VASOPRESSIN- vasopressin injection
HF Acquisition Co LLC, DBA HealthFirst

VASOSTRICT(TM) (VASOPRESSIN INJECTION, USP) 20 UNITS PER mL

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VASOSTRICT ® safely and effectively. See full prescribing information for VASOSTRICT ®.

Vasostrict ® (vasopressin injection) for intravenous use
Initial U.S. Approval: 2014

INDICATIONS AND USAGE

Vasostrict® is indicated to increase blood pressure in adults with vasodilatory shock (e.g., post-cardiotomy or sepsis) who remain hypotensive despite fluids and catecholamines. (1)

DOSAGE AND ADMINISTRATION

Dilute Vasostrict® with normal saline (0.9% sodium chloride) or 5% dextrose in water (D5W) to either 0.1 units/mL or 1 unit/mL for intravenous administration. Discard unused diluted solution after 18 hours at room temperature or 24 hours under refrigeration. (2-2.1)
Post-cardiotomy shock: 0.03 to 0.1 units/minute (2-2.2)
Septic shock: 0.01 to 0.07 units/minute (2-2.2)

DOSAGE FORMS AND STRENGTHS

Injection: 20 units per mL (3)

CONTRAINDICATIONS

Vasostrict® is contraindicated in patients with known allergy or hypersensitivity to 8-L-arginine vasopressin or chlorobutanol. (4)

WARNINGS AND PRECAUTIONS

Can worsen cardiac function. (5-5.1)

ADVERSE REACTIONS

The most common adverse reactions include decreased cardiac output, bradycardia, tachyarrhythmias, hyponatremia and ischemia (coronary, mesenteric, skin, digital). (6)

To report SUSPECTED ADVERSE REACTIONS, contact Par Pharmaceutical at 1-800-828-9393 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Pressor effects of catecholamines and Vasostrict® are expected to be additive. (7-7.1)
Indomethacin may prolong effects of Vasostrict®. (7-7.2)
Co-administration of ganglionic blockers or drugs causing SIADH may increase the

pressor response. (7-7.3, 7-7.5)
Co-administration of drugs causing diabetes insipidus may decrease the pressor response. (7-7.6)

USE IN SPECIFIC POPULATIONS

Pregnancy: May induce uterine contractions. (8-8.1)
Pediatric Use: Safety and effectiveness have not been established. (8-8.4)
Geriatric Use: No safety issues have been identified in older patients. (8-8.5)

Revised: 12/2016

FULL PRESCRIBING INFORMATION

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

1 INDICATIONS & USAGE

Vasostrict® is indicated to increase blood pressure in adults with vasodilatory shock (e.g., post-cardiotomy or sepsis) who remain hypotensive despite fluids and catecholamines.

2 DOSAGE & ADMINISTRATION

2.1 Preparation of Diluted Solutions

Dilute Vasostrict® in normal saline (0.9% sodium chloride) or 5% dextrose in water (D5W) prior to use for intravenous administration. Discard unused diluted solution after 18 hours at room temperature or 24 hours under refrigeration.

Table 1 Preparation of diluted solutions

Fluid restriction? Final concentration Mix

Vasostrict® Diluent

No 0.1 units/mL 2.5 mL (50 units) 500 mL

Yes 1 unit/mL 5 mL (100 units) 100 mL

Inspect parenteral drug products for particulate matter and discoloration prior to use, whenever solution and container permit.

2.2 Administration

The goal of treatment is optimization of perfusion to critical organs, but aggressive treatment can compromise perfusion of organs, like the gastrointestinal tract, whose function is difficult to monitor. The following advice is empirical. In general, titrate to the lowest dose compatible with a clinically acceptable response.

For post-cardiotomy shock, start with a dose of 0.03 units/minute. For septic shock, start with a dose of 0.01 units/minute. If the target blood pressure response is not achieved, titrate up by 0.005 units/minute at 10- to 15-minute intervals. The maximum dose for post-cardiotomy shock is 0.1 units/minute and for septic shock 0.07 units/minute. After target blood pressure has been maintained for 8 hours without the use of catecholamines, taper Vasostrict® by 0.005 units/minute every hour as tolerated to maintain target blood pressure.

3 DOSAGE FORMS & STRENGTHS

Vasostrict® (vasopressin injection, USP) is a clear, practically colorless solution for intravenous administration available as 20 units/mL in a single dose vial and 200 units/10 mL (20 units/mL) in a multiple dose vial.

