SUMMARY OF PRODUCT CHARACTERISTICS:

1. NAME OF THE MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Ketamine Hydrochloride USP

Equivalent to Ketamine……50.0 mg

Benzethonium Chloride USP……0.01 % w/v

(As preservative)

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection

Clear, colorless liquid.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

KETAMAX is recommended:

- As an anaesthetic agent for diagnostic and surgical procedures. When used by intravenous or intramuscular injection, KETAMAX is best suited for short procedures. With additional doses, or by intravenous infusion, KETAMAX 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 catheterization 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.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Posology:

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.

Preoperative preparations:

KETAMAX can be safely used alone when the stomach is 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.

Note: Ketamine is chemically incompatible with barbiturates and diazepam because of precipitate formation. Therefore, these should not be mixed in the same syringe or infusion fluid.

Onset and duration:

As with other general anaesthetic agents, the individual response to KETAMAX is somewhat varied depending on the dose, route of administration, age of patient, and concomitant use of other agents, so that dosage recommendation cannot be absolutely fixed. 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.

A. KETAMAX as the sole anaesthetic agent:

Intravenous Infusion: The use of KETAMAX 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.

General Anaesthesia Induction:

An infusion corresponding to 0.5 - 2 mg/kg as total induction dose.

Maintenance of anaesthesia:

Anaesthesia may be maintained using a microdrip infusion of 10 - 45 microgram/kg/min (approximately 1 – 3 mg/min). The rate of infusion will depend on the patient's reaction and response to anaesthesia. The dosage required may be reduced when a long acting neuromuscular blocking agent is used.

Intermittent Injection:

Induction:

Intravenous Route:

The initial dose of KETAMAX administered intravenously may range from 1 mg/kg to 4.5mg/kg (in terms of ketamine base).The average amount required to produce 5 to 10 minutes of surgical anaesthesia has been 2.0 mg/kg. It is recommended that intravenous administration be accomplished slowly (over a period of 60 seconds). More rapid administration may result in respiratory depression and enhanced pressor response.

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.

Intramuscular Route:

The initial dose of KETAMAX 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.

Dosage in Hepatic Insufficiency:

Dose reductions should be considered in patients with cirrhosis or other types of liver impairment.

Dosage in Obstetrics

Data are lacking for intramuscular injection and maintenance infusion of ketamine in the parturient population, and recommendations cannot be made.

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 KETAMAX by either the intravenous or intramuscular route.

Each additional dose is from ½ 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 KETAMAX 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.

B. KETAMAX as induction agent prior to the use of other general anaesthetics:

Induction is accomplished by a full intravenous or intramuscular dose of KETAMAX as defined above. If KETAMAX has been administered intravenously and the principal anaesthetic is slow-acting, a second dose of KETAMAX may be required 5 to 8 minutes following the initial dose. If KETAMAX has been administered intramuscularly and the principal anaesthetic is rapid-acting, administration of the principal anaesthetic may be delayed up to 15 minutes following the injection of KETAMAX.

C. KETAMAX as supplement to anaesthetic agents:

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

D. 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.

4.3 CONTRAINDICATIONS

Hypersensitivity to the active substance.

Ketamax is contra-indicated in persons in whom an elevation of blood pressure would constitute a serious hazard. Ketamax should not be used in patients with eclampsia or pre-eclampsia, severe coronary or myocardial disease, cerebrovascular accident or cerebral trauma.

4.4 SPECIAL WARNING AND PRECAUTIONS FOR USE

To be used only in hospitals by or under the supervision of experienced medically qualified anaesthetists except under emergency conditions.

As with any general anaesthetic agent, resuscitative equipment should be available and ready for use. Respiratory depression may occur with over dosage of ketamine, in which case supportive ventilation should be employed. Mechanical support of respiration is preferred to the administration of analeptics.

The intravenous dose should be administered over a period of 60 seconds. More rapid administration may result in transient respiratory depression or apnoea and enhanced pressor response. Because pharyngeal and laryngeal reflexes usually remain active, mechanical stimulation of the pharynx should be avoided unless muscle relaxants, with proper attention to respiration, are used. In surgical procedures involving visceral pain pathways, ketamine should be supplemented with an agent which obtunds visceral pain.

