Important Prescribing Information

October 16, 2017

Subject: Temporary importation of intravenous drug products to address drug shortages

Dear Healthcare Professional,

In order to address market shortages of critical drug products including those impacted by the aftermath of Hurricane Maria, Baxter Healthcare Corporation (Baxter) is coordinating with the U.S. Food and Drug Administration (FDA) to increase the availability of products from Baxter's manufacturing facility in Canada. You may be provided with additional letters for other imported products you receive. Please read each letter in its entirety because each letter may contain different, product-specific information.

Baxter has initiated temporary importation of the products tabulated below. These products are manufactured by Baxter's manufacturing facility in Canada and are marketed in Canada. At this time, no other entity except Baxter is authorized by the FDA to import or distribute these products in the United States. FDA has not approved the listed products manufactured by Baxter's manufacturing facility in Canada.

Effective immediately, and during this temporary period, Baxter will offer the following:

Product name and description	Size	Product code	Pack factor	NDC
0.9% Sodium Chloride Injection USP in VIAFLEX Container	50 mL	JB1301P	96	0338-9579-96
	100 mL	JB1302P	96	0338-9583-96
	250 mL	JB1322P	30	0338-9604-30
	500 mL	JB1323	24	0338-9608-24
	1000 mL	JB1324	12	0338-9612-12
5% Dextrose Injection USP in VIAFLEX Container	50 mL	JB0081P	96	0338-9533-96
	100 mL	JB0082P	96	0338-9530-96
0.9% Sodium Chloride Injection USP in MINI-BAG Plus Container	50 mL	JB0042	96	0338-9531-96
	100 mL	JB0043P	72	0338-9535-72
5% Dextrose Injection USP in MINI-BAG Plus Container	50 mL	JB0040	96	0338-9536-96
	100 mL	JB0041P	72	0338-9539-72
Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection USP (4mg/mL) in VIAFLEX Container	1g/250 mL	JB0972P	30	0338-9590-30
	2g/500 mL	JB0973	24	0338-9586-24

It is important to note the following:

- The imported Canadian products have a dual-language label with English and French.
- The imported products' administration port system is fully compatible with IV set spike heads on Baxter IV sets marketed in the United States.
- **The barcode may not register accurately on the U.S. scanning systems.** Institutions should manually input the product into their systems to confirm that barcode systems do not provide incorrect information when the product is scanned. Alternative procedures should be followed to assure that the correct drug product is being used and administered to individual patients.

There are some differences in the labeling between the U.S. marketed products and the Canadian products. Please see the product comparison tables at the end of this letter for:

- Table 1. Key differences in 0.9% Sodium Chloride Injections, USP
- Table 2. Key differences in 5% Dextrose Injections, USP
- Table 3. Key differences in Lidocaine Hydrochloride and Dextrose Injection, USP

Please refer to the FDA-approved package insert for the full prescribing information of each drug product as follows:

- 0.9% Sodium Chloride Injection, USP (click here)
- 5% Dextrose Injection, USP (click here)
- 0.9% Sodium Chloride Injection USP in MINI-BAG Plus Container (click here)
- 5% Dextrose Injection USP in MINI-BAG Plus Container (click here)
- Lidocaine Hydrochloride and 5% Dextrose Injection USP (click here)

If you have any questions about the information contained in this letter or the use of the imported products, please contact Baxter's Medical Information Service at 1-800-933-0303.

To place an order, please contact Baxter's Center for Service by calling 1-888-229-0001.

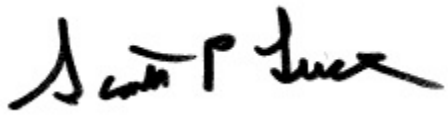
To report product quality issues, please contact Baxter Product Surveillance at 1-800-437-5176.

To report adverse events associated with these imported products, please call Baxter at 1-866-888-2472, or fax: 1-800-759-1801. Adverse events or quality problems experienced with the use of this product may also be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax:

- Complete and submit the report **Online**: www.fda.gov/medwatch/report.htm

- **Regular mail or Fax**: Download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

