KETAMINE HYDROCHLORIDE- ketamine hydrochloride injection
Par Pharmaceutical Inc.

Ketamine Hydrochloride Injection, USP

CIII

SPECIAL NOTE

EMERGENCE REACTIONS HAVE OCCURRED IN APPROXIMATELY 12 PERCENT OF PATIENTS.

THE PSYCHOLOGICAL MANIFESTATIONS VARY IN SEVERITY BETWEEN PLEASANT DREAM-LIKE STATES, VIVID IMAGERY, HALLUCINATIONS, AND EMERGENCE DELIRIUM. 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 USE OF KETAMINE HYDROCHLORIDE INJECTION.

THE INCIDENCE OF THESE EMERGENCE PHENOMENA IS LEAST IN THE ELDERLY (OVER 65 YEARS OF AGE) PATIENT. ALSO, THEY ARE LESS FREQUENT WHEN THE DRUG IS GIVEN INTRAMUSCULARLY AND THE INCIDENCE IS REDUCED AS EXPERIENCE WITH THE DRUG IS GAINED.

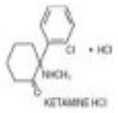
THE INCIDENCE OF PSYCHOLOGICAL MANIFESTATIONS DURING EMERGENCE, PARTICULARLY DREAM-LIKE OBSERVATIONS AND EMERGENCE DELIRIUM, MAY BE REDUCED BY USING LOWER RECOMMENDED DOSAGES OF KETAMINE HYDROCHLORIDE INJECTION IN CONJUNCTION WITH INTRAVENOUS DIAZEPAM DURING INDUCTION AND MAINTENANCE OF ANESTHESIA. (See **DOSAGE AND ADMINISTRATION** Section.) ALSO, THESE REACTIONS MAY BE REDUCED IF VERBAL, TACTILE, AND VISUAL STIMULATION OF THE PATIENT IS MINIMIZED DURING THE RECOVERY PERIOD. THIS DOES NOT PRECLUDE THE MONITORING OF VITAL SIGNS.

IN ORDER TO TERMINATE A SEVERE EMERGENCE REACTION, THE USE OF A SMALL HYPNOTIC DOSE OF A SHORT-ACTING OR ULTRA SHORT-ACTING BARBITURATE MAY BE REQUIRED.

WHEN KETAMINE HYDROCHLORIDE INJECTION IS USED ON AN OUTPATIENT BASIS, THE PATIENT SHOULD NOT BE RELEASED UNTIL RECOVERY FROM ANESTHESIA IS COMPLETE AND THEN SHOULD BE ACCOMPANIED BY A RESPONSIBLE ADULT.

DESCRIPTION

Ketamine hydrochloride is a nonbarbiturate anesthetic chemically designated *dl* 2-(0-chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride. It is formulated as a slightly acid (pH 3.5-5.5) sterile solution for intravenous or intramuscular injection in concentrations containing the equivalent of either 10, 50 or 100 mg ketamine base per milliliter and contains not more than 0.1 mg/mL Phemerol® (benzethonium chloride) added as a preservative. The 10 mg/mL solution has been made isotonic with sodium chloride.



CLINICAL PHARMACOLOGY

Ketamine hydrochloride is a rapid-acting general anesthetic producing an anesthetic state characterized by profound analgesia, normal pharyngeal-laryngeal reflexes, normal or slightly enhanced skeletal muscle tone, cardiovascular and respiratory stimulation, and occasionally a transient and minimal respiratory depression.

A patent airway is maintained partly by virtue of unimpaired pharyngeal and laryngeal reflexes. (See **WARNINGS** and **PRECAUTIONS** Sections.)

The biotransformation of ketamine hydrochloride includes N-dealkylation (metabolite I), hydroxylation of the cyclohexone ring (metabolites III and IV), conjugation with glucuronic acid and dehydration of the hydroxylated metabolites to form the cyclohexene derivative (metabolite II).

