

PRESCRIBING INFORMATION

PENTASPAN* (10% Pentastarch in 0.9% Sodium Chloride Injection) Injection

THERAPEUTIC CLASSIFICATION

Plasma Volume Expander

ACTION AND CLINICAL PHARMACOLOGY

The colloidal properties of pentastarch render it useful as a plasma volume expander. Intravenous infusion of PENTASPAN (pentastarch) results in expansion of the plasma volume in excess of the volume infused. This expansion persists for approximately 18 to 24 hours and is expected to improve the hemodynamic status for 12 to 18 hours.

Pentastarch molecules below 50,000 molecular weight are rapidly eliminated by renal excretion. A single dose of approximately 500 mL of PENTASPAN results in elimination in the urine of approximately 70% of the dose within 24 hours, and approximately 80% of the dose within one week. The remaining percentage of the administered dose is presumed to be eliminated at a slower rate. Although this process is variable, it generally results in an intravascular pentastarch concentration below the level of detection by one week. The hydroxyethyl group is not cleaved, but remains intact and attached to glucose units when excreted.

INDICATIONS AND CLINICAL USE

PENTASPAN (pentastarch) is indicated when plasma volume expansion is desired as an adjunct in the management of shock due to hemorrhage, surgery, sepsis, burns or other trauma. It is not a substitute for red blood cells or coagulation factors in plasma.

CONTRAINDICATIONS

PENTASPAN(pentastarch) is contraindicated in patients with known hypersensitivity to hydroxyethyl starch, or with bleeding disorders, or with congestive heart failure where volume overload is a potential problem. PENTASPAN should not be used in renal disease with oliguria or anuria not related to hypovolemia.

WARNINGS

General

Administration of large volumes of PENTASPAN(pentastarch) will decrease haemoglobin concentration and dilute plasma proteins excessively. Administration should be kept below the

recommended ceiling of 2000 mL in 24 hours (see Dosage and Administration).

As with other plasma volume expanders, large volumes of PENTASPAN will alter the coagulation mechanisms inasmuch as a prolongation of prothrombin, partial thromboplastin and clotting times will occur. The physician should also be alert to the possibility of transient prolongation of bleeding time.

Hypersensitivity has been seen (wheezing, urticaria and hypotension). Anaphylactic/anaphylactoid reactions have been reported with PENTASPAN; a causal relationship has not been established. If hypersensitivity effects occur, discontinue the drug and, if necessary, administer appropriate therapy.

Use in Pregnancy

PENTASPAN has been shown to be embryocidal in New Zealand rabbits and in Swiss mice when given in doses 5 times the human dose. There are no adequate and well-controlled clinical studies using pentastarch in pregnant women. PENTASPAN should not be used during pregnancy unless potential benefits justify the potential risk to the fetus.

Nursing Mothers

It is not known whether pentastarch is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when PENTASPAN is administered to a nursing woman.

Pediatric Use

The safety and effectiveness of PENTASPAN in children have not been established.

PRECAUTIONS

PENTASPAN (pentastarch), like all plasma volume expanders, is not a substitute for red blood cells or coagulation factors in plasma.

The possibility of circulatory overload should be kept in mind.

Caution should be used when the risk of pulmonary edema and/or congestive heart failure is increased. Special care should be exercised in patients who have impaired renal clearance since this is the principal route by which pentastarch is eliminated.

The serum chemistries of sixteen normal volunteers who were given PENTASPAN in doses of 500 to 2000 mL (2x1000mL infusions on separate days) were essentially unchanged from pre- to seven days post-infusion, except for dilutional effects. There were no clinically significant abnormal values except for one creatinine phosphokinase level following an episode of venospasm. However, indirect bilirubin levels of 8.3 mg/L (normal 0 - 7 mg/L) have been reported in 2 out of 20 normal subjects who received multiple infusions of a 6% hetastarch product. Total bilirubin was within normal limits at all times; indirect bilirubin returned to

normal by 96 hours following the final infusion. The significance, if any, of these elevations is not known; however, caution should be observed before administering PENTASPAN to patients with a history of liver disease.

Caution should be exercised when administering PENTASPAN to patients allergic to corn because such patients can also be allergic to PENTASPAN.

Elevated serum amylase levels may be observed temporarily following administration of PENTASPAN although no association with pancreatitis has been demonstrated. A 6% hetastarch injection product has not been shown to increase serum lipase. Similar effects may be expected with PENTASPAN.

ADVERSE REACTIONS

Coagulation disorders or hemorrhage have been reported in association with the use of PENTASPAN(pentastarch) as a plasma volume expander. Headache, diarrhea, nausea, weakness, temporary weight gain, insomnia, fatigue, fever, edema, paresthesia, acne, malaise, shakiness, dizziness, chest pain, chills, nasal congestion, anxiety, and increased heart rate have also been reported in clinical studies involving PENTASPAN.

