HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LIDOCAINE HYDROCHLORIDE safely and effectively. See full prescribing information for LIDOCAINE HYDROCHLORIDE.

LIDOCAINE HYDROCHLORIDE injection, for intravenous use
Initial U.S. Approval: 1948

---------- INDICATIONS AND USAGE----------
Lidocaine Hydrochloride (HCl) is indicated in the acute management of life-threatening ventricular arrhythmias. (1)

----------DOSAGE AND ADMINISTRATION----------
Adults
Recommended Intravenous Bolus: 1 mg/kg to 1.5 mg/kg at 25 to 50 mg/min. Additional 0.5mg/kg to 0.75mg/kg bolus as needed every 5-10 minutes up to a maximum cumulative dose of 3 mg/kg in one hour. Do not administer more than 300 mg/hour.

Recommended Intravenous Infusion: Following bolus, 0.014 to 0.057 mg/kg/min.

Pediatric Patients
Recommended dosage is 1 mg/kg administered as an intravenous bolus, followed by continuous intravenous infusion at 30 mcg/kg/min.

---------- DOSAGE FORMS AND STRENGTHS----------
Injection: 100 mg in 5 mL (20 mg/mL) in a single-dose vial (3)

---------- CONTRAINDICATIONS ----------
Hypersensitivity to lidocaine, any of its formulation components, or local anesthetics of the amide type. (4)

---------- WARNINGS AND PRECAUTIONS----------
- Central Nervous System Depression or Irritability: Central nervous system depression (sedation) or irritability (twitching), which may progress to convulsions accompanied by respiratory depression and/or respiratory arrest. Monitor for premonitory signs and assurance of adequate oxygenation. (5.1)
- Cardiovascular Toxicity: If hypotension or excessive depression of cardiac conductivity is seen, discontinue lidocaine HCl. In patients with hypovolemia, severe congestive heart failure, and shock, use lidocaine HCl with hemodynamic monitoring. (5.2)
- Malignant Hyperthermia: If signs of malignant hyperthermia occur begin immediate treatment for malignant hyperthermia and discontinue lidocaine HCl. (5.3)
- Methemoglobinemia: If signs or symptoms of methemoglobinemia occur begin immediate treatment for methemoglobinemia and discontinue lidocaine HCl. (5.4)

---------- ADVERSE REACTIONS ----------
Most adverse reactions are directly related to lidocaine's antiarrhythmic action. Bradycardia, cardiac arrhythmia, hypotension, dyspnea, dizziness, and confusion have been reported. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

---------- DRUG INTERACTIONS----------
- Effects of Other Drugs on Lidocaine HCl: Strong inhibitors of CYP1A2 systemic lidocaine exposure.
- Moderate inducers of CYP1A2: Decrease systemic lidocaine exposure.
- Beta-adrenergic blockers: Reduce the amount of lidocaine presented for metabolism (12.3)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Lidocaine Hydrochloride (HCl) Injection administered intravenously is indicated in the acute management of life-threatening ventricular arrhythmias.

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing and Administration Considerations

- At the time of administration of lidocaine HCl, ECG monitoring, emergency resuscitative equipment, persons trained for resuscitation, and drugs must be immediately available to manage possible adverse reactions involving the cardiovascular, respiratory, or central nervous system.
- Correct electrolyte disturbances, especially hypokalemia or hypomagnesemia, prior to use and monitor and correct throughout therapy.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

2.2 Recommended Dosage in Adults

Intravenous Bolus

The recommended dosage of lidocaine HCl is 1 mg/kg to 1.5 mg/kg administered as an intravenous bolus under ECG monitoring at the rate of approximately 25 mg/min to 50 mg/min. If needed, administer an additional bolus of lidocaine HCl at a recommended dose of 0.5 mg/kg to 0.75 mg/kg as an intravenous bolus every 5-10 minutes up to a maximum cumulative dose of 3 mg/kg within one hour. Do not administer more than 300 mg of lidocaine HCl during a one-hour period.

For Continuous Intravenous Infusion

Following intravenous bolus, initiate continuous intravenous infusion of lidocaine HCl at 0.014 mg/kg/min to 0.057 mg/kg/min if needed. Discontinue lidocaine HCl as soon as the patient's basic cardiac rhythm is stable or at the earliest signs of CNS toxicity *[see Warnings and Precautions (5.1)]*.

