

Summary of Product Characteristics

Heparin Sodium Injection IP

HEPARIN[®]
25000 IU INJECTION

Composition :

Each ml contains :

Heparin Sodium IP 5000 IU

(Derived from Porcine Intestinal Mucosa)

Benzyl Alcohol IP 0.95% w/v

Water for Injections IP q.s.

1. **Name of medicinal product** Active ingredient: Heparin Sodium

Heparin Sodium

Prescription status

Prescription only medicine

3. Qualitative and quantitative composition

3.1 Pharmacotherapeutic group

Anticoagulant

3.2. Active ingredients by class and quantity

3.2.1 Medically active ingredients:

1 ml solution for injection contains 5,000 (I.U.) Heparin Sodium (from porcine intestinal mucosa).

Activity: min 150 IU/ml mg, max 200 IU/ml mg \pm 25.0 - 33.3 mg

3.2.2 Other active ingredients:

1 ml solution for injection contains 10 mg benzyl alcohol

3.3 Other ingredients:

Sodium Chloride, Water for Injections

4. Indications

Treatment of thrombo-embolic disorders as deep vein thrombosis, acute arterial embolism or thrombosis, thrombophlebitis, pulmonary embolism, fat embolism.

Prophylaxis of deep vein thrombosis and thromboembolic events.

5. Contraindications

Absolute contraindications

Heparin allergy or hypersensitivity to other components of the preparation HEPARIN INJECTION IP 5,000 UNITS/ML.

Patients with present or previous thrombotic phenomena (Type II) caused by heparin.

Diseases accompanied by increased bleeding tendency (e.g. haemorrhagic diathesis, clotting factor deficiencies (except disseminated intravascular coagulation during the phase of hypercoagulation)) severe hepatic, renal or pancreatic diseases, severe thrombocytopenia.

Diseases with a suspicion of damage to the vascular system, such as: gastric ulcers and/or intestinal ulcers, hypertension above 150 mmHg diastolic, intra-cerebral hemorrhage, injury or surgery of the central nervous system, eye surgeries, retinopathy (severe retina problems), intrauterine hemorrhage, aneurysm of cerebral arteries, sub-acute bacterial endocarditis (inflammation of the endocardium).

Risk of miscarriage (Abortus imminens).

Spinal anaesthesia, epidural anaesthesia, lumbar puncture.

Relative contraindications

Suspicion of a malignant disease with tendency to hemorrhages

Renal and urethral calculi

Chronic alcoholism

An especially meticulous medical monitoring is required:

During pregnancy, especially in case of long term use

in elderly patients, especially women

When concomitantly treated with fibrinolytics or oral anticoagulants, with platelet aggregation inhibitors (for example Acetylsalicylic Acid, Ticlopidin, Clopidogrel) and/or glycoprotein IIb/IIIa receptor antagonists.

When concomitantly treated with drugs that increase serum potassium level. The serum potassium level should be monitored in high-risk patients (patients with increased risk of hyperkalemia such as diabetes mellitus, impaired renal function or treatment with serum-potassium level raising medication).

Warnings:

Because of its benzyl alcohol content HEPARIN INJECTION IP 5,000 UNITS/ML must not be used in neonates, especially not in those showing signs of immaturity.

Use in pregnancy and lactation

Heparin does not cross the placenta and does not appear in breast milk. Up to date, no incidence of fetal malformations caused by heparin use in pregnancy has been reported. Increased risk of abortions and stillbirths has been reported. Complications in pregnant women caused by treatment or by the disease itself cannot be excluded.

The use of epidural anaesthesia during labour, for women being medically treated or anti-coagulated, is absolutely contraindicated.

6. Side effects

Depending on the dose of HEPARIN INJECTION IP 5,000 UNITS/ML, increased hemorrhages especially cutaneous hemorrhages, hemorrhage of the mucous membranes, wounds, in the area of the gastrointestinal tract, the urinary tract and the genitourinary tract should be taken into consideration.

Occasionally at the beginning of the treatment, a slight temporary decrease of the thrombocyte count (Thrombocytopenia Type I) with values between 100,000 and 150,000/ μ l (caused by a temporary activation of the thrombocytes) can be observed. Complications usually do not occur. The treatment is therefore to be continued.

Thrombocytopenia has been reported to occur in patients receiving heparin with a reported incidence of 0 to 30%. Platelet counts should be obtained at baseline and periodically during heparin administration. Mild thrombocytopenia (count greater than 100,000/mm³) may remain stable or reverse even if heparin is continued. If the count falls below 100,000/mm³ or if recurrent thrombosis develops (see Heparin-induced Thrombocytopenia and Heparin-induced Thrombocytopenia and Thrombosis), the heparin product should be discontinued and, if necessary, an alternative anticoagulant administered.

The patient must be informed that he must not be treated with drugs containing heparin in the future. Guidelines for use of platelet values: see section 14.

