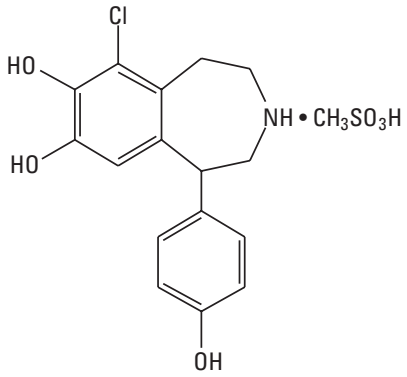
Corlopam®

brand of Fenoldopam Mesylate Injection, USP

DESCRIPTION

CORLOPAM (Fenoldopam Mesylate Injection, USP) is a dopamine D_1-like receptor agonist. The product is formulated as a solution to be diluted for intravenous infusion. Chemically it is 6-chloro-2,3,4,5-tetrahydro-1-(4-hydroxyphenyl)-[1*H*]-3-benzazepine-7,8-diol methanesulfonate with the following structure:



fenoldopam mesylate

Fenoldopam mesylate is a white to off-white powder with a molecular weight of 401.87 and a molecular formula of $C_{16}H_{16}ClNO_3 \bullet CH_3SO_3H$. It is sparingly soluble in water, ethanol and methanol, and is soluble in propylene glycol.

Ampules: Each 1 mL contains, in sterile aqueous solution, citric acid 3.44 mg; fenoldopam mesylate equivalent to fenoldopam 10 mg; propylene glycol 518 mg; sodium citrate dihydrate 0.61 mg; sodium metabisulfite 1 mg.

CLINICAL PHARMACOLOGY

Mechanism of Action

Fenoldopam is a rapid-acting vasodilator. It is an agonist for D_1-like dopamine receptors and binds with moderate affinity to α_2-adrenoceptors. It has no significant affinity for D_2-like receptors, α_1 and β adrenoceptors, $5HT_1$ and $5HT_2$ receptors, or muscarinic receptors. Fenoldopam is a racemic mixture with the R-isomer responsible for the biological activity. The R-isomer has approximately 250-fold higher affinity for D_1-like receptors than does the S-isomer. In non-clinical studies, fenoldopam had no agonist effect on presynaptic D_2-like dopamine receptors, or α- or β-adrenoceptors, nor did it affect angiotensin-converting enzyme activity. Fenoldopam may increase norepinephrine plasma concentration.

In animals, fenoldopam has vasodilating effects in coronary, renal, mesenteric and peripheral arteries. All vascular beds, however, do not respond uniformly to fenoldopam. Vasodilating effects have been demonstrated in renal efferent and afferent arterioles. In humans, increases in renal blood flow were demonstrated in hypertensive and normal subjects treated with intravenous fenoldopam in two small controlled trials. No beneficial clinical effect on renal function has been shown in patients with heart failure or hepatic or severe renal disease.

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Pharmacokinetics

Administered as a constant infusion at rates of 0.01 to 1.6 µg/kg/min, fenoldopam produced steady-state plasma concentrations that were proportional to infusion rates. The elimination half-life was about 5 minutes in mild to moderate hypertensives, with little difference between the R (active) and S isomers. Steady state concentrations are attained in about 20 minutes (4 half-lives). The steady state plasma concentrations of fenoldopam, at comparable infusion rates, were similar in normotensive subjects and in patients with mild to moderate hypertension or hypertensive emergencies (Table 1).

Table 1

CORLOPAM Plasma Concentrations in Normotensive, Mild to Moderate and Malignant Hypertensive Patients

CORLOPAM PLASMA CONCENTRATION (ng/mL)

	Patient Populations		
CORLOPAM Infusion Rate (µg/kg/min)	Normotensive Subjects n=10	Mild to Moderate Hypertensive Patients n=7	Malignant Hypertension Patients n=20
0.1	3.2	4.0	3.3

Clearance of parent (active) fenoldopam is not altered in patients with end-stage renal disease on continuous ambulatory peritoneal dialysis (CAPD) and is not affected on average, in severe hepatic failure. The effects of hemodialysis on the pharmacokinetics of fenoldopam have not been evaluated.

In radiolabeled studies in rats, no more than 0.005% of fenoldopam crossed the blood-brain barrier.

