# Instructions for Medical Use
# Lidocaine-Liqvo with epinephrine
## 1 % and 2 % solution for injection

**Trade Name**: Lidocaine-Liqvo with epinephrine
**International Nonproprietary Name:** Lidocaine, Epinephrine.
**Pharmaceutical Form:** Solution for injection.
**Strength:** 1 % and 2 % with epinephrine 1:100000
**Composition:** *active ingredients:* lidocaine hydrochloride - 10 mg/mL or 20 mg/mL, epinephrine hydrotartrate equivalent to epinephrine - 0.01 mg/mL; *inactive ingredients:* sodium chloride, sodium metabisulfite, citric acid, benzalkonium chloride, water for injection.
**Description:** Clear, colorless or slightly yellowish solution.
**Pharmacotherapeutical Group:** Local anesthetic.
**Code ATC:** N01BB52
**PHARMACOLOGICAL EFFECT**
***Pharmacodynamics***
Lidocaine is a local anaesthetic of the amide type. It causes all types of local anesthesia: terminal, infiltration, conduction. The local anesthetic action consists in neuronal membrane stabilization by reducing its penetration for sodium ions, which prevents action potential occurrence and impulse conduction. It rapidly hydrolyzes in a slightly alkaline media of tissues and after a short latent period acts within 60-90 minutes. Anesthetic activity decreases with tissue acidosis.
Epinephrine - adrenoceptor agonist, constricts blood vessels and prolongs lidocaine action.
***Pharmacokinetics***
Lidocaine is readily absorbed from the gastrointestinal tract, from mucous membranes and through damaged skin also in case of intramuscular administration.
The elimination half-life is 2 hours.
Lidocaine is metabolized in liver with formation of two pharmacologically active metabolites. It eliminates with urine: approximately 90% of dose is excreted in the form of metabolites and less than 10% - unchanged.
Lidocaine crosses the blood-brain and placental barriers.
**Indications for Use**
All types of local anesthesia (infiltration and conduction anesthesia, peripheral nerve blocks) in dentistry, ophthalmology, otorhinolaryngology, obstetrics, gynecology, surgery, dermatology.
Lidocaine-Liqvo with epinephrine 1% is indicated in children above 1 to 12 years of age. Lidocaine-Liqvo with epinephrine 1% and 2% is indicated in adults and children above 12 years of age.
**Contraindications**
Increased sensitivity to lidocaine or any other components of drug product, to other local anesthetics of the amide type, in children bellow 12 years for 2% lidocaine solution, in children bellow 1 year for 1% lidocaine solution.
The use of a vasoconstrictor (epinephrine) is contraindicated for anaesthesia of fingers, toes, tip of nose, ears and penis.
The drug product should be *used* ***with caution*** in patients with epilepsy, complete or partial heart block, arterial hypertension, cerebrovascular and cardiovascular diseases, respiratory depression, severe *liver or kidney impairment*, hyperthyroidism, diabetes, elderly and debilitated patients.
**Dosage And Administration**
Not for intravenous administration.
*The dosage regimen is set individually* according to the indications, the clinical situation and the used dosage form.
The drug product should be administered slowly in the lowest concentration and lowest dose, giving the desired effect. The clinician's experience and the knowledge of the patient's physical status are of important for select the dose.
The below provided table is an indicative guide of drug dosing at the most commonly used blockades. The "Dose" values in column reflect the expected range of average required dose.

| Type of block | Lidocaine concentration, % | Dose | | Indication |
|---|---|---|---|---|
| | | ml | mg | |
| Infiltration anesthesia | 1 | up to 15 | up to 150 | Surgical operations |
| Intercostal nerves (per nerve) | 1 | 2-5 max.15 ml | 20-50 max.150 mg | Surgical operations, Rib fracture |
| Genital area | 1 | 10 | 100 | Instrumental childbirth |
| Paracervical anesthesia (each side) | 1 | 10 | 100 | Surgical operation, Cervical dilatation, Anestesia during labor |
| Sciatic | 2 | 15 | 300 | Surgical operations |