Sincerely,



Scott P. Luce
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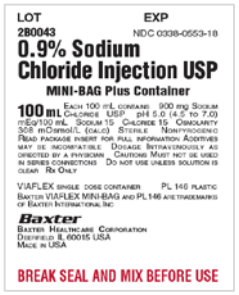
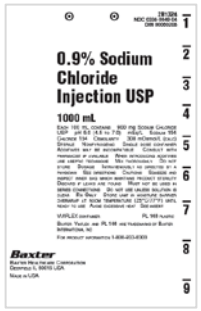
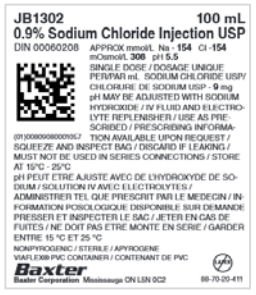
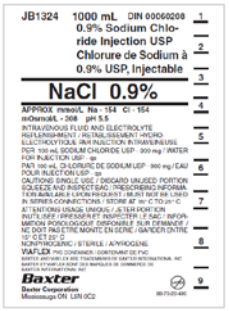
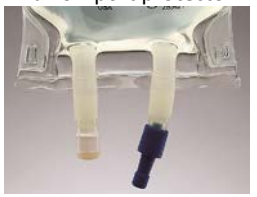
USMP/MG61/17-0005 10/17

Product Comparison Tables

Table 1. Key differences in 0.9% Sodium Chloride Injections

	US FDA approved product			Import product		
						
	MINI-BAG Plus	**Small volume parenteral**	**Large volume parenteral**	**MINI-BAG Plus**	**Small volume parenteral**	**Large volume parenteral**
Product name	**0.9% Sodium Chloride Injection, USP**			**0.9% Sodium Chloride Injection, USP**		
Indications	0.9% Sodium Chloride Injection, USP is indicated as a source of water and electrolytes and may also be used as diluent for reconstitution of a powdered drug product packaged in a vial with a 20 mm closure.	Sodium Chloride Injection, USP is indicated as a source of water and electrolytes. 0.9% Sodium Chloride Injection, USP is also indicated for use as a priming solution in hemodialysis procedures.		0.9% Sodium Chloride Injection, USP is indicated as a source of water and electrolytes. 0.9% Sodium Chloride Injection, USP can be used as a vehicle or diluent for compatible products for parenteral administration. 0.9% Sodium Chloride Injection, USP is also indicated for use as a priming solution in hemodialysis procedures		
Active ingredients *	Each 100 mL contains 900 mg Sodium Chloride, USP			Each 100 mL contains 900 mg Sodium Chloride, USP		
	Sodium 154 mEq/L Chloride 154 mEq/L			APPROX mmol/L: Sodium 154 Chloride 154		
Additional information	pH is 5.0 (4.5 to 7.0) Osmolarity 308 mOsmol/L (calc)			APPROX pH 5.5 Osmolarity 308 mOsm/L		
Storage conditions	Room temperature (25°C/77°F)	Room temperature (25°C/77°F); brief exposure up to 40°C/(104°F) does not adversely affect the product	Room temperature (25°C/77°F)	Store at 15°C - 25°C		
Container	MINI-BAG Plus / VIAFLEX (PVC)	VIAFLEX Container (PVC)	VIAFLEX Container (PVC)	MINI-BAG Plus / VIAFLEX (PVC)	VIAFLEX Container (PVC)	VIAFLEX Container (PVC)
Administration ports	Pull off port protector with 20 mm vial adapter 	Pull off port protector 	Pull off port protector 	Pull off port protector with 20 mm vial adapter 	Pull off port protector 	Pull off port protector 

* For monovalent ions, such as sodium and chloride, the numeric value of the millimole and milliequivalent are identical

Table 2. Key differences in 5% Dextrose Injections

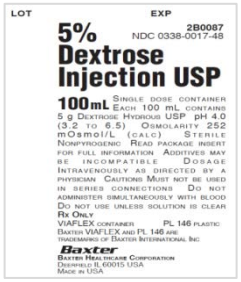
	US FDA approved product		Import product	
				
	MINI-BAG Plus	**Small volume parenteral**	**MINI-BAG Plus**	**Small volume parenteral**
Product name	**5% Dextrose Injection, USP**		**5% Dextrose Injection, USP**	
Indications	5% Dextrose Injection, USP is indicated as a source of water and calories and may also be used as diluent for reconstitution of a powdered drug product packaged in a vial with a 20 mm closure.	Dextrose Injection, USP is indicated as a source of water and calories.	5% Dextrose Injection, USP is indicated as a source of water and calories.	
Active ingredients	Each 100 mL contains 5 g Dextrose Hydrous USP		Each 100 mL contains 5 g Dextrose Hydrous USP	
Additional information	pH 4.0 (3.2 to 6.5)		pH 4.0	
	Osmolarity 252 mOsmol/L (calc)		Osmolarity 252 mOsmol/L (calc)	
Storage conditions	Room temperature (25°C/77°F)	Room temperature (25°C/77°F); brief exposure up to 40°C/104°F does not adversely affect the product.	Store at 15°C - 25°C	
Container	MINI-BAG Plus/VIAFLEX (PVC)	VIAFLEX Container (PVC)	MINI-BAG Plus / VIAFLEX (PVC)	VIAFLEX Container (PVC)
Administration ports	Pull off port protector with 20 mm vial adapter 	Pull off port protector 	Pull off port protector with 20 mm vial adapter 	Pull off port protector 

