
PHENYLEPHRINE HYDROCHLORIDE INJECTION, USP 10mg PER mL 1mL VIAL

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PHENYLEPHRINE HYDROCHLORIDE safely and effectively. See full prescribing information for PHENYLEPHRINE HYDROCHLORIDE. PHENYLEPHRINE HYDROCHLORIDE injection, for intravenous use Initial U.S. Approval: 2012

INDICATIONS AND USAGE

Phenylephrine Hydrochloride is an alpha-1 adrenergic receptor agonist indicated for increasing blood pressure in adults with clinically important hypotension resulting primarily from vasodilation, in such settings as septic shock or anesthesia. (1)

DOSAGE AND ADMINISTRATION

Dilute before administration. (2.1)

Dosing for Perioperative Hypotension

Intravenous bolus administration: 50 mcg to 250 mcg (2.4) Intravenous continuous infusion: 0.5 mcg/kg/minute to 1.4 mcg/kg/minute titrated to effect (2.4)

Dosing for Patients with Vasodilatory Shock

Intravenous continuous infusion: 0.5 mcg/kg/minute to 6 mcg/kg/minute titrated to effect (2.5)

DOSAGE FORMS AND STRENGTHS

Injection: 10 mg per mL supplied as a 1 mL single dose vial (3, 11, 16)

CONTRAINDICATIONS

Hypersensitivity to it or any of its components (4)

WARNINGS AND PRECAUTIONS

Severe bradycardia and decreased cardiac output (5.2) Extravasation: during intravenous administration may cause necrosis or sloughing of tissue (5.4) Concomitant use with oxytocic drugs: pressor effect of sympathomimetic pressor amines is potentiated (5.5)

ADVERSE REACTIONS

Most common adverse reactions: nausea and vomiting, headache, nervousness (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

Agonistic effects with monoamine oxidase inhibitors (MAOI), β -adrenergic blocking agents, α -2 adrenergic agonists, steroids, tricyclic antidepressants, norepinephrine transport inhibitors, ergot alkaloids, centrally-acting sympatholytic agents and atropine sulfate (7.1) Antagonistic effects on and by α -adrenergic blocking agents (7.2)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 3/2019

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1 INDICATIONS & USAGE

Phenylephrine Hydrochloride is an alpha-1 adrenergic receptor agonist indicated for increasing blood pressure in adults with clinically important hypotension resulting primarily from vasodilation, in such settings as septic shock or anesthesia.

2 DOSAGE & ADMINISTRATION

2.1 General Administration Instructions

Phenylephrine hydrochloride must be diluted before administration as bolus intravenous infusion or continuous intravenous infusion.

Inspect the solution for particulate matter and discoloration prior to administration. The diluted solution should not be held for more than 4 hours at room temperature or for more than 24 hours under refrigerated conditions. Discard any unused portion.

During phenylephrine hydrochloride administration:

Correct intravascular volume depletion. Correct acidosis. Acidosis may reduce the effectiveness of phenylephrine.

2.2 Preparing a 100 mcg/mL Solution for Bolus Intravenous Administration

For bolus intravenous administration, withdraw 10 mg (1 mL of a 10 mg/mL concentration) of phenylephrine injection and dilute with 99 mL of 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP. This will yield a final concentration of 100 mcg/mL. Withdraw an appropriate dose from the 100 mcg/mL solution prior to bolus intravenous administration.

2.3 Preparing a Solution for Continuous Intravenous Infusion

For continuous intravenous infusion, withdraw 10 mg (1 mL of 10 mg/mL concentration) of phenylephrine hydrochloride injection and add to 500 mL of 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (providing a final concentration of 20 mcg/mL).

2.4 Dosing for Perioperative Setting

In adult patients undergoing surgical procedures with either neuraxial anesthesia or general anesthesia:

50 mcg to 250 mcg by intravenous bolus administration. The most frequently reported initial bolus dose is 50 mcg or 100 mcg.

0.5 mcg/kg/min to 1.4 mcg/kg/min by intravenous continuous infusion, titrated to blood pressure goal.