Following intravenous administration, the ketamine concentration has an initial slope (alpha phase) lasting about 45 minutes with a half-life of 10 to 15 minutes. This first phase corresponds clinically to the anesthetic effect of the drug. The anesthetic action is terminated by a combination of redistribution from the CNS to slower equilibrating peripheral tissues and by hepatic biotransformation to metabolite I. This metabolite is about 1/3 as active as ketamine in reducing halothane requirements (MAC) of the rat. The later half-life of ketamine (beta phase) is 2.5 hours.

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 somatesthetic sensory blockade. It may selectively depress the thalamoneocortical system before significantly obtunding the more ancient cerebral centers and pathways (reticular-activating and limbic systems).

Elevation of blood pressure begins shortly after injection, reaches a maximum within a few minutes and usually returns to preanesthetic values within 15 minutes after injection. In the majority of cases, the systolic and diastolic blood pressure peaks from 10% to 50% above preanesthetic levels shortly after induction of anesthesia, but the elevation can be higher or longer in individual cases (see **CONTRAINDICATIONS** Section).

Ketamine has a wide margin of safety; several instances of unintentional administration of overdoses of ketamine hydrochloride (up to ten times that usually required) have been followed by prolonged but complete recovery.

Ketamine hydrochloride has been studied in over 12,000 operative and diagnostic procedures, involving over 10,000 patients from 105 separate studies. During the course of these studies ketamine hydrochloride was administered as the sole agent, as induction for other general agents, or to supplement low-potency agents.

Specific areas of application have included the following:

1. debridement, painful dressings, and skin grafting in burn patients, as well as other superficial surgical procedures.
2. neurodiagnostic procedures such as pneumonencephalograms, ventriculograms, myelograms, and lumbar punctures. See also **Precaution** concerning increased intracranial pressure.
3. diagnostic and operative procedures of the eye, ear, nose, and mouth, including dental extractions.
4. diagnostic and operative procedures of the pharynx, larynx, or bronchial tree. NOTE: Muscle relaxants, with proper attention to respiration, may be required (see **PRECAUTIONS** Section).
5. sigmoidoscopy and minor surgery of the anus and rectum, and circumcision.
6. extraperitoneal procedures used in gynecology such as dilatation and curettage.
7. orthopedic procedures such as closed reductions, manipulations, femoral pinning, amputations, and biopsies.
8. as an anesthetic in poor-risk patients with depression of vital functions.

9. in procedures where the intramuscular route of administration is preferred.
10. in cardiac catheterization procedures.

In these studies, the anesthesia was rated either "excellent" or "good" by the anesthesiologist and the surgeon at 90% and 93%, respectively; rated "fair" at 6% and 4%, respectively; and rated "poor" at 4% and 3%, respectively. In a second method of evaluation, the anesthesia was rated "adequate" in at least 90%, and "inadequate" in 10% or less of the procedures.

INDICATIONS AND USAGE

Ketamine hydrochloride injection is indicated as the sole anesthetic agent for diagnostic and surgical procedures that do not require skeletal muscle relaxation. Ketamine hydrochloride is best suited for short procedures but it can be used, with additional doses, for longer procedures.

Ketamine hydrochloride injection is indicated for the induction of anesthesia prior to the administration of other general anesthetic agents.

Ketamine hydrochloride injection is indicated to supplement low-potency agents, such as nitrous oxide.

Specific areas of application are described in the **CLINICAL PHARMACOLOGY** Section.

CONTRAINDICATIONS

Ketamine hydrochloride is contraindicated in those in whom a significant elevation of blood pressure would constitute a serious hazard and in those who have shown hypersensitivity to the drug.

WARNINGS

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

Postoperative confusional states may occur during the recovery period. (See Special Note.)

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

PRECAUTIONS

General

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.

Because pharyngeal and laryngeal reflexes are usually active, ketamine hydrochloride 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 hydrochloride is used alone. Muscle relaxants, with proper attention to respiration, may be required in both of these instances.

Resuscitative equipment should be ready for use.

The *incidence of emergence reactions may be reduced* if verbal and tactile stimulation of the patient is minimized during the recovery period. This does not preclude the monitoring of vital signs (see Special Note).

