titrated to the patient's requirements.

As with all parenteral drug products, intravenous admixtures should be inspected visually for clarity, particulate matter, precipitation, discolouration and leakage prior to administration whenever solution and container permit. Solutions showing haziness, particulate matter, precipitate, discolouration or leakage should not be used. Discard unused portion. Do not use if precipitate appears.

**Onset and Duration**
Because of rapid induction following the initial intravenous injection, the patient should be in a supported position during administration.

The onset of action of Ketamine Hydrochloride Injection USP is rapid; an intravenous dose of 2 mg/kg of body weight usually produces surgical anesthesia within 30 seconds after injection, with the anesthetic effect usually lasting five to ten minutes. If a longer effect is desired, additional increments can be administered intravenously or intramuscularly to maintain anesthesia without producing significant cumulative effects.

Intramuscular doses, from experience primarily in children, in a range of 9 to 13 mg/kg usually produce surgical anesthesia within three to four minutes following injection, with the anesthetic effect usually lasting 12 to 25 minutes.

**Use of Ketamine Hydrochloride Injection USP as the Sole Anesthetic Agent**
**Induction**
Intravenous Route: The initial dose of Ketamine Hydrochloride Injection USP administered intravenously may range from 1 to 4.5 mg/kg. The average amount required to produce five to ten minutes of surgical anesthesia has been 2 mg/kg.

Rate of Administration: It is recommended that Ketamine Hydrochloride Injection USP 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 Hydrochloride Injection USP administered intramuscularly may range from 6.5 – 13 mg/kg. A dose of 10 mg/kg will usually produce 12 to 25 minutes of surgical anesthesia.

**Maintenance of Anesthesia**
Increments of ½ to the full induction dose, either intravenous or intramuscular may be repeated as needed for maintenance of anesthesia. Nystagmus, movements in response to stimulation, and vocalization may indicate lightening of anesthesia.

**Use of Ketamine Hydrochloride Injection USP Prior to the Administration of Other General Anesthetic Agents**
Ketamine Hydrochloride Injection USP is clinically compatible with the commonly used general and local anesthetic agents when an adequate respiratory exchange is maintained. When Ketamine Hydrochloride Injection USP is used as an induction agent, prior to the administration of other general anesthetic agents:

1. The full induction dose of Ketamine Hydrochloride Injection USP should be given IV over 60 seconds.

2. At the completion of the induction dose of Ketamine Hydrochloride Injection, the anesthetist should proceed immediately with the chosen general anesthetic procedure. A second dose of Ketamine Hydrochloride Injection USP (half the original induction dose) may be required at five to eight minutes following the initial induction dose when using an agent such as methoxyflurane where some considerable time is required for full surgical anesthesia to be established with the gaseous anesthetic. Otherwise, lightening in the depth of anesthesia may occur and the patient may enter the stage of excitement, associated with vocalization and purposeful movements.

**Recovery**
Following the procedure, the patient should be observed but left undisturbed. This does not preclude the monitoring of vital signs.

**Information for Patients**

As appropriate, especially in cases where early discharge is possible, the duration of ketamine and other drugs employed during the conduct of anesthesia should be considered. Patients should be cautioned that driving an automobile, operating hazardous machinery or engaging in hazardous activities should not be undertaken for 24 hours or more (depending upon the dosage of ketamine and consideration of other drugs employed) after anesthesia.

**Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice*

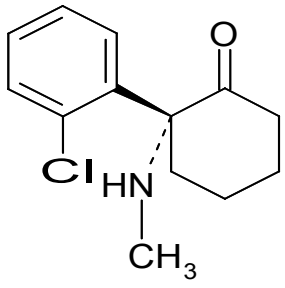
## PHARMACEUTICAL INFORMATION

**Proper Name:** ketamine hydrochloride

**Chemical Name:** (1) 2-(2-Chlorophenyl)-2-(methylamino)-cyclohexanone hydrochloride
(2) (±)-2-(*o*-Chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride

**Molecular Formula**: $C_{13}H_{16}ClNOxHCl$

**Structural Formula:**




**HCl**

**Molecular Weight:** 274.2

**Description:** White, crystalline powder, having a slight, characteristic odour. Freely soluble in water, hydrochloric acid 0.1N and methanol; soluble in ethanol; Sparingly soluble in chloroform and practically insoluble in ether.

**Melting Point:** 259°C
**pH:** 3.5-4.1, in a solution (1 in 10)
**pKa:** 7.4 base

## COMPOSITION

**Ketamine Hydrochloride Injection USP,** 10 mg/mL, 2 mL multidose vial (for maintenance therapy) and 20 mL multidose vial: Each mL contains: ketamine (as hydrochloride) 10 mg, benzethonium chloride 0.01% as a preservative, sodium chloride 6.4 mg, sodium hydroxide and/or hydrochloric acid to adjust pH, and water for injection.

**Ketamine Hydrochloride Injection USP,** 50 mg/mL, 2 mL multidose vial (for maintenance therapy) and 10 mL multidose vial: Each mL contains: ketamine (as hydrochloride) 50 mg, benzethonium chloride 0.01% as a preservative, sodium hydroxide and/or hydrochloric acid to adjust pH, and water for injection.

## STABILITY AND STORAGE RECOMMENDATIONS

Store between 15 and 30°C. Protect from light and heat. Discard 28 days after initial use.

## AVAILABILITY OF DOSAGE FORMS

**Ketamine Hydrochloride Injection USP** 10 mg/mL is available in 2 mL multidose vials (for maintenance therapy) boxes of 10, and 20 mL multidose vials, boxes of 1.

**Ketamine Hydrochloride Injection USP** 50 mg/mL is available in 2 mL multidose vials (for maintenance therapy) boxes of 10, and 10 mL multidose vials, boxes of 1.

**Latex-Free Stoppers**: Stoppers contain no dry natural rubber.

## REFERENCES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3. White PF, Way WL, and Trevor AJ. Ketamine – Its Pharmacology and Therapeutic Uses. Anesthesiology 1982; 56:119-136.

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5. White PF. Ketamine update: its clinical uses in anesthesia. Seminars in Anesthesia 1988; 7(2):113-126.

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