Excretion and Metabolism

Radiolabeled studies show that about 90% of infused fenoldopam is eliminated in urine, 10% in feces. Elimination is largely by conjugation, without participation of cytochrome P-450 enzymes. The principal routes of conjugation are methylation, glucuronidation, and sulfation. Only 4% of the administered dose is excreted unchanged. Animal data indicate that the metabolites are inactive.

Special Population: The pharmacokinetics of fenoldopam were not influenced by age, gender, or race in hypertensive emergency patients. Effects of renal and hepatic dysfunction are described above. There have been no formal drug-drug interaction studies using intravenous fenoldopam.

Pharmacodynamics and Clinical Studies

In a randomized double-blind, placebo-controlled, 5-group study in 32 patients with mild to moderate essential hypertension (diastolic blood pressure between 95 and 119 mm Hg), and a mean baseline pressure of about 154/98 mm Hg, and heart rate of about 75 bpm, fixed-rate IV infusions of CORLOPAM produced dose-related reductions in systolic and diastolic blood pressure. Infusions were maintained at a fixed rate for 48 hours. Table 2 shows the results of the study. The onset of response was rapid at all infusion rates, with the 15-minute response representing 50-100% of the one-hour response in all groups. There was some suggestion of partial tolerance at 48 hours in the two higher dose infusions, but a substantial effect persisted through 48 hours. When infusions were stopped, blood pressure gradually returned to pretreatment values with no evidence of rebound. This study suggests that there is no greater response to 0.8 µg/kg/min than to 0.4 µg/kg/min.

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Table 2
PHARMACODYNAMIC EFFECTS OF FENOLDOPAM IN MILD TO MODERATE HYPERTENSIVE PATIENTS

Time Point and Mean Change From Time Zero ± SE	Infusion Rate (µg/kg/min)				
	Placebo n = 7	0.04 n = 7	0.1 n = 7	0.4 n = 5	0.8 n = 6
15 Minutes of Infusion*					
Systolic BP	0 ± 6	-15 ± 6	-19 ± 8	-14 ± 4	-24 ± 6
Diastolic BP	0 ± 2	-5 ± 3	-12 ± 4	-15 ± 3	-20 ± 4
Heart rate	+2 ± 2	+3 ± 2	+5 ± 1	+16 ± 3	+19 ± 3
30 Minutes of Infusion*					
Systolic BP	-6 ± 5	-17 ± 6	-18 ± 6	-14 ± 8	-26 ± 6
Diastolic BP	-6 ± 3	-7 ± 3	-16 ± 4	-14 ± 3	-20 ± 2
Heart rate	+2 ± 2	+3 ± 2	+10 ± 2	+18 ± 3	+23 ± 3
1 Hour of Infusion*					
Systolic BP	-15 ± 4	-22 ± 7	-22 ± 7	-26 ± 9	-22 ± 9
Diastolic BP	-5 ± 3	-9 ± 2	-18 ± 4	-19 ± 4	-21 ± 1
Heart rate	+1 ± 3	+5 ± 2	+12 ± 3	+19 ± 4	+25 ± 4
4 Hours of Infusion*					
Systolic BP	-14 ± 5	-16 ± 9	-31 ± 15	-22 ± 11	-25 ± 7
Diastolic BP	-14 ± 8	-8 ± 4	-19 ± 9	-25 ± 3	-20 ± 1
Heart rate	+5 ± 3	+6 ± 3	+10 ± 4	+21 ± 2	+27 ± 7
24 Hours of Infusion*					
Systolic BP	-20 ± 6	-23 ± 8	-35 ± 7	-22 ± 6	-23 ± 11
Diastolic BP	-11 ± 6	-11 ± 5	-23 ± 10	-22 ± 5	-13 ± 3
Heart rate	+6 ± 3	+5 ± 3	+13 ± 2	+17 ± 4	+15 ± 3
48 Hours of Infusion*					
Systolic BP	-12 ± 8	-31 ± 6	-22 ± 8	-9 ± 6	-14 ±10
Diastolic BP	-9 ± 5	-10 ± 6	-9 ± 7	-9 ± 2	-9 ±3
Heart rate	+1 ± 2	0 ± 4	+1 ± 4	+12 ± 3	+8 ± 3

*Mean change from time zero ± S.E.