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

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

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

An increase in cerebrospinal fluid pressure has been reported following administration of ketamine hydrochloride. Use with extreme caution in patients with preanesthetic elevated cerebrospinal fluid pressure.

Information for Patients

As appropriate, especially in cases where early discharge is possible, the duration of ketamine hydrochloride and other drugs employed during the conduct of anesthesia should be considered. The 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 hydrochloride and consideration of other drugs employed) after anesthesia.

Drug Interactions

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

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

Usage in Pregnancy

Since the safe use in pregnancy, including obstetrics (either vaginal or abdominal delivery), has not been established, such use is not recommended (see **ANIMAL PHARMACOLOGY AND TOXICOLOGY, Reproduction**).

Geriatric Use

Clinical studies of ketamine hydrochloride did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Pediatric Use

Safety and effectiveness in pediatric patients below the age of 16 have not been established.

ADVERSE REACTIONS

Cardiovascular: Blood pressure and pulse rate are frequently elevated following administration of ketamine hydrochloride alone. However, hypotension and bradycardia have been observed. Arrhythmia has also occurred.

Respiration: Although respiration is frequently stimulated, severe depression of respiration or apnea may occur following rapid intravenous administration of high doses of ketamine hydrochloride. Laryngospasms and other forms of airway obstruction have occurred during ketamine hydrochloride anesthesia.

Eye: Diplopia and nystagmus have been noted following ketamine hydrochloride administration. It also may cause a slight elevation in intraocular pressure measurement.

Genitourinary: Severe irritative and inflammatory urinary tract and bladder symptoms including cystitis have been reported in individuals with history of chronic ketamine use or abuse.

Psychological: (See Special Note.)

Neurological: In some patients, enhanced skeletal muscle tone may be manifested by tonic and clonic movements sometimes resembling seizures (see **DOSAGE AND ADMINISTRATION** Section).

Gastrointestinal: Anorexia, nausea and vomiting have been observed; however, this is not usually severe and allows the great majority of patients to take liquids by mouth shortly after regaining consciousness (see **DOSAGE AND ADMINISTRATION** Section).

General: Anaphylaxis. Local pain and exanthema at the injection site have infrequently been reported. Transient erythema and/or morbilliform rash have also been reported.

For medical advice about adverse reactions contact your medical professional. To report SUSPECTED ADVERSE REACTIONS, contact JHP at 1-866-923-2547 or MEDWATCH at 1-800-FDA-1088 (1-800-332-1088) or http://www.fda.gov/medwatch/.

DRUG ABUSE AND DEPENDENCE

Ketamine has been reported being used as a drug of abuse.

Reports suggest that ketamine produces a variety of symptoms including, but not limited to anxiety, dysphoria, disorientation, insomnia, flashbacks, hallucinations, and psychotic episodes.

Ketamine dependence and tolerance are possible following prolonged administration. A withdrawal syndrome with psychotic features has been described following discontinuation of long-term ketamine use. Therefore, ketamine should be prescribed and administered with caution.

OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

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

If the ketamine hydrochloride dose is augmented with diazepam, the two drugs must be given separately. Do not mix ketamine hydrochloride and diazepam in syringe or infusion flask. For additional information on the use of diazepam, refer to the **WARNINGS** and **DOSAGE AND ADMINISTRATION** Sections of the diazepam insert.

Preoperative Preparations:

1. While vomiting has been reported following ketamine hydrochloride administration, some airway protection may be afforded because of active laryngeal-pharyngeal reflexes. However, since aspiration may occur with ketamine hydrochloride and since protective reflexes may also be diminished by supplementary anesthetics and muscle relaxants, the possibility of aspiration must be considered. Ketamine hydrochloride is recommended for use in the patient whose stomach is not empty when, in the judgment of the practitioner, the benefits of the drug outweigh the possible risks.
2. Atropine, scopolamine, or another drying agent should be given at an appropriate interval prior to induction.

