INDICATIONS AND USAGE

Vasostriç® is indicated to increase blood pressure in adults with vasodilatory shock (e.g., post-cardiotomy or sepsis) who remain hypotensive despite fluids and catecholamines. [see Clinical Pharmacology (12.3)].

DOSE AND ADMINISTRATION

2.1 Preparation of Diluted Solutions

Dilute Vasostriç 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.

Use in patients with known allergy or hypersensitivity to 8-L-arginine vasopressin or chlorobutanol. (4)

WARNINGS AND PRECAUTIONS

Use with caution in patients with impaired cardiac function. (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, Inc. at 1-800-828-9393 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

REvised: 03/2015

Suggested Table 1 Preparation of diluted solutions

<table>
<thead>
<tr>
<th>Fluid restriction?</th>
<th>Final concentration</th>
<th>Mix</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>0.1 units/mL</td>
<td>500 mL</td>
</tr>
<tr>
<td>Yes</td>
<td>1 unit/mL</td>
<td>5 mL (100 units)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100 mL</td>
</tr>
</tbody>
</table>

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 Vasostriç by 0.005 units/minute every hour as tolerated to maintain target blood pressure.

3 DOSAGE FORMS AND STRENGTHS

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

4 CONTRAINDICATIONS

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

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 Vasostriç on cardiac index and systemic vascular resistance [see Clinical Pharmacology (12.3)].

7.3 Ganglionic Blocking Agents

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

7.4 Furosemide

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

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* Sections or subsections omitted from the full prescribing information are not listed.
12.1 Mechanism of Action
One mg is equivalent to 530 units. V1 receptors are directly coupled to phospholipase C, resulting in release of calcium, leading to doses triggers contractions of smooth muscles in the gastrointestinal tract mediated by muscular.

12.2 Pharmacodynamics
At therapeutic doses exogenous vasopressin elicits a vasocostrictive effect in most vascular beds including the splanchic, 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_{2} receptors. At lower concentrations typical for the antidiuretic hormone vasopressin inhibits water diuresis via renal V_{2} 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.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category C

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-cardiomyopathy 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.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenicity, 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-cardiomyopathy vasodilatory shock.

16 HOW SUPPLIED/STORAGE AND HANDLING
Vasostrict (vasopressin injection, USP) is supplied in vials as follows:

<table>
<thead>
<tr>
<th>1 mL Vial</th>
<th>Until manufacturer expiration date</th>
<th>12 months or until manufacturer expiration date, whichever is earlier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opened (After First Puncture)</td>
<td>48 hours</td>
<td></td>
</tr>
</tbody>
</table>

NDC 42023-164-25 (carton)

Manufactured by: Par Pharmaceutical Companies, Inc.

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