SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ketamin Abcur 10 mg/ml, solution for injection
Ketamin Abcur 50 mg/ml, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml solution for injection contains ketamine hydrochloride equivalent to 10 mg ketamine.
1 ampoule of 5 ml contains ketamine hydrochloride equivalent to 50 mg ketamine.

Each ml solution for injection contains ketamine hydrochloride equivalent to 50 mg ketamine.
1 ampoule of 5 ml contains ketamine hydrochloride equivalent to 250 mg ketamine.
1 ampoule of 10 ml contains ketamine hydrochloride equivalent to 500 mg ketamine.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).
Clear colourless solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Induction and maintenance of anaesthesia for diagnostic and surgical procedures either as a single anaesthetic agent or in combination with other anaesthetic agents. Prior to the induction or to supplement regional anaesthesia.

Ketamin Abcur is indicated in children and adults.

4.2 Posology and method of administration

Ketamin Abcur should only be administered by or under supervision of medically qualified anaesthetists. Equipment to ensure the vital functions should be available.

Ketamin Abcur is not indicated or recommended for long-term use (see sections 4.1 and 4.4).

Adults, elderly (over 65 years) and children:

Premedication: Atropine or glycopyrrolate should be given preoperatively to inhibit mucus secretion. Benzodiazepine derivate such as midazolam, as premedication (intravenous or rectal), can be given to supress the initial hyperkinetic circulation and reduce the frequency of anxiety during awakening.

Posology

Intramuscular: For intramuscular administration the higher strength, Ketamin Abcur 50 mg/ml, should be chosen to minimize the volume.

i.m. injection	*Dose (mg/kg body weight)*	*Onset time (min)*	*Duration (min)*
Induction	10.0 (6.5–13.5)	3-5	12-25
Maintenance	½ the induction dose		

Intravenous: Administration of intravenous bolus dose should be slow (at least 60 seconds). More rapid administration may result in transient respiratory depression.

i.v. injection	*Dose (mg/kg body weight)*	*Onset time (min)*	*Duration (min)*

Induction	2.0 (1.0–4.5)	1	5-15
Maintenance	½ the induction dose or transition to infusion. See below.		

Conversion table: Dose in mg/kg body weight to dose in ml/kg body weight

Dose *mg/kg body weight*	*Dose* *ml/kg body weight* *Ketamin Abcur 10 mg/ml*	*Dose* *ml/kg body weight* *Ketamin Abcur 50 mg/ml*
1.0	0.10	0.02
2.0	0.20	0.04
4.5	0.45	0.09
6.5	0.65	0.13
10.0	1.00	0.20
13.5	1.35	0.27

Infusion: Infusion gives a more even course of anaesthesia. The total dose of ketamine is often lower than with intermittent injections and awakening occurs faster. During ventilation with oxygen/nitrous oxide, a dose of ketamine in the lower range may be sufficient.

Infusion	*Dose*
Induction	2.0-6.0 mg/kg body weight
Maintenance	2.0-6.0 mg/kg body weight and hour

The dose above is equivalent to about 1 drop/kg body weight and minute of ketamine 1 mg/ml solution for infusion.

Dosing in obstetrics: For use in obstetrics, during vaginal delivery or cesarean section, an intravenous dose in the interval 0.2-1.0 mg/kg is recommended, see section 4.6.

Dosing in hepatic impairment: Dose reduction should be considered for patients with cirrhosis or hepatic impairment for other reasons (see section 4.4).

Dosing in renal impairment
Dose reduction is usually not required.

Combination with other anaesthetic agents: Ketamine can advantageously be combined with benzodiazepine derivates, such as midazolam. Ketamine and midazolam can be mixed in the same infusion (10 ml Ketamin Abcur 50 mg/ml + 7.5 ml midazolam 5 mg/ml per 500 ml solution for infusion).

Induction (i.v. injection)	
ketamine	2 mg/kg body weight
midazolam	0.15 mg/kg body weight

Maintenance (continuous infusion)	
ketamine	1 mg/kg bodyweight and hour
midazolam	0.075 mg/kg body weight and hour

Method of administration

For instructions on dilution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Patients in whom an increase in blood pressure poses a serious risk. Eclampsia or pre-eclampsia.

4.4 Special warnings and precautions for use

Ketamin Abcur should be used with caution in patients with:
- hypovolemia, dehydration or heart disease, especially coronary artery disease (e.g. congestive heart failure, myocardial ischemia and myocardial infarction), because of the substantial increase in myocardial oxygen consumption.