2.3 Recommended Dosage in Pediatric Patients

Although controlled clinical studies to establish pediatric dosing schedules have not been conducted, the recommended dosage is 1 mg/kg administered as an intravenous bolus. Following bolus, initiate continuous intravenous infusion at a rate of 30 mcg/kg/min as needed.

3 DOSAGE FORMS AND STRENGTHS

Injection: 100 mg in 5 mL (20 mg per mL) supplied as a clear, colorless solution in a single-dose vial.

4 CONTRAINDICATIONS

Lidocaine HCl is contraindicated in patients with severe hypersensitivity to lidocaine, any of its formulation components, or local anesthetics of the amide type. Serious and life-threatening hypersensitivity reactions have been reported.

5 WARNINGS AND PRECAUTIONS

5.1 Central Nervous System Depression or Irritability

Lidocaine HCl can cause central nervous system (CNS) toxicity ranging from sedation to convulsions with respiratory compromise. Early signs may include sedation or irritability (twitching), which may progress to convulsions accompanied by respiratory depression and/or respiratory arrest. Monitor for premonitory signs and ensure adequate oxygenation. Establishment of an artificial airway with ventilatory support may be necessary. Monitor for and treat convulsions. Discontinue lidocaine HCl as soon as the patient's basic cardiac rhythm is stable or at the earliest signs of CNS toxicity *[see Dosage and Administration (2.2)]*.

5.2 Cardiovascular Toxicity

Lidocaine HCl can cause cardiovascular toxicity. If hypotension or excessive depression of cardiac conductivity (such as prolongation of the PR interval and widening QRS complex and the appearance of aggravation of arrhythmias) occur, discontinue lidocaine HCl.

Lidocaine HCl may increase the risk of cardiovascular toxicity in patients with underlying cardiovascular disease or hemodynamic instability. In patients with hypovolemia, severe congestive heart failure, and shock, use lidocaine HCl with hemodynamic monitoring.

In patients with sinus bradycardia or incomplete heart block, the administration of lidocaine HCl without prior acceleration in heart rate may promote more frequent and serious ventricular arrhythmias or complete heart block.

Occasional acceleration of ventricular rate may occur when lidocaine HCl is administered to patients with atrial fibrillation.

5.3 Malignant Hyperthermia

Lidocaine HCl is associated with malignant hyperthermia. If signs of malignant hyperthermia occur (unexplained or unexpected tachycardia, tachypnea, respiratory acidosis, or metabolic acidosis), begin immediate treatment for malignant hyperthermia and discontinue lidocaine HCl.

5.4 Methemoglobinemia

Lidocaine HCl is associated with methemoglobinemia. If clinically significant signs or symptoms of methemoglobinemia occur (cyanosis, headache, rapid pulse, shortness of breath, lightheadedness, or fatigue), begin immediate treatment for methemoglobinemia and discontinue lidocaine HCl. Patients with glucose-6-phosphate dehydrogenase deficiency, congenital or idiopathic methemoglobinemia, cardiac or pulmonary compromise, exposure to oxidizing agents or their metabolites, or infants <6 months old are more susceptible and should be closely monitored for signs and symptoms of methemoglobinemia.

6 ADVERSE REACTIONS

The following adverse reactions have been identified during post-approval use of lidocaine HCl. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiovascular

Bradycardia, cardiac arrhythmia, circulatory shock, coronary artery vasospasm, edema, flushing, heart block, hypotension, and local thrombophlebitis.

Ear and labyrinth

Tinnitus.

Gastrointestinal

Nausea, vomiting.

Immune System

Anaphylactoid reaction, anaphylaxis, hypersensitivity reaction.

Nervous System

Headache, shivering, agitation, anxiety, apprehension, coma, confusion, disorientation, dizziness, drowsiness, euphoria, hallucination, hyperesthesia, hypoesthesia, intolerance to temperature, lethargy, loss of consciousness, metallic taste, nervousness, paresthesia, psychosis, seizure, slurred speech, tremor, twitching, weakness.

Respiratory

Bronchospasm, dyspnea, respiratory depression.