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 is rapid; an intravenous dose of 2 mg/kg (1 mg/lb) 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, in a range of 9 to 13 mg/kg (4 to 6 mg/lb) usually produce surgical anesthesia within 3 to 4 minutes following injection, with the anesthetic effect usually lasting 12 to 25 minutes.

Dosage:

As with other general anesthetic agents, the individual response to ketamine hydrochloride 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 against the patient's requirements.

Induction:

Intravenous Route:

The initial dose of ketamine hydrochloride administered intravenously may range from 1 mg/kg to 4.5 mg/kg (0.5 to 2 mg/lb). The average amount required to produce five to ten minutes of surgical anesthesia has been 2 mg/kg (1 mg/lb).

Alternatively, in adult patients an induction dose of 1 mg to 2 mg/kg intravenous ketamine at a rate of 0.5 mg/kg/min may be used for induction of anesthesia. In addition, diazepam in 2 mg to 5 mg doses, administered in a separate syringe over 60 seconds, may be used. In most cases, 15 mg of intravenous diazepam or less will suffice. The incidence of psychological manifestations during emergence, particularly dream-like observations and emergence delirium, may be reduced by this induction dosage program.

Note: The 100 mg/mL concentration of ketamine hydrochloride *should not* be injected intravenously without proper dilution. It is recommended the drug be diluted with an equal volume of either Sterile Water for injection, USP, Normal Saline, or 5% Dextrose in Water.

Rate of Administration:

It is recommended that ketamine hydrochloride 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 administered intramuscularly may range from 6.5 to 13 mg/kg (3 to 6 mg/lb). A dose of 10 mg/kg (5 mg/lb) will usually produce 12 to 25 minutes of surgical anesthesia.

Maintenance of Anesthesia:

The maintenance dose should be adjusted according to the patient's anesthetic needs and whether an additional anesthetic agent is employed.

Increments of one-half to the full induction dose may be repeated as needed for maintenance of anesthesia. However, it should be noted that purposeless and tonic-clonic 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.

It should be recognized that the larger the total dose of ketamine hydrochloride administered, the longer will be the time to complete recovery.

Adult patients induced with ketamine hydrochloride augmented with intravenous diazepam may be

maintained on ketamine hydrochloride given by slow microdrip infusion technique at a dose of 0.1 to 0.5 mg/minute, augmented with diazepam 2 to 5 mg administered intravenously as needed. In many cases 20 mg or less of intravenous diazepam total for combined induction and maintenance will suffice. However, slightly more diazepam may be required depending on the nature and duration of the operation, physical status of the patient, and other factors. The incidence of psychological manifestations during emergence, particularly dream-like observations and emergence delirium, may be reduced by this maintenance dosage program.

Dilution:

To prepare a dilute solution containing 1 mg of ketamine per mL, aseptically transfer 10 mL from a 50 mg per mL vial or 5 mL from a 100 mg per mL vial to 500 mL of 5% Dextrose Injection, USP or Sodium Chloride (0.9%) Injection, USP (Normal Saline) and mix well. The resultant solution will contain 1 mg of ketamine per mL.

The fluid requirements of the patient and duration of anesthesia must be considered when selecting the appropriate dilution of ketamine hydrochloride injection. If fluid restriction is required, ketamine hydrochloride injection can be added to a 250 mL infusion as described above to provide a ketamine hydrochloride concentration of 2 mg/mL.

Ketamine hydrochloride injection 10 mg/mL vials are not recommended for dilution.

Supplementary Agents:

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

The regimen of a reduced dose of ketamine hydrochloride supplemented with diazepam can be used to produce balanced anesthesia by combination with other agents such as nitrous oxide and oxygen.

HOW SUPPLIED

Ketamine hydrochloride injection is supplied as the hydrochloride in concentrations equivalent to ketamine base.

NDC 42023-137-10 — Each 20-mL multi-dose vial contains 10 mg/mL. Supplied in cartons of 10.

NDC 42023-138-10 — Each 10-mL multi-dose vial contains 50 mg/mL. Supplied in cartons of 10.

NDC 42023-139-10 — Each 5-mL multi-dose vial contains 100 mg/mL. Supplied in cartons of 10.

