KETAMINE HYDROCHLORIDE INJECTION USP

Composition: Each vial with 10 mL solution for injection contains 500 mg ketamine (as ketamine hydrochloride).
Excipients: benzethonium chloride 0.1 mg/mL, water for injections.

Indications: KETAMINE HYDROCHLORIDE INJECTION USP is recommended:
1. As the sole anaesthetic agent for diagnostic and surgical procedures that do not require skeletal muscle relaxation. KETAMINE HYDROCHLORIDE INJECTION USP is best suited for short procedures but it can be used with additional doses, for longer procedures;
2. For the induction of anaesthesia prior to administration of other general anaesthetic agents;
3. To supplement low potency agents, such as nitrous oxide;
4. In obstetrics, for vaginal delivery or in caesarian section. Maternal side effects of awareness and dreaming can be reduced by the injection of diazepam or related drugs after the birth of the infant.

Specific areas of application included the following:
1. Debridement, painful dressings and skin grafting in burn patients, as well as other superficial surgical procedures;
2. Neurodiagnostic, such as pneumoencephalograms, ventriculograms, myelograms and lumbar punctures;
3. Diagnostic and operative procedures of the eye, 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)
5. Sigmoidoscopy and minor surgery of the anus, rectum and circumcision;
6. Extraperitoneal procedures used in gynaecology, such as dilation and curettage;
7. Orthopaedic procedures, such as closed reductions, manipulations, femoral pinning, amputation and biopsies;
8. As an anaesthetic in poor-risk patients with depression of vital functions;
9. In procedures where the intramuscular route of administration is preferred;
10. In cardiac catherisation procedures.

Preoperative Preparation:
1. When vomiting has been reported following KETAMINE HYDROCHLORIDE INJECTION USP administration, airway protection is usually afforded because of active laryngeal-pharyngeal reflexes. However, because these reflexes may also be diminished by supplementary anaesthetics or muscular relaxants, the possibility of aspiration must be considered. KETAMINE HYDROCHLORIDE INJECTION USP is recommended for use in the patient whose stomach is not empty, only when in the judgment of the practitioner, the benefits of the drug outweighs the possible risks.
2. Atropine, Scopolamine or other “drying agents” should be given at an appropriate interval prior to induction

Dosage and Administration:
Dosage: As with other general anaesthetic drugs, the individual response to KETAMINE HYDROCHLORIDE INJECTION USP is somewhat varied depending on the dose, route of administration and age of patient, so that the dosage recommended cannot be absolutely fixed. The drug should be titrated against the patient’s requirements.
Onset and duration: Because of rapid induction following the initial intravenous injections, the patient should be in a supported position during administration. The onset of action of KETAMINE HYDROCHLORIDE INJECTION USP is rapid and intravenous dose of 2 mg/kg body weight usually produces surgical anaesthesia within 30 seconds after injection, with the anaesthetic effect usually lasting 5 to 10 minutes. If a longer effect is desired, additional increments can be administered intravenously or intramuscularly to maintain anaesthesia without producing significant cumulative effect. Intramuscular doses from experience (primarily in children, in a range of 9 to 13 mg/kg) usually produce anaesthesia within 3 to 4 minutes following administration, with the anaesthetic effect usually lasting 12 to 25 minutes.
Induction: Intravenous route: The initial dose of KETAMINE HYDROCHLORIDE INJECTION USP administered intravenously may range from 1 mg/kg to 4.5 mg/kg. The average amount required to produce 5 to 10 minutes of surgical anaesthesia has been 2 mg/kg.
Rate of administration: It is recommended that KETAMINE HYDROCHLORIDE INJECTION USP is 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 ranges from 6.5 to 13 mg/kg. A dose of 10 mg/kg will usually produce 12 to 25 minutes of surgical anaesthesia.
Maintenance of anaesthesia: Increments of one half to the full induction dose may be repeated, as needed, for maintenance of anaesthesia. However, it should be noted that 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. It should be recognized that the larger the total dose of KETAMINE HYDRO-CHLORIDE INJECTION USP administered, the longer will be the time to complete recovery.

Supplementary agents: KETAMINE HYDROCHLORIDE INJECTION USP is clinically compatible with commonly used general and local anaesthetic agents when an adequate respiratory exchange is maintained.

Contraindications

KETAMINE HYDROCHLORIDE INJECTION USP must not be administered in the following cases:
– Hypersensitivity to ketamine or to any of the excipients outlined in section 6.1.
– Poorly controlled or untreated high blood pressure (arterial hypertension – systolic/diastolic blood pressure >180/100 mmHg at rest).
– Preeclampsia and eclampsia.
– Untreated or insufficiently treated hyperthyroidism.
– Situations where relaxed uterus muscles are required, e.g. impending rupture of the uterus, umbilical cord prolapse.