Table 3. Key differences in Lidocaine Hydrochloride and Dextrose Injection, USP

	US FDA approved product	Import product	
	Lidocaine Hydrochloride and 5% Dextrose Injection USP	**Lidocaine Hydrochloride and Dextrose Injection USP**	
			
	Lidocaine Hydrochloride and 5% Dextrose (4mg/mL) 500 mL bag	**Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection (4mg/mL) - 250 mL**	**Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection (4mg/mL) - 500 mL**
Ingredients	Each 100 mL contains: Lidocaine HCl USP 400 mg Dextrose Hydrous USP 5 g	Each 100 mL contains: Lidocaine HCl USP 400 mg Dextrose Hydrous USP 5 g	Each 100 mL contains: Lidocaine HCl USP 400 mg Dextrose Hydrous USP 5 g
Additional information	pH 4.0 (3.0 to 7.0) Osmolarity 282 mOsmol/L (calc)	pH approximately 5.0 Osmolarity approximately 282 mOsmol/L	pH approximately 5.0 Osmolarity approximately 282 mOsmol/L
Indications and Usage	Lidocaine hydrochloride administered intravenously is specifically indicated in the acute management of (1) ventricular arrhythmias occurring during cardiac manipulations, such as cardiac surgery and (2) life-threatening arrhythmias which are ventricular in origin, such as occur during acute myocardial infarction.	The intravenous administration of Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection is indicated in the treatment of ventricular tachycardia and premature ventricular beats of a life-threatening nature which may occur during cardiac manipulation such as surgery or catheterization or during acute myocardial infarction, digitalis toxicity or other cardiac diseases. Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection is indicated when fluid restriction is desirable.	
Contraindi-cations	Hypersensitivity reactions, including anaphylactic reactions, have been reported with lidocaine. Lidocaine hydrochloride is contraindicated in patients with a history of hypersensitivity to local anesthetics of the amide type. Lidocaine is contraindicated in patients with Stokes-Adams syndrome, Wolff-Parkinson-White syndrome, or with severe degrees of sinoatrial, atrioventricular, or intraventricular block.	Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection is contraindicated in patients with: 1. Known hypersensitivity to local anesthetics of the amide type, such as prilocaine, mepivacaine or bupivacaine, or to other components of the solution; 2. Adams-Stokes syndrome, or severe degrees of sinoatrial, atrioventricular or intraventricular block. Solutions containing dextrose may be contraindicated in patients with known allergy to corn or corn products. The safety of Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection in the treatment of arrhythmias in children has not been established.	
Warnings	**Please refer to the FDA-approved package insert for the full prescribing information** Constant monitoring with an electrocardiograph is essential - Signs of excessive depression of cardiac conductivity, such as prolongation of the PR interval, widening of the QRS interval and the appearance or aggravation of arrhythmias, should be followed by prompt cessation of the intravenous infusion of this agent. Hypersensitivity, including anaphylaxis, has been reported with lidocaine-containing solutions. Stop the infusion immediately if signs of hypersensitivity develop. Acceleration of ventricular rate may occur in patients with atrial fibrillation or flutter treated with lidocaine. In patients with sinus bradycardia or incomplete heart block, the administration of lidocaine hydrochloride intravenously for the elimination of ventricular ectopic beats without prior acceleration in heart r ate (e.g., by isoproterenol or by electric pacing) may promote more frequent and serious ventricular arrhythmias or complete heart block (see Contraindications). Because lidocaine is metabolized mainly in the liver and excreted by the kidneys, patients with renal or hepatic insufficiency may be at increased risk for toxicity.	Constant ECG monitoring is essential for the proper administration of Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection intravenously. Signs of excessive depression of cardiac conductivity, such as prolongation of PR interval and QRS complex, and the appearance of aggravation of arrhythmias, should be followed by prompt cessation of the intravenous infusion. It is mandatory to have emergency resuscitative equipment and drugs immediately available to manage possible adverse reactions involving the cardiovascular, respiratory, or central nervous systems. Anaphylactic reactions may occur following administration of lidocaine hydrochloride. In emergency situations, when a ventricular rhythm disorder is suspected, and ECG equipment is not available, a single dose may be administered when the physician in attendance has determined that the potential benefits outweigh the possible risks. If possible, emergency resuscitative equipment and drugs should be available.	

