KANOX 50MG/ML INJECTION (10ML VIAL)

DESCRIPTION: **Kanox 50mg/ml Injection (10ml vial)**: A clear, colourless solution

COMPOSITION: Each ml contains Ketamine Hydrochloride equivalent to Ketamine 50 mg. Each vial contains total of Ketamine Hydrochloride equivalent to Ketamine 500 mg

PHARMACODYNAMICS: Ketamine is a rapid-acting, general anaesthetic producing an anaesthetic state characterised 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 relatively unimpaired pharyngeal and laryngeal reflexes (see Warnings and Precautions). The anaesthetic state produced by Ketamine has been termed "dissociative anaesthesia" in that it appears to selectively interrupt association pathways of the brain before producing somaesthetic sensory blockade. Ketamine may selectively depress the thalamo neocortical system before significantly obtunding the more ancient cerebral centres and pathways (reticular-activating and limbic system). Elevation of blood pressure begins shortly after injection, reaches a maximum within a few minutes and usually returns to preanaesthetic values within 15 minutes after injection. The median peak rise from 20 to 25% of preanaesthetic values. Ketamine has a wide margin of safety; several instances of unintentional administration of overdoses of Ketamine (up to 10 times that usually required) have been followed by prolonged but complete recovery.

PHARMACOKINETICS:
Absorption: Rapid
Distribution: Rapidly distributed into highly perfused tissues including the brain.
Biotransformation: Hepatic. However, termination of anaesthetic effects may be caused by the redistribution from brain to the tissues.
Half Life: Distribution - Approximately 7 to 11 minutes. Elimination - Approximately 2 to 3 hours.
Time to Induction of Anaesthesia: Intravenous (following a dose of 1 to 2 mg per kg of bodyweight (mg/kg)) - Sensation of dissociation: 15 seconds. Anaesthesia 30 seconds. Intramuscular (following a dose of 5 to 10 mg/kg) - Anaesthesia: 3 to 4 minutes.
Duration of Anaesthesia: Intravenous (following a dose of 2 mg/kg) - 5 to 10 minutes. Intramuscular (following a dose of 10 mg/kg) - 12 to 25 minutes.
Time to recovery: Rapid
Elimination: Renal. 90%. About 4% as unchanged ketamine. Fecal. Up to 5%.

INDICATION: Ketamine is recommended:
1. As the sole anaesthetic agent for diagnostic and surgical procedures that do not require skeletal muscle relaxation. Ketamine 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 the 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.

RECOMMENDED DOSAGE:
Pre-operative preparation:
1. While vomiting has been reported following Ketamine administration, airway protection is usually afforded because of active laryngeal-pharyngeal reflexes. However, because these reflexes may also be diminished by supplementary anaesthetics or muscle relaxants, the possibility of aspiration must be considered. Ketamine is recommended for use in the patient whose stomach is not empty, only when, in the judgement of the practitioner, the benefits of the drug outweigh the possible risks.
2. Atropine, hyoscine, or other "drying" agents should be given at an appropriate interval prior to induction.

Dosage: As with other general anaesthetic agents, the individual response to Ketamine 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 injection, the patient should be in a supported position during administration. The onset of action of Ketamine is rapid, and intravenous dose of 2 mg/kg of bodyweight 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 surgical anaesthesia within three to four minutes following administration, with the anaesthetic effect usually lasting 12 to 25 minutes.
Induction: Intravenous route: The initial dose of Ketamine 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 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 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 recognised that the larger the total dose of Ketamine is administered, the longer will be the time to complete recovery.
Supplementary Agents: Ketamine is clinically compatible with commonly used general and local anaesthetic agents when an adequate respiratory exchange is maintained.

ROUTE OF ADMINISTRATION: for i.m./i.v. injection

CONTRAINDICATIONS: Ketamine is contra-indicated in those in whom a significant elevation of blood pressure would constitute a serious hazard and those who have shown hypersensitivity to the drug.
-increase intra-ocular or CSF pressure
-eclampsia or pre-eclampsia
-prone to hallucinations

WARNINGS & PRECAUTIONS:
Warnings:
1. Ketamine 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. Postoperative confusional states may occur during the recovery period (see Adverse Reactions: Physiological).
4. Respiratory depression may occur with overdosage or too rapid a rate of administration of Ketamine, in which case, supportive ventilation should be employed. Mechanical support of respiration is preferred to administration of analeptics.

