NAME OF THE MEDICINAL PRODUCT

Heparin Sodium B. Braun 25 000 IU/5 ml Solution for Injection/Infusion

COMPOSITION

1 ml solution for injection/infusion contains 5 000 IU of heparin sodium (porcine mucosa) according to WHO standard.
1 vial (5 ml) contains 25 000 IU of heparin sodium.

Excipients with known effect:
1 ml of solution for injection/infusion contains 12.5 mg benzyl alcohol.

Excipients: Benzyl alcohol (antimicrobial preservative): 12.5 mg/ml, hydrochloric acid (for pH adjustment), sodium chloride, sodium hydroxide (for pH adjustment), water for injection.

THERAPEUTIC INDICATIONS

Therapy of acute venous and arterial thromboembolism (including early treatment of myocardial infarction and unstable angina pectoris); prophylaxis of thromboembolism; prevention of blood clotting during extracorporeal circulation (e.g. cardiopulmonary bypass, haemodialysis).

CONTRAINDICATIONS

The medicinal product must not be used in the following conditions:
Hypersensitivity to the active substance or to any of the excipients listed, active bleeding, heparin-induced thrombocytopenia of type II either known from the patient's history or being suspected on grounds of clinical observations.

Diseases and organ lesions associated with haemorrhagic diathesis, such as:
Coagulopathies, thrombocytopenia, severe diseases of liver and pancreas.

Diseases where there is a suspicion of vascular damage, e.g.:
Ulcers in the gastro-intestinal tract, uncontrolled and severe arterial hypertension with a diastolic blood pressure higher than 110 mm Hg, intracranial haemorrhage, cerebral arterial aneurysm, retinopathies, bleeding into the vitreum, ophthalmic surgical procedures or injury, active tuberculosis, infectious endocarditis.

Imminent abortion.

Because Heparin Sodium B. Braun contains benzyl alcohol, its use is contraindicated in neonates, especially in immature pre-term neonates.

UNDESIRABLE EFFECTS

The most frequent undesirable effects are bleeding events from any organ or tissue.
Besides this, local reactions at the site of administration may occur.
Heparin-induced thrombocytopenia of type II occurs rarely < 1/1 000) but this adverse reaction may become serious. It is assumed to be a hypersensitivity reaction mediated by specific antibodies. Details see below.

Other undesirable effects may include local or systemic allergic reactions.

Undesirable effects are listed according to their frequencies as follows:

Very common:	(≥ 1/10)
Common:	(≥ 1/100 to < 1/10)
Uncommon:	(≥ 1/1 000 to < 1/100)
Rare:	(≥ 1/10 000 to < 1/1 000)
Very rare:	(< 1/10 000)
Not known:	Frequency cannot be estimated from the available data

All reactions that are derived from post-marketing experience (spontaneous reports and literature) only are based on a patient population which is largely unknown. Therefore exact incidences cannot be provided and are referred to with the frequency ‘not known’.

Blood and lymphatic system disorders
Common: Heparin-induced thrombocytopenia type I.
At the beginning of heparin therapy mild heparin-induced thrombocytopenia type I (platelet count 100 000 – 150 000 per microlitre), without thrombosis. The thrombocytopenia usually occurs within the first 5 days of treatment, and is probably due to a direct effect on platelets.
Not known: Eosinophilia

Nervous system disorders
Not known: Permanent or temporary paralysis due to subarachnoidal or epidural haematomas after neuraxial anaesthesia.

Skin and subcutaneous tissue disorders
Uncommon: Transient alopecia following long-term administration, skin necroses

Musculoskeletal, connective tissue and bone disorders
Not known: Osteoporosis (after long-term administration of heparin)

Endocrine disorders
Rare: Hypoaldosteronism, resulting in hyperkalaemia and metabolic acidosis, especially in patients with impaired kidney function and diabetes mellitus

Vascular disorders
Very common: Haemorrhage. Depending on the dose, increased incidence of bleeding from any organ or tissue

General disorders and administration site conditions
Common: Local tissue reactions at the injection site, such as induration, redness, discolouration, and minor haematomae

Immune system disorders
Uncommon: Allergic reactions of all types and severities, with various manifestations (e.g. urticaria, pruritus, dyspnoea, bronchospasm, hypotension)
Rare: Toxic or allergic reactions to benzyl alcohol. Severe heparin-induced, antibody-mediated thrombocytopenia (Heparin-induced thrombocytopenia type II, details see below)
Very rare: Anaphylactic shock especially in sensitized patients having previously received heparin, onset of type II thrombocytopenia with a delay of up to several weeks after the end of heparin administration
Not known: Type IV hypersensitivity reaction (e. g. erythematous papules and plaques located at injection site) which may occur with a latency of up to several months

Hepatobiliary disorders
Very common: Hepatic enzymes increased (increases of the serum concentrations of transaminases (AST, ALT), gamma-glutamyl transpeptidase, lactate dehydrogenase and lipase, possible resulting in increased free fatty acids). These reactions are, however, reversible

Reproductive system and breast disorders
Very rare: Priapism

Information on particular undesirable effects
Heparin induced thrombocytopenia type II
Severe heparin-induced, antibody-mediated thrombocytopenia (type II thrombocytopenia, HIT II), is characterised by platelet counts markedly below 100 000 per microlitre or a rapid decrease to less than 50 per cent of the initial value and accompanied by arterial or venous thromboses or embolism, consumption coagulopathy, skin necroses at the site of injection. The anticoagulatory effect of heparin may be reduced.

In patients without pre-existing hypersensitivity to heparin the decrease of the platelet count typically begins between 5 to 14 days after commencement of the heparin therapy. In patients with existing antibodies to heparin such decrease may begin already after a few hours. The greater the degree of trauma and thus the release of PF4, the more likely patients went on to develop HIT antibodies and clinical HIT.

As soon as type II thrombocytopenia occurs, heparin administration must be discontinued immediately.

Emergency treatment depends on the nature and severity of the symptoms. Re-exposure of the patient to parenteral heparin is absolutely contraindicated.

Patients undergoing extracorporeal circulation
Principally the same ADRs that occur in other patients might occur. Haemodialysis patients might be at an increased risk for developing anaphylactic or anaphylactoid reactions.

WARNINGS

Keep out of sight and reach of children. Do not administer if solution appears impaired, that is opacity, precipitate, discoloration, or when the container is damaged.

NOTE
Prescription only
Not all products are registered and approved for sale in all countries or regions. Indications of use may also vary by country and region. Please contact your country representative for product availability and information.

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