



For the use of a registered medical Practitioner or Hospital or Laboratory only



Hydroxyethyl Starch 130/0.4

PVHES

6% w/v Solution for Injection for I.V. Infusion
Blood Substitute and Plasma Protein Fraction

WARNING:

- Do not use HES solutions in critically ill adult patients including those with sepsis, and those admitted to the ICU as it increases the risk of Mortality
- Avoid use in patients with pre-existing renal dysfunction.
- Discontinue use of HES at the first sign of renal injury.
- Need for renal replacement therapy has been reported up to 90 days after HES administration. Continue to monitor renal function for at least 90 days in all patients.
- Avoid use in patients undergoing open heart surgery in association with cardiopulmonary bypass due to excess bleeding.
- Discontinue use of HES at the first sign of coagulopathy.

DESCRIPTION:

6% hydroxyethyl starch 130/0.4 in 0.9% sodium chloride injection is a clear to slightly opalescent, colorless to slightly yellow, sterile, non-pyrogenic, isotonic solution for intravenous administration using sterile equipment, the final solution pH is 4.0 to 5.5.

The hydroxyethyl starch is a synthetic colloid for use in plasma volume replacement. The chemical name of hydroxyethyl starch is poly(O-2-hydroxyethyl) starch.

COMPOSITION:

Each 100ml contains:	
Hydroxyethyl Starch (130/0.4)	6.0 gms
Sodium Chloride BP	0.9 gms
Water for Injections BP	q. s.
Average Molecular Weight	130,000 Dalton
Degree of substitution	0.38-0.45
mOsmol/L	308
mEq/L	Na ⁺ 154 Cl ⁻ 154

CLINICAL PHARMACOLOGY:

Mechanism of Action : need to be added as per following

Hydroxyethyl starch in a colloidal solution which expands plasma volume when administered intravenously. This effect depends on the mean molecular weight (130,000 daltons; range 110,000 – 150,000 daltons), the molar substitution by hydroxyethyl groups (0.4; range 0.38 – 0.45) on glucose units of the starch, the pattern of hydroxyethyl substitution (C2/C6 ratio) of approximately 9:1, and the concentration (6%), as well as the dosage and infusion rate.

Hydroxyethyl starch is a derivative of thin boiling waxy corn starch, which mainly consists of a glucose polymer (amylopectin) predominantly composed of α-1-4-connected glucose units with several α-1-6-branches. Substitution of hydroxyethyl groups on the glucose units of the polymer reduces the normal degradation of amylopectin by α-amylase in the body. The low molar substitution (0.4) is the main pharmacological determinant for the beneficial effects of Hydroxyethyl starch on pharmacokinetics, intravascular volume and hemodilution. To describe the molecular weight and molar substitution characteristics of the hydroxyethyl starch, the compound is designated as hydroxyethyl starch 130/0.4.

PHARMACODYNAMICS:

After isovolemic exchange of blood with 500 ml of Hydroxyethyl starch in healthy volunteers, blood volume is maintained for at least 6 hours.

PHARMACOKINETICS:

The pharmacokinetic profile of hydroxyethyl starch is complex and largely dependent on its molar substitution as well as its molecular weight. When administered intravenously, molecules smaller than the renal threshold (60,000-70,000 daltons) are readily and rapidly excreted in the urine, while molecules with higher molecular weights are metabolized by plasma α-amylase prior to excretion via the renal route. The mean in vivo molecular weight of hydroxyethyl starch in plasma is 70,000 – 80,000 daltons immediately following infusion and remains above the renal threshold throughout the treatment period.

Following intravenous administration of 500 mL hydroxyethyl starch to healthy volunteers, plasma levels of hydroxyethyl starch remain at 75% of peak concentration at 30 minutes post-infusion and decrease to 14% at 6 hours post-infusion. Plasma levels of hydroxyethyl starch return to baseline levels 24 hours following infusion. Plasma clearance, volume of distribution, and elimination half-life of hydroxyethyl starch in healthy volunteers following IV administration of 500 mL is 31.4 mL/min, 5.9 liters, and 12 hours, respectively. Approximately 62 % of hydroxyethyl starch is excreted in urine within 72 hours.

The pharmacokinetics of hydroxyethyl starch are similar following single and multiple dose administration. No significant plasma accumulation occurred after daily administration of 500 mL of a 10% solution containing hydroxyethyl starch 130/0.4 over a period of 10 days.

THERAPEUTIC INDICATIONS:

6% hydroxyethyl starch 130/0.4 in 0.9% sodium chloride injection is indicated for the treatment and prophylaxis of hypovolemia in adults and children. It is not a substitute for red blood cells or coagulation factors in plasma.

DOSAGE AND ADMINISTRATION:

hydroxyethyl starch is administered by intravenous infusion only. The daily dose and rate of infusion depend on the patient's blood loss, on the maintenance or restoration of hemodynamics and on the hemodilution (dilution effect). hydroxyethyl starch can be administered repetitively over several days.

The initial 10 to 20 mL should be infused slowly, keeping the patient under close observation due to possible anaphylactoid reactions.

Adult Dose: Up to 50 mL of hydroxyethyl starch per kg of body weight per day. This dose is equivalent to 3500 mL of hydroxyethyl starch for a 70 kg patient.

Pediatric Dose: The safety and efficacy have not been established in the age group of 2 to 12 years

PREPARATION FOR ADMINISTRATION (USE ASEPTIC TECHNIQUE):

- Close flow control clamp of administration set.
- Insert spike of infusion set into infusion port.
- Suspend container from hanger.
- Follow manufacture's recommended procedures for the administration.
- Discontinue administration and notify physician immediately if patient exhibits signs of adverse reactions.
- If leaks are found, discard unit as sterility may be impaired

CONTRAINDICATIONS:

Do not use hydroxyethyl starch (HES) in critically ill adult patients, including patients with sepsis, due to increased risk of mortality and renal replacement therapy.