Warnings:
1. KETAMINE HYDROCHLORIDE INJECTION USP should be used by or under the direction of physicians experienced in administering general anaesthetics and in 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. Prolonged recovery time may occur if barbiturates and/or narcotics are used concurrently with KETAMINE HYDROCHLORIDE INJECTION USP.
4. Postoperative confusional states may occur during the recovery period (see Adverse effects – psychological).
5. Respiratory depression may occur with overdosage or too rapid a rate of administration of KETAMINE HYDROCHLORIDE INJECTION USP, in which case, supportive ventilation should be employed. Mechanical support of respiration is preferred to administration of analeptics.
6. Cases of hepatic disorders, in particular cholestatic of cholangitis type, that may be severe, have been reported in case of prolonged and/or repeated use or in case of abuse/misuse. In some cases of very prolonged use at high doses, these lesions have led to liver transplantations. Discontinuation of treatment should be considered in case of disturbances of liver function.
7. Some published studies in children have observed cognitive deficits after repeated or prolonged exposures to anaesthetic/sedative agents early in life. These studies have substantial limitations, and it is not clear if the observed effects are due to the anaesthetic/sedation drug administration or other factors such as the surgery or underlying illness.

Precautions:
1. Because pharyngeal and laryngeal reflexes are usually active, KETAMINE HYDROCHLORIDE INJECTION USP 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 INJECTION USP is used alone. Muscle relaxants, with proper attention to respiration, may be required in both of these instances.
2. Resuscitative equipment should be ready for use.

3. 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 Adverse effects – psychological)
4. The intravenous dose should be administered over a period of 60 seconds. More rapid administration may result in respiratory depression or apnoea and enhance pressor response.
5. In surgical procedures involving visceral pain pathway, KETAMINE HYDROCHLORIDE INJECTION USP should be supplemented with an agent which obtunds visceral pain.
6. Use with caution in the chronic alcoholic and the acutely alcohol-intoxicated patient.
7. An increase in cerebrospinal fluid pressure has been reported following administration of KETAMINE HYDRO-CHLORIDE INJECTION USP.

Use with extreme caution in patients with pre-anaesthetic elevated cerebrospinal fluid pressure.

Adverse Effects:

Cardiovascular: Blood pressure and pulse rate are frequently elevated following administration of KETAMINE HYDROCHLORIDE INJECTION USP. However, hypotension and bradycardia have been observed. Arrhythmia has also occurred.

Respiration: Although respiration is frequently stimulated, severe depression of respiration or apnoea may occur following rapid intravenous administration of high doses of KETAMINE HYDROCHLORIDE INJECTION USP. Laryngospasm and other forms of airway obstruction have occurred during KETAMINE HYDROCHLORIDE INJECTION USP anaesthesia.

Eye: Diplopia and nystagmus have been noted following KETAMINE HYDROCHLORIDE INJECTION USP administration. KETAMINE HYDROCHLORIDE INJECTION USP may cause a slight elevation in intraocular pressure measurement.

Psychological: Emergence reactions have occurred in approximately 12% of patients. The psychological manifestations vary in severity between pleasant dream-like status, vivid imagery, hallucinations and emergence delirium. In some cases these states have been accompanied by confusion, excitement and irrational behaviour which a few patients recall as unpleasant experience. The duration ordinarily lasts 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 USP. The incidence of these emergence phenomena is least in the young (15 years of age or less) and elderly (over 65 years of age) patients. Also they are less frequent when the drug is given intramuscularly. 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 addition, the use of a small hypnotic dose of a short- acting barbiturate may be required to terminate a severe emergence reaction. The incidence of emergence reactions is reduced as experience with the drug is gained. When KETAMINE HYDROCHLORIDE INJECTION USP is on an out-patient basis, the patient should not be released until recovery from anaesthesia is completed and then should be accompanied by a responsible adult.

Neurological: In some patients, enhanced skeletal muscular tone may be manifested by tonic and clonic movements, sometimes resembling seizures (see Dosage and Administration).

Gastrointestinal: Anorexia, nausea and vomiting have been observed. However, these are not usually severe and allows the great majority of patients to take liquids by mouth, shortly after regaining consciousness (see Dosage and Administration)

Hepatobiliary disorders: Unknown frequency: Liver function test abnormal, cholangitis, cholestasis in case of prolonged treatment at high doses or in case of abuse.

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

Use in pregnancy:

Studies in animals have shown reproductive toxicity (see Preclinical safety data section).

The use of KETAMINE HYDROCHLORIDE INJECTION USP during pregnancy must be carefully assessed by the physician.

Pharmacological properties

Preclinical safety data: Reproductive toxicity: Published animal studies of some anaesthetic/sedation drugs have reported adverse effects on brain development in early life and late pregnancy. These studies have demonstrated that anaesthetic and sedation drugs that block N-methyl-D-aspartate (NMDA) receptors and/or potentiate gamma-aminobutyric acid (GABA) activity during the period of rapid brain growth or synaptogenesis may result in neuronal and oligodendrocyte cell loss in the developing brain and alterations in synaptic morphology and neurogenesis when used for longer than 3 hours. The clinical significance of these non-clinical findings is yet to be determined. However, based on comparisons across species, the window of vulnerability to these changes is believed to correlate with exposures in the third trimester through the first several months of life, but may extend out to approximately 3 years of age in humans.

Drug Interaction: No known drug interactions

Incompatibilities: Barbiturates and KETAMINE HYDROCHLORIDE INJECTION USP, being chemically incompatible, because of precipitate formation, should not be injected from the same syringe.

Storage Conditions: Store at or below 30 °C. Protect from light.

Packing: KETAMINE HYDROCHLORIDE INJECTION USP Injection – 10 vials of 10 mL

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Date of last revision: November 2020

SIN05966P