

PACKAGE LEAFLET
for medical use of a medicinal product

LIDOCAINE-DARNITSA

Qualitative and quantitative composition:

active substance: lidocaine;

1 mL of the solution contains 20 mg of lidocaine hydrochloride;

excipients: sodium chloride, sodium hydroxide, water for injection.

Pharmaceutical form. Solution for injection.

Basic physical and chemical properties: clear colorless or slightly coloured liquid.

Pharmacotherapeutic group.

Preparations for local anesthesia. Lidocaine. ATC code N01B B02.

Pharmacological properties.

Pharmacodynamic properties.

A local anesthetic that provides terminal anesthesia, infiltration and conduction anesthesia. The relative toxicity of lidocaine hydrochloride depends on the concentration of the solution. In low concentrations (0.5 %), it does not significantly differ in toxicity from novocaine, with an increase in concentration (1 % and 2 %), toxicity increases.

Pharmacokinetic properties.

When applied topically on the mucous membranes, lidocaine is absorbed to varying degrees depending on the dose and place of application (the maximum concentration is reached in 10-20 minutes); absorption is affected by the rate of perfusion through the mucous membrane. When administered intramuscularly, the maximum concentration is reached in 5-15 minutes. Binding to plasma proteins is 60-80 % (depending on the dose).

It easily passes through histohematic barriers, including the blood-brain barrier. First, it enters tissues with a good blood supply (the heart, lungs, brain, liver, spleen), then it enters adipose and muscle tissues. It passes through the placenta, 40-55 % of the concentration of the drug that was administered to the woman in labor is detected in the body of the neonate.

It is metabolized by 90 % in the liver by oxidative N-dealkylation with the production of active metabolites: monoethyl-glycin xylidine and glycin xylidine which have half-lives of 2 and 10 hours, respectively. It possesses the first pass effect.

In impaired liver function, the elimination half-life may become more than 2-fold higher. 5-20 % is excreted in the urine as a parent drug.

Clinical particulars.

Therapeutic indications.

Local anesthesia (terminal, infiltration and conduction anesthesia) in surgery, ophthalmology, dentistry, otorhinolaryngology; peripheral nerve block and nerve plexus block in various pain syndromes.

Contraindications.

Individual hypersensitivity to drug ingredients as well as to other anaesthetics of the amide type; epileptiform seizures associated with the administration of lidocaine hydrochloride in the medical history; 2nd and 3d degree AV block, complete transverse heart block; sick sinus syndrome; Wolf-Parkinson-White syndrome, Adams-Stokes syndrome; severe heart failure (degree II-III); pronounced hypotension; severe bradycardia; cardiogenic shock; complete AV block; myasthenia gravis; hypovolemia; porphyria; severe renal and/or hepatic insufficiency; retrobulbar administration to patients with glaucoma; blood clotting disorders, anticoagulant therapy; infections at the injection site; non-contact patients.

Interaction with other medicinal products and other forms of interaction.

Chlorpromazine, pethidine, bupivacaine, quinidine, disopyramide, amitriptyline, imipramine, nortriptyline – if co-administered with lidocaine, the concentration of the latter in blood plasma decreases.

Antiarrhythmic drugs (including amiodarone, verapamil, quinidine, disopyramide, ajmaline) – if co-administered with lidocaine, the cardiodepressive effect increases, in particular, the QT interval becomes prolonged and in isolated cases, AV block or ventricular fibrillation may develop. Concomitant use with amiodarone may lead to seizures.

Procainamide – in co-administration with lidocaine, delusions and hallucinations are possible.

Novocaine, novocainamide – in co-administration with lidocaine, excitation of the central nervous system, hallucinations are possible.

Curare-like drugs – in co-administration with lidocaine, muscle relaxation increases (paralysis of the respiratory muscles is possible).

Ethanol – in co-administration with lidocaine, it increases the depressing effect of the latter on respiration.

Vasoconstrictors (epinephrine, methoxamine, phenylephrine) – in co-administration with lidocaine, they enhance the slowing down of the lidocaine absorption and prolong the effect of the latter.

Cimetidine – in co-administration, it reduces the hepatic clearance of lidocaine (reduced metabolism due to the inhibition of microsomal oxidation) and increases its concentration and the risk of toxic effects.

Guanadrel, guanethidine, mecamlamine, trimetaphan – in co-administration for spinal and epidural anesthesia with lidocaine, the risk of pronounced hypotension and bradycardia increases.