In a multicenter, randomized, double-blind comparison of four infusion rates, CORLOPAM was administered as constant rate infusions of 0.01, 0.03, 0.1 and 0.3 µg/kg/min for up to 24 hours to 94 patients experiencing hypertensive emergencies (defined as diastolic blood pressure ≥ 120 mm Hg with evidence of compromise of end-organ function involving the cardiovascular, renal, cerebral or retinal systems). Infusion rates could be doubled after one hour if clinically indicated. There were

dose-related, rapid-onset, decreases in systolic and diastolic blood pressures and increases in heart rate (Table 3).

Table 3

PHARMACODYNAMIC EFFECTS OF FENOLDOPAM IN HYPERTENSIVE EMERGENCY PATIENTS

Time Point and Pharmacodynamic Parameters	Infusion Rate µg/kg/min 0.01 n = 25	0.03 n = 24	0.1 n = 22	0.3 n = 23
Pre-Infusion Baseline				
Systolic BP - mean ± SE	210 ± 21	208 ± 26	205 ± 24	211 ± 17
Diastolic BP - mean ± SE	136 ± 16	135 ± 11	133 ± 14	136 ± 15
Heart rate - mean ± SE	87 ± 20	84 ± 14	81 ± 19	80 ± 14
15 minutes of Infusion*				
Systolic BP	-5 ±4	-7 ± 4	-16 ± 4	-19 ± 4
Diastolic BP	-5 ± 3	-8 ± 3	-12 ± 2	-21 ± 2
Heart rate	-2 ± 3	+1 ± 1	+2 ± 1	+11 ± 2
30 Minutes of Infusion*				
Systolic BP	-6 ± 4	-11 ± 4	-21 ± 3	-16 ± 4
Diastolic BP	-10 ± 3	-12 ± 3	-17 ± 3	-20 ± 2
Heart rate	-2 ± 3	-1 ± 1	+3 ± 2	+12 ± 3
1 Hour of Infusion*				
Systolic BP	-5 ± 3	-9 ± 4	-19 ± 4	-22 ±4
Diastolic BP	-8 ± 3	-13 ± 3	-18 ± 2	-23 ± 2
Heart rate	-1 ± 3	0 ± 2	+3 ± 2	+11 ± 3
4 Hours of Infusion*				
Systolic BP	-14 ± 4	-20 ± 5	-23 ± 4	-37 ± 4
Diastolic BP	-12 ± 3	-18 ± 3	-21 ± 3	-29 ± 3
Heart rate	-2 ± 4	0 ± 2	+4 ± 2	+11 ± 2

* Mean change from baseline ± S.E.

Two hundred and thirty six severely hypertensive patients (DBP ≥ 120 mm Hg), with or without end-organ compromise, were randomized to receive in two open-label studies either fenoldopam or nitroprusside. The response rate was 79% (92/117) in the fenoldopam group and 77% (90/119) in the nitroprusside group. Response required a decline in supine diastolic blood pressure to less than 110 mm Hg if the baseline were between 120 and 150 mm Hg, inclusive, or by ≥ 40 mm Hg if the baseline were ≥ 150 mm Hg. Patients were titrated to the desired effect. For fenoldopam, the dose ranged from 0.1 to 1.5 µg/kg/min; for nitroprusside, the dose ranged from 1.0 to 8.0 µg/kg/min. As in the study in mild to moderate hypertensives, most of the effect seen at one hour is present at 15 minutes. The additional effect seen after 1 hour occurs in all groups and may not be drug-related (there was no placebo group to evaluate this).

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INDICATIONS AND USAGE

CORLOPAM is indicated for the in-hospital, short-term (up to 48 hours) management of severe hypertension when rapid, but quickly reversible, emergency reduction of blood pressure is clinically indicated, including malignant hypertension with deteriorating end-organ function. Transition to oral therapy with another agent can begin at any time after blood pressure is stable during CORLOPAM infusion.

CONTRAINDICATIONS

None known.

WARNINGS

Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

PRECAUTIONS

Intraocular Pressure: In a clinical study of 12 patients with open-angle glaucoma or ocular hypertension (mean baseline intraocular pressure was 29.2 mm Hg with a range of 22.0-33.0 mm Hg), infusion of CORLOPAM at escalating doses ranging from 0.05-0.5 µg/kg/min over a 3.5 hour period caused a dose-dependent increase in intraocular pressure (IOP). At the peak effect, the intraocular pressure was raised by a mean of 6.5 mm Hg (range -2.0 to +8.5 mm Hg, corrected for placebo effect). Upon discontinuation of the CORLOPAM infusion, the IOP returned to baseline values within 2 hours. CORLOPAM administration to patients with glaucoma or intraocular hypertension should be undertaken with caution.