	US FDA approved product	Import product
	Lidocaine Hydrochloride and 5% Dextrose Injection USP	**Lidocaine Hydrochloride and Dextrose Injection USP**
Precautions	**Please refer to the FDA-approved package insert for the full prescribing information** **General:** If malignant hyperthermia develops, discontinue administration immediately and institute therapeutic countermeasures as clinically indicated. Lidocaine hydrochloride should not be added to blood transfusion assemblies because of the possibilities of pseudoagglutination or hemolysis. **Laboratory Tests:** Clinical evaluation and periodic laboratory determinations are necessary to monitor changes in fluid balance, electrolyte concentrations, and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient warrants such evaluation. **Carcinogenesis, Mutagenesis, and Impairment of Fertility:** Long term animal studies have not been performed to evaluate carcinogenic potential, mutagenic potential or the effect on fertility of lidocaine hydrochloride. **Pregnancy:** Teratogenic Effects: Reproduction studies have been performed in rats at doses up to five times the maximum human dose and have revealed no significant findings. There are, however, no adequate and well-controlled studies in pregnant women. Lidocaine may cross the placental barrier. **Nursing Mothers:** Lidocaine is present in human milk. Limited data available on lidocaine's effects on the breastfed child have not revealed a consistent pattern of associated adverse events. **Pediatric Use** Safety and effectiveness in pediatric patients have not been established. **Geriatric Use** In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.	Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection should be used with caution in patients with bradycardia, severe digitalis intoxication, first or second degree heart block in the absence of a pacemaker, or hypokalaemia (See CONTRAINDICATIONS and WARNINGS). In unconscious patients circulatory collapse should be watched for, since CNS effects may not be apparent as an initial manifestation of toxicity. Caution should be observed in patients with cardiac decompensation and hypotension or posterior diaphragmal infarction with a tendency towards development of heart block. Intravenous administration of lidocaine hydrochloride is sometimes accompanied by a hypotensive response, and, in overdosage, this may be precipitous. For this reason the intravenous dose should not exceed 100 mg in a single injection and no more than 200 – 300 mg in a one hour period (See DOSAGE and ADMINISTRATION). When high doses are used and the patient's myocardial function is impaired, combination with other drugs which reduce the excitability of cardiac muscle requires caution. Repeated doses of Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug or its metabolites. Tolerance to elevated blood levels varies with the status of the patient. Debilitated, elderly patients and acutely ill patients should be given reduced doses commensurate with their age and physical condition. Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection should also be used with caution in patients with epilepsy, impaired cardiac conduction, bradycardia, impaired hepatic function or renal function and in severe shock. **Use in the Elderly** A reduction in dosage may be necessary for elderly patients, particularly those with compromised cardiovascular and/or hepatic function and/or prolonged infusion. Elderly patients should be given reduced doses corresponding to their age and physical status. **Impaired Renal Function** Caution should be employed in the repeated use of Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection in patients with severe renal disease, since possible accumulation of lidocaine or its metabolites may lead to toxic phenomena. **Impaired Hepatic Function** Caution should be employed in the repeated use of Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection in patients with severe liver disease, since possible accumulation of lidocaine or its metabolites may lead to toxic phenomena. **Use in Pregnancy** It is reasonable to assume that lidocaine has been used, mainly as a local anesthetic, by a large number of pregnant women and women of child-bearing age. No specific disturbances to the reproductive process have so far been reported, e.g., no increased incidence of malformations. However, care should be taken during early pregnancy when maximum organogenesis takes place. There are no adequate and well-controlled studies with intravenous administration of lidocaine in pregnant women. **Use in Nursing Mothers** Lidocaine is excreted in the breast milk, but in such small quantities that there is generally no risk of affecting the infant at therapeutic dose levels. **Use in Neonates** Through their lower enzyme capacity, *very rarely*, neonates