7 DRUG INTERACTIONS

7.1 Effects of Other Drugs on Lidocaine HCl

Table 1. Drug Interactions with Lidocaine HCl

Strong CYP1A2 Inhibitors	
Intervention:	Closely monitor for adverse effects when lidocaine HCl is used concomitantly with CYP1A2 inhibitors.
Clinical Impact:	Lidocaine HCl is a CYP1A2 substrate. Strong inhibitors of CYP1A2 have been shown to increase systemic lidocaine exposure *[see Clinical Pharmacology (12.3)]*, which may increase the risk of lidocaine adverse reactions.
Moderate CYP1A2 Inducers	
Intervention:	Monitor efficacy and titrate dose within dosing thresholds to desired therapeutic effect when lidocaine HCl is used concomitantly with CYP1A2 inducers.
Clinical Impact:	Lidocaine HCl is a CYP1A2 substrate. Moderate inducers of CYP1A2 have been shown to decrease systemic lidocaine exposure *[see Clinical Pharmacology (12.3)]*, which may lead to decreased efficacy and need for higher dosing to achieve desired therapeutic effect.
Beta-adrenergic Blockers	
Intervention:	Closely monitor for adverse effects when lidocaine HCl is used concomitantly with beta-adrenergic blockers.
Clinical Impact:	Ninety percent of lidocaine HCl metabolism occurs in the liver. Beta-adrenergic blockers may reduce blood flow to the liver via reduced cardiac output, reducing the amount of lidocaine presented for metabolism. This may increase systemic lidocaine exposure and the risk of lidocaine adverse effects.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are risks to the mother and fetus associated with untreated ventricular arrhythmias; therefore, life-sustaining therapy for ventricular arrhythmias should not be withheld (see *Clinical Considerations*). Available published data and decades of clinical use with lidocaine in pregnant women have not identified any drug-associated risks of major birth defects, miscarriage, or adverse maternal or fetal outcomes.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk

The incidence of ventricular tachycardia is increased and may be more symptomatic during pregnancy. Ventricular arrhythmias most often occur in pregnant women with underlying cardiomyopathy, congenital heart disease, valvular heart disease, or mitral valve prolapse. Breakthrough arrhythmias may also occur during pregnancy, as therapeutic treatment levels may be difficult to maintain due to the increased volume of distribution and increased drug metabolism inherent in the pregnant state.

Maternal adverse reactions

During treatment of systemic toxicity, which may appear as maternal hypotension or fetal bradycardia, the pregnant woman should be maintained in the left lateral decubitus position if possible or manual displacement of the uterus off the great vessels be accomplished. Elevating the patient's legs will also help prevent decreases in blood pressure. The fetal heart rate also should be monitored continuously, and electronic fetal monitoring is highly advisable.

8.2 Lactation

Risk Summary

Published data report the presence of lidocaine and its metabolites in human milk in low amounts, along with poor oral bioavailability. There are no data on the effect of lidocaine on the breastfed infant or the effect on milk production.

8.4 Pediatric Use

Lidocaine hydrochloride is used for the acute management of life-threatening ventricular arrhythmias in pediatric patients. Safety and effectiveness of lidocaine hydrochloride in pediatric patients have not been established by controlled clinical studies *[see Dosage and Administration (2.3)].*

10 OVERDOSAGE

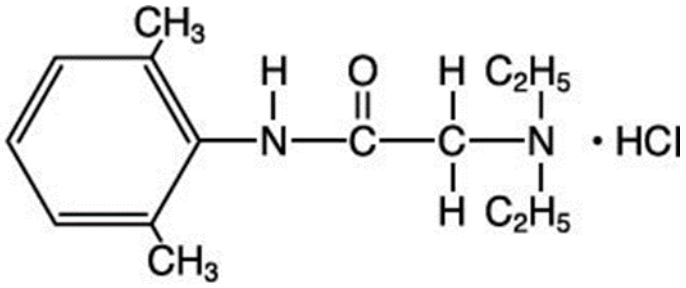
Management of Overdosage:

- In the case of severe reaction, discontinue the use of lidocaine HCl.

- Institute emergency resuscitative procedures and administer the emergency drugs necessary to manage the severe reaction. For severe convulsions, small increments of diazepam or an ultra-short-acting barbiturate or if those are not available a short-acting barbiturate; or if the patient is under anesthesia, a short-acting muscle relaxant may be given intravenously. Patency of the airway and adequacy of ventilation must be assured.
- Should circulatory depression occur, vasopressors, such as ephedrine, or metaraminol may be used. Should cardiac arrest occur, immediate initiation of standard CPR procedures should commence.

