VASOPRESSIN IN 0.9% SODIUM CHLORIDE- vasopressin solution
Long Grove Pharmaceuticals, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VASOPRESSIN IN SODIUM CHLORIDE INJECTION safely and effectively. See full prescribing information for VASOPRESSIN IN SODIUM CHLORIDE INJECTION.
VASOPRESSIN injection, for intravenous use
Initial U.S. Approval: 2014

INDICATIONS AND USAGE

- Vasopressin in Sodium Chloride Injection is indicated to increase blood pressure in adults with vasodilatory shock who remain hypotensive despite fluids and catecholamines. (1)

DOSAGE AND ADMINISTRATION

- This product does not require further dilution prior to administration. (2.1)
- Post-cardiotomy shock: 0.03 units/minute to 0.1 units/minute by intravenous infusion (2.2)
- Septic shock: 0.01 units/minute to 0.07 units/minute by intravenous infusion (2.2)

DOSAGE FORMS AND STRENGTHS

Injection: in a premixed single-dose, ready to use vial. (3)

- 20 units/100 mL (0.2 units/mL) in 0.9% Sodium Chloride
- 40 units/100 mL (0.4 units/mL) in 0.9% Sodium Chloride
- 50 units/50 mL (1 unit/mL) in 0.9% Sodium Chloride

CONTRAINDICATIONS

- Vasopressin in Sodium Chloride Injection is contraindicated in patients with known allergy or hypersensitivity to 8-L-arginine vasopressin or chlorobutanol. (4)

WARNINGS AND PRECAUTIONS

- Can worsen cardiac function. (5.1)
- Reversible diabetes insipidus (5.2)

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 Long Grove Pharmaceuticals LLC at 1-855-642-2594 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Pressor effects of catecholamines and Vasopressin in Sodium Chloride Injection are expected to be additive. (7.1)
- Indomethacin may prolong effects of Vasopressin in Sodium Chloride Injection. (7.2)
- Co-administration of ganglionic blockers or drugs causing SIADH may increase the pressor response. (7.3, 7.4)
- Co-administration of drugs causing diabetes insipidus may decrease the pressor response. (7.5)

USE IN SPECIFIC POPULATIONS

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

Revised: 10/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Vasopressin in Sodium Chloride Injection is indicated to increase blood pressure in adults with vasodilatory shock who remain hypotensive despite fluids and catecholamines.

2 DOSAGE AND ADMINISTRATION

2.1 Preparation of Solution

Inspect parenteral drug products for particulate matter and discoloration prior to use,

whenever solution and container permit.

This product does not require further dilution prior to administration.

2.2 Administration

In general, titrate to the lowest dose compatible with a clinically acceptable response.

The recommended starting dose is:

Post-cardiotomy shock: 0.03 units/minute by intravenous infusion

Septic Shock: 0.01 units/minute by intravenous infusion

Titrate up by 0.005 units/minute at 10- to 15-minute intervals until the target blood pressure is reached. There are limited data for doses above 0.1 units/minute for postcardiotomy shock and 0.07 units/minute for septic shock. Adverse reactions are expected to increase with higher doses.

After target blood pressure has been maintained for 8 hours without the use of catecholamines, taper Vasopressin in Sodium Chloride Injection by 0.005 units/minute every hour as tolerated to maintain target blood pressure.

3 DOSAGE FORMS AND STRENGTHS

Vasopressin in Sodium Chloride Injection is a clear, colorless premixed solution for intravenous administration in a single-dose, ready to use vial available as:

- 20 units/100 mL (0.2 units/mL) in 0.9% Sodium Chloride
- 40 units/100 mL (0.4 units/mL) in 0.9% Sodium Chloride
- 50 units/50 mL (1 unit/mL) in 0.9% Sodium Chloride

4 CONTRAINDICATIONS

Vasopressin in Sodium Chloride Injection 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

A decrease in cardiac index may be observed with the use of vasopressin.

5.2 Reversible Diabetes Insipidus

Patients may experience reversible diabetes insipidus, manifested by the development of polyuria, a dilute urine, and hypernatremia, after cessation of treatment with vasopressin. Monitor serum electrolytes, fluid status and urine output after vasopressin discontinuation. Some patients may require readministration of vasopressin or administration of desmopressin to correct fluid and electrolyte shifts.

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

Postmarketing Experience

Reversible diabetes insipidus *[see Warnings and Precautions (5.2)]*

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. Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.

7.2 Indomethacin

Use with *indomethacin* may prolong the effect of Vasopressin in Sodium Chloride Injection on cardiac index and systemic vascular resistance. Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed [*see Clinical Pharmacology (12.3)*].

7.3 Ganglionic Blocking Agents

Use with *ganglionic blocking agents* may increase the effect of Vasopressin in Sodium Chloride Injection on mean arterial blood pressure. Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed [*see Clinical Pharmacology (12.3)*].