- mild to moderate hypertension and tachyarrhythmias.
- increased cerebrospinal fluid pressure and CNS injuries or diseases, as an increase in cerebrospinal pressure has been reported during ketamine anaesthesia.
- increased intraocular pressure (e.g. glaucoma) and ocular examination or operations, where an increase in intraocular pressure is inappropriate.
- chronic or acute alcohol intoxication.
- neurotic features or psychiatric history (e.g. schizophrenia and acute psychosis).
- acute intermittent porphyria.
- hyperthyroidism or patients on thyroid replacement (increased risk of hypertension and tachycardia).
- pulmonary or upper respiratory infection (ketamine sensitises the gag reflex, and can potentially cause laryngospasm).
- intracranial lesions, head injury, eyeball injury or hydrocephalus.

The onset of anaesthesia is accompanied by transient tachycardia, an increase in blood pressure and cardiac output, which return to baseline within 15 minutes after the injection. In clinical studies, the mean increase in blood pressure has been between 20 to 25% above baseline. Depending on the patient's general condition, the increase in blood pressure can be considered a side effect or a beneficial effect of ketamine.

Ketamine is metabolised in the liver, so hepatic clearance is required for the clinical effects to cease. Prolongation of the effect may occur in patients with cirrhosis or other impaired liver function. Dose reduction should be considered in these patients.

Ketamine has been given as a only agent with good safety when the ventricle has not been emptied. However, since the need for supplementary anesthetics or muscle relaxants cannot always be predicted, it is recommended that the patient fasts for 4-6 hours before surgery to avoid aspiration. Since pharyngeal reflexes are usually preserved, mechanical stimulation of the pharynx should be avoided unless adequate muscle relaxants are used.

Long-Term Use

Ketamine is not indicated or recommended for long-term use (see sections 4.1 and 4.2).

Cases of cystitis including haemorrhagic cystitis, acute kidney injury, hydronephrosis, and ureteral disorders have been reported in patients treated with ketamine for long periods (outside the current indication), particularly when ketamine has been abused. These adverse reactions develop over a period of time ranging from 1 month to several years in patients treated with ketamine for long periods.

Hepatotoxicity, such as mixed liver injury, cholestatic liver injury and biliary dilatation, has also been reported in patients with long-term use (>3 days), see section 4.8.

Drug abuse and dependence

There have been reports of ketamine being used as a drug of abuse. Reports indicate that ketamine causes a range of symptoms including, but not limited to, flashbacks, hallucinations, depression, anxiety, insomnia or confusion (see section 4.8). Other adverse reactions have also been reported: see "Long-Term Use".

Ketamine dependence and tolerance may develop in individuals with a history of drug abuse and dependence. For this reason, ketamine should be prescribed and administered with caution.

Ketamin Abcur contains sodium

1 ampoule of 10 mg/ml contains less than 1 mmol sodium (23 mg), i.e. essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Theophylline

Combination with theophylline or aminophylline should be avoided, as there is clinical and experimental evidence of lowered seizure threshold when theophylline or aminophylline is combined with ketamine. Unpredictable seizures with extensor activity have been reported with the simultaneous administration of these agents.

Suxametone

Ketamine may prolong the muscle relaxant effect of suxametone. The combination may require dose adjustment.

Atracurium

Ketamine may potentiate the neuromuscular blocking effects of atracurium including respiratory depression with apnoea.

Diazepam

Premedication with diazepam prolongs the half-life of ketamine with an increased effect as a result. The combination may require dose adjustment.

Vasopressin

A synergistic blood pressure-increasing effect has been observed with the simultaneous administration of ketamine and vasopressin.

Sympathomimetics (directly or indirectly) and vasopressin may enhance the sympathomimetic effects of ketamine.

Concomitant use of ergometrine may lead to blood pressure increase.

Barbiturates, narcotics, inhalation anaesthetics, alcohol, muscular relaxants, etc.

Barbiturates, narcotics, and inhalation anesthetics, if used concomitantly with Ketamine, may prolong recovery. Concomitant use of ketamine (especially at high doses or if it is administered rapidly) with halogenated anaesthetics may increase the risk of developing bradycardia, hypotension or decreased cardiac output.

Concomitant administration of ketamine and other sedatives (e.g. *ethanol, phenothiazines, sedating H_1-blockers or muscle relaxants*) may potentiate CNS depression and/or increase risk of respiratory depression. In the case of concomitant administration of other anxiolytics, sedatives and hypnotics, it may be necessary to reduce the ketamine dose. Ketamine has been reported to antagonise the hypnotic effect of thiopental.

Thyroid hormones
Patients taking thyroid hormones are at increased risk of developing hypertension and tachycardia when receiving ketamine.

Antihypertensive agents
The risk of hypotension increases with the concomitant administration of antihypertensive agents and ketamine.

