PRESCRIBING INFORMATION

[Pr]Vasopressin Injection, USP

Vasopressin Injection

Sterile Solution

20 USP units / mL

Synthetic

For Intramuscular (IM) or Subcutaneous (SC) Injection

Antidiuretic Agent

Fresenius Kabi Canada Ltd.
165 Galaxy Blvd, Suite 100
Toronto, ON M9W 0C8

Date of Initial Authorization:
OCT 03, 1994

Date of Revision:
MAR 28, 2022

Submission Control Number: 255357

RECENT MAJOR LABEL CHANGES

2 CONTRAINDICATIONS	03/2022
3 SERIOUS WARNINGS AND PRECAUTIONS BOX	03/2022

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Vasopressin Injection, USP (vasopressin) is indicated for prevention and treatment of postoperative abdominal distention, in abdominal roentgenography to dispel interfering gas shadows, and in diabetes insipidus.

1.1 Pediatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use.

2 CONTRAINDICATIONS

Vasopressin Injection, USP is contraindicated in patients having cardiorenal disease with hypertension, advanced arteriosclerosis, coronary thrombosis, angina pectoris, epilepsy or toxemia of pregnancy. Anaphylaxis or hypersensitivity to the drug or its components are also contraindications.

Vasopressin Injection, USP is contraindicated in patients with chronic nephritis with nitrogen retention. See 7 WARNINGS AND PRECAUTIONS.

Vasopressin Injection, USP is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

Vasopressin Injection, USP should not be used in patients with vascular disease, especially disease of the coronary arteries, except with extreme caution. In such patients, even small doses may precipitate anginal pain, and with larger doses, the possibility of myocardial infarction should be considered.

Vasopressin Injection, USP may produce water intoxication. The early signs of drowsiness, listlessness, and headaches should be recognized to prevent terminal coma and convulsions.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

When determining the dose of Vasopressin Injection, USP for a given case, the following should be kept in mind:

It is particularly desirable to give a dose not much larger than is just sufficient to elicit the desired physiologic response. Excessive doses may cause undesirable side actions – blanching of the skin, abdominal cramps, nausea – which, though not serious, may be alarming to the patient. Spontaneous recovery from such side effects occurs in a few minutes. It has been found that one or two glasses of water given at the time the Vasopressin Injection, USP is administered reduces such symptoms.

Parental drug products should be inspected visually for particulate matter and discolouration prior to administration wherever solution and container permit.

4.2 Recommended Dose and Dosage Adjustment

Vasopressin Injection, USP may be administered intramuscularly (IM) or subcutaneously (SC).

Ten units (0.5 mL) of Vasopressin Injection, USP will usually elicit full physiologic response in adult patients; 5 units (0.25 mL) will be adequate in many cases. Vasopressin Injection, USP should be given IM at three or four hour intervals as needed. (For an additional discussion of dosage, consult the sections below).

Abdominal Distention

For the average postoperative adult patient, give 5 units (0.25 mL) initially, and then increase to 10 units (0.5 mL) at subsequent injections, if necessary. It is recommended that vasopressin be given IM and that injections be repeated at three or four hour intervals as required.

Vasopressin used in this manner will frequently prevent, or relieve, postoperative distention.

Abdominal Roentgenography

For the average case, two Vasopressin Injection, USP of 10 units (0.5 mL) each are suggested. The first should be given two hours and the second, one-half hour before films are exposed.

Diabetes Insipidus

The dose by injection is 5 to 10 units (0.25 to 0.5 mL) repeated two or three times daily as needed.

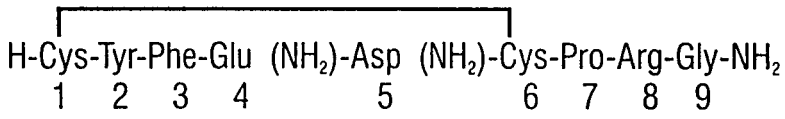
5 OVERDOSAGE

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Vasopressin Injection, USP is a sterile, nonpyrogenic solution of synthetic vasopressin of the posterior pituitary gland. It is substantially free from the oxytocic principle and is standardized to contain 20

pressor units/mL. The chemical name is Vasopressin, 8-L-arginine and has the following structural formula:



$C_{46}H_{65}N_{15}O_{12}S_2$ **1084.23 g/mol**

Each mL contains: 20 USP Vasopressin units; chlorobutanol (anhydrous) 5 mg as preservative; Water for Injection q.s. Glacial acetic acid and/or sodium hydroxide for pH adjustment (2.5 - 4.5).