are at risk of methaemoglobinaemia. Methaemoglobinaemia can become clinically overt (cyanosis), and treatment with methylene blue may be considered necessary. **Use in Patients with Acute Porphyria** Theoretical evidence suggests that lidocaine may have porphyrogenic properties. The clinical significance of this is unknown. Caution should be exercised if intravenous Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection is administered to patients with acute porphyria. **Carcinogenesis, Mutagenesis, Impairment of Fertility** Studies of lidocaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted. **Drug Interactions** Lidocaine is mainly metabolized in the liver by CYP1A2 and CYP3A4 to its two major metabolites, monoethylglycinexylidine (MEGX) and glycinexylidine (GX), both of which are pharmacologically active. Lidocaine has a high hepatic extraction ratio. Only a small fraction (3%) of lidocaine is excreted unchanged in the urine. The hepatic clearance of lidocaine is expected to depend largely on blood flow. Since the affinity of lidocaine to CYP1A2 and CYP3A4 is very low compared to therapeutic plasma concentrations, it is less likely that the metabolism of substrates for these enzymes will be inhibited when coadministered with lidocaine. However, there is a potential for influence of other drugs on the plasma levels/effect of lidocaine, e.g. strong inhibitors or inducers of CYP1A2 and/or CYP3A4 and drugs that affect liver blood flow (see Table 1).
Adverse Events	Systemic reactions of the following types have been reported: Nervous System Disorders: respiratory depression and arrest; unconsciousness; convulsions; tremors; twitching; vomiting; blurred or double vision; drowsiness; dizziness; light-headedness; tinnitus; sensation of heat, cold or numbness; euphoria; apprehension; agitation; confused state; paresthesia; dysarthria. Cardiovascular System: cardiovascular arrest; bradycardia which may lead to cardiac arrest; hypotension, Ventricular fibrillation, Ventricular tachycardia, Ventricular arrhythmia, Asystole. Gastrointestinal Disorders: Hypoesthesia oral, Nausea, Hematologic Effects: methemoglobinemia. Psychiatric Disorders: Disorientation Allergic reactions, including anaphylactic reactions, may occur but are infrequent. There have been no reports of cross sensitivity between lidocaine hydrochloride and procainamide or between lidocaine hydrochloride and quinidine.	Adverse experiences following the administration of lidocaine are similar in nature to those observed with other amide type agents. These adverse experiences are, in general, dose related and may result from high plasma levels caused by excessive dosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Common adverse reactions are those from the central and peripheral nervous system. They occur in 5-10% of the patients and are mostly dose-related. The following definitions of frequencies are used: Very common (≥ 10%), common (1 – 9.9%), uncommon (0.1 – 0.9%), rare (0.01 – 0.09%) and very rare (< 0.01%). Systemic reactions of the following types have been reported: **Central Nervous System** CNS manifestations are excitatory and/or depressant. Common adverse reactions are circumoral paresthesia, dizziness and drowsiness. Rare adverse reactions would include persistent dizziness, lightheadedness, nervousness, apprehension, euphoria, confusion, hyperacusis, tinnitus, blurred vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, apnea, respiratory depression and arrest. The excitatory manifestations may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest. Drowsiness following the administration of lidocaine is usually an early sign of a high lidocaine plasma level and may occur as a consequence of rapid absorption. **Cardiovascular System** Rare cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, asystole and cardiovascular collapse which may lead to cardiac arrest. Arrhythmias, including ventricular tachycardia /ventricular fibrillation have also been reported. **Hematologic System** Very rarely, neonatal methaemoglobinaemia can occur (see Precautions). Methemoglobinemia was also reported in adults. **Immune System** Allergic reactions, including anaphylactic reactions, are characterized by cutaneous lesions, urticaria, edema, or in the most severe and very rare instances, hypersensitivity including anaphylactic shock. Allergic reactions of the amide type are rare and may occur as a result of sensitivity either to the drug itself, or to other components of the formulation. Idiosyncratic reactions have been reported at low doses in some patients. Cross- sensitivity between Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection (lidocaine hydrochloride and dextrose injection, USP) and procainamide or Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection and quinidine have not been reported.