4 CONTRAINDICATIONS

Vasostrict® is contraindicated in patients with known allergy or hypersensitivity to 8-L-arginine vasopressin or chlorobutanol.

5 WARNINGS AND PRECAUTIONS

5.1 Worsening Cardiac Function

Use in patients with impaired cardiac response may worsen cardiac output.

6 ADVERSE REACTIONS

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

Bleeding/lymphatic system disorders: Hemorrhagic shock, decreased platelets, intractable bleeding

Cardiac disorders: Right heart failure, atrial fibrillation, bradycardia, myocardial ischemia

Gastrointestinal disorders: Mesenteric ischemia

Hepatobiliary: Increased bilirubin levels

Renal/urinary disorders: Acute renal insufficiency

Vascular disorders: Distal limb ischemia

Metabolic: Hyponatremia

Skin: Ischemic lesions

7 DRUG INTERACTIONS

7.1 Catecholamines

Use with catecholamines is expected to result in an additive effect on mean arterial blood pressure and other hemodynamic parameters.

7.2 Indomethacin

Use with indomethacin may prolong the effect of Vasostrict® on cardiac index and systemic vascular resistance [see Clinical Pharmacology (12-12.3)].

7.3 Ganglionic Blocking Agents

Use with ganglionic blocking agents may increase the effect of Vasostrict® on mean arterial blood pressure [see Clinical Pharmacology (12-12.3)].

7.4 Furosemide

Use with furosemide increases the effect of Vasostrict® on osmolar clearance and urine flow [see Clinical Pharmacology (12-12.3)].

7.5 Drugs Suspected of Causing SIADH

Use with drugs suspected of causing SIADH (e.g., SSRIs, tricyclic antidepressants, haloperidol, chlorpropamide, enalapril, methyldopa, pentamidine, vincristine, cyclophosphamide, ifosfamide, felbamate) may increase the pressor effect in addition to the antidiuretic effect of Vasostrict®.

7.6 Drugs Suspected of Causing Diabetes Insipidus

Use with drugs suspected of causing diabetes insipidus (e.g., demeclocycline, lithium, foscarnet, clozapine) may decrease the pressor effect in addition to the antidiuretic effect of Vasostrict®.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Risk Summary: There are no adequate or well-controlled studies of Vasostrict® in pregnant women. It is not known whether vasopressin can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Animal reproduction studies have not been conducted with vasopressin [see Clinical Pharmacology (12-12.3)].

Clinical Considerations: Because of increased clearance of vasopressin in the second and third trimester, the dose of Vasostrict® may need to be up-titrated to doses exceeding 0.1 units/minute in post-cardiotomy shock and 0.07 units/minute in septic shock.

Vasostrict® may produce tonic uterine contractions that could threaten the continuation of pregnancy.

8.3 Nursing Mothers

It is not known whether vasopressin is present in human milk. However, oral absorption by a nursing infant is unlikely because vasopressin is rapidly destroyed in the gastrointestinal tract. Consider advising a lactating woman to pump and discard breast milk for 1.5 hours after receiving vasopressin to minimize potential exposure to the breastfed infant.

8.4 Pediatric Use

Safety and effectiveness of Vasostrict® in pediatric patients with vasodilatory shock have not been established.

8.5 Geriatric Use

Clinical studies of vasopressin 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 [see Warnings and Precautions (5), Adverse Reactions (6), and Clinical Pharmacology (12-12.3)].

10 OVERDOSAGE

Overdosage with Vasostrict® can be expected to manifest as consequences of vasoconstriction of various vascular beds (peripheral, mesenteric, and coronary) and as hyponatremia. In addition, overdosage may lead less commonly to ventricular tachyarrhythmias (including Torsade de Pointes), rhabdomyolysis, and non-specific

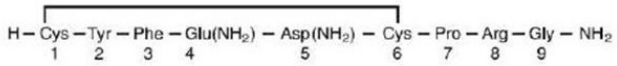
gastrointestinal symptoms.

Direct effects will resolve within minutes of withdrawal of treatment.