Vasopressin Injection, USP, 20 USP units/mL, 1 mL in 2 mL (partially filled) flip-top multiple-use vials (USP Type I glass vial, gray bromobutyl stopper and aluminum seal) is available in packages of 25.

The stopper is not made with natural rubber latex.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

Vasopressin Injection, USP should be used cautiously in the presence of migraine, asthma, heart failure or any state in which a rapid addition to extracellular water may produce hazard for an already overburdened system.

Chronic nephritis with nitrogen retention contraindicates the use of Vasopressin Injection, USP until reasonable nitrogen blood levels have been attained.

Regular monitoring of blood urea nitrogen (BUN) levels is required in patients with chronic nephritis to ensure an adequate level is maintained.

8 ADVERSE REACTIONS

8.5 Post-Market Adverse Reactions

Local or systemic allergic reactions may occur in hypersensitive individuals.

The following side effects have been reported following the administration of vasopressin with the following frequency:

Not known – cannot be estimated from the available data

Immune system disorders: hypersensitivity, anaphylaxis.

Metabolism and nutrition disorders: hyperhydration/water intoxication.

Nervous system disorders: headache, vertigo, tremor.

Cardiac disorders: chest pain due to angina, cardiac arrest.

Vascular disorders: peripheral ischaemia, pallor, hypertension.

Respiratory, thoracic and mediastinal disorders: bronchospasm.

Gastrointestinal disorders: flatulence, nausea, vomiting, diarrhoea, abdominal pain.

Skin and subcutaneous tissue disorders: gangrene, hyperhidrosis, urticaria.

Renal and urinary disorders: fluid retention

General disorders and administration site conditions: non-cardiac chest pain.

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 1 - Established or Potential Drug-Drug Interactions

Proper/Common name	Effect	Clinical comment
Alcohol	Alcohol may decrease the antidiuretic effect of vasopressin when given concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Carbamazepine	Carbamazepine may potentiate the antidiuretic effect of vasopressin when used concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Chlorpropamide	Chlorpropamide may potentiate the antidiuretic effect of vasopressin when used concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Clofibrate	Clofibrate may potentiate the antidiuretic effect of vasopressin when used concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Demeclocycline	Demeclocycline may decrease the antidiuretic effect of vasopressin when given concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Fludrocortisone	Fludrocortisone may potentiate the antidiuretic effect of vasopressin when used concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Ganglion blocking agents or drugs causing SIADH	Ganglion blocking agents or drugs causing SIADH may produce a marked increase in sensitivity to the pressor effect of vasopressin.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.

Heparin	Heparin may decrease the antidiuretic effect of vasopressin when given concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Lithium	Lithium may decrease the antidiuretic effect of vasopressin when given concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Noradrenaline	Noradrenaline may decrease the antidiuretic effect of vasopressin when given concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Tricyclic antidepressants	Tricyclic antidepressants may potentiate the antidiuretic effect of vasopressin when used concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.
Urea	Urea may potentiate the antidiuretic effect of vasopressin when used concurrently.	Hemodynamic monitoring is recommended; adjust the dose of vasopressin as needed.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Vasopressin Injection, USP is a synthetic water-soluble pressor principle identical in sequence to arginine vasopressin.

10.2 Pharmacodynamics

Vasopressin exerts its antidiuretic action by increasing reabsorption of water by the renal tubules. Vasopressin can cause contraction of smooth muscle of the gastrointestinal tract and of all parts of the vascular bed, especially the capillaries, small arterioles, and venules with less effect on the smooth musculature of the large veins.

The direct effect on the contractile elements is neither antagonized by adrenergic blocking agents nor prevented by vascular denervation.

10.3 Pharmacokinetics

Absorption

Following subcutaneous or intramuscular administration of vasopressin injection, the duration of antidiuretic activity is variable, but effects are usually maintained for 2-8 hours.

Distribution

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

Metabolism

The majority of the dose of vasopressin is metabolized and rapidly destroyed in the liver and kidneys. Vasopressin has a plasma half-life of about 10 to 20 minutes.

Elimination

Approximately 5% of a subcutaneous dose of vasopressin is excreted unchanged in the urine four hours after dosing.

11 STORAGE, STABILITY AND DISPOSAL

Store at 15 °C and 30 °C. Discard within 14 days after initial use. Do not permit to freeze.

Stability: Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit.

12 SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions for Vasopressin Injection, USP.

This Prescribing Information was prepared by:

Fresenius Kabi Canada Ltd.
165 Galaxy Blvd, Suite 100
Toronto, ON M9W 0C8

Questions or concerns? 1-877-821-7724

Last Revised: MAR 28, 2022