

HAES STERIL 6% ; HAES STERIL 10% Solution for Infusion

COMPOSITION:	Haes Steril 6%	Haes Steril 10%
1000 ml solution for infusion contains:		
Medical active ingredients:		
Poly (O-2-hydroxyethyl) starch = (Hydroxyethyl starch: HES) (Degree of molar substitution 0.40 - 0.55) (Average molecular weight: 200,000 Da)	60.00 g	100.00 g
Sodium Chloride (Na ⁺ 154 mmol/l Cl ⁻ 154 mmol/l)	9.00 g (Theoretical osmolarity 309 mosm/l)	9.00 g

List of excipients: Sodium Hydroxide, Hydrochloric Acid, Water for Injections.

Pharmaceutical form: Solution for infusion

Therapeutic indications: Therapy and prophylaxis of hypovolaemia (volume deficiency) and shock (volume replacement therapy) in connection with: • Surgery (haemorrhagic shock) • Trauma (traumatic shock, injuries) • Infections (septic shock) • Burns (burn shock)

Contraindications:

1. Bleeding (haemorrhagic) disorders.
2. Congestive heart failure (cardiac insufficiency).
3. Renal failure with oliguria or anuria not related to hypovolemia.
4. Known hypersensitivity to hydroxyethyl starch.

In the event of fibrinogen deficiency Haes Steril should be administered only in potentially fatal emergencies until such time as blood is on hand for substitution. Although teratogenicity studies have failed to reveal any embryotoxic effects, Haes Steril should not be used during pregnancy.

Nursing mothers: it is not known whether hydroxyethyl starch is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Haes Steril is administered to a nursing woman.

Pediatric use: the safety and effectiveness of Haes Steril in children have not been established.

Side Effects: Haes Steril too can lead to death, life threatening, anaphylactoid reactions, such as have been reported in recent years following colloidal volume substitutes. The clinical picture in such cases may range from mild subjective complaints, via circulatory disturbances, shock and bronchospasm to respiratory and cardiac arrest.

In the event of intolerance reactions, the infusion is to be discontinued immediately and the standard immediate (emergency) measures have to be initiated.

- a) In case of subject complaints (dorsalgia, nausea, etc.), discontinuation of infusion.
- b) In case of allergic skin reactions, administration of antihistamines (H₁ and H₂ antagonists), discontinuation of infusion.
- c) In the event of a rise in heart rate and fall in systolic blood pressure to below 90 mmHg, administration of corticosteroids I.V. (e.g., 100 mg prednisolone), discontinuation of infusion.
- d) In case of difficult of breathing and shock, administration of high dose corticosteroids (e.g., 1 gram prednisolone), Oxygen, adrenaline (drip) and volume replenishment, changing the volume substitute, discontinuation of infusion.
- e) In case of respiratory or cardiac arrest, resuscitating, discontinuation of infusion.
- f) Cardiovascular, circulatory overload and pulmonary oedema.
- g) Other: vomiting, peripheral oedema of the lower extremities, submaxillary and parotid glandular enlargement, mild influenza-like symptoms, headaches and muscle pains.

Hematology: Haes Steril can, in case of rising doses, influence the coagulation mechanism, without triggering clinical hemorrhage. On administration of high doses, however, the physician should take into account the possibility of a prolongation of the bleeding time.

The fall in the haematocrit value and dilution of the plasma proteins should also be noted.

Interactions: If a mixture with other drugs is necessary, hygienic injection, complete mixing and compatibility has to be taken care of. The results of compatibility tests are provided on request.

Precautions: Caution should be used when administering Haes Steril to patients allergic to corn, because such patients can also be allergic to Haes Steril.

Elevated serum amylase levels may be observed temporarily following administration of Haes Steril, although no association with pancreatitis has been demonstrated.

Application and Dosage:

In the light of possible anaphylactoid reaction the initial 10-20 ml Haes Steril are to be infused slowly, keeping the patient under close observation.