Tachycardia: CORLOPAM causes a dose-related tachycardia (Table 2 and Table 3), particularly with infusion rates above 0.1 µg/kg/min. Tachycardia diminishes over time but remains substantial at higher doses.

Hypotension: CORLOPAM may occasionally produce symptomatic hypotension and close monitoring of blood pressure during administration is essential. (See Adverse Reactions.) It is particularly important to avoid systemic hypotension when administering the drug to patients who have sustained an acute cerebral infarction or hemorrhage.

Hypokalemia: Decreases in serum potassium occasionally to values below 3.0 meq/L were observed after less than 6 hours of fenoldopam infusion. It is not clear if the hypokalemia reflects a pressure natriuresis with enhanced potassium-sodium exchange or a direct drug effect. During clinical trials, electrolytes were monitored at intervals of 6 hours. Hypokalemia was treated with either oral or intravenous potassium supplementation. Patient management should include appropriate attention to serum electrolytes.

Drug Interactions: Although there have been no formal interaction studies, intravenous CORLOPAM has been administered safely with drugs such as digitalis and sublingual nitroglycerin. There is limited experience with concomitant antihypertensive agents such as beta-blockers, alpha-blockers, calcium channel-blockers, ACE inhibitors, and diuretics (both thiazide-like and loop).

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 24-month study, mice treated orally with fenoldopam at 12.5, 25, or 50 mg/kg/day, reduced to 25 mg/kg/day on day 209 of study, showed no increase above controls in the incidence of neoplasms. Female mice in the highest dose group had an

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increased incidence and degree of severity of a fibro-osseous lesion of the sternum compared with control or low-dose animals. Compared to controls, female mice in the middle- and upper-dose groups had a higher incidence and degree of severity of chronic nephritis. These pathologic lesions were not seen in male mice treated with fenoldopam.

In a 24-month study, rats treated orally with fenoldopam at 5, 10 or 20 mg/kg/day, with the mid- and high-dose groups increased to 15 or 25 mg/kg/day, respectively, on day 372 of the study, showed no increase above controls in the incidence or type of neoplasms. Compared with the controls, rats in the mid- and high-dose groups had a higher incidence of hyperplasia of collecting duct epithelium at the tip of the renal papilla.

In *in vitro* assays, fenoldopam did not induce bacterial gene mutation in the Ames test or mammalian gene mutation in the Chinese hamster ovary (CHO) cell assay. In the *in vitro* chromosomal aberration assay with CHO cells, fenoldopam was associated with statistically significant and dose-dependent increases in chromosomal aberrations, and in the proportion of aberrant metaphases. However, no chromosomal damage was seen in the *in vivo* mice micronucleus or bone marrow assays. The data support the conclusion that fenoldopam is not genotoxic or clastogenic.

Oral fertility and general reproduction performance studies in male and female rats at 12.5, 37.5 or 75 mg/kg/day revealed no impairment of fertility or reproduction performance due to fenoldopam.

Pregnancy: *Pregnancy Category B.* Oral reproduction studies have been performed in rats and rabbits at doses of 12.5 to 200 mg/kg/day and 6.25 to 25 mg/kg/day, respectively. Studies have revealed maternal toxicity at the highest doses tested but no evidence of impaired fertility or harm to the fetus due to fenoldopam. However, there are no adequate and well-controlled studies in pregnant women. Since animal reproduction studies are not always predictive of human response, fenoldopam should be used in pregnancy only if clearly needed.

Nursing Mothers: Fenoldopam is excreted in milk in rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when CORLOPAM is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

CORLOPAM causes a dose-related fall in blood pressure and increase in heart rate (see Precautions, Tachycardia, and Hypotension). In controlled clinical studies of severe hypertension in patients with end-organ damage, 3% (4/137) of patients withdrew because of excessive falls in blood pressure. Increased heart rate could, in theory, lead to ischemic cardiac events or worsened heart failure, although these events have not been observed. The most common events reported as associated with CORLOPAM use are headache, cutaneous dilation (flushing), nausea, and hypotension, each reported in more than 5% of patients.

Adverse reactions in controlled trials in hypertension

Adverse events occurring more than once in any dosing group (once if potentially important or plausibly drug-related) in the fixed-dose constant-infusion studies are presented in the following Table by infusion-rate group. There was no clear dose relationship, except possibly for headache, nausea, flushing.