β -blockers – in co-administration, they slow down lidocaine metabolism in the liver, increase the effects of lidocaine (including toxic ones), and increase the risk of bradycardia and hypotension. Concomitant use of β -blockers and lidocaine requires the reduction of the dose of the latter.

Cardiac glycosides – in co-administration with lidocaine, the cardiotonic effect of cardiac glycosides decreases.

Digitalis glycosides – if there is intoxication, lidocaine may increase the severity of the AV block.

Sleeping pills or sedatives – in co-administration with lidocaine, an enhancement of the depressing effect of sleeping pills and sedatives on the CNS is possible.

Opioid analgesics (morphine) – in co-administration with lidocaine, the analgesic effect of opioid analgesics increases, however, respiratory depression also increases.

Monoamine oxidase inhibitors (furazolidone, procarbazine, selegiline) – in co-administration with lidocaine, the risk of hypotension increases and the local anesthetic effect of the latter

becomes prolonged. Lidocaine should not be used parenterally during treatment with monoamine oxidase inhibitors.

Anticoagulants (including ardeparin, dalteparin, danaparoid, enoxaparin, heparin, warfarin) – in co-administration with lidocaine, they increase the risk of bleeding.

General anesthetics – in co-administration with lidocaine, the latter increases the depressing effect of general anesthetics (hexobarbital, sodium thiopental intravenously) on the respiratory center.

Polymyxin B – in co-administration with lidocaine, respiratory function monitoring is necessary.

Rifampicin – in co-administration with lidocaine, reduction of the concentration of the latter in the blood is possible.

Propafenone – in co-administration with lidocaine, increased duration and severity of side effects from the side of the central nervous system is possible.

Prenylamine – in co-administration with lidocaine, the risk of development of ventricular arrhythmia of the "pirouette" type increases.

Anticonvulsants, barbiturates (phenytoin) – in co-administration with lidocaine, acceleration of lidocaine metabolism in the liver, reduction of concentration in the blood, and enhancement of cardiodepressive effect is possible.

Isadrin, glucagon – in co-administration with lidocaine, lidocaine clearance increases.

Norepinephrine, mexiletine – in co-administration with lidocaine, the clearance of the latter decreases (toxicity increases); hepatic blood flow decreases.

Acetazolamide, thiazide and loop diuretics – in co-administration with lidocaine as a result of the development of hypokalemia, they reduce the effect of the latter.

Midazolam – in co-administration with lidocaine, the concentration of the latter in blood plasma increases.

Drugs that cause neuromuscular transmission blockade – in co-administration with lidocaine, the effect of drugs that cause neuromuscular transmission blockade increases, since the latter reduce the conduction of nerve impulses.

Special warnings and precautions for use.

Lidocaine can be administered only by a healthcare provider.

When cleaning the injection site with disinfectant solutions containing heavy metals, the risk of developing a local reaction like soreness and swelling increases.

During the use of lidocaine, ECG monitoring is mandatory. In case of sinus node disorders, prolongation of the P-Q interval, widening of the QRS complex, or development of new arrhythmia, the dose should be reduced or the drug should be discontinued.

Before using lidocaine in heart diseases (hypokalemia reduces the effectiveness of lidocaine), it is necessary to normalize the level of potassium in the blood.

When performing planned subarachnoid anesthesia, monoamine oxidase inhibitors should be discontinued at least 10 days before anesthesia.

When performing local anesthesia, special caution should be exercised when injecting the drug into areas containing many blood vessels. During the injection, avoid contact with blood vessels.

When injected into vascularized tissues, an aspiration test is recommended.

Barbiturates are recommended before the administration of high-dose lidocaine.

Caution should be exercised with the aim to avoid accidental subdural or intravascular administration of the drug. It is necessary to establish close monitoring of the systemic cardiovascular and central nervous system toxic effect of the drug (since the doses prescribed for epidural anesthesia are always higher than for subdural anesthesia).

Extreme caution should be used when performing paravertebral anesthesia in patients with neurological diseases, spinal deformity, septicemia and severe arterial hypertension.

Lower doses of the drug should be administered in the head and neck area, including retrobulbar and dental administration, as well as when used for stellate ganglion blockade, since systemic toxic effects of the drug can enter the cerebral circulation through the retrograde flow.

Extreme caution should be exercised with retrobulbar administration, as severe side effects are possible: collapse, shortness of breath, convulsions, reversible blindness.