Special caution is recommended in the case of patients with disturbed coagulation, heart failure and pulmonary oedema, renal failure and chronic hepatic diseases.

Application as intravenous infusion: The daily dose and rate of infusion are to be determined according to blood loss and haemoconcentration. The therapeutic limit is based on the haemodilution effects. In younger patients without cardiovascular or pulmonary risks a haematocrit value of 30% is regarded as borderline for the use of colloidal volume substitutes.

1) Recommended dosage for the therapy and prophylaxis of volume deficiency and shock (volume substitution therapy) – unless otherwise prescribed – Daily dose up to 20 ml/kg b.w./day (= 1500 ml/75 kg b.w./day = 2.0 g HES/kg b.w./day). Normally 500 to 1000 ml/day.

Rates of infusion:

- a) In haemorrhagic shock up to 20 ml/kg b.w./hour (= 0.33 ml/kg b.w./minute = 1500 ml/75 kg b.w./hour = 25 ml/75 kg b.w./minute).
- b) In septic and burn shock lower rates of infusion.
- c) In children under 10 years of age 15 ml /kg b.w./hour (= 0.25 ml/kg b.w./minute). Do not exceed.

Duration of application: there is no pharmacological or clinical evidence to give cause for concern with regard to a repeated application. The duration and extent of the treatment are to be determined according to the duration and extent of the hypovolaemia.

2) Recommended dosage for haemodilution therapy – unless otherwise prescribed – Daily dose: a) 500 ml/day (medium dose). b) 2 × 500 ml in 8-12 hours (125-83 ml/hour).

If administration is by pressure infusion, all air should be withdrawn or expeller from the bag through the medication prior to infusion. The recommended haemodilution therapy with Haes Steril (is analogous to 10% (6%) Dextran 40) recommended daily over a period of 7-10 days. Whereby administration may be performed hypervolaemic (without blood-letting) or isovolaemic (with blood-letting).

Further details – Description of Haes Steril:

Hydroxyethyl starch is manufactured from amylopectin and is characterized by molecular weight and degree of substitution. The average molecular weight is approximately 200,000 Da, and the degree of substitution is approximately 0.5, i.e., approximately 5 hydroxyethyl groups are present in 10 glucose units of the amylopectin skeleton. The main chain in HES (poly-(O-2-hydroxyethyl) starch) is made up of alpha 1,4-linked glucose units and branched via alpha 1,6 bonds. On its close structural relationship to glycogen a high somatic tolerance and only a low risk of anaphylactoid reactions may be anticipated for Haes Steril. Haes Steril is characterized by the high stability of the solution and does not flocculate in the event of temperature fluctuation.

Effects of Haes Steril: with reference to its colloidal properties Haes Steril is comparable to 10% (6%) Dextran 40 solution. Following the infusion of Haes Steril in normovolaemic test subjects. There is an increase of plasma volume equivalent to approximately 140% of the volume infused. Within 340 minutes the increase in plasma volume drops to 50% of the infused volume. Thus the expansion brings about an improvement in circulation and microcirculation over a period of approximately 4 hours. Haes Steril is degraded continuously by serum amylase and eliminated predominantly via the kidneys. Whereby approximately 70% appears in the urine within 24 hours at which point only 2% can still be detected in the plasma.

Special precautions for storage: Do not store above 25°C.

Nature and contents of container:

Colourless glass bottle with halobutyl rubber closure and aluminium cap: 250ml, 500 ml.

Polyolefine bag (Freeflex®): 250 ml, 500 ml

Polyethylene bottle (Bottlepack): 500 ml.

Instructions for use and handling: Do not use HAES-steril after the expiry date! Use only clear solutions and undamaged containers. Do not use if the solution is cloudy and if the container is damaged. Keep out of reach of children!

Israeli Drug License number: Haes Steril 6% - 100.64.28469.00 ; Haes Steril 10% - 100.73.28386.00

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Importer: Genmedix Ltd., VAT # 51-095136-1, P.O.B. 8500, Netanya 42504

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