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

Ketamine should be used with caution in patients with the following conditions:

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

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, particularly with extended use (>3 days) or drug abuse.

Since an increase in cerebrospinal fluid (CSF) pressure has been reported during ketamine anaesthesia, KETAMAX should be used with special caution in patients with preanaesthetic elevated cerebrospinal fluid pressure.

Use with caution in patients with globe injuries and increased intraocular pressure (e.g. glaucoma) because the pressure may increase significantly after a single dose of ketamine.

Use with caution in patients with neurotic traits or psychiatric illness (e.g. schizophrenia and acute psychosis).

Use with caution in patients with acute intermittent porphyria.

Use with caution in patients with seizures.

Use with caution in patients with hyperthyroidism or patients receiving thyroid replacement (increased risk of hypertension and tachycardia).

Use with caution in patients with pulmonary or upper respiratory infection (ketamine sensitizes the gag reflex, potentially causing laryngospasm).

Use with caution in patients with intracranial mass lesions, a presence of head injury, or hydrocephalus.

Emergence Reactions

The psychological manifestations vary in severity between pleasant dream-like states, vivid imagery, hallucinations, nightmares or illusions and emergence delirium (often consisting of dissociative or floating sensations). In some cases these states have been accompanied by confusion, excitement, and irrational behaviour which a few patients recall as an unpleasant experience. Emergence delirium phenomena may occur during the recovery period. The incidence of these 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.

Cardiovascular:

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

Elevation of blood pressure begins shortly after the injection of Ketamine, reaches a maximum within a few minutes and usually returns to pre-anaesthetic values within 15 minutes after injection. The median peak rise of blood pressure in clinical studies has ranged from 20 to 25 percent of pre-anaesthetic values. Depending on the condition of the patient, this elevation of blood pressure may be considered a beneficial effect, or in others, an adverse reaction.

Long-Term Use

Cases of cystitis including haemorrhagic cystitis have been reported in patients being given ketamine on a longterm basis. This adverse reaction develops in patients receiving long term ketamine treatment after a time ranging from 1 month to several years. Ketamine is not indicated nor recommended for long term use. Hepatotoxicity has also been reported in patients with extended use (> 3 days).

Drug Abuse and Dependence

Ketamine has been reported as being 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. Cases of cystitis including haemorrhagic cystitis and cases of hepatotoxicity have also been reported. If used on a daily basis for a few weeks, dependence and tolerance may develop, particularly in individuals with a history of drug abuse and dependence. Therefore the use of Ketamax should be closely supervised and it should be prescribed and administered with caution.

SPECIAL PRECAUTIONS FOR STORAGE AFTER DILUTION:

Chemical and physical in-use stability has been demonstrated for 48 hours at 25°C protected from light. From a microbiological point of view, the product should be used immediately. If not used immediately, in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution have taken place in controlled validated aseptic conditions.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Prolonged recovery time may occur if barbiturates and/or narcotics are used concurrently with ketamine, Diazepam is known to increase the half-life of ketamine and prolongs its pharmacodynamic effects. Dose adjustments may therefore be needed.

Ketamine is chemically incompatible with barbiturates and diazepam because of precipitate formation. Therefore, these should not be mixed in the same syringe or infusion fluid.

Ketamine may potentiate the neuromuscular blocking effects of atracurium and tubocurarine including respiratory depression with apnea.

The use of halogenated anesthetics concomitantly with ketamine can lengthen the elimination half-life of ketamine and delay recovery from anesthesia. Concurrent use of ketamine (especially in high doses or when rapidly administered) with halogenated anesthetics can increase the risk of developing bradycardia, hypotension or decreased cardiac output.

The use of Ketamine with other central nervous system (CNS) depressants (e.g. ethanol, phenothiazines, sedating H1 blockers or skeletal muscle relaxants) can potentiate CNS depression and/or increase risk of developing respiratory depression. Reduced doses of ketamine may be required with concurrent administration of other anxiolytics, sedatives and hypnotics.

Ketamine has been reported to antagonize the hypnotic effect of thiopental, Patients taking thyroid hormones have an increased risk of developing hypertension and tachycardia when given ketamine, Concomitant use of antihypertensive agents and ketamine increases the risk of developing hypotension. Sympathomimetics (directly or indirectly acting) and vasopressin may enhance the sympathomimetic effects of ketamine.