11 DESCRIPTION

Vasopressin is a polypeptide hormone that causes contraction of vascular and other smooth muscles and antidiuresis. Vasostrict® is a sterile, aqueous solution of synthetic arginine vasopressin for intravenous administration. The 1 mL solution contains vasopressin 20 units/mL, Water for Injection, USP, and sodium acetate buffer adjusted to a pH of 3.8. The 10 mL solution contains vasopressin 20 units/mL, chlorobutanol, NF 0.5% as a preservative, and Water for Injection, USP and, sodium acetate buffer adjusted to a pH of 3.8.

The chemical name of vasopressin is Cyclo (1-6) L-Cysteinyl-L-Tyrosyl-L-Phenylalanyl-L-Glutaminyl-L-Asparaginyl-L-Cysteinyl-L-Prolyl-L-Arginyl-L-Glycinamide. It is a white to off-white amorphous powder, freely soluble in water. The structural formula is:



Molecular Formula: C46H65N15O12S2 Molecular Weight: 1084.23

One mg is equivalent to 530 units.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The vasoconstrictive effects of vasopressin are mediated by vascular V1 receptors. Vascular V1 receptors are directly coupled to phopholipase C, resulting in release of calcium, leading to vasoconstriction. In addition, vasopressin stimulates antidiuresis via stimulation of V2 receptors which are coupled to adenyl cyclase.

12.2 Pharmacodynamics

At therapeutic doses exogenous vasopressin elicits a vasoconstrictive effect in most vascular beds including the splanchnic, renal and cutaneous circulation. In addition,

vasopressin at pressor doses triggers contractions of smooth muscles in the gastrointestinal tract mediated by muscular V1-receptors and release of prolactin and ACTH via V3 receptors. At lower concentrations typical for the antidiuretic hormone vasopressin inhibits water diuresis via renal V2 receptors.

In patients with vasodilatory shock vasopressin in therapeutic doses increases systemic vascular resistance and mean arterial blood pressure and reduces the dose requirements for norepinephrine. Vasopressin tends to decrease heart rate and cardiac output. The pressor effect is proportional to the infusion rate of exogenous vasopressin. Onset of the pressor effect of vasopressin is rapid, and the peak effect occurs within 15 minutes. After stopping the infusion the pressor effect fades within 20 minutes. There is no evidence for tachyphylaxis or tolerance to the pressor effect of vasopressin in patients.

12.3 Pharmacokinetics

At infusion rates used in vasodilatory shock (0.01-0.1 units/minute) the clearance of vasopressin is 9 to 25 mL/min/kg in patients with vasodilatory shock. The apparent t1/2 of vasopressin at these levels is ≤10 minutes. Vasopressin is predominantly metabolized and only about 6% of the dose is excreted unchanged in urine. Animal experiments suggest that the metabolism of vasopressin is primarily by liver and kidney. Serine protease, carboxipeptidase and disulfide oxido-reductase cleave vasopressin at sites relevant for the pharmacological activity of the hormone. Thus, the generated metabolites are not expected to retain important pharmacological activity.

Drug-Drug Interactions

Indomethacin more than doubles the time to offset for vasopressin's effect on peripheral vascular resistance and cardiac output in healthy subjects [see Drug Interactions (7-7.2)].

The ganglionic blocking agent tetra-ethylammonium increases the pressor effect of vasopressin by 20% in healthy subjects [see Drug Interactions (7-7.3)].

Furosemide increases osmolar clearance 4-fold and urine flow 9-fold when co-administered with exogenous vasopressin in healthy subjects [see Drug Interactions (7-7.4)].

Halothane, morphine, fentanyl, alfentanyl and sufentanyl do not impact exposure to endogenous vasopressin.

Special Populations

Pregnancy: Because of a spillover into blood of placental vasopressinase the clearance of exogenous and endogenous vasopressin increases gradually over the course of a pregnancy. During the first trimester of pregnancy the clearance is only slightly increased. However, by the third trimester the clearance of vasopressin is increased about 4-fold and at term up to 5-fold. After delivery the clearance of vasopressin returns to pre-conception baseline within two weeks.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No formal carcinogenicity or fertility studies with vasopressin have been conducted in

animals. Vasopressin was found to be negative in the in vitro bacterial mutagenicity (Ames) test and the in vitro Chinese hamster ovary (CHO) cell chromosome aberration test. In mice, vasopressin has been reported to have an effect on function and fertilizing ability of spermatozoa.