Drugs that inhibit CYP3A4 enzyme activity typically decrease hepatic clearance, which may lead to increased plasma concentrations of CYP3A4 substrate drugs, such as ketamine. When ketamine is co-administered with drugs that inhibit CYP3A4 (e.g. itraconazole, fluconazole, clarithromycin, erythromycin, verapamil, diltiazem) enzyme, a reduced dosage of ketamine may be required to achieve the desired clinical outcome.

Drugs that induce CYP3A4 enzyme activity typically increase hepatic clearance, which may lead to decreased plasma concentrations of CYP3A4 substrate drugs, such as ketamine. When ketamine is co-administered with drugs that induce CYP3A4 enzymes (e.g. phenytoin, carbamazepine, St. John's wort), increased dosage of ketamine may be required to obtain the desired clinical result.

4.6 Fertility, pregnancy and lactation

Pregnancy
No controlled clinical studies have been conducted during pregnancy. The safety of use during pregnancy has not been established and therefore such use is not recommended, except for administration during caesarean section and vaginal delivery. Ketamine readily crosses the placenta. Animal studies have shown reproductive toxicological effects (see section 5.3).

Some newborns exposed to ketamine when the mother received intravenous doses of ≥1.5 mg/kg during labor have experienced respiratory depression and low Apgar scores, requiring neonatal resuscitation.

Marked increases in maternal blood pressure and uterine muscle tone have been observed at intravenous doses of more than 2 mg/kg.

Breast-feeding
Ketamine passes into breast milk but the risk of harm to the child seems unlikely at therapeutic doses. However, the necessary data are lacking, so its use cannot be recommended.

4.7 Effects on ability to drive and use machines

After treatment with ketamine, the ability to react may be impaired. This should be taken into account when increased attention is required, e.g. when driving.

The patient should refrain from driving or operating machinery for at least 24 hours after ketamine anesthesia. After outpatient anesthesia, the patient should be accompanied home and should refrain from alcohol for the next 24 hours.

4.8 Undesirable effects

Side effects are mostly related to dose and injection rate and are reversible.
CNS side effects are more common if Ketamine is given as the sole anesthetic.

The following adverse reactions have been observed and reported in treatment with ketamine with the following frequencies: Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (frequency cannot be estimated from available data).

MedDRA system organ class database	**Common (≥1/100, <1/10)**	**Uncommon (≥1/1 000, <1/100)**	**Rare (≥1/10 000, <1/1 000)**	**Not known (frequency cannot be estimated from available data)**
Immune system disorders			anaphylactic reaction*	
Metabolism and nutrition disorders		anorexia		
Psychiatric disorders	hallucination, abnormal dreams, nightmare, confusion, agitation, abnormal behaviour	Anxiety, worry	delirium*, flashback*, dysphoria*, insomnia, disorientation	
Nervous system disorders	nystagmus, tonic clonic movements			
Eye disorders	diplopia			

MedDRA system organ class database	**Common (≥1/100, <1/10)**	**Uncommon (≥1/1 000, <1/100)**	**Rare (≥1/10 000, <1/1 000)**	**Not known (frequency cannot be estimated from available data)**
Cardiac disorders		bradycardia, arrhythmia		
Vascular disorders		hypotension		
Respiratory, thoracic and mediastinal disorders		respiratory depression, laryngospasm	obstructive pulmonary disease *, apnoea*	
Gastrointestinal disorders	nausea, vomiting, salivary hypersalivation*			
Hepatobilary disorders				drug induced liver injury**
Skin and subctaneous tissue disorders	erythema, mobilliform rash	exanthem		
Musculoskeletal and connective tissue disorders		increased muscle tone		
General disorders and administration site conditions		injection site pain, injection site rash		

MedDRA system organ class database	Common (≥1/100, <1/10)	Uncommon (≥1/1 000, <1/100)	Rare (≥1/10 000, <1/1 000)	Not known (frequency cannot be estimated from available data)
Investigations	increased blood pressure, increased heart rate, increased respiratory rate	increased intraocular pressure		abnormal liver function test*

* Adverse reaction frequency calculated from safety data collected after launch
** In case of long-term use (>3 days) or drug abuse

Awakening from anesthesia is often accompanied by vivid dreams, with or without psychomotor activity, which may be manifested by nightmares or hallucinations, confusion, emergence delirium (often with dissociative or floating sensations), and irrational behavior. The incidence of these reactions is reduced by combining Ketamine with benzodiazepine derivatives. Transient respiratory depression due to CNS effects may be seen with intravenous induction and is dependent on dose size and injection rate

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V*.

4.9 Overdose

Symptoms:
Clinical signs of overdose are convulsions, cardiac arrhythmias and respiratory arrest.

Management:

Respiratory arrest should be treated with assisted or controlled ventilation until satisfactory spontaneous breathing has returned.