Table 4
ADVERSE EVENTS* FROM FIXED-DOSE INFUSION STUDIES BY DOSE GROUP

		CORLOPAM Doses (µg/kg/min)					
Body System	**Event**	**Placebo (n = 7)**	**0.01 (n = 26)**	**0.03-0.04 (n = 31)**	**0.1 (n = 28)**	**0.3-0.4 (n = 29)**	**0.6-0.8 (n = 11)**
Body, General	Headache	1	5	4	7	8	6
	Injection site reaction	0	1	3	0	3	2
Cardiovascular	ST-T abnormalities (primarily T-wave inversion)	0	2	4	0	1	0
	Flushing	0	0	0	0	1	3
	Hypotension**	0	0	0	2	0	2
	Postural hypotension	0	2	0	0	0	0
	Tachycardia**	0	0	0	0	0	2
Digestive	Nausea	0	3	0	3	5	4
	Vomiting	0	2	0	2	1	2
	Abdominal pain/ fullness	0	2	0	0	2	1
	Constipation	0	0	0	0	0	2
	Diarrhea	0	0	0	0	2	0
Metabolic and Nutritional	Increased creatinine**	0	0	2	0	0	0
	Hypokalemia**	0	2	2	0	1	0
Nervous	Nervousness/ anxiety	0	0	1	0	0	2
	Insomnia	0	2	0	0	0	0
	Dizziness	0	1	1	2	2	0
Respiratory	Nasal congestion	0	0	0	0	0	2
Skin and Appendages	Sweating	0	0	0	1	1	2
Urogenital	Urinary tract infection	0	2	0	1	0	0
Musculoskeletal	Back pain	0	1	0	1	2	2

*Includes events reported by 2 or more patients receiving CORLOPAM treatment across all dose groups.

**Investigator defined; no protocol definition.

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Adverse effects in overall data base

The adverse event incidences listed below are based on observations of over 1,000 CORLOPAM treated patients and not listed in the Table above.

Events reported with a frequency between 0.5-5% in patients treated with IV CORLOPAM

Cardiovascular:	extrasystoles, palpitations, bradycardia, heart failure, ischemic heart disease, myocardial infarction, angina pectoris
Metabolic:	elevated BUN, elevated serum glucose, elevated transaminase, elevated LDH
General Body:	non-specific chest pain, pyrexia
Hematologic/Lymphatic:	leukocytosis, bleeding
Respiratory:	dyspnea, upper respiratory disorder
Genitourinary:	oliguria
Musculoskeletal:	limb cramp

ANIMAL TOXICOLOGY

Unusual toxicologic findings (arterial lesions in the rat) with fenoldopam are summarized below. These findings have not been observed in mice or dogs. No evidence of a similar lesion in humans has been observed.

Arterial lesions characterized by medial necrosis and hemorrhage have been seen in renal and splanchnic arteries of rats given fenoldopam mesylate by continuous intravenous infusion at doses of 1 to 100 µg/kg/min for 24 hours. The incidence of these lesions is dose related. Arterial lesions morphologically identical to those observed with fenoldopam have been reported in rats infused with dopamine. Data suggest that the mechanism for this injury involves activation of D_1-like dopaminergic receptors. Such lesions have not been seen in dogs given doses up to 100 µg/kg/min by continuous intravenous infusion for 24 hours, nor were they seen in dogs infused at the same dose for 6 hours daily for 24 days. The clinical significance of this finding is not known.

Oral administration of fenoldopam doses of 10 to 15 mg/kg/day or 20 to 25 mg/kg/day to rats for 24 months induced a higher incidence of polyarteritis nodosa compared to controls. Such lesions were not seen in rats given 5 mg/kg/day of fenoldopam or in mice given the drug at doses up to 50 mg/kg/day for 24 months.

OVERDOSAGE

Intentional CORLOPAM overdosage has not been reported. The most likely reaction would be excessive hypotension which should be treated with drug discontinuation and appropriate supportive measures.