7.4 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 Vasopressin in Sodium Chloride Injection. Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.

7.5 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 Vasopressin in Sodium Chloride Injection. Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on Vasopressin in Sodium Chloride Injection use in pregnant women to inform a drug associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted.

Clinical Considerations

Dose adjustments during pregnancy and the postpartum period: Because of increased clearance of vasopressin in the second and third trimester, the dose of Vasopressin in Sodium Chloride Injection may need to be increased [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)*].

Maternal adverse reactions: Vasopressin in Sodium Chloride Injection may produce tonic uterine contractions that could threaten the continuation of pregnancy.

8.2 Lactation

There are no data on the presence of Vasopressin in Sodium Chloride Injection in either human or animal milk, the effects on the breastfed infant, or the effects on milk production.

8.4 Pediatric Use

Safety and effectiveness of Vasopressin in Sodium Chloride Injection 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 (12.3)*].

10 OVERDOSAGE

Overdosage with Vasopressin in Sodium Chloride Injection 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.

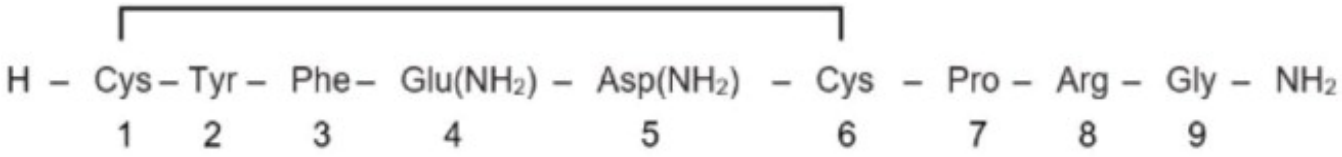
Direct effects will resolve within minutes of withdrawal of treatment.

11 DESCRIPTION

Vasopressin is a polypeptide hormone. Vasopressin in Sodium Chloride Injection is a sterile, aqueous solution of synthetic arginine vasopressin for intravenous administration.

Each mL of the 0.2 unit/mL strength contains 0.2 units vasopressin, 0.0672 mg aspartic acid, 0.0180 mg boric acid, 0.05 mg chlorobutanol, 9 mg sodium chloride and Water for Injection, USP. Each mL of the 0.4 unit/mL strength contains 0.4 units vasopressin, 0.0672 mg aspartic acid, 0.0180 mg boric acid, 0.10 mg chlorobutanol, 9 mg sodium chloride and Water for Injection, USP. Each mL of the 1 unit/mL strength contains 1 unit vasopressin, 0.0672 mg aspartic acid, 0.0180 mg boric acid, 0.25 mg chlorobutanol, 9 mg sodium chloride and Water for Injection, USP.

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: $C_{46}H_{65}N_{15}O_{12}S_2$ Molecular Weight: 1084.23

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Vasopressin causes vasoconstriction by binding to V_1 receptors on vascular smooth muscle coupled to the Gq/11-phospholipase C-phosphatidyl-inositol-triphosphate pathway, resulting in the release of intracellular calcium. In addition, vasopressin stimulates antidiuresis via stimulation of V_2 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 V_1-receptors and release of prolactin and ACTH via V_3 receptors. At lower concentrations typical for the antidiuretic hormone

vasopressin inhibits water diuresis via renal V_2 receptors. In addition, vasopressin has been demonstrated to cause vasodilation in numerous vascular beds that are mediated by V_2, V_3, oxytocin and purinergic P2 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. The pressor effect reaches its peak 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

Vasopressin plasma concentrations increase linearly with increasing infusion rates from 10 micro-units/kg/min to 200 micro-units /kg/min. Steady state plasma concentrations are achieved after 30 minutes of continuous intravenous infusion.

Distribution

Vasopressin does not appear to bind plasma protein. The volume of distribution is 140 mL/kg.

Elimination

At infusion rates used in vasodilatory shock (0.01 units/minute to 0.1 units/minute), the clearance of vasopressin is 9 to 25 mL/min/kg in patients with vasodilatory shock. The apparent $t_{1/2}$ of vasopressin at these levels is ≤10 minutes.

Metabolism

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.

Excretion

Vasopressin is predominantly metabolized and only about 6% of the dose is excreted unchanged into urine.

Specific 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 preconception baseline within two weeks.

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 (7.2)*].

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

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

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 HANDLING

Vasopressin in Sodium Chloride Injection is a clear, colorless solution for intravenous administration available as:

NDC 81298-8552-3: A carton of 10 single dose vials. Each vial contains vasopressin 20 units/100 mL (0.2 units/mL).

NDC 81298-8554-3: A carton of 10 single dose vials. Each vial contains vasopressin 40 units/100 mL (0.4 units/mL).