11 DESCRIPTION

Lidocaine HCl, chemical name: acetamide, 2-(diethylamino)-N-(2,6- dimethylphenyl)-monohydrochloride has the following structural formula:



Lidocaine HCl, USP is a class Ib antiarrhythmic for intravenous use. It is a sterile, nonpyrogenic solution prepared from lidocaine with the aid of sodium hydroxide and/or hydrochloric acid for pH adjustment.

Each mL contains: Lidocaine HCl 20 mg; Sodium Chloride 6 mg; Water for Injection q.s. Hydrochloric acid and/or sodium hydroxide may have been added for pH adjustment (pH 5.0 to 7.0). The container is for single use; solution contains no preservative.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Lidocaine exerts its antiarrhythmic effect by raising the electrical stimulation threshold of the ventricle during diastole. In usual therapeutic doses, lidocaine produces no change in myocardial contractility, systemic arterial pressure or absolute refractory period. Lidocaine primarily blocks voltage and pH dependent sodium channels, which results in a decrease in conduction velocity. It prolongs the relative refractory period as compared to the action potential duration. It is predominately a blockade of the inactive sodium channels that causes the decrease in action potential and an increase in refractory period.

12.2 Pharmacodynamics

Following single intravenous bolus dosing, the onset of action is 45 to 90 seconds with a duration of 10 to 20 minutes.

Therapeutic doses of lidocaine can be used safely in patients with conduction abnormalities. No significant changes in heart rate, blood pressure, QRS duration, or QT interval changes were noted with lidocaine administration in patients with conduction abnormalities. Therapeutic effects of lidocaine are generally associated with plasma levels of 6 to 25 μmol/L (1.5 to 6 mcg free base per

mL). The blood to plasma distribution ratio is approximately 0.84. Objective adverse manifestations become increasingly apparent with increasing plasma levels above 6 mcg free base per mL.

Hemodynamic Effects

Bolus doses of lidocaine up to 2 mg/kg have been shown to be safe with minimal changes in arterial pressure or heart rate.

Patients were given 6 mg/kg of lidocaine diluted in 50 ml of 5% dextrose over 22 minutes. There were no significant changes in mean heart rate, blood pressure, Atrioventricular nodal conduction time (AH), His-Purkinje conduction time, or QRS duration between control values and during or after the lidocaine infusion.

Cardiac Electrophysiology

At a dose 4 times the maximum recommended human dose (MRHD), lidocaine does not prolong the QT interval to any clinically relevant extent. Patients were given 6 mg/kg of lidocaine diluted in 50 ml of 5% dextrose over 22 minutes: slight but insignificant changes between mean QRS or QT duration before and after lidocaine administration were observed.

12.3 Pharmacokinetics

Distribution

In plasma, lidocaine is predominantly bound to alpha-1-acid glycoprotein. Protein binding is dependent on drug concentration and plasma-concentration of the alpha-1-acid glycoprotein. At 1-4 mcg/mL, the drug is 60-80% bound to alpha-1-acid glycoprotein. Distribution may be decreased in patients with heart failure and liver disease. Lidocaine HCl crosses the blood brain barrier.

Elimination

Elimination is biphasic with an initial half-life of approximately 8 minutes following a single IV bolus. The terminal half-life is approximately 1.5 to 2 hours following a single IV bolus. Prolonged elimination occurs in patients with continuous infusion >24 hours, heart failure, liver disease, shock, and severe renal impairment.

Metabolism

Lidocaine HCl is 90% hepatically cleared via CYP1A2 and CYP3A4. It is a minor substrate of CYP2A6 and CYP2B6. N-dealkylation is a major pathway of lidocaine metabolism and yields the metabolites, monoethylglycinexylidide (MEGX) and glycinexylidide (GX). The pharmacological actions of these metabolites are similar to but less potent than, those of lidocaine HCl.

Excretion

Lidocaine HCl is excreted in the urine, approximately 90% as metabolites and 10% as unchanged drug. Renal impairment can lead to accumulation of active metabolites (MEGX and GX) which may cause CNS toxicity.

Specific Populations

Geriatric Patients

For elderly patients over the age of 65, studies indicate that lidocaine clearance is unchanged, the volumes of distribution is slightly larger compared to younger subjects.

Racial or Ethnic Groups

The pharmacokinetics of lidocaine were investigated in 17 healthy young adult volunteers (seven White, five Asian and five Black). There were no significant differences in the PK of lidocaine among these racial groups.