Convulsion should be treated with intravenous diazepam. If this treatment does not produce desired result, intravenous administration of phenytoin or thiopental is recommended.

No specific antidote is available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: general anaesthetic, ATC code: N01AX03

Ketamine contains ketamine in racemic form as the active substance. Ketamine produces a so-called dissociative anesthesia by selectively interrupting association pathways in the brain. In subanesthetic doses, ketamine has an analgesic effect that is probably due to interaction with biogenic amine and endogenous opiate systems. Ketamine usually does not affect the reflexes in the pharynx and larynx and muscle tone remains normal or increases slightly. Cardiovascular and respiratory stimulating effects allow ketamine to be given to high-risk patients in hypovolemic shock. Ketamine's bronchodilator effect enables its use in patients with bronchial asthma and in respiratory treatment of status asthmaticus. The effect on secretion and the gastrointestinal tract is attenuated by premedication with an anticholinergic. The analgesic effect can be used as a complement to regional anesthesia or in mass casualty situations/disaster contexts..

Ketamine is clinically compatible with most common anesthetics and muscle relaxants provided that respiration is maintained.

An intravenous dose of 2.0 mg/kg body weight produces surgical anesthesia within one minute of injection and the anesthetic effect persists for 5-15 minutes. Intramuscular dosage of 10.0 mg/kg body weight produces surgical anesthesia within 3-5 minutes of injection with a duration of 12-25 minutes. To achieve prolonged anesthesia or analgesia, Ketamine can be given by infusion via drip or syringe pump for uniform administration. Intravenous or intramuscular injection can be repeated.

5.2 Pharmacokinetic properties

Absorption
Ketamine is rapidly absorbed following parentral administration.The bioavailability after intramuscular administration is 90 %.

Distribution
Plasma protein binding is approximately 50 %. Lipid solubility is high. Ketamine readily crosses the placenta and is rapidly distributed to highly perfused tissues (e.g. heart, lungs and brain), followed by muscle and peripheral tissues and then fat. Ketamine has a biphasic plasma profile with a distribution phase lasting approximately 45 minutes with a distribution half-life of 10-15 minutes, which clinically corresponds to the anesthetic effect of the drug. Maximum plasma concentrations of ketamine are approximately 1.8-2.0 mikrog/ml 5 minutes after an intravenous bolus injection of 2 mg/kg and approximately 1.7-2.2 mikrog/ml 15 minutes after an intramuscular injection of 6 mg/kg in adults and children.

Biotransformation
Ketamine is metabolized in the liver. The terminal elimination half-life in plasma is approximately 80 minutes for adults and somewhat shorter for children.
Ketamine undergoes N-demethylation in the liver (via the cytochrome P450 system) and hydroxylation of the cyclohexanone ring with the formation of water-soluble conjugates that are excreted in the urine. The CYP3A4 enzyme is the enzyme primarily responsible for the N-demethylation of ketamine to norketamine
in human liver microsomes, with the enzymes CYP2B6 and CYP2C9 contributing to a lesser extent.
Further oxidation also occurs with the formation of cyclohexanone derivatives. The unconjugated N-demethylated metabolite has been shown to be less than one-sixth as potent as ketamine. The unconjugated demethylcyclohexanone derivative has been shown to be less than onetenth as potent as ketamine.

Elimination
Results from studies in adult humans showed that on average 91% of the dose is found in urine and 3% faeces.

5.3 Preclinical safety data

Published studies in animals (including primates) at doses resulting in light to moderate anaesthesia show that the use of anaesthetic agents during the period of rapid brain growth or synaptogenesis results in cell loss in the developing brain that may be associated with long-term cognitive deficits. The clinical significance of these nonclinical findings is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

10 mg/ml:
Sodium chloride
Water for injections

50 mg/ml:
Water for injections

6.2 Incompatibilities

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

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Before first opening: 3 years
After opening: Chemical and physical in-use stability has been demonstrated for 48 hours at 25°C. From 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 reconstitution/dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

No special storage conditions.

6.5 Nature and contents of container

Ketamin Abcur 10 mg/ml: 5 ml glass ampoules (type I) in boxes of 5, 10, 20, 50 or 100 ampoules.
Ketamin Abcur 50 mg/ml: 5 ml glass ampoules (type I) in boxes of 5, 10, 20, 50 or 100 ampoules.
10 ml glass ampoules (type I) in boxes of 5, 10, 20, 50 or 100 ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Ketamin Abcur can be diluted with 50 mg/ml (5%) glucose solution and 9 mg/ml (0.9%) sodium chloride.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Abcur AB
Box 1452
251 14 Helsingborg
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

11-Feb-2026