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

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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 minimised during the recovery period. This does not preclude the monitoring of vital signs (see Adverse Reactions: 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 pathways, Ketamine should be supplemented with an agent which obtunds visceral pain.
6. Use with caution in the chronic alcoholic and the acutely alcohol-intoxicated patients.
7. An increase in cerebrospinal fluid pressure has been reported following administration of Ketamine. Use with extreme caution in patients with pre-anaesthetic elevated cerebrospinal fluid pressure.

INTERACTION WITH OTHER MEDICAMENTS:
1. Barbiturates and Ketamine are chemically incompatible because of precipitate formation.
2. Ketamine used concurrently with barbiturates and/or narcotics may prolong recovery time.
3. Concurrent use of Ketamine with halogen hydrocarbon inhalation anaesthetics such as: Enflurane, Halothane, Isoflurane, Methoxyflurane, may prolong recovery from anaesthesia.
4. Concurrent use of antihypertensives or CNS depression-producing medications with Ketamine, especially high-dose or rapidly administered Ketamine may increase the risk of hypotension and/or respiratory depression.
5. Ketamine should be administered with caution to patients receiving thyroid hormones because of the risk of hypertension and tachycardia.

USE IN PREGNANCY & LACTATION:
Use in Pregnancy: Ketamine crosses the placenta. This should be borne in mind during operative obstetric procedures in pregnancy. No controlled clinical studies in pregnancy have been conducted. The use in pregnancy has not been established, and such use is not recommended, with the exception of administration during surgery for abdominal delivery or vaginal delivery.
Some neonates exposed to ketamine at maternal intravenous doses ≥1.5 mg/kg during delivery have experienced respiratory depression and low Apgar scores requiring newborn resuscitation.
Marked increases in maternal blood pressure and uterine tone have been observed at intravenous doses greater than 2 mg/kg.
Data are lacking for intramuscular injection and maintenance infusion of ketamine in the parturient population, and recommendations cannot be made.
Although extensive animal studies have not shown any adverse effects on the foetus, the use of Ketamine in the first trimester of pregnancy must be carefully assessed by the physician.
Use in Lactation: The safe use of ketamine during lactation has not been established, and such use is not recommended.

SIDE EFFECTS:
Cardiovascular: Blood pressure and pulse rate are frequently elevated following administration of Ketamine. 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. Laryngo-spasm and other forms of airway obstruction have occurred during Ketamine anaesthesia.
Eye: Diplopia and nystagmus have been noted following Ketamine administration. Ketamine may also cause a slight elevation in intraocular pressure measurement.
Psychological: Emergency reactions have occurred in approximately 12% 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 behaviour which a few patients recall as an 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 post-operatively. No residual psychological effects are known to have resulted from use of Ketamine. 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 intramuscularly. These reactions may be reduced if verbal, tactile and visual stimulation of the patient is minimised 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 or ultra-short acting barbiturate may be required to terminate a severe emergence reaction. The incidence of emergence reactions is induced as experience with the drug is gained. When Ketamine is used on an out-patient basis, the patient should not be released until recovery from anaesthesia is complete and then should be accompanied by a responsible adult.
Neurological: In some patients, enhanced skeletal muscle 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, 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**).
General: Local pain and exanthema at the injection site have infrequently been reported. Transient erythema and/or morbiliform rash have also been reported.

SYMPTOMS AND TREATMENT OF OVERDOSE:
Respiratory depression can result from an overdosage of Ketamine. 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.

INCOMPATIBILITIES: If diazepam is administered concurrently with ketamine, the two medications should be given separately. The two medications should not be mixed in a syringe or added to the same intravenous infusion solution. Ketamine and barbiturates should not be injected from the same syringe because they will form a precipitate.

STORAGE CONDITIONS: Store below 25ºC. Protect from light. KEEP OUT OF REACH OF CHILDREN. *JAUHKAN DARIPADA KANAK-KANAK*
Stability after opening: Please store in refrigerator for not more than 4 weeks. Do not freeze. Discard if any physical changes observed.

SHELF LIFE:
Please refer to outer package.

PACK SIZE:
Pack in a box of 5 and 25 x 10ml vials.

PRODUCT REGISTRATION HOLDER & MANUFACTURER:
DUOPHARMA (M) SDN BHD
Lot 2599, Jalan Seruling 59 Kawasan 3,
Taman Klang Jaya, 41200 Klang, Selangor, MALAYSIA.

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