	US FDA approved product	Import product
	Lidocaine Hydrochloride and 5% Dextrose Injection USP	**Lidocaine Hydrochloride and Dextrose Injection USP**
Drug Interactions	Pharmacodynamics Interactions Digitalis derivatives: Monitor toxicity when lidocaine is used in patients with digitalis toxicity accompanied by supraventricular arrhythmia and/or atrioventricular block (see Contraindications). When lidocaine is administered with other antiarrhythmic drugs such as amiodarone, phenytoin, procainamide, propranolol or quinidine, the cardiac effects may be additive or antagonistic and toxic effects may be additive. Pharmacokinetics Interactions Concomitant treatment with drugs which are inhibitors of CYP1A2 and/or CYP3A4 has the potential to increase lidocaine plasma levels by decreasing lidocaine clearance and thereby prolonging the elimination half-life. Monitor toxicity when administering lidocaine with CYP1A2 and/or CYP3A4 inhibitors. Concomitant use of lidocaine at steady-state concentrations of the CYP1A2 inhibitor fluvoxamine increases intravenous lidocaine plasma AUC and C_{max} by 71% and 22%, and decreases MEGX AUC and C_{max} by 54% and 65%. Fluvoxamine decreases the plasma clearance of lidocaine by 41%-60% and prolonged the mean half-life by one hour. Monitor toxicity when coadministering these medications. Concomitant use of lidocaine with propofol, a hypnotic agent and CYP3A4 inhibitor, may increase lidocaine plasma levels by reducing lidocaine clearance. Monitor toxicity when coadministering lidocaine with propofol. Concomitant treatment with drugs which are inducers of CYP1A2 and/or CYP3A4 (e.g., phenytoin) has the potential to decrease lidocaine plasma levels and higher doses may be required. Concomitant use of lidocaine with a weak CYP1A2 and CYP3A4 inhibitor has been reported to increase lidocaine plasma levels by 24% – 75% and may result in toxic accumulation of the drug. Monitor toxicity when coadministering lidocaine with cimetidine. Beta-adrenergic blockers (e.g. propranolol): Concomitant use of lidocaine with beta-adrenergic blockers may increase lidocaine plasma levels by decreasing hepatic blood flow and thereby decrease lidocaine clearance. Monitor for toxicity when coadministering lidocaine with drugs that decrease hepatic blood flow.	**Table 1. Established or Potential Drug-Drug Interactions** **Name** / **Reference** / **Effect** / **Clinical comment** Strong inhibitors of CYP1A2 (fluvoxamine) / Clinical trial / Coadministration of fluvoxamine, reduced [41%] the elimination of lidocaine in healthy subjects. Given concomitantly with lidocaine, strong inhibitors of CYP1A2 can cause a metabolic interaction leading to increased lidocaine plasma concentrations. / Therefore, coadministration of lidocaine should be avoided in patients treated with strong inhibitors of CYP1A2, such as fluvoxamine. CYP1A2 inducers (Phenytoin) / Theoretical / During concomitant administration of lidocaine and CYP1A2 inducers, plasma levels/effect of lidocaine may decrease. / Higher dose of lidocaine may be required. Strong inhibitors of CYP3A4 (erythromycin, itraconazole) / Clinical trial / Erythromycin and itraconazole have each been shown to have a **modest** or no effect on the pharmacokinetics of intravenous lidocaine (0-18% decreased elimination with erythromycin but no effect with itraconazole). / No dose adjustment seems required. CYP3A4 inducers (carbamazepine, phenobarbital, phenytoin, / Clinical trial / Concomitant administration with carbamazepine, phenobarbital, phenytoin, and primidone, may slightly decrease plasma levels of lidocaine (<10%). / No dose adjustment seems required. Beta-blockers (propranolol, metoprolol, nadolol) / Clinical trial / Propranolol, metoprolol, and nadolol have been reported to reduce intravenous lidocaine clearance, probably through effects on hepatic blood flow and/or metabolism, and may increase the plasma concentration of lidocaine by about 30%, less with metoprolol. / Therefore, concomitant administration of beta-blockers with lidocaine should be avoided. If not possible, close monitoring and dose adjustment may be required. Cimetidine / Clinical trial / Cimetidine has an unspecific inhibitory effect on CYP (including CYP1A2 and CYP3A4) mediated metabolism and reduces hepatic blood flow. Clinical experiments showed that the concomitant administration of cimetidine reduces the systemic clearance of lidocaine and increases lidocaine serum concentration by as much as 50%. Thus, therapeutic serum levels of lidocaine may rise to toxic levels when cimetidine is used concomitantly. Ranitidine has not displayed this effect. / Therefore, concomitant administration with lidocaine should be avoided. If not possible, close monitoring and dose adjustment of lidocaine and/or cimetidine may be required. Amiodarone / Clinical trial, Case study / Like cimetidine, amiodarone has an unspecific inhibitory effect on CYP mediated metabolism. Concomitant administration has resulted in increased plasma levels of lidocaine and may result in toxic effects. / Therefore, concomitant administration with lidocaine should be avoided. If not possible, close monitoring and dose adjustment of lidocaine and/or amiodarone may be required.