Type II Heparin-induced Thrombocytopenia (HIT) and Type II HIT and Thrombosis can occur hours to days after the discontinuation of heparin therapy. Patients presenting with thrombocytopenia or thrombosis after discontinuation of heparin should be evaluated for Type II HIT and Type II HIT and Thrombosis.

2. **Most important incompatibilities**

Physical and chemical incompatibilities Heparin may not be administered down with other medication in a hypodermic syringe or an infusion.

10. Single and daily dosage

Heparin must be dosed individually!

The dose depends on the coagulation parameters, nature and course of the disease, the patient's response, side effects, body weight and age. Different heparin sensitivity and the possible development of heparin tolerance during the course of treatment must be taken into account.

1. **Thrombo-embolism prophylaxis (low-dose treatment)**

For the prophylaxis of thrombo-embolism subcutaneous injection is recommended.

Pre- and postoperative thrombo-embolism prophylaxis:

Preoperative: 5,000 7,500 I.U. subcutaneous approximately 2 hours before the operation.

Postoperative: depending on the risk of thrombosis, usually 5,000 I.U. s.c. every 8-12 hours for 7,500 I.U. every 12 hours until either the patient is ambulatory or until sufficient Vitamin K antagonist. Laboratory diagnostic controls (coagulation times) for the dosage adjustment might be required in individual cases.

2. **Interaction with other medicinal products**

Substances that can influence plasma blood coagulation or the cells involved in this process may cause a tendency toward increased bleeding. (Such substances are, for example, acetyl salicylic acid, Ticlopidin, Clopidogrel, glycoprotein IIb/IIIa receptor antagonists, coumarine derivatives, fibrinolytics, glypiridam, sulfonamides, high dose penicillin therapy). An enhanced heparin effect in concomitant administration of non steroidal anti-inflammatory drugs (such as Phenbutazone, Indomethacin, Dexamethasone, Flunoxazone) is possible.

When alkaline medications such as tricyclic psychotropics, antihistamines and quinine are concomitantly administered, salt formation with heparin can cause loss of efficacy of both drugs.

An intravenous infusion of nitroglycerine might cause a reduction of the effectiveness of Heparin A removal of nitroglycerine might cause a rapid increase of aPTT. Close controls of PTT together with a dosage adjustment of heparin are necessary with the simultaneous infusion of nitroglycerine. An increased effect of other drugs, e.g. Propofolol, can occur through plasma protein binding displacement.

Medication increasing serum potassium levels can only be used under especially close medical monitoring together with HEPARIN INJECTION IP 5,000 UNITS/ML.

In addition, heparin shows numerous interactions with other preparations, whose clinical significance is being evaluated differently.

3. Warnings

With infants, children and patients with kidney and/or liver insufficiency a meticulous monitoring and special care is required. The same applies also for thrombo-embolism prophylaxis ("low dose" treatment).

During treatment with HEPARIN INJECTION IP 5,000 UNITS/ML intra-muscular injections are to be avoided due to risk of hematomas.

Patients treated with HEPARIN INJECTION IP 5,000 UNITS/ML (over 22,500 I.U./dose) should avoid all and any risk of being injured.

Heparin induced thrombocytopenia:

Thrombocytopenia has been reported to occur in patients receiving heparin with a reported incidence of 0 to 30%. Platelet counts should be obtained at baseline and periodically during heparin administration. Mild thrombocytopenia (count greater than 100,000/mm³) may remain stable or reverse even if heparin is continued. However, thrombocytopenia of any degree should be monitored closely, if the count falls below 100,000/mm³ or if recurrent thrombosis develops (see Heparin-induced Thrombocytopenia and Heparin-induced Thrombocytopenia and Thrombosis), the heparin product should be discontinued and, if necessary, an alternative anticoagulant administered.

Type II Heparin-induced Thrombocytopenia (HIT) is a serious antibody-mediated reaction resulting from irreversible aggregation of platelets. Type II HIT may progress to the development of venous and arterial thromboses; a condition referred to as Heparin-induced Thrombocytopenia and Thrombosis (HITT). Thrombotic events may also be the initial presentation for HITT. These serious thromboembolic events include stroke, myocardial infarction, pulmonary embolism, cerebral venous thrombosis, limb ischemia, deep vein thrombosis, pulmonary embolism, mesenteric thrombosis, renal arterial thrombosis, skin necrosis, gangrene of the extremities that may lead to amputation, and possibly death. Thrombocytopenia of any degree should be monitored closely. If the platelet count falls below 100,000/ μ l or if recurrent thrombosis develops, the heparin product should be promptly discontinued and alternative anticoagulants considered if patients require continued anticoagulation.

Type II Heparin-induced Thrombocytopenia (HIT) and Type II HIT and Thrombosis can occur up to several weeks after the discontinuation of heparin therapy. Patients presenting with thrombocytopenia or thrombosis after discontinuation of heparin should be evaluated for Type II HIT and Type II HIT and Thrombosis.

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