NDC 81298-8550-3: A carton of 10 single dose vials. Each vial contains vasopressin 50 units/50 mL (1 unit/mL).

Store unopened vials refrigerated at 2°C to 8°C (36°F to 46°F). Do not freeze. Keep vials in original carton to protect from light.

Vials may be held up to three (3) 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 three (3) months 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 Vasopressin in Sodium Chloride Injection beyond the manufacturer's expiration date stamped on the vial.

Manufactured for:
Long Grove Pharmaceuticals, LLC
Rosemont, IL 60018

Made in India

Principal Display Panel – 20 Units per 100 mL Carton Label

Vasopressin
in 0.9% Sodium Chloride Injection

20 Units per 100 mL (0.2 units per mL)

For intravenous infusion

Ready to use
10 x 100 mL Single-Dose Vials
Discard Unused Portion

NDC 81298-8552-3

Rx only

Recommended Dosage: See Prescribing Information.

LONG GROVE™
PHARMACEUTICALS

Principal Display Panel – 40 Units per 100 mL Carton Label

Vasopressin
in 0.9% Sodium Chloride Injection

40 Units per 100 mL (0.4 units per mL)

For intravenous infusion

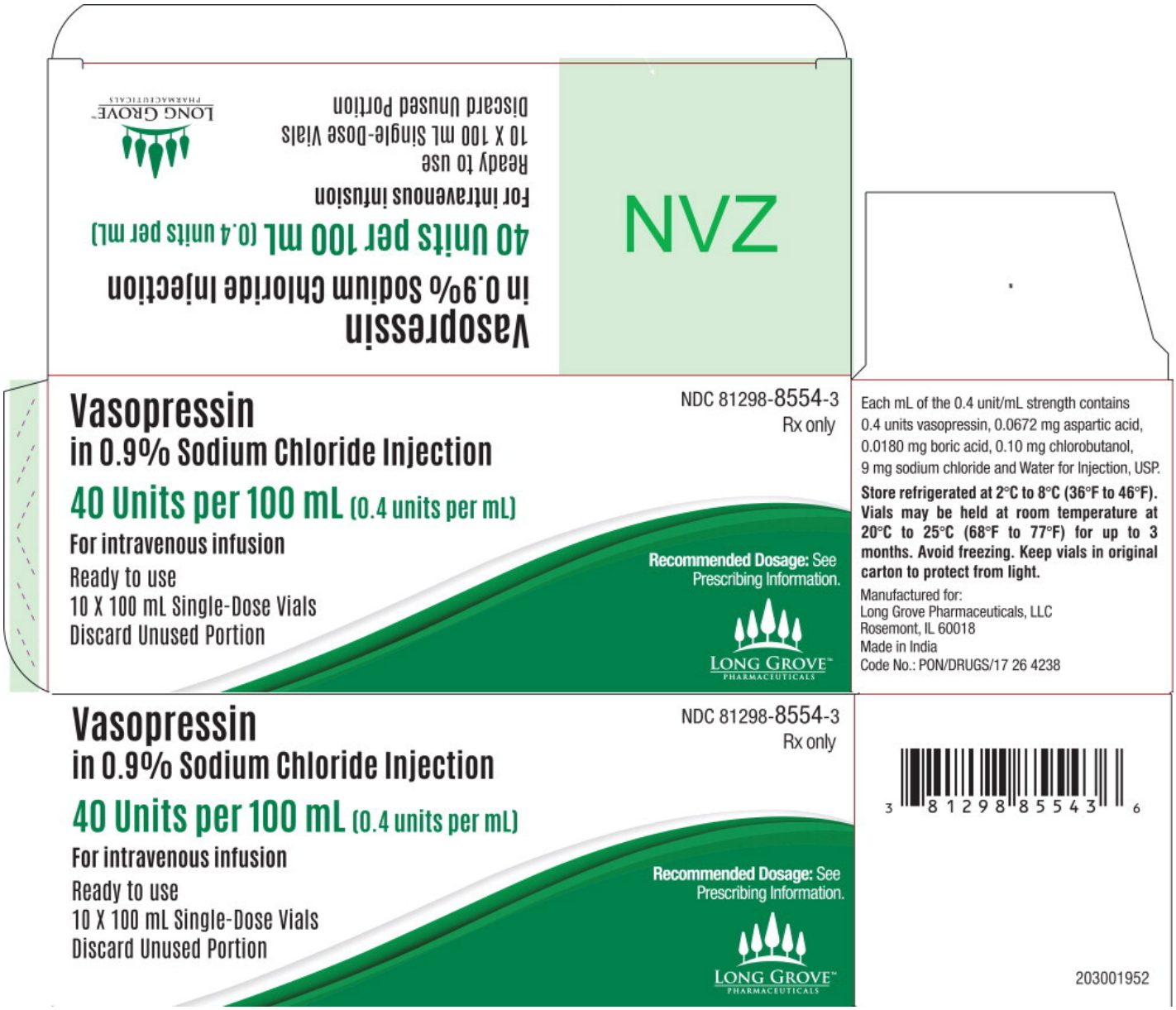
Ready to use
10 x 100 mL Single-Dose Vials
Discard Unused Portion

NDC 81298-8554-3

Rx only

Recommended Dosage: See Prescribing Information.