14 CLINICAL STUDIES

Increases in systolic and mean blood pressure following administration of vasopressin were observed in 7 studies in septic shock and 8 in post-cardiotomy vasodilatory shock.

16 HOW SUPPLIED/STORAGE AND HANDELING

VASOSTRICT(TM) (VASOPRESSIN INJECTION, USP) is supplied in the following dosage forms.
NDC 51662-1314-1
VASOSTRICT(TM) (VASOPRESSIN INJECTION, USP) 20 UNITS PER mL 1mL VIAL

NDC 51662-1314-2

VASOSTRICT(TM) (VASOPRESSIN INJECTION, USP) 20 UNITS PER mL 1mL VIAL in 1 pouch

HF Acquisition Co LLC, DBA HealthFirst
Mukilteo, WA 98275

Also supplied in the following manufacture supplied dosage forms

Vasostrict® (vasopressin injection, USP) is a clear, practically colorless solution for intravenous administration available as:

NDC 42023-164-25: A carton of 25 single dose vials each containing vasopressin 1 mL at 20 units/mL.

NDC 42023-190-01: A carton of 1 multiple dose vial containing vasopressin 10 mL at 200 units/10 mL (20 units/mL).

Store between 2°C and 8°C (36°F and 46°F). Do not freeze.

Vials may be held up to 12 months upon removal from refrigeration to room temperature storage conditions (20°C to 25°C [68°F to 77°F], USP Controlled Room Temperature), anytime within the labeled shelf life. Once removed from refrigeration, unopened vial should be marked to indicate the revised 12 month expiration date. If the manufacturer’s original expiration date is shorter than the revised expiration date, then the shorter date must be used. Do not use Vasostrict® beyond the manufacturer’s expiration date stamped on the vial.

After initial entry into the 10 mL vial, the remaining contents must be refrigerated. Discard the refrigerated 10 mL vial after 30 days after first puncture.

The storage conditions and expiration periods are summarized in the following table.

	Unopened Refrigerated 2°C to 8°C (36°F to 46°F)	Unopened Room Temperature 20°C to 25°C (68°F to 77°F) Do not store above 25°C (77°F)	Opened (After First Puncture)
1 mL Vial	Until manufacturer expiration date	12 months or until manufacturer expiration date, whichever is earlier	N/A
10 mL Vial	Until manufacturer expiration date	12 months or until manufacturer expiration date, whichever is earlier	30 days

SPL UNCLASSIFIED

Distributed by:

HF Acquisition Co LLC, DBA HealthFirst

Mukilteo, WA 98275

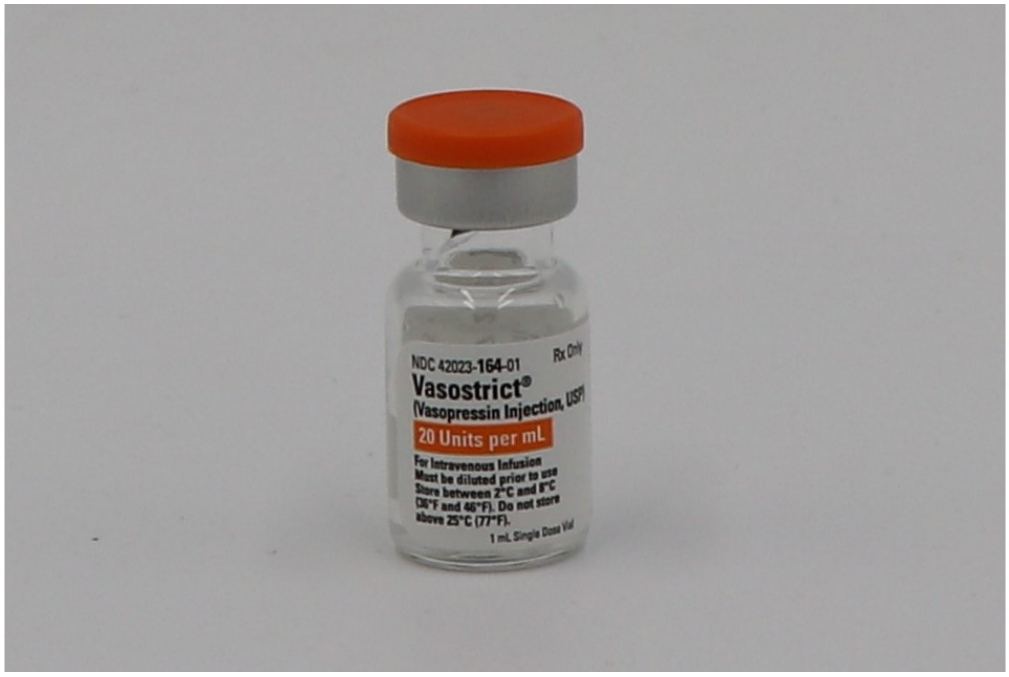
Also distributed by the manufacture in the following manufacture supplied dosage forms