For adults and children above 12 years of age the maximum recommended single dose of lidocaine hydrochloride with epinephrine is 7 mg/kg of body weight, however, in the all cases the maximum dose must not exceed 500 mg.
*Pediatric Patients:*
It is recommended to use a low concentration (1%) of lidocaine solutions in children 1 to 12 years of age. The maximum dose of lidocaine hydrochloride with epinephrine for children should not exceed 7 mg/kg of body weight (0,7 ml). In children with a high body weight a gradual reduction of the dosage is often necessary and should be based on the ideal body weight.
Elderly and debilitated patients should be given the smallest doses commensurate with their age and physical condition.
**Side Effects**
Like other local anesthetics adverse reactions to lidocaine are rare and caused by increased plasma concentration due to accidental intravascular injection, excess dose or rapid absorption from areas with abundant blood supply; either due to hypersensitivity, idiosyncrasy or poor drug tolerance by some patients.
Systemic toxicity reactions are mainly manifested by the central nervous and/or cardiovascular system.
*Immune system disorders:* rare (≥ 1/ 10,000 to < 1/ 1,000) - hypersensitivity reactions (allergic or anaphylactic reactions).
*Nervous system disorders:* common (≥ 1/ 100 to < 1/ 10) - dizziness, paresthesia; uncommon (≥ 1/ 1,000 to < 1/ 100) - reactions of CNS toxicity (convulsions, numbness of tongue, circumoral paresthesia, tinnitus, tremor, dysarthria, hyperacusis, CNS depression); rare (≥1/10,000 to <1/1,000) – neuropathy, peripheral nerve injury, arachnoiditis.
*Eye disorders:* rare - diplopia, visual impairment.
*Cardiovascular disorders:* common - bradycardia, hypotension, hypertension; rare - arrhythmias, cardiac arrest.
*Respiratory disorders:* rare - respiratory depression.
*Gastrointestinal disorders:* common - nausea, vomiting.
**Overdose**
In the event of overdose, systemic toxic reactions may developed, which primary involve the central nervous and (or) cardiovascular systems.
In the event of overdose, symptoms of systemic toxicity reactions appears later 15–60 minutes after injection due to the slower increase of local anesthetic blood concentration.
Accidental intravascular injections of drug product may cause immediate systemic toxic reactions developed immediately after injection (within few seconds or minutes).
CNS reactions are similar for all amide local anesthetics, while cardiovascular reactions are more dependent on the used drug and its dose.
*Central nervous system toxicity*
Systemic toxicity manifestations from the central nervous system develop gradually: the first symptoms are visual disturbances, numbness around the mouth, numbness of tongue, hyperacusis, tinnitus, dizziness. Dysarthria, tremor and muscle twitching are more serious manifestations of systemic toxicity and may

precede the appearance of generalized seizures (these signs must not be mistaken for the patient's neurotic behavior). Loss of consciousness, convulsion from several seconds to several minutes, accompanied by a violation of breathing, the hypoxia rapid development and hypercapnia due to increased muscle activity and inadequate ventilation have been developed at the progression of intoxication.
In severe cases apnoea may occur. Anesthetics toxic effects have been increases at emerging acidosis, hyperkalaemia, hypocalcaemia.
Functions recovery *occurs fairly rapidly* due to anesthetic redistribution from the CNS and its subsequent metabolism and excretion, unless large amounts of the drug have been injected.
*Cardiovascular system toxicity*
Cardiovascular system symptoms are generally preceded by signs of toxicity in the central nervous system, which may be overlooked in patients under heavy sedation (benzodiazepines or barbiturates) or under general anesthesia.
Hypotension, bradycardia, arrhythmia and even cardiac arrest may occur as a result of high systemic concentrations of local anesthetics. In rare cases cardiac arrest is not accompanied previous symptomatology from the CNS.
In children, early local anesthetic toxicity signs are sometimes more difficult to detect because it found so difficult to explain by children, or in the case of regional anesthesia combined with general anesthesia.
*Treatment of acute toxicity*
If signs of acute systemic toxicity appear, injection of the local anaesthetic should be stopped immediately.
In case of convulsion and CNS depression patient needs in adequate treatment, for maintaining oxygenation, stopping seizures, maintaining the activity of the cardiovascular system. Oxygenation should be provided with oxygen, and if necessary, the transition to artificial pulmonary ventilation. If cardiovascular depression occurs (hypotension, bradycardia), appropriate treatment (intravenous fluids, vasopressor, chronotropic and or inotropic agents should be considered). If circulatory failure or cardiac arrest should occur, immediate standard resuscitation should be instituted. Optimal oxygenation, ventilation and circulatory support as well as treatment of acidosis are of vital importance. In case of cardiac arrest longer resuscitation measures may be required.
When treatment of systemic toxicity in children it is necessary to adjust the dose commensurate with age and weight.