Patients with Renal Impairment

Patients with renal impairment may accumulate the metabolite of lidocaine because of the dependence of glycinexylidide elimination on renal function. In patients not undergoing hemodialysis, lidocaine clearance was reduced with decrease in renal function. No such changes were observed in patients undergoing intermittent hemodialysis.

Patients with Hepatic Impairment

Prolonged elimination of lidocaine is seen in patients with cirrhosis, as the metabolism of lidocaine depends on liver blood flow and Cytochrome P450. In patients with moderate and severe hepatic impairment (Child-Pugh class B and C, respectively) the half-life of lidocaine was increased 2.5 and 3.5-fold, respectively compared to patients with mild hepatic impairment (Child-Pugh class A).

Drug Interaction Studies

Pharmacokinetic studies of erythromycin, a moderate CYP3A4 inhibitor, have reported <20% or no decrease in lidocaine clearance or AUC when given in combination with IV lidocaine. However, these studies have shown an increase of 30-70% in the AUC of the MEGX metabolite.

A study with rifampin, a strong CYP3A4 inducer, showed increase in clearance by 15% and decrease in AUC by 11% following a single dose of IV lidocaine.

A study with fluvoxamine, a strong CYP1A2 inhibitor, showed decrease in clearance by 41% and decrease in AUC and C_{max} by 22% and 71%, respectively, following a single dose of IV lidocaine.

A pharmacokinetic study with propranolol, a weak CYP1A2 inhibitor and beta blocker, showed a decrease in clearance of 41-47% following single doses of IV lidocaine, with an increase in AUC and C_{max} of 113% and 79%, respectively. Another pharmacokinetic study with propranolol and lidocaine continuous infusion showed a 17-25% decrease in lidocaine clearance. A pharmacokinetic study with nadolol showed a decrease in clearance of 17% *[see Drug Interactions (7)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies of lidocaine HCl in animals to evaluate the carcinogenic and mutagenic potential have not been conducted.

Impairment of Fertility

No significant reduction in fertility occurred in Sprague-Dawley rats when lidocaine was given via continuous subcutaneous infusion via osmotic minipumps up to doses of 126 mg/m^2/hr (approximately 1.1 times the MRHD as mg/m^2/hr).

16 HOW SUPPLIED/STORAGE AND HANDLING

Lidocaine Hydrochloride Injection, USP

Product Code	Unit of Sale	Strength	Each
20805	NDC 63323-208-05 Unit of 25	2% 100 mg per 5 mL (20 mg per mL)	NDC 63323-208-01 5 mL Single Dose Vial

Store at 20°C to 25°C (68°F to 77°F) *[see USP Controlled Room Temperature]*.

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

Preservative Free.

Discard Unused Portion.

Use only if solution is clear and seal is intact.

17 PATIENT COUNSELING INFORMATION

Nervous System Reactions:

Advise patients to recognize early symptoms of nervous system reactions, such as headache, shivering, agitation, anxiety, apprehension, coma, confusion, disorientation, dizziness, drowsiness, euphoria, hallucination, hyperesthesia, hypoesthesia, intolerance to temperature, lethargy, loss of consciousness or slurred speech, and to report any of these symptoms to a healthcare provider immediately *[see Warnings and Precautions (5.1) and Adverse Reactions (6.2)].*

Cardiovascular events:

Advise patients to be alert for the symptoms of cardiovascular events, including chest pain, shortness of breath, weakness, confusion, dizziness, or slurring of speech, and to report any of these symptoms to a healthcare provider immediately *[see Warnings and Precautions (5.2) and Adverse Reactions (6.2)].*

Malignant Hyperthermia:

If the patient or a member of the patient's family has a history of malignant hyperthermia or if the patient has a history of Duchenne muscular dystrophy or other latent neuromuscular disease, inform a healthcare provider immediately. Early signs and symptoms include tachycardia, tachypnea, and respiratory and metabolic acidosis *[see Warnings and Precautions (5.3)].*

Methemoglobinemia*:*

Inform patients that use of lidocaine HCl may cause methemoglobinemia, a serious condition that must be treated promptly. Advise patients or caregivers to seek immediate medical attention if they or someone in their care experience the following signs or symptoms: pale-, gray-, or blue-colored skin (cyanosis); headache; rapid heart rate; shortness of breath; lightheadedness; or fatigue *[see Warnings and Precautions (5.4)]*.

Manufactured by:

FRESENIUS KABI

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