2.5 Dosing for Septic or Other Vasodilatory Shock

In adult patients with septic or other vasodilatory shock:

No bolus.

0.5 mcg/kg/min to 6 mcg/kg/min by intravenous continuous infusion, titrated to blood pressure goal. Doses above 6 mcg/kg/min do not show significant incremental increase in blood pressure.

3 DOSAGE FORMS & STRENGTHS

Injection: 10 mg per mL phenylephrine hydrochloride is supplied as a 1 mL single dose vial.

4 CONTRAINDICATIONS

The use of phenylephrine hydrochloride is contraindicated in patients with:

Hypersensitivity to it or any of its components

5 WARNINGS AND PRECAUTIONS

5.1 Exacerbation of Angina, Heart Failure, or Pulmonary Arterial Hypertension

Because of its pressor effects, phenylephrine hydrochloride can precipitate angina in patients with severe arteriosclerosis or history of angina, exacerbate underlying heart failure, and increase pulmonary arterial pressure.

5.2 Bradycardia

Phenylephrine hydrochloride can cause severe bradycardia and decreased cardiac output.

5.3 Risk in Patients with Autonomic Dysfunction

The pressor response to adrenergic drugs, including phenylephrine, can be increased in patients with autonomic dysfunction, as may occur with spinal cord injuries.

5.4 Skin and Subcutaneous Necrosis

Extravasation of phenylephrine can cause necrosis or sloughing of tissue.

5.5 Pressor Effect with Concomitant Oxytocic Drugs

Oxytocic drugs potentiate the pressor effect of sympathomimetic pressor amines including phenylephrine hydrochloride [see Drug Interactions (7.1)], with the potential for hemorrhagic stroke.

5.7 Peripheral and Visceral Ischemia

Phenylephrine hydrochloride can cause excessive peripheral and visceral vasoconstriction and ischemia to vital organs, particularly in patients with extensive peripheral vascular disease.

5.8 Renal Toxicity

Phenylephrine hydrochloride can increase the need for renal replacement therapy in patients with septic shock. Monitor renal function.

6 ADVERSE REACTIONS

The following adverse reactions associated with the use of phenylephrine hydrochloride were identified in the literature. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or to establish a causal relationship to drug exposure.

Cardiac disorders: Bradycardia, AV block, ventricular extrasystoles, myocardial ischemia

Gastrointestinal disorders: Nausea, vomiting

General disorders and administrative site conditions: Chest pain, extravasation

Immune system disorders: Sulfite sensitivity

Nervous system disorders: Headache, nervousness, paresthesia, tremor

Psychiatric disorders: Excitability

Respiratory: Pulmonary edema, rales

Skin and subcutaneous tissue disorders: Diaphoresis, pallor, piloerection, skin blanching, skin necrosis with extravasation

Vascular disorders: Hypertensive crisis

7 DRUG INTERACTIONS

7.1 Agonists

The pressor effect of phenylephrine hydrochloride is increased in patients receiving:

Monoamine oxidase inhibitors (MAOI), such as selegiline. β -adrenergic blockers α -2 adrenergic agonists, such as clonidine Steroids Tricyclic antidepressants Norepinephrine transport inhibitors, such as atomoxetine Ergot alkaloids, such as methylergonovine maleate Centrally-acting sympatholytic agents, such as guanfacine or reserpine Atropine sulfate

7.2 Antagonists

 α -adrenergic blocking agents, including phenothiazines (e.g., chlorpromazine) and amiodarone block phenylephrine and are in turn blocked by phenylephrine.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with intravenous phenylephrine. It is also not known whether phenylephrine can cause fetal harm when administered to a pregnant woman or can

affect reproduction capacity. Phenylephrine hydrochloride should be given to a pregnant woman only if clearly needed.

8.2 Labor and Delivery

The most common maternal adverse reactions reported in studies of phenylephrine use during neuraxial anesthesia during cesarean delivery include nausea and vomiting, which are commonly associated with hypotension, bradycardia, reactive hypertension, and transient arrhythmias. Phenylephrine does not appear to cause a decrease in placental perfusion sufficient to alter either the neonate Apgar scores or blood-gas status.