It should be kept in mind that lidocaine has a pronounced antiarrhythmic effect and can itself act as an arrhythmogenic factor. Therefore, before the drug administration, it is necessary to collect medical history regarding the presence of signs of arrhythmia and use the drug with caution in people with complaints of arrhythmias in the past.

Use with caution and in lower doses in patients with moderate heart failure, moderate hypotension, incomplete atrioventricular block, intraventricular conduction disorders, moderate liver and kidney function disorders (creatinine clearance not less than 10 mL/min), respiratory disorders, epilepsy, after heart surgery, with a genetic predisposition to hyperthermia, weakened patients and elderly patients.

Intramuscular lidocaine administration may increase the concentration of creatinine, which may lead to the misdiagnosis of acute myocardial infarction.

By local anesthesia of tissues with marked vascularization (for example, the neck in case of thyroid surgery), caution should be taken to avoid intravascular administration of the drug.

The safety of amide anesthetics use is uncertain in patients prone to malignant hyperthermia, so its use in such cases should be avoided.

Lidocaine should be used with caution in patients with circulatory insufficiency, hypovolemia, hypotension, hepatic and renal insufficiency.

Use with caution in patients with central nervous system disorders who use narcotics, as acute cardiac system side effects may occur. With the long-term use, it is necessary to monitor the level of electrolytes in the blood. Use with caution in patients who are prone to seizures, in a state of shock, with hypoxia.

Fertility, pregnancy and lactation.

The use of the drug during pregnancy is contraindicated.

If it is necessary to use the drug, breast-feeding should be discontinued.

Effects on ability to drive and use machines.

After using the drug, no activities should be taken that require the psychomotor speed.

Posology and method of administration.

Before using lidocaine hydrochloride, it is mandatory to conduct a skin test for hypersensitivity to the drug, as evidenced by swelling and redness of the injection site.

For local anesthesia, apply as an injection (subcutaneously, intramuscularly) and topically to the mucous membranes. Intravascular administration of the drug should be avoided.

For conduction anesthesia (including anesthesia of the brachial and sacral plexuses), inject 5-10 mL of the solution (100-200 mg of the drug).

For anesthesia of digits of the extremities, the nose, ears, inject 2-3 mL of the solution (40-60 mg of the drug). The maximum dose of the drug for adults when used for conduction anesthesia is 10 mL (200 mg of lidocaine hydrochloride).

For all types of injectable anesthesia, it is possible to combine lidocaine with epinephrine (1:50000-1:100000; prepare ex tempore, add 1 drop of 0.1 % epinephrine solution per 5-10 mL of 2 % lidocaine solution), except cases where the systemic effect of epinephrine (adrenalin) is undesirable (hypersensitivity to epinephrine, arterial hypertension, diabetes mellitus, glaucoma) or short-term anesthetic effect is needed. Epinephrine slows down the absorption of lidocaine and prolongs its action.

For anesthesia in ophthalmology, 2 drops of the solution should be instilled into the conjunctival sac 2-3 times with an interval of 30-60 seconds immediately before the examination or surgery.

For terminal anesthesia, apply lidocaine solution to the mucous membranes in a volume of no more than 20 mL for adults at a dose of up to 2 mg/kg of body weight, the duration of anesthesia is 15-30 minutes. The maximum dose of the solution for adults is 20 mL.

In children with all types of peripheral anesthesia, the total dose of lidocaine hydrochloride should not exceed 3 mg/kg of body weight.

Children.

The drug is not used in children under 12 years of age.

Overdose.

The main symptoms are associated with central nervous system and cardiovascular depression: fatigue, somnolence, depression, dizziness, disorientation, tonic-clonic seizures, coma, tremor, visual disturbances, tinnitus, atrioventricular block, asphyxia, nausea, vomiting, euphoria, psychomotor agitation, asthenia, apnea, bradycardia, low blood pressure, collapse. The first symptoms of an overdose in healthy individuals occur when the concentration of lidocaine hydrochloride in the blood exceeds 0.006 mg/kg; convulsions occur at 0.01 mg/kg.