Distributed by:
Par Pharmaceutical
Chestnut Ridge, NY 10977

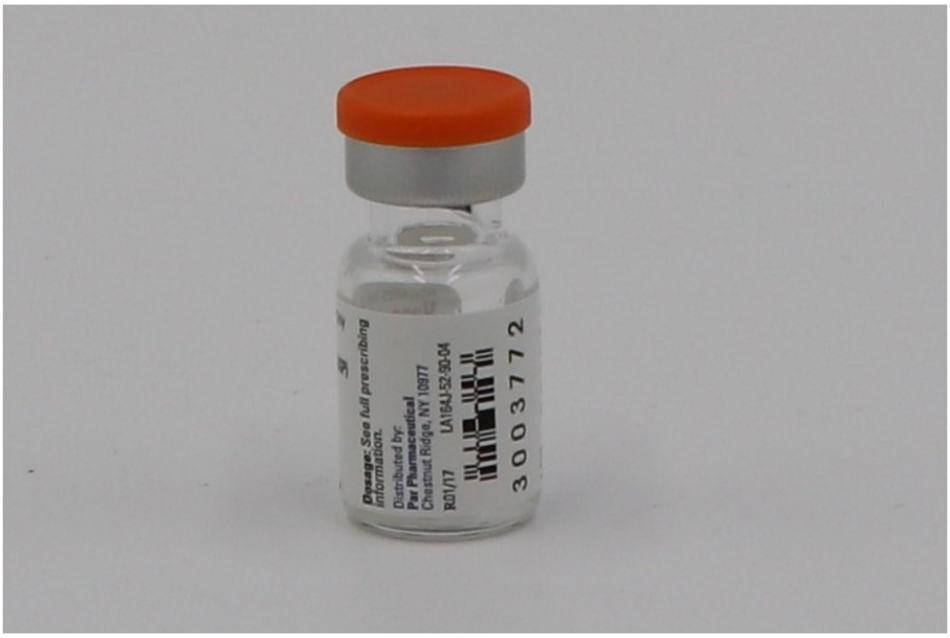
R12/16
OS164J-01-90-08

Vasostrict® is a registered trademark of Par Pharmaceutical Companies, Inc.

