innohep®

Anticoagulant

Tinzaparin sodium

Vials of 2 ml
Tinzaparin sodium 10,000 anti-Xa IU/ml, preserved with benzyl alcohol.
Tinzaparin sodium 20,000 anti-Xa IU/ml, preserved with benzyl alcohol, stabilized with sodium bisulphite.

Syringe of 0.25 ml, 0.35 ml or 0.45 ml
Tinzaparin sodium 10,000 anti-Xa IU/ml.

Syringe of 0.5 ml, 0.7 ml or 0.9 ml
Tinzaparin sodium 20,000 anti-Xa IU/ml, stabilized with sodium bisulphite.

Properties
Tinzaparin sodium is a low molecular weight heparin produced by enzymatic depolymerization of conventional heparin.
The molecular mass is between 1,000 and 14,000 dalton, with a peak maximum molecular mass of approx. 4,500 dalton.
Tinzaparin sodium is an anti-thrombotic agent.
innohep® has a bioavailability of about 90% following subcutaneous injection. The absorption half-life is 200 minutes, peak plasma activity being observed after 4–6 hours.
The elimination half-life is about 80 minutes. Tinzaparin sodium is eliminated, primarily with the urine, as unchanged drug.

The pharmacokinetics/pharmacodynamics of **innohep®** are monitored by anti-Xa activity. There is a linear dose-response relationship between plasma activity and the dose administered.

The biological activity of **innohep®** is expressed in anti-Xa international units.

Indications
Treatment of deep-vein thrombosis and pulmonary embolism.

Prevention of postoperative deep-vein thrombosis in patients undergoing general and orthopaedic surgery.

Prevention of clotting in in-dwelling intravenous lines for extracorporeal circulation and haemodialysis.

Dosage
Treatment of DVT and PE:
The recommended dose is 175 anti-Xa IU/kg body-weight s.c. once daily.

Thromboprophylaxis in patients with moderate risk of thrombosis (general surgery):
On the day of operation 3,500 anti-Xa IU s.c. 2 hours before surgery and postoperatively once daily 3,500 anti-Xa IU for 7–10 days.

Thromboprophylaxis in patients with high risk of thrombosis (e.g. total hip replacement):
On the day of operation 4,500 anti-Xa IU s.c. 12 hours before surgery or 50 anti-Xa IU/kg body-weight s.c. 2 hours before surgery and then once daily until the patient has been mobilized.

For short-term haemodialysis (less than 4 hours):
A bolus dose of 2,000–2,500 anti-Xa IU into the arterial side of the dialyser (or intravenously) at the beginning of dialysis.

Long-term haemodialysis (more than 4 hours):
A bolus dose of 2,500 anti-Xa IU into the arterial side of the dialyser (or intravenously) at the beginning of dialysis, followed by an infusion of 750 anti-Xa IU/hour.

Dose adjustment: Increase or decrease of the bolus dose, if required, can be made in steps of 250–500 anti-Xa IU until a satisfactory response is obtained.

Elderly:
Renal function should be assessed with e.g. the Cockcroft-Gault formula to estimate creatinine clearance levels.

No dose reduction is needed in elderly patients with normal renal function. (See **Special precautions**).

Renal impairment:
No dose reduction is needed in patients having creatinine clearance levels down to 20 ml/min. However, precaution is recommended when treating patients with severe renal impairment (creatinine clearance < 30 ml/min). (See **Special precautions**).

Overdose
An overdose of **innohep®** may be complicated by haemorrhage. At recommended doses there should be no need for an antidote, but in the event of accidental administration of an overdose, the effect of **innohep®** can be reversed by intravenous administration of 1% protamine sulphate solution.
The dose of protamine sulphate required per neutralization should be accurately determined by titrating with the plasma of the patient. As a rule, 1 mg of protamine sulphate neutralizes the effect of 100 anti-Xa IU of tinzaparin.

Adverse effects
innohep® is safe with regard to bleeding risks, when applied at the doses recommended, provided that patients with increased bleeding potential (bleeding disorders, severe thrombocytopenia) are excluded or treated with special care.
Priapism and skin necrosis have been reported in only a few cases.

Contraindications
Known hypersensitivity to any of the constituents.
The 20,000 anti-Xa IU/ml formulation of **innohep®** contains sodium bisulphite, which may cause allergic reactions, including anaphylaxis in predisposed patients. In the remaining formulations without sulphite, this risk does not exist.
Other contraindications are generalized or focal haemorrhagic tendency. Uncontrolled severe hypertension. Acute cerebral insults. Septic endocarditis.

Special precautions
innohep® should be given with caution to patients with hepatic insufficiency. Precaution is recommended in the treatment of patients with severe renal impairment (creatinine clearance < 30 ml/min).

Precaution is recommended in the treatment of elderly patients with renal impairment. Renal function should be assessed and in patients with severe renal impairment (creatinine clearance < 30 ml/min), monitoring of anti-factor Xa activity should be considered.
innohep® should not be administered by intramuscular injection due to risk of local haematoma formation.

Patients receiving **innohep®** concurrently with spinal or epidural anaesthesia should be closely monitored for signs or symptoms of neurological injury.

Interactions
Concomitant administration of other drugs affecting haemostasis, e.g. vitamin K antagonists and dextran, may enhance the anticoagulant effect of **innohep®**.

Use during Pregnancy and Lactation
Data on a