8.3 Nursing Mothers

It is not known whether this drug is excreted in human milk.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of phenylephrine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. 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.

8.6 Hepatic Impairment

In patients with liver cirrhosis [Child Pugh Class A (n=3), Class B (n=5) and Class C (n=1)], dose-response data indicate decreased responsiveness to phenylephrine. Consider using larger doses than usual in hepatic impaired subjects.

8.7 Renal Impairment

In patients with end stage renal disease (ESRD) undergoing hemodialysis, dose-response data indicates increased responsiveness to phenylephrine. Consider using lower doses of phenylephrine hydrochloride in ESRD patients.

10 OVERDOSAGE

Overdose of phenylephrine hydrochloride can cause a rapid rise in blood pressure. Symptoms of overdose include headache, vomiting, hypertension, reflex bradycardia, and cardiac arrhythmias including ventricular extrasystoles and ventricular tachycardia, and may cause a sensation of fullness in the head and tingling of the extremities.

Consider using an α -adrenergic antagonist.

11 DESCRIPTION

Phenylephrine hydrochloride is a synthetic sympathomimetic agent in sterile form for parenteral injection. Chemically, phenylephrine hydrochloride is (-)-m-Hydroxy- α -[(methylamino)methyl]benzyl alcohol hydrochloride and has the following structural formula:

Phenylephrine hydrochloride is very soluble in water, freely soluble in ethanol, and insoluble in chloroform and ethyl ether. Phenylephrine hydrochloride is sensitive to light.

Phenylephrine Hydrochloride Injection, USP is a clear, colorless, aqueous solution that is essentially free of visible foreign matter. Each mL contains: Phenylephrine Hydrochloride 10 mg; Sodium Chloride 3.5 mg; Sodium Citrate Dihydrate 4 mg; and Citric Acid Monohydrate 1 mg in water for injection. The pH may be adjusted in the range of 3.5 to 5.5 with Sodium Hydroxide and/or Hydrochloric Acid, if necessary.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Phenylephrine hydrochloride is an α -1 adrenergic receptor agonist.

12.2 Pharmacodynamics

Phenylephrine is the active moiety. Metabolites are inactive at both the α -1 and α -2 adrenergic receptors. Following parenteral administration of phenylephrine hydrochloride, increases in systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, and total peripheral vascular resistance are observed. The onset of blood pressure increase following an intravenous bolus phenylephrine hydrochloride administration is rapid and the effect may persist for up to 20 minutes. As mean arterial pressure increases following parenteral doses, vagal activity also increases, resulting in reflex bradycardia.

Most vascular beds are constricted, including renal, splanchnic, and hepatic.

12.3 Pharmacokinetics

Following an intravenous infusion of phenylephrine hydrochloride, the effective half-life was approximately 5 minutes. The steady-state volume of distribution (340 L) exceeded the body volume by a factor of 5, suggesting a high distribution into certain organ compartments. The average total serum clearance (2095 mL/min) was close to one-third of the cardiac output.

A mass balance study showed that phenylephrine is extensively metabolized by the liver with only 12% of the dose excreted unchanged in the urine. Deamination by monoamino oxidase is the primary metabolic pathway resulting in the formation of the major metabolite (m-hydroxymandelic acid) which accounts for 57% of the

14 CLINICAL STUDIES

Increases in systolic and mean blood pressure following administration of phenylephrine were observed in 42 literature-based studies in the perioperative setting, including 26 studies where phenylephrine was used in low-risk (ASA 1 and 2) pregnant women undergoing neuraxial anesthesia during cesarean delivery, 3 studies in non-obstetric surgery under neuraxial anesthesia, and 13 studies in patients undergoing surgery under general anesthesia. Mean arterial blood pressure increases were also observed in two double-blind, active-controlled studies in patients with septic shock.