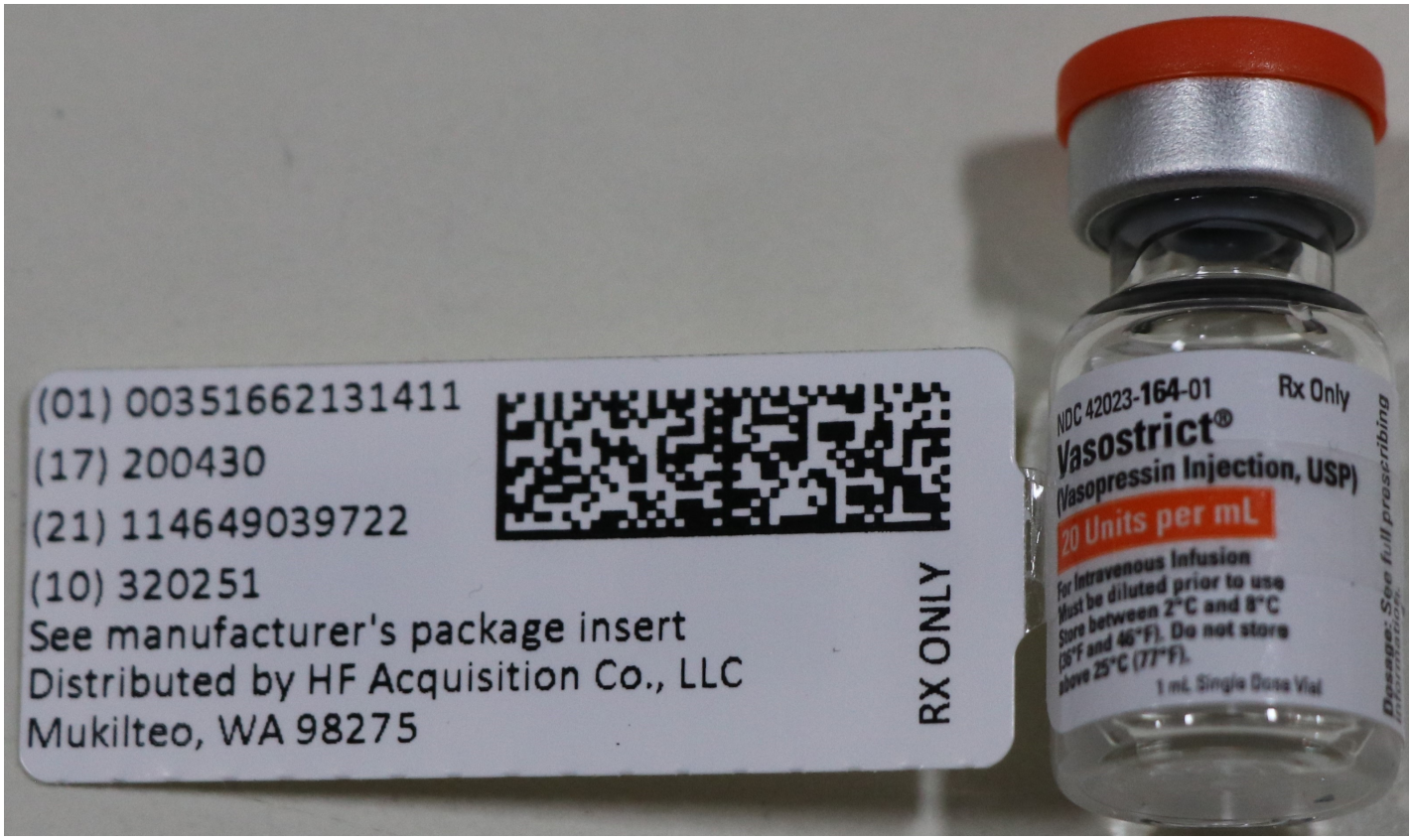
PRINCIPAL DISPLAY PANEL, VIAL FRONT



PRINCIPAL DISPLAY PANEL, VIAL BACK



PRINCIPAL DISPLAY PANEL, SERIALIZED VIAL



PRINCIPAL DISPLAY PANEL, SERIALIZED LABEL ONLY

PRINCIPAL DISPLAY PANEL - SERIALIZED POUCH 51662-1314-2

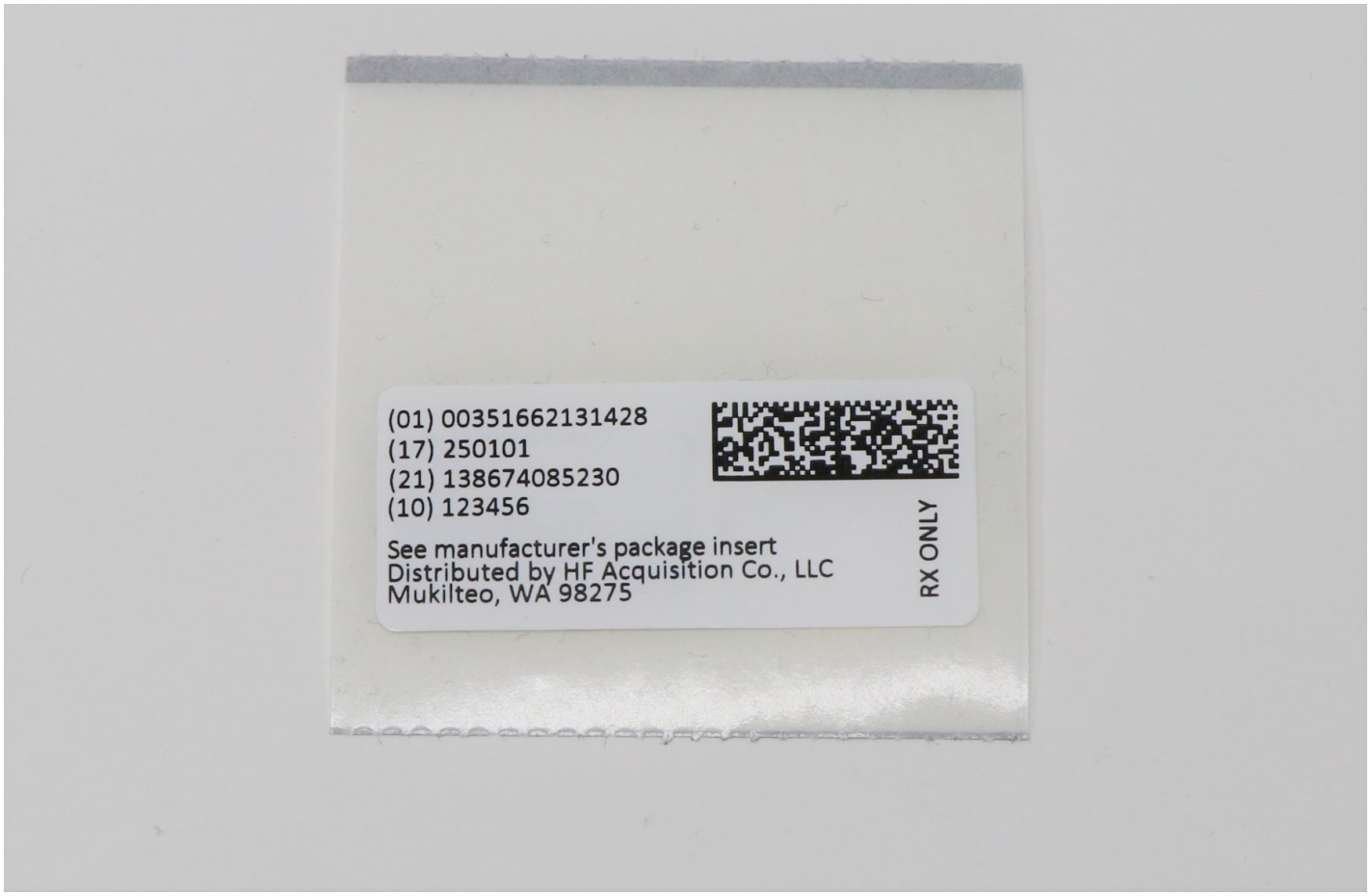
VASOSTRICT™ (VASOPRESSIN INJECTION, USP) 20 UNITS PER mL 1mL VIAL

NDC: 51662-1314-2
LOT: 123456
EXP: 2025-01-01

(01) 00351662131428
(10) 123456
(17) 250101
(21) 138674085230

FOR INTRAVENOUS INFUSION. MUST BE DILUTED PRIOR TO USE. STORE BETWEEN 2°C AND 8°C (36°F AND 46°F). DO NOT STORE ABOVE 25°C (77°F). VIALS MAY BE HELD AT 20°C TO 25°C (68°F TO 77°F) FOR UP TO 12 MONTHS. DOSAGE: SEE FULL PRESCRIBING INFORMATION. DISCARD PREPARED INFUSION SOLUTIONS AFTER 18 HOURS AT ROOM TEMPERATURE OR 24 HOURS REFRIGERATED.

See manufacturer's package insert
ORIGINAL MFG NDC: 42023-164-25
RX ONLY
Manufactured by HF Acquisition Co., LLC
Mukilteo, WA 98275



VASOPRESSIN

vasopressin injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:51662-1314(NDC:42023-164)
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
VASOPRESSIN, UNSPECIFIED (UNII: Y87Y826H08) (VASOPRESSIN, UNSPECIFIED - UNII:Y87Y826H08)	VASOPRESSIN, UNSPECIFIED	20 [USP'U] in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	
SODIUM ACETATE (UNII: 4550K0SC9B)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:51662-1314-1	1 mL in 1 VIAL; Type 0: Not a Combination Product	11/17/2018	
2	NDC:51662-1314-2	1 in 1 POUCH	11/01/2021	
2		1 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA204485	11/17/2018	

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

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

Establishment

Name	Address	ID/FEI	Business Operations
HF Acquisition Co LLC, DBA HealthFirst		045657305	relabel(51662-1314)

Revised: 11/2021 HF Acquisition Co LLC, DBA HealthFirst