- Do not use HES in patients with severe liver disease.
- Do not use HES in patients with known hypersensitivity to hydroxyethyl starch
- Do not use HES in clinical conditions with volume overload.

- Do not use HES in patients with pre-existing coagulation or bleeding disorders.
- Do not use HES in patients with renal failure with oliguria or anuria not related to hypovolemia.
- Do not use HES in patients receiving dialysis treatment.
- Do not use HES in patients with severe hyponatremia or severe hyperchloremia.
- Do not use HES in patients with intracranial bleeding.

WARNING & PRECAUTIONS:

Anaphylactoid reactions (mild influenza-like symptoms, bradycardia, tachycardia, bronchospasm, non-cardiac pulmonary edema) occur with solutions containing hydroxyethyl starch. If a hypersensitivity reaction occurs, administration of the drug should be discontinued immediately and the appropriate treatment and supportive measures should be undertaken until symptoms have resolved.

Fluid Equilibrium: Avoid fluid overload; adjust dosage in patients with cardiac or renal dysfunction

Fluid status and rate of infusion should be assessed regularly during treatment, especially in patients with cardiac insufficiency or severe kidney dysfunction.

In cases of severe dehydration, a crystalloid solution should be given first. Generally, sufficient fluid should be administered in order to avoid dehydration.

Monitoring: Laboratory Tests: Clinical evaluation and periodic laboratory determinations are necessary to monitor fluid balance, serum electrolyte concentrations, kidney function, acid-base balance, and coagulation parameters during prolonged parenteral therapy or whenever the patient's condition warrants such evaluation. Monitor liver function in patients receiving Hydroxyethyl starch

Interference with Laboratory Tests: Elevated serum amylase levels may be observed temporarily following administration of the HES and can interfere with the diagnosis of pancreatitis.

At high dosages, the dilutional effects may result in decreased levels of coagulation factors and other plasma proteins and a decrease in hematocrit.

USE IN SPECIFIC POPULATION:

Pregnancy: There are no adequate and well-controlled studies in pregnant women. Hydroxyethyl starch should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Foods, Drugs, Devices and Cosmetic act prohibits dispensing without prescription

Labor and Delivery: Information on the use of Hydroxyethyl starch during labor or delivery is unknown. Use if clearly needed.

Renal Impairment: Hydroxyethyl starch is mainly excreted by the kidneys, and the risk of adverse reactions may be greater in patients with impaired renal function. Volume status, infusion rate, and urine output should be closely monitored. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection.

Nursing Mothers: It is not known whether this drug is excreted in human milk, because many drugs are excreted in human milk, caution should be exercised when Hydroxyethyl starch is administered to a nursing woman.

Children: Hydroxyethyl starch may be given to premature infants and newborns only after a careful risk/benefit evaluation. The safety and efficacy of Hydroxyethyl starch have not been established in the age group of 2 to 12 years.

Dosage in children should be adapted to individual patient colloid needs, taking into account underlying disease, hemodynamics and hydration status.

Geriatric Use: There is no any differences in safety or effectiveness in responses between the elderly and younger patients

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY:

Long-term studies in animals to evaluate the carcinogenic potential of hydroxyethyl starch have not been performed. No mutagenic effects occur with hydroxyethyl starch 130/0.4
Fertility studies on directly exposed animals have not been performed.

ADVERSE REACTIONS:

Anaphylactoid/hypersensitivity reactions (mild influenza-like symptoms, bradycardia, tachycardia, bronchospasm, non-cardiac pulmonary edema) can occur. Most common adverse reactions (incidence >1%) are pruritus, elevated serum amylase haemodilution (resulting in dilution of blood components, e.g., coagulation factors and other plasma proteins, and in a decrease in Hematocrit)

Anaphylactoid reactions occur rarely in <0.1% after administration of hydroxyethyl starch solutions. Disturbances of blood coagulation beyond dilution effects can occur rarely in <0.1% depending on the dosage with the administration of hydroxyethyl starch solutions

CAUTION:

Foods, Drugs, Devices and Cosmetic Act Prohibits dispensing without prescription

DRUG INTERACTIONS:

No interactions with other drugs or nutritional products are known.

The safety and compatibility of additives have not been established.

OVERDOSE:

As with all plasma volume substitutes, overdosage can lead to overloading of the circulatory system (e.g. pulmonary edema). In this case, the infusion should be stopped immediately and if necessary, a diuretic should be administered.

SPECIAL INSTRUCTIONS:

- Parenteral products should be inspected for particulate matter and discoloration prior to administration whenever solution and container permit.
- Do not administer unless the solution is clear, free from particles and the IV container is undamaged.
- hydroxyethyl starch should be used immediately after insertion of the administration set.
- Do not vent.
- If administered by pressure infusion, air should be withdrawn or expelled from the bag through the medication/administration port prior to infusion.
- Discontinue the infusion if an adverse reaction occurs.
- It is recommended that administration sets be changed at least once every 24 hours.
- For single use only. Discard unused portion.

STORAGE:

Store at temperatures not exceeding 30°C. Do not freeze.

For suspected adverse drug reaction, report to the FDA: www.fda.gov/ph and

pv@biocarelifesciences.com.

PRESENTATION: 500 mL Non - PVC Plastic Bag (Box of 1's)

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Distributed by:



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