Concomitant use with ergometrine may lead to an increase in blood pressure.

When ketamine and theophylline or aminophylline are given concurrently, a clinically significant reduction in then seizure threshold may be observed. Unpredictable extensor-type seizures have been reported with concurrent administration of these agents. Drugs that inhibit CYP3A4 enzyme activity generally decrease hepatic clearance, resulting in increased plasma concentration of CYP3A4 substrate medications, such as ketamine. Coadministration of ketamine with drugs that inhibit CYP3A4 enzyme may require a decrease in ketamine dosage to achieve the desired clinical outcome. Drugs that induce CYP3A4 enzyme activity generally increase hepatic clearance, resulting in decreased plasma concentration of CYP3A4 substrate medications, such as ketamine. Coadministration of ketamine with drugs

that induce CYP3A4 enzyme may require an increase in ketamine dosage to achieve the desired clinical outcome.

4.6 FERTILITY, PREGNANCY AND LACTATION

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 new born 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.

Lactation

The safe use of ketamine during lactation has not been established, and such use is not recommended.

Studies in animals have shown reproductive toxicity.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINE

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. 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

4.8 UNDESIRABLE EFFECTS

The order of frequency are Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Not known (frequency cannot be estimated from the available data) The following Adverse Events have been reported:

Immune system disorders

Rare: Anaphylactic reaction*

Metabolism and nutrition disorders
Uncommon: Anorexia
Psychiatric disorders
Common: Hallucination, Abnormal dreams, Nightmare, Confusion, Agitation, Abnormal behaviour
Uncommon: Anxiety
Rare: Delirium* Flashback*, Dysphoria*, Insomnia, Disorientation*
Nervous system disorders
Common: Nystagmus, Hypertonia, Tonic clonic movements
Eye disorders
Common: Diplopia
Not Known: Intraocular pressure increased
Cardiac disorders
Common: Blood pressure increased, Heart rate increased
Uncommon: Bradycardia, Arrhythmia
Vascular disorders
Uncommon: Hypotension
Respiratory, thoracic and mediastinal disorders\
Common: Respiratory rate increased
Uncommon: Respiratory depression, Laryngospasm
Rare: Obstructive airway disorder*, Apnoea*
Gastrointestinal disorders
Common: Nausea, Vomiting
Rare: Salivary hypersecretion*
Hepatobiliary disorders
Not Known: Liver function test abnormal, Drug-induced liver injury**
Skin and subcutaneous tissue disorders
Common: Erythema, Rash morbilliform
Renal and urinary disorders
Rare: Cystitis*, Haemorrhagic cystitis*
General disorders and administration site conditions
Uncommon: Injection site pain, Injection site rash
* AE frequency estimated from post-marketing safety database
** Extended period use (> 3 days) or drug abuse

4.9 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 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

INCOMPATIBILITIES:

Ketamine is chemically incompatible with barbiturates and diazepam because of precipitate formation. Therefore, these should not be mixed in the same syringe or infusion fluid.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

ATC code: N01AX03, **Pharmacotherapeutic group:** General anaesthetics.

Pharmacodynamics:

Ketamine is a rapidly acting general anaesthetic for intravenous or intramuscular use with a distinct pharmacological action. Ketamine hydrochloride produces dissociative anaesthesia characterized by catalepsy, amnesia, and marked analgesia which may persist into the recovery period. Pharyngeal-laryngeal reflexes remain normal and skeletal muscle tone may be normal or can be enhanced to varying degrees. Mild cardiac and respiratory stimulation and occasionally respiratory depression occur.

Mechanism of Action:

Ketamine induces sedation, immobility, amnesia and marked analgesia. 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 somesthetic sensory blockade. It may selectively depress the thalamoneocortical system before significantly obtunding the more ancient cerebral centres 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.