Dosage and Administration	**Please refer to the FDA-approved package insert for the full prescribing information** Therapy of ventricular arrhythmias is often initiated with a single IV bolus of 1.0 to 1.5 mg/kg at a rate of 25 to 50 mg/min. of lidocaine hydrochloride injection. Following acute treatment by bolus in patients in whom arrhythmias tend to recur and who are incapable of receiving oral antiarrhythmic agents, intravenous infusion of Lidocaine Hydrochloride and 5% Dextrose Injection, USP is administered continuously at the rate of 1 to 4 mg/min (0.020 to 0.050 mg/kg/min in the average 70 kg adult). The 0.4% solution (4 mg/mL) can be given at a rate of 15 to 60 mL/hr (0.25 to 1 mL/min). The 0.8% solution (8 mg/mL) can be given at a rate of 7.5 to 30 mL/hr (0.12 to 0.5 mL/min). Precise dosage regimen is determined by patient characteristics and response. Infusion rate should be reduced by approximately one-half to compensate for decreased rate of clearance after prolonged infusion (24 hours) (see Clinical Pharmacology). Failure to adjust the rate of infusion in keeping with this altered ability to eliminate lidocaine may result in toxic accumulation of the drug in the patient's serum. Intravenous infusions of lidocaine hydrochloride must be administered under constant ECG monitoring to avoid potential overdosage and toxicity. Intravenous infusion should be terminated as soon as the patient's basic cardiac rhythm appears to be stable or at the earliest signs of toxicity (see OVERDOSAGE). It should rarely be necessary to continue intravenous infusions beyond 24 hours. As soon as possible and when indicated, patients should be changed to an oral antiarrhythmic agent for maintenance therapy. **Pediatric**: Clinical studies to establish pediatric dosing schedules have not been conducted. The usual dosage is a bolus dose of 1 mg/kg followed by an infusion rate of 20 mcg to 50 mcg/kg/min. The bolus dose should be repeated if infusion is not initiated within 15 minutes of the initial bolus dose. **Hepatic impairment** is likely to decrease clearance and increase exposure level of	**Single Intravenous Injection** The usual dose is 50 to 100 mg Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection (lidocaine hydrochloride and dextrose injection, USP) administered under ECG and blood pressure monitoring. This dose may be administered at the rate of approximately 25 to 50 mg/min. Sufficient time should be allowed to enable a slow circulation to carry the drug to the site of action. If the initial injection of 50 to 100 mg does not produce a desired response, a second dose may be repeated after 10 minutes. NO MORE THAN 200 TO 300 MG OF LIDOCAINE HYDROCHLORIDE 0.4% AND 5% DEXTROSE INJECTION SHOULD BE ADMINISTERED DURING A ONE HOUR PERIOD. **Continuous Intravenous Infusion** Following intravenous injection, Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection may be administered by intravenous infusion at a rate of 1-2 mg/min (approximately 15-30µg/kg/min in the average 70 kg patient) in those patients in whom the arrhythmia tends to recur, and who are incapable of receiving oral antiarrhythmic therapy. Intravenous infusions of Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection must be administered under constant ECG and blood pressure monitoring and with meticulous regulation of infusion rate, in order to avoid potential overdosage and toxicity. Intravenous infusions should be terminated as soon as the patient's basic cardiac rhythm appears to be stable or at the earliest signs of toxicity. It should rarely be necessary to continue intravenous infusion beyond 24 hours. As soon as possible, and when indicated, patients should be changed to an oral antiarrhythmic agent for maintenance therapy. Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection should be used only when fluid restriction is desirable. When administering Lidocaine Hydrochloride 0.4% and 5% Dextrose Injection by continuous intravenous infusion, it is necessary to use an infusion pump or a precision volume control I.V. set. It is recommended that the administration set be replaced at least once every 24 hours. Directions for use of VIAFLEX plastic containers: Do not remove unit from overwrap until ready for use. The overwrap is a moisture barrier. The inner bag maintains the sterility of the product. After removing overwrap, check for leaks by firmly squeezing the inner bag. If leaks are found, discard solution as sterility may be impaired. **Warning**: Do not use plastic containers in series connections. Such use could result in air embolism due to residual air (approximately 15 mL) being drawn from the