16 HOW SUPPLIED/STORAGE AND HANDLING

Phenylephrine Hydrochloride Injection, USP, is supplied as follows:

NDC:51662-1576-1 PHENYLEPHRINE HYDROCHLORIDE INJECTION, USP 10mg PER mL 1mL VIAL

NDC:51662-1576-2 PHENYLEPHRINE HYDROCHLORIDE INJECTION, USP 10mg PER mL 1mL VIAL in 1 Pouch

NDC:51662-1576-3 PHENYLEPHRINE HYDROCHLORIDE INJECTION, USP 10mg PER mL 1mL VIAL in a Pouch, 25 Pouches/Case

HF Acquisition Co LLC, DBA HealthFirst 11629 49th Pl W.

Mukilteo, WA 98275

Also supplied in the following manufacture supplied dosage forms

Store at 20° to 25°C (68° to 77°F), excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Protect from light. Keep covered in carton until time of use. For single use only. Discard unused portion.

17 PATIENT COUNSELING INFORMATION

Inform patients, families, or caregivers that the primary side effect of phenylephrine is hypertension and rarely, hypertensive crisis. Patients may experience bradycardia (slow heart rate), which in some cases may produce

heart block or other cardiac arrhythmias, extra ventricular beats, myocardial ischemia in patients with underlying cardiac disease, and pulmonary edema (fluid in the lungs) or rales. Common, less serious symptoms include the following:

chest pain

skin or tissue damage if the drug leaks out of the venous catheter into the surrounding tissue headache, nervousness, tremor, numbness/tingling (paresthesias) in hands or feet nausea, vomiting excitability, dizziness, sweating, flushing

Lake Zurich, IL 60047

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PRINCIPAL DISPLAY PANEL - 51662-1576-1 - VIAL AND SERIALIZED VIAL LABELING, 1mL VIAL (10mg per mL)

Principal Display Panel NDC 51662-1576-2 Pouch

Pouch

Vial

Principal Display Panel NDC 51662-1576-3 Case

Case

RFID

PHENYLEPHRINE HYDROCHLORIDE phenylephrine hydrochloride injection											
Product Information											
Product Type			HUMAN PRESCRIPTION DRUG Item Code (Source)		Source)	NDC:51662-1576(NDC:63323-751)					
Route of Administration			INTRAVENOUS								
Active Ingredient/Active Moiety											
Ingre			edient Name		Ba	Basis of Strength		Strength			
PHENYLEPHRINE HYDROCHLORIDE (UNII: 0			4JA59TNSJ) (PHENYLEPHRINE - UNII:1WS297W6MV) PHE		PHENYLEP	NYLEPHRINE HYDROCHLORIDE		10 mg in 1 mL			
Inactive Ingredients											
Ingredient Name								renath			
								Strength			
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)											
WATER (UNII: 059QF0K00R)											
SODIUM HYDROXIDE (UNII: 55X04QC32I)											
NITROGEN (UNII: N762921K75)											
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)											
HYDROCHLORIC ACID (UNII: QTT17582CB)											
Pa	ackaging										
#	Item Code		Package Description	M	larketing S	tart Date	Marketin	ng End Date			
1	NDC:51662-1576-1	1 mL in 1 VIAL, SINGL	E-DOSE; Type 0: Not a Combination P	roduct 06/	30/2021						
2	NDC:51662-1576-3	25 in 1 CASE		07/	10/2022						
2	NDC:51662-1576-2	1 in 1 POUCH									
2		1 mL in 1 VIAL, SINGL	E-DOSE; Type 0: Not a Combination P	roduct							
Marketing Information											
	Marketing Catego	ory Applicat	ion Number or Monograph Cita	tion M	larketing St	art Date	Marketin	ng End Date			
AN	IDA	ANDA210665		06/3	0/2021						

Registrant - HF Acquisition Co LLC, DBA HealthFirst (045657305)

Establishment										
Name	Address	ID/FEI	Business Operations							
HF Acquisition Co LLC, DBA HealthFirst		045657305	relabel(51662-1576)							

Revised: 2/2024

HF Acquisition Co LLC, DBA HealthFirst