Store between 20° to 25°C (68° to 77°F). (See USP controlled room temperature.)

Protect from light.

Rx Only.

ANIMAL PHARMACOLOGY AND TOXICOLOGY

Toxicity:

The acute toxicity of ketamine hydrochloride has been studied in several species. In mature mice and rats, the intraperitoneal LD_{50} values are approximately 100 times the average human intravenous dose and approximately 20 times the average human intramuscular dose. A slightly higher acute toxicity observed in neonatal rats was not sufficiently elevated to suggest an increased hazard when used in pediatric patients. Daily intravenous injections in rats of five times the average human intravenous dose and intramuscular injections in dogs at four times the average human intramuscular dose demonstrated excellent tolerance for as long as 6 weeks. Similarly, twice weekly anesthetic sessions of one, three, or six hours' duration in monkeys over a four- to six-week period were well tolerated.

Interaction with Other Drugs Commonly Used for Preanesthetic Medication:

Large doses (three or more times the equivalent effective human dose) of morphine, meperidine, and atropine increased the depth and prolonged the duration of anesthesia produced by a standard anesthetizing dose of ketamine hydrochloride in Rhesus monkeys. The prolonged duration was not of sufficient magnitude to contraindicate the use of these drugs for preanesthetic medication in human clinical trials.

Blood Pressure:

Blood pressure responses to ketamine hydrochloride vary with the laboratory species and experimental conditions. Blood pressure is increased in normotensive and renal hypertensive rats with and without adrenalectomy and under pentobarbital anesthesia.

Intravenous ketamine hydrochloride produces a fall in arterial blood pressure in the Rhesus monkey and a rise in arterial blood pressure in the dog. In this respect the dog mimics the cardiovascular effect observed in man. The pressor response to ketamine hydrochloride injected into intact, unanesthetized dogs is accompanied by a tachycardia, rise in cardiac output and a fall in total peripheral resistance. It causes a fall in perfusion pressure following a large dose injected into an artificially perfused vascular bed (dog hindquarters), and it has little or no potentiating effect upon vasoconstriction responses of epinephrine or norepinephrine. The pressor response to ketamine hydrochloride is reduced or blocked by chlorpromazine (central depressant and peripheral α-adrenergic blockade), by β-adrenergic blockade, and by ganglionic blockade. The tachycardia and increase in myocardial contractile force seen in intact animals does not appear in isolated hearts (Langendorff) at a concentration of 0.1 mg of ketamine hydrochloride or in Starling dog heart-lung preparations at a ketamine hydrochloride concentration of 50 mg/kg of HLP. These observations support the hypothesis that the hypertension produced by ketamine hydrochloride is due to selective activation of central cardiac stimulating mechanisms leading to an increase in cardiac output. The dog myocardium is not sensitized to epinephrine and ketamine hydrochloride appears to have a weak antiarrhythmic activity.

Metabolic Disposition:

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 resulted 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-labeled 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 µg/mL, and CSF levels were about 0.2 µg/mL, 1 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 the 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 hydrochloride. Repeated doses of ketamine hydrochloride administered to animals did not produce any detectable increase in microsomal enzyme activity.

Reproduction:

Male and female rats, when given five times the average human intravenous dose of ketamine hydrochloride for three consecutive days about one week before mating, had a reproductive performance equivalent to that of saline-injected controls. When given to pregnant rats and rabbits intramuscularly at twice the average human intramuscular dose during the respective periods of organogenesis, the litter characteristics were equivalent to those of saline-injected controls. A small

group of rabbits was given a single large dose (six times the average human dose) of ketamine hydrochloride on Day 6 of pregnancy to simulate the effect of an excessive clinical dose around the period of nidation. The outcome of pregnancy was equivalent in control and treated groups.

To determine the effect of ketamine hydrochloride on the perinatal and postnatal period, pregnant rats were given twice the average human intramuscular dose during Days 18 to 21 of pregnancy. Litter characteristics at birth and through the weaning period were equivalent to those of the control animals. There was a slight increase in incidence of delayed parturition by one day in treated dams of this group. Three groups each of mated beagle bitches were given 2.5 times the average human intramuscular dose twice weekly for the three weeks of the first, second, and third trimesters of pregnancy, respectively, without the development of adverse effects in the pups.