Treatment: discontinuation of the drug, oxygen therapy, vasoconstrictors (norepinephrine, mesatonum), anticonvulsants, cholinolytics. The patient should stay in a horizontal position; fresh air, oxygen supply and/or artificial respiration should be provided. Central nervous system symptoms should be treated by using short-acting benzodiazepines or barbiturates. If an overdose occurs during anesthesia, a short-acting muscle relaxant should be used. For treatment of bradycardia and conduction disorders, use atropine (0.5-1 mg intravenously), for arterial hypotension use sympathomimetics in combination with β -adrenergic agonists. In case of cardiac arrest, immediate resuscitation measures are indicated. It is possible to perform intubation, artificial lung ventilation. Dialysis is ineffective in the treatment of acute overdosage with lidocaine. There is no specific antidote.

Undesirable effects.

The following undesirable effects may occur during the drug administration:

cardiovascular disorders: decreased blood pressure, tachycardia – if co-administered with a vasoconstrictor, bradycardia, peripheral vasodilation, collapse, tachycardia, palpitations, chest pain, heart pain, arrhythmia, slowing of cardiac conduction, AV heart block, ventricular fibrillation, cardiac arrest; in very rare cases – arterial hypertension;

central and peripheral nervous system disorders: central nervous system agitation (when used in high doses), anxiety, dizziness, confusion, somnolence, sleep disorders, headache, weakness, motor restlessness, euphoria, nystagmus, loss of consciousness, sensitivity disorders, paresthesias, numbness of the tongue and lips (when used in dentistry); in patients with hypersensitivity – euphoria, tremor, trismus, muscle twitching, motor restlessness, convulsions (its risk increases with hypercapnia and acidosis); persistent anesthesia, paresis or palsy of lower extremities and loss of sphincter control (for example, cauda equina syndrome) – is a cause of this more often than other local anesthetics, motor and sensory block, dysarthria, dysphagia, coma;

eye disorders: visual impairment, blurred vision, diplopia, nystagmus, flickering of "flies" in front of the eyes, midriasis, photophobia, reversible blindness, conjunctivitis;

ear disorders: auditory disorders, tinnitus, hyperacusia;

psychiatric disorders: anorexia, irritability, restlessness, hallucinations, depression, anxiety, sleep disorders, agitation;

respiratory, thoracic and mediastinal disorders: rhinitis, dyspnea, difficulty breathing, feeling of suffocation, respiratory depression, bronchospasm, paralysis of the respiratory muscles, respiratory paralysis (more often develops with subarachnoid anesthesia), respiratory arrest;

gastrointestinal disorders: nausea, vomiting, involuntary defecation, abdominal pain;

Renal and urinary disorders: involuntary urination;

skin and subcutaneous tissue disorders: hyperemia, pruritus, rash, urticaria;
reproductive system disorders: decreased libido and/or potency;
immune system disorders: hypersensitivity reactions, including angioedema, generalized exfoliative dermatitis, anaphylactic shock, anaphylactic reactions; immune system suppression;
administration site conditions: a slight burning sensation that resolves with the development of the anesthetic effect (within 1 minute), edema, hyperemia, itching, rash, thrombophlebitis, localized nerve damage at the injection site; in case of spinal or epidural anesthesia, there may be back and leg pain, partial/complete spinal block accompanied by a decrease in blood pressure, impaired defecation, involuntary urination, impotence, loss of sensitivity in the perineal area (the probability of these effects increases with the high dose administration or in case of accidental administration of lidocaine into the intrathecal space when the dose intended for administration into the epidural space enters the intrathecal space); in individual cases, after such an intervention, motor, sensory and/or autonomic function resolve slowly (after several months) or incompletely;
general disorders: persistent anesthesia, hypothermia, feeling of heat, cold or numbness of the extremities, malignant hyperthermia, increased sweating, pale skin, syndrome of edema, weakness.

Shelf life. 3 years.

Special precautions for storage.

Keep in the original package at $\leq 25^{\circ}\text{C}$. Do not freeze.

Keep out of reach of children.

Incompatibilities.

The drug should not be mixed with other medicinal products in the same container, except for the solvents specified in the section "Posology and method of administration".

Lidocaine precipitates when mixed with amphotericin, methohexitone, or sulfadiazine. Depending on the pH of the solution, lidocaine may not be compatible with ampicillin.

Nature and contents of container.

2 mL in an ampoule; 5 ampoules in a blister; 2 blisters in a pack.

Category of release. Prescription only medicine.

Manufacturer. PrJSC "Pharmaceutical firm "Darnitsa".

The manufacturer's location and address of the place of business.

13 Boryspilska Street, Kyiv, 02093 Ukraine

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