It is uncertain whether any of these adverse experiences are attributable to the drug, medical procedures, concurrent adjunctive medication, or a combination of these factors.

Hypersensitivity has been seen (wheezing, urticaria and hypotension).

Anaphylactic/anaphylactoid reactions have been reported with PENTASPAN (see WARNINGS).

SYMPTOMS AND TREATMENT OF OVERDOSAGE

The treatment of overdosage of PENTASPAN (pentastarch) would be essentially symptomatic and supportive.

DOSAGE AND ADMINISTRATION

PENTASPAN (pentastarch) is administered by intravenous infusion only. Total dosage and rate of infusion depend upon the amount of blood or plasma lost. In adults, the amount usually administered is 500 to 2000 mL. Total dosage does not usually exceed 2000 mL per day or approximately 28 mL per kg of body weight for the typical 70 kg patient. In acute hemorrhagic shock, an administration rate approaching 20 mL per kg per hour may be used. Use beyond 72 hours has not been studied.

Parenteral drug products should be inspected for particulate matter and discoloration prior to administration whenever solution and container permit.

The solution is intended for intravenous administration using sterile equipment. It is recommended that intravenous administration apparatus be replaced at least once every 24 hours.

PHARMACEUTICAL INFORMATION

Drug Substance

Proper Name: Pentastarch (USAN)

Chemical Name: Low molecular weight, low molar substitution hydroxyethyl starch

Structural Formula:

Amylopectin derivative in which R₂, R₃, and R₆ are H or CH₂CH₂OH, or R₆ is a branching point in the starch polymer connected through a 1-6 linkage to additional α-D-glucopyranosyl units.

Average Molecular Weight: 200,000 - 300,000

Pentastarch is an artificial colloid derived from a waxy starch composed almost entirely of amylopectin. Hydroxyethyl ether groups are introduced into the glucose units of the starch and the resultant material is hydrolyzed to yield a product with a molecular weight suitable for use as a plasma volume expander. Pentastarch is characterized by its molar substitution, and also by its molecular weight.

The degree of substitution is 0.40 - 0.50 which means pentastarch has approximately 45 hydroxyethyl groups for every 100 glucose units. The average molecular weight of pentastarch is 200,000 - 300,000. Hydroxyethyl groups are attached by an ether linkage primarily at C-2 of the glucose unit and to a lesser extent at C-3 and C-6. The polymer resembles glycogen, and the polymerized glucose units are joined primarily by 1-4 linkages with occasional 1-6 branching linkages. The degree of branching is approximately 1:20 which means that there is one 1-6 branch for every 20 glucose polymer units.

Composition

PENTASPAN is supplied sterile and nonpyrogenic in 250 and 500 mL plastic, intravenous infusion bags. The composition of each 100 mL is as follows:

Pentastarch	10.0 g
Sodium Chloride USP	0.9 g
Water for Injection USP	qs
pH adjusted with Sodium Hydroxide	

Approximate Concentration of Electrolytes (mEq/Litre): Sodium 154, Chloride 154

pH: Approx. 5.0

Calculated osmolality: Approx. 326 mOsm/Kg

Stability and Storage

PENTASPAN is supplied sterile and nonpyrogenic in 250 mL and 500 mL plastic, intravenous infusion bags. Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended that the product be stored at room temperature (15-25°C).

PENTASPAN is a clear, pale yellow to amber solution. Exposure to prolonged adverse storage conditions may result in a change to a turbid deep brown or the formation of a crystalline precipitate. Do not use the solution if these conditions are evident.

Special Instructions

Caution - Before administering to patient, review these directions:

Visual Checking

1. Do not remove the plastic infusion container from its overwrap until immediately before use.
2. While the overwrap is intact, identify the solution (PENTASPAN), lot number and expiration date.
3. Check that the solution is clear.
4. Inspect the intact unit for signs of obvious damage. If present, the unit should not be used.

Removal of Overwrap

A peelable area is located in the lower right hand corner of the unit (the label facing upward and the port facing downward). Pull apart the two edges. You can also tear at any notch located at either end of the unit. After removing overwrap, check for minute leaks by squeezing container firmly. If leaks are found, discard unit as sterility may be impaired.

Preparation for Administration (Use aseptic technique)

1. Close flow control clamp of administration set.
2. Twist off plug from port designated "Infusion Set Port".
3. Insert spike of infusion set into port with a twisting motion until the set is firmly sealed.
4. Suspend container from hanger.
5. Follow manufacturer's recommended procedures for the administration set.
6. Discontinue administration and notify physician immediately if patient exhibits signs of adverse reactions.

DOSAGE FORMS

Availability

PENTASPAN (pentastarch) is supplied sterile and nonpyrogenic in 250 mL and 500 mL plastic, intravenous infusion bags.

A complete Product Monograph is available upon request

Bristol-Myers Squibb Canada
Montreal, Canada

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