	US FDA approved product	Import product
	Lidocaine Hydrochloride and 5% Dextrose Injection USP	**Lidocaine Hydrochloride and Dextrose Injection USP**
	lidocaine. Administer lidocaine at lower maintenance infusion rate with close monitoring of toxicity in patients with hepatic impairment. **Renal Impairment**: In patients with severe renal impairment (eGFR less than 30 mL/min/1.73 m^2), administer lidocaine at lower maintenance infusion rate with close monitoring of toxicity. Lidocaine is incompatible with the following due to precipitate formation (includes but is not limited to): Amphotericin, Cephazolin sodium, Phenytoin sodium. Because dosages of this drug are titrated to response, **no additives should be made to Lidocaine Hydrochloride and 5% Dextrose Injection, USP**.	primary container before administration of the fluid from the secondary container is completed. To Open Tear overwrap down the side at the slit and remove solution container. Do not add supplementary medication. Preparation for Administration 1. Suspend container from eyelet support. 2. Remove plastic protector from outlet port at bottom of container. 3. Attach administration set. Refer to complete directions accompanying set.
Overdosage	Signs and symptoms of overdose may include: • Central nervous system effects, e.g., coma, loss of consciousness, CNS depression, seizure, tonic-clonic muscle jerks, tremor, nystagmus, tingling of tongue and lips, tinnitus, drowsiness, disorientation, and lightheadedness. • Cardiorespiratory effects, e.g., cardiovascular collapse and cardiorespiratory arrest (sometimes fatal), respiratory depression and arrest, hypotension, myocardial depression, arrhythmias, including asystole, heart block, ventricular arrhythmias, tachycardia, and bradycardia. Discontinue lidocaine administration in the event of an overdose. There is no specific antidote for overdose of lidocaine. The risk of overdose can be minimized by close monitoring during treatment. Emergency procedures should include appropriate corrective, resuscitative, and other supportive measures (See WARNINGS).	Symptoms of idiosyncratic reactions are described under ADVERSE REACTIONS. **Symptoms** Lidocaine toxicity may appear at serum concentrations greater than 8 mg/L. The most serious effects of lidocaine intoxication are on the central nervous system and cardiovascular system and overdosage can result in dizziness, delirium, severe hypotension, conduction defects, bradycardia, asystole, arrhythmias, including ventricular tachycardia/fibrillation, cardiovascular collapse which may lead to cardiac arrest, apnea, seizures, coma, respiratory arrest and death. *Central nervous system* toxicity is a graded response, with symptoms and signs of escalating severity. The first symptoms are circumoral paresthesia, numbness of the tongue, lightheadedness, hyperacusis and tinnitus. Visual disturbance and muscular tremors are more serious and precede the onset of generalized convulsions. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly following convulsions due to the increased muscular activity, together with the interference with normal respiration. In severe cases apnea may occur. Acidosis increases the toxic effects. Recovery is due to redistribution and metabolism of the drug. Recovery may be rapid unless large amounts of the drug have been administered. *Cardiovascular effects* may be seen in cases with high systemic concentrations. Severe hypotension, bradycardia, arrhythmia and cardiovascular collapse may be the result in such cases. Cardiovascular toxic effects are generally preceded by signs of toxicity in the central nervous system, unless the patient is receiving a general anesthetic or is heavily sedated with drugs such as a benzodiazepine or barbiturate. **Treatment** The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness. At the first sign of change, oxygen should be administered. The first step in the management of convulsions consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. An anticonvulsant should be given i.v. if the convulsions do not stop spontaneously in 15-20 seconds. Thiopental 100-150 mg i.v. will abort the convulsions rapidly. Alternatively, diazepam 5-10 mg i.v. may be used, although its action is slower. Succinylcholine will stop the muscle convulsions rapidly, but will require tracheal intubation and controlled ventilation, and should only be used by those familiar with these procedures. Hypotension may be counteracted by giving sympathicomimetic drugs (e.g., adrenaline). Adrenergic agents of both α-adrenoceptor stimulating (e.g., metaraminol) and β-adrenoceptor stimulating type (e.g., isoprenaline) are generally effective. The bradycardia may be treated with parasympatholytic agents (e.g., atropine). Should circulatory arrest occur, immediate cardiopulmonary resuscitation should be instituted. Optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance, since hypoxia and acidosis will increase the systemic toxicity of local anesthetics. Epinephrine (0.1-0.2 mg as intravenous or intracardial injections) should be given as soon as possible and repeated, if necessary. For management of suspected drug overdose, contact your regional Poison Control Centre immediately.
Storage conditions	Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended the product be stored at room temperature (25°C); brief exposure up to 40°C does not adversely affect the product.	Store at room temperature (15-25°C).
Administration ports	Pull off port protector 	Pull off port protector