5.2 Pharmacokinetics Properties

Absorption

Ketamine is rapidly absorbed following intra-muscular administration

Distribution

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. In humans at an intravenous bolus dose of 2.5 mg/kg, the distribution phase of ketamine lasts about 45 minutes, with a half-life of 10 to 15 minutes, which is associated with the duration of the anaesthetic effect (about 20 minutes). Plasma ketamine concentrations are about 1.8 to 2.0 μg/mL at 5 minutes after an intravenous bolus injection of 2 mg/kg dose and about 1.7 to 2.2 μg/mL at 15 minutes after an intramuscular injection of 6 mg/kg dose in adults and children. In parturients receiving an intramuscular dose of 250 mg (approximately 4.2 mg/kg), placental transfer rate of ketamine from maternal artery to umbilical vein was 47% at the time of delivery (1.72 versus 0.75 μg/mL). Average delivery time for these parturients was 12 minutes from the time of ketamine injection to vaginal delivery of a newborn.

Biotransformation

Biotransformation takes place in liver. Termination of anaesthetic is partly by redistribution from brain to other tissues and partly by metabolism. CYP3A4 enzyme is the primary enzyme responsible for ketamine Ndemethylation to norketamine in human liver microsomes; with CYP2B6 and CYP2C9 enzymes as minor contributors.

Elimination

Elimination half-life is approximately 2-3 hours, and excretion renal, mostly as conjugated metabolites.

5.3 Preclinical safety data

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Carcinogenesis:
Long-term animal studies have not been conducted to evaluate the carcinogenic potential of ketamine.

Mutagenesis:
In a published report, ketamine was clastogenic in the in vitro chromosomal aberration assay.

Impairment of Fertility:
Adequate studies to evaluate the impact of ketamine on male or female fertility have not been conducted. Male and female rats were treated with 10 mg/kg ketamine IV (0.8 times the average human induction dose of 2 mg/kg IV based on body surface area) on Days 11, 10, and 9 prior to mating. No impact on fertility was noted; however, this study design does not adequately characterize the impact of a drug on fertility endpoints.

Animal Toxicology and/or Pharmacology:
Published studies in animals demonstrate that the use of anesthetic agents during the period of rapid brain growth or synaptogenesis results in widespread neuronal and oligodendrocyte cell loss in the developing brain and alterations in synaptic morphology and neurogenesis. 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. In primates, exposure to 3 hours of an anesthetic regimen that produced a light surgical plane of anesthesia did not increase neuronal cell loss, however, treatment regimens of 5 hours or longer increased neuronal cell loss. Data in rodents and in primates suggest that the neuronal and oligodendrocyte cell losses are associated with subtle but prolonged cognitive deficits in learning and memory. The clinical significance of these nonclinical findings is not known, and healthcare providers should balance the benefits of appropriate anesthesia in neonates and young children who require procedures against the potential risks suggested by the nonclinical data.
In published studies, intraperitoneal administration of ketamine at doses greater than 40 mg/kg induced vacuolation in neuronal cells of the posterior cingulate and retrosplenial cortices in adult

rats, similar to what has been reported in rodents administered other NMDA receptor antagonists. These vacuoles were demonstrated to be reversible and did not progress to degeneration or neuronal death up to doses of 80 mg/kg (1.2 times the human dose of 10 mg/kg based on body surface area). A no-effect level for neuronal vacuolation was 20 mg/kg intraperitoneal (0.3 times a human dose of 10 mg/kg on a body surface area basis). The window of vulnerability to these changes is believed to correlate with exposures in humans from the onset of puberty through adulthood. The relevance of this finding to humans is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzethonium chloride

Water for injection

6.2 Incompatibilities

Ketamine is chemically incompatible with barbiturates and diazepam because of precipitate formation. Therefore, these should not be mixed in the same syringe or infusion fluid.

6.3 Shelf life

3 years.

Proposed shelf life (after reconstitution or dilution): Store at 30°C and 2 to 8°C for 48 hours.

Proposed shelf life (after first opening container): Store at 25°C for 72 hours

6.4 Special precautions for storage

Store below 30ºC, protected from light.

Storage after Dilution

Chemical and physical in-use stability has been demonstrated for 48 hours at 25°C protected from light. From a microbiological point of view, the product should be used immediately. If not used immediately, in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution have taken place in controlled validated aseptic conditions..

6.5 Nature and contents of container

The product is available in 10 ml amber vial USP Type-I with 20 mm bromobutyl rubber stopper and 20 mm Ice blue flip off seal with “Troikaa embossed”. Further such 1 labelled vial packed in a printed carton along with package insert.

6.6 Special precautions for disposal

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

Not Applicable

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not Applicable

10. DATE OF REVISION OF THE TEXT

Not Applicable