LONG GROVE™
PHARMACEUTICALS



Principal Display Panel – 50 Units per 50 mL Carton Label

Vasopressin
in 0.9% Sodium Chloride Injection

50 Units per 50 mL (1 units per mL)

For intravenous infusion

Ready to use
10 x 50 mL Single-Dose Vials
Discard Unused Portion

NDC 81298-8550-3

Rx only

Recommended Dosage: See Prescribing Information.

LONG GROVE™
PHARMACEUTICALS

Vasopressin
in 0.9% Sodium Chloride Injection
50 Units per 50 mL (1 unit per mL)
For intravenous infusion

Ready to use
10 X 50 mL Single-Dose Vials
Discard Unused Portion

NDC 81298-8550-3
Rx only

Recommended Dosage: See prescribing information.

LONG GROVE PHARMACEUTICALS

Each mL of the 1 unit/mL strength contains 1 unit vasopressin, 0.0672 mg aspartic acid, 0.0180 mg boric acid, 0.25 mg chlorobutanol, 9 mg sodium chloride and Water for Injection, USP.

Store refrigerated at 2°C to 8°C (36°F to 46°F). Vials may be held at 20°C to 25°C (68°F to 77°F) for up to 3 months. Avoid freezing. Keep vials in original carton to protect from light.

Manufactured for:
Long Grove Pharmaceuticals, LLC
Rosemont, IL 60018
Made in India
Code No.: PON/DRUGS/082 22 288

Vasopressin
in 0.9% Sodium Chloride Injection
50 Units per 50 mL (1 unit per mL)
For intravenous infusion

Ready to use
10 X 50 mL Single-Dose Vials
Discard Unused Portion

NDC 81298-8550-3
Rx only

Recommended Dosage: See prescribing information.

LONG GROVE PHARMACEUTICALS

3 81298 85503 0

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NVZ

VASOPRESSIN IN 0.9% SODIUM CHLORIDE

vasopressin solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:81298-8552
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
VASOPRESSIN (UNII: Y4907O6MFD) (VASOPRESSIN - UNII:Y4907O6MFD)	VASOPRESSIN	0.2 [USP'U] in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
CHLOROBUTANOL (UNII: HM4YQM8WRC)	0.05 mg in 1 mL
ASPARTIC ACID (UNII: 30KYC7MIAI)	0.0672 mg in 1 mL
BORIC ACID (UNII: R57ZHV85D4)	0.0180 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	9 mg in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:81298-8552-3	10 in 1 CARTON	07/12/2024	
1	NDC:81298-8552-1	100 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA217766	07/12/2024	

VASOPRESSIN IN 0.9% SODIUM CHLORIDE

vasopressin solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:81298-8554
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
VASOPRESSIN (UNII: Y4907O6MFD) (VASOPRESSIN - UNII:Y4907O6MFD)	VASOPRESSIN	0.4 [USP'U] in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
CHLOROBUTANOL (UNII: HM4YQM8WRC)	0.10 mg in 1 mL
ASPARTIC ACID (UNII: 30KYC7MIAI)	0.0672 mg in 1 mL
BORIC ACID (UNII: R57ZHV85D4)	0.0180 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	9 mg in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:81298-8554-3	10 in 1 CARTON	07/12/2024	
1	NDC:81298-8554-1	100 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA217766	07/12/2024	

VASOPRESSIN IN 0.9% SODIUM CHLORIDE

vasopressin solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:81298-8550
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
VASOPRESSIN (UNII: Y4907O6MFD) (VASOPRESSIN - UNII:Y4907O6MFD)	VASOPRESSIN	1.0 [USP'U] in 1 mL

Inactive Ingredients

Ingredient Name	Strength
CHLOROBUTANOL (UNII: HM4YQM8WRC)	0.25 mg in 1 mL
ASPARTIC ACID (UNII: 30KYC7MIAI)	0.0672 mg in 1 mL
BORIC ACID (UNII: R57ZHV85D4)	0.0180 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	9 mg in 1 mL
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:81298-8550-3	10 in 1 CARTON	07/12/2024	07/12/2024
1	NDC:81298-8550-1	50 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA217766	07/12/2024	07/12/2024

Labeler - Long Grove Pharmaceuticals, LLC (081134465)

Revised: 6/2025 Long Grove Pharmaceuticals, LLC