DOSAGE AND ADMINISTRATION

The optimal magnitude and rate of blood pressure reduction in acutely hypertensive patients have not been rigorously determined, but, in general, both delay and too rapid decreases appear undesirable in sick patients. An initial CORLOPAM dose may be chosen from Tables 2 and 3 in the Clinical Pharmacology Section that produces the desired magnitude and rate of blood pressure reduction in a given clinical situation. Doses below 0.1 µg/kg/min have very modest effects and appear only marginally useful in this population. In general, as the initial dose increases, there is a greater and more rapid blood pressure reduction. However, lower initial doses (0.03-0.1 µg/kg/min) titrated slowly

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have been associated with less reflex tachycardia than have higher initial doses (≥ 0.3 µg/kg/min). In clinical trials, doses from 0.01-1.6 µg/kg/min have been studied. Most of the effect of a given infusion rate is attained in 15 minutes.

CORLOPAM should be administered by continuous intravenous infusion. **A bolus dose should not be used.** Hypotension and rapid decreases of blood pressure should be avoided. The initial dose should be titrated upward or downward, no more frequently than every 15 minutes (and less frequently as goal pressure is approached) to achieve the desired therapeutic effect. The recommended increments for titration are 0.05-0.1 µg/kg/min.

Use of a calibrated, mechanical infusion pump is recommended for proper control of infusion rate during CORLOPAM infusion. In clinical trials, CORLOPAM treatment was safely performed **without** the need for intra-arterial blood pressure monitoring; blood pressure and heart rate were monitored at frequent intervals, typically every 15 minutes. Frequent blood pressure monitoring is recommended.

Use of beta-blockers in conjunction with CORLOPAM has not been studied in hypertensive patients and, if possible, concomitant use should be avoided. If the drugs are used together, caution should be exercised because unexpected hypotension could result from beta-blocker inhibition of the reflex response to fenoldopam.

The CORLOPAM infusion can be abruptly discontinued or gradually tapered prior to discontinuation. Oral antihypertensive agents can be added during CORLOPAM infusion or following its discontinuation. Patients in controlled clinical trials have received intravenous CORLOPAM for as long as 48 hours.

PREPARATION OF INFUSION SOLUTION

WARNING: CONTENTS OF AMPULES MUST BE DILUTED BEFORE INFUSION. EACH AMPULE IS FOR SINGLE USE ONLY.

Dilution:

The CORLOPAM Injection ampule concentrate must be diluted in 0.9% Sodium Chloride Injection USP or 5% Dextrose Injection USP using the following dilution schedule:

mL of Concentrate (mg of drug)	Added to	Final Concentration
4 mL (40 mg)	1000 mL	40 µg/mL
2 mL (20 mg)	500 mL	40 µg/mL
1 mL (10 mg)	250 mL	40 µg/mL

The drug dose rate must be individualized according to body weight and according to the desired rapidity and extent of pharmacodynamic effect. The following Table provides the calculated infusion volume in mL/min for a range of drug doses and body weights. The infusion should be administered using a calibrated mechanical infusion pump that can accurately and reliably deliver the desired infusion rate.

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Table 5
INFUSION RATES (mL/min) TO ACHIEVE A GIVEN DRUG DOSE RATE (µg/kg/min)

Body Weight (kg)	Drug Dose Rate				
	0.025 µg/kg/min	**0.05** µg/kg/min	**0.1** µg/kg/min	**0.2** µg/kg/min	**0.3** µg/kg/min
	Infusion Rates (mL/min)				
40	0.025	0.05	0.10	0.20	0.30
50	0.031	0.06	0.13	0.25	0.38
60	0.038	0.08	0.15	0.30	0.45
70	0.044	0.09	0.18	0.35	0.53
80	0.050	0.10	0.20	0.40	0.60
90	0.056	0.11	0.23	0.45	0.68
100	0.063	0.13	0.25	0.50	0.75
110	0.069	0.14	0.28	0.55	0.83
120	0.075	0.15	0.30	0.60	0.90
130	0.081	0.16	0.33	0.65	0.98
140	0.088	0.18	0.35	0.70	1.05
150	0.094	0.19	0.38	0.75	1.13

The diluted solution is stable under normal ambient light and temperature conditions for at least 24 hours. Diluted solution that is not used within 24 hours of preparation should be discarded. Parenteral products should be inspected visually. If particulate matter or cloudiness is observed, the drug should be discarded.

HOW SUPPLIED

List	Container	Concentration	Fill	Quantity
2304	Single-dose ampule	10 mg/mL	1 mL	one per carton
2304	Single-dose ampule	10 mg/mL	2 mL	one per carton

Store at 2 to 30°C.

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