**Drug interaction**

Lidocaine should be used with caution in patients receiving other local anesthetics or agents structurally related to amide-type local anesthetics (e.g. anti-arrhythmics, such as mexiletine), since the systemic toxic effects are additive.
Specific interaction studies with lidocaine and anti-arrhythmic drugs class III (e.g. amiodarone) have not been performed, but caution is advised.
The toxicity of lidocaine may increase at simultaneous use with cimetidine and propranolol (due to increasing of lidocaine concentration) when lidocaine is given in high doses over a long time period. Such interactions should be of no clinical importance following short term treatment with lidocaine at recommended doses. Use caution when prescribing solutions containing epinephrine, tricyclic antidepressants, MAO inhibitors, ergot alkaloids and general anesthetics because severe prolonged hypertension may be occur.
Phenothiazine and butyrophenone derivatives may reduce the vasopressor effect of epinephrine.
Simultaneous use of solutions containing epinephrine, with general inhalation anesthesia (halothane, enfluran) increases risk of arrhythmia.
Non-cardioselective beta-blockers such as propranolol enhance pressor effects of epinephrine, which may lead to severe hypertension and bradycardia.

**Cautions**

For local anesthesia only. Unacceptable intravenous administration. Injection should be made slowly with a preliminary or permanent aspiration to avoid intravascular injection. The lowest effective dose is recommended for use. The drug product should be used in the presence of resuscitation equipment and drug product to prevent toxic reactions.
Patients treated with antiarrhythmic drugs class III (e.g. amiodarone) should be under close surveillance and ECG monitoring considered, since cardiac effects may be additive.
Avoid the use of the drug in patients with acute porphyria, since lidocaine is probably porphyrinogenic.
Paracervical block can sometimes cause bradycardia or tachycardia of foetal, and careful monitoring of the foetal heart rate is required.
The lidocaine solution should be injected with *caution* into highly vascularized tissues to avoid intravasal drug exposure (for example, to the head or neck area), in such cases, drug smaller doses are indicated.
There have been post-marketing reports of chondrolysis in patients receiving post-operative intra-articular continues infusions of local anesthetics. In most cases, the chondrolysis have noted into the shoulder joint. Due to multiple contributing factors and inconsistency in the scientific literature regarding mechanism of action, causality has not been established. Prolonged intra-articular continuous infusion is not an approved indication for lidocaine.
The drug product contains sodium metabisulphite, which may cause allergic reactions (including anaphylactic symptoms and life-threatening) and bronchospasm especially in patients with bronchial asthma are sensitive to sulfites.
Preservative containing lidocaine solutions should not be used epidurally, intracisternally, intrathecally, intra- or retro-bulbary or by any route giving access to the cerebrospinal fluid. The volume in a single dose should not exceed 15 ml.
The effect of lidocaine may be reduced at injection into inflamed or infected tissues.
Lidocaine solution containing epinephrine cannot be used as an antiarrhythmic agent.
Since the drug product contains 64 mg of sodium in each vial (20 ml), use with caution in patients observing a salt-free diet.

***Pregnancy and breast-feeding***

Although there is no evidence from animal studies of harm to the foetus, drug product should not be given during early pregnancy except in cases of acute necessity if the potential benefit justifies the potential risk to the fetus. Epinephrine may decrease uterine blood flow and contractility, especially after inadvertent injection into maternal blood vessels.
Lidocaine may enter the mother's milk, but in such small amounts that there is generally no risk of this affecting the neonate. It is not known whether epinephrine enters breast milk or not, but it is unlikely to affect the breast-fed child. Drug product using is possible in breastfeeding.

***Effects on ability to drive and use machines***

After administration of lidocaine it is not recommended to refrain from potentially hazardous activities that require high concentration and speed of psychomotor reactions.

**Release form**

Per 20 ml solution for injection 2 % and 1 % with epinephrine 1: 100000 in glass vials. Per 10 vials along with the instruction for medical drug are placed in a cardboard blocks.

**Storage conditions**

Store below 25°C, protect from light. Keep out of reach of children.

**Shelf life**

2 years. Do not use after expiry date indicated on the packing.

**Delivery terms**

Prescription medicine.

**Marketing Authorisation Holder and Manufacturer**

"LIQVOR" CJSC
Kochinyan 7/9, 0089 Yerevan
Republic of Armenia
Tel: (+374) 60 37 88 00
e-mail: info@liqvor.com