Prescribing Information as of February 2013.

Manufactured and Distributed by:
JHP Pharmaceuticals, LLC
Rochester, MI 48307

3003216A

PRINCIPAL DISPLAY PANEL - 20 mL Vial Carton

NDC 42023-137-10
Rx Only

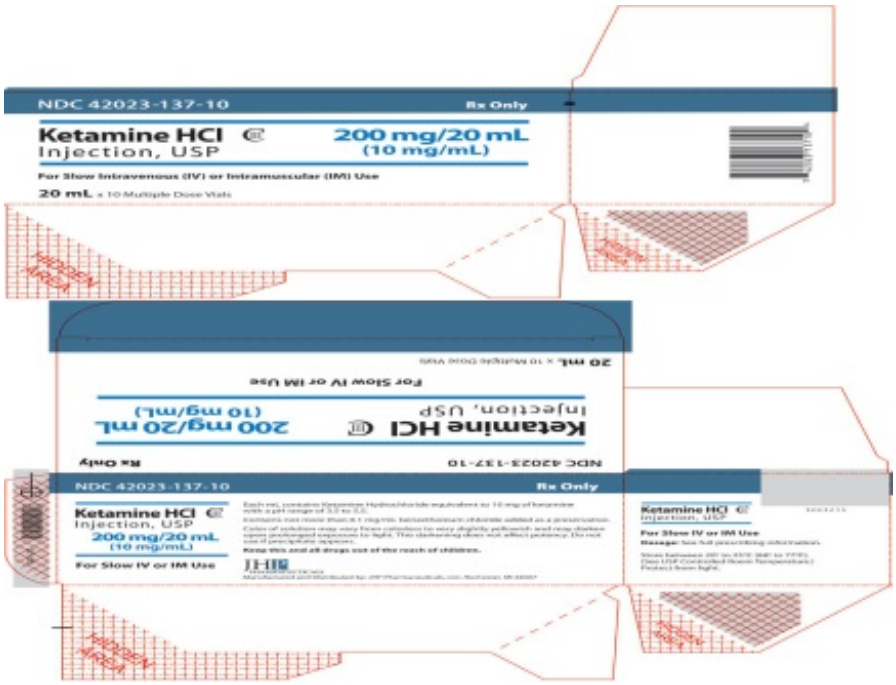
Ketamine HCl
Injection, USP

CIII

200 mg/20 mL
(10 mg/mL)

For Slow Intravenous (IV) or Intramuscular (IM) Use

20 mL x 10 Multiple Dose Vials



PRINCIPAL DISPLAY PANEL - 10 mL Vial Carton

NDC 42023-138-10
Rx Only

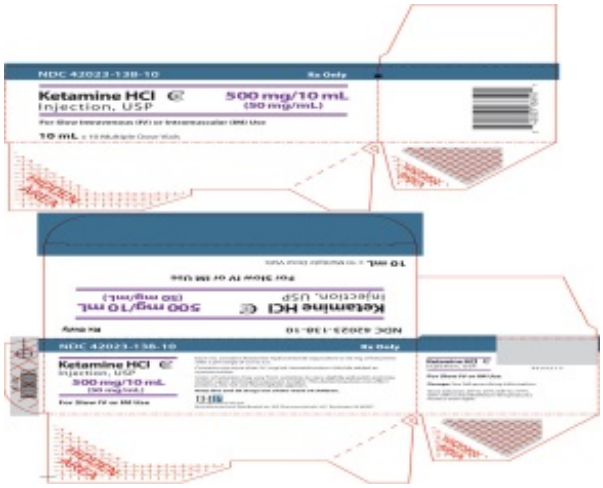
Ketamine HCl
Injection, USP

CIII

500 mg/10 mL
(50 mg/mL)

