Vasostrict (vasopressin injection) for intravenous use

Initial U.S. Approval: 2014

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Vasostrict™

Vasopressin Injection, USP

For Intravenous Use

Vasostrict™ (vasopressin injection) 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. (2.1)

Post-cardiotomy shock: 0.03 to 0.1 unit/minute (2.2)

Septic shock: 0.07 to 0.2 units/minute (2.2)

Dosage Forms and Strengths

Injection: 20 units per mL; packaged as 1 mL per vial (3)

Contraindications

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

Warnings and Precautions

Can worsen cardiac function. (5.1)

Adverse Reactions

The most common adverse reactions include decreased cardiac output, bradycardia, tachyarrhythmias, hypotension and ischemia (coronary, mesenteric, skin, digital). (8)

To report Suspected Adverse Reactions, contact Par Pharmaceutical, Inc. at 1-800-828-9393 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Table 1 Preparation of Diluted Solutions

<table>
<thead>
<tr>
<th>Fluid restriction?</th>
<th>Final concentration</th>
<th>Vasostrict</th>
<th>Diluent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>0.1 units/mL</td>
<td>0.5 mL (50 units)</td>
<td>500 mL</td>
</tr>
<tr>
<td>Yes</td>
<td>1 unit/mL</td>
<td>5 mL (100 units)</td>
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Dosage and Administration

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

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

Administration

The goal of treatment is optimization of perfusion to critical organs, but aggressive treatment may 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 unit/minute and for septic shock 0.07 units/minute. After target blood pressure has been maintained for 6 hours without the use of catecholamines, taper Vasostrict by 0.005 units/minute every hour as tolerated to maintain target blood pressure.

Doseage Forms and Strengths

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Warnings and Precautions

1. Worsening Cardiac Function

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

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: Dialysis disequilibrium

Metabolic: Hypokalemia

Skin: Ichthyosis

Drug Interactions

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

Indomethacin

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

Ganglionic Blocking Agents

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

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.

Full Prescribing Information

4 Contraindications

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13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
No formal carcinogenicity or fertility studies with vasopressin have been conducted in animals.
13.2 Developmental toxicity
In pregnant woman or can affect reproduction capacity. Animal reproduction studies have not been
performed in animals. It is also not known whether vasopressin crosses the placenta or enters breast milk.
Vasostrict may produce tonic uterine contractions that could threaten the continuation of
pregnancy. If pregnancy does occur, the patient should be monitored closely.
Drug-Drug Interactions
Furosemide increases osmolar clearance 4-fold and urine flow 9-fold when co-administered with
vasopressin to minimize potential exposure to the breastfed infant.

Vasostrict (vasopressin injection, USP) is supplied in vials as follows:
Vasostrict is a registered trademark of Par Pharmaceutical Companies, Inc.

Vasostrict is a synthetic octapeptide that is extensively used in the management of different forms of
critical illness, such as septic shock. It is typically administered as a slow intravenous infusion at a rate of
0.01 to 0.1 units per minute. Vasostrict is a potent vasoconstrictor, competitively binding to the V1
receptors on vascular smooth muscle cells, thereby increasing blood pressure and systemic vascular
resistance. Its use is contraindicated in patients with hypertension, hyperthyroidism, acute asthma, and
non-vasopressin-refractory hypertensive crisis.

In patients with vasodilatory shock vasopressin in therapeutic doses increases systemic vascular
resistance and mean arterial blood pressure and reduces the dose requirements for catecholamines. Vasopressin in
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