For Slow Intravenous (IV) or Intramuscular (IM) Use

10 mL x 10 Multiple Dose Vials



PRINCIPAL DISPLAY PANEL - 5 mL Vial Carton

NDC 42023-139-10
Rx Only

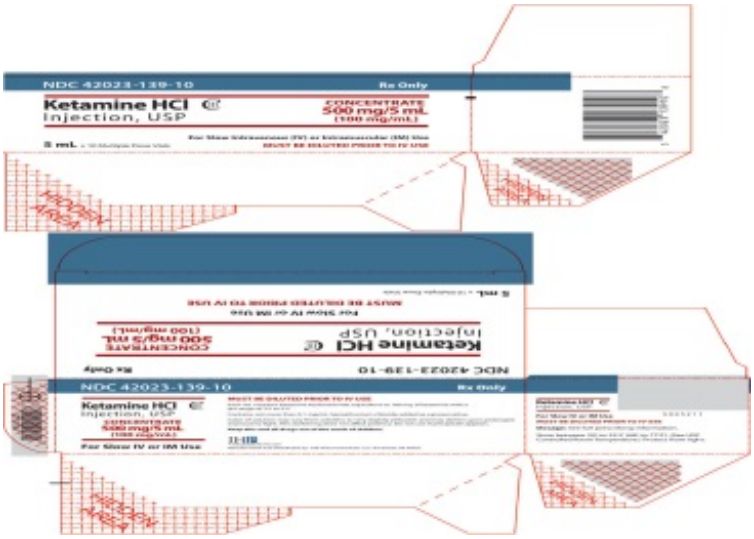
Ketamine HCl
Injection, USP

CIII

CONCENTRATE
500 mg/5 mL
(100 mg/mL)

For Slow Intravenous (IV) or Intramuscular (IM) Use

5 mL x 10 Multiple Dose Vials
MUST BE DILUTED PRIOR TO IV USE



KETAMINE HYDROCHLORIDE

ketamine hydrochloride injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:42023-137
Route of Administration	INTRAVENOUS, INTRAMUSCULAR	**DEA Schedule**	CIII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ketamine hydrochloride (UNII: O18YUO0I83) (ketamine - UNII:690G0D6V8H)	ketamine	10 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
benzethonium chloride (UNII: PH41D05744)	
sodium chloride (UNII: 451W47IQ8X)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:42023-137-10	10 in 1 CARTON	06/01/2012	05/06/2018
1		20 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA016812	06/01/2012	05/06/2018

KETAMINE HYDROCHLORIDE

ketamine hydrochloride injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:42023-138
Route of Administration	INTRAVENOUS, INTRAMUSCULAR	**DEA Schedule**	CIII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ketamine hydrochloride (UNII: O18YUO0I83) (ketamine - UNII:690G0D6V8H)	ketamine	50 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
benzethonium chloride (UNII: PH41D05744)	
sodium chloride (UNII: 451W47IQ8X)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:42023-138-10	10 in 1 CARTON	06/01/2012	04/29/2018
1		10 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA016812	06/01/2012	04/29/2018

KETAMINE HYDROCHLORIDE

ketamine hydrochloride injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:42023-139
Route of Administration	INTRAVENOUS, INTRAMUSCULAR	**DEA Schedule**	CIII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ketamine hydrochloride (UNII: O18YUO0I83) (ketamine - UNII:690G0D6V8H)	ketamine	100 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
benzethonium chloride (UNII: PH41D05744)	
sodium chloride (UNII: 451W47IQ8X)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:42023-139-10	10 in 1 CARTON	06/01/2012	05/12/2018
1		5 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA016812	06/01/2012	05/12/2018

Labeler - Par Pharmaceutical Inc. (092733690)

Registrant - Par Sterile Products, LLC (808402890)

Establishment

Name	Address	ID/FEI	Business Operations
Par Sterile Products, LLC		808402890	MANUFACTURE(42023-137, 42023-138, 42023-139) , ANALYSIS(42023-137, 42023-138, 42023-139)

Revised: 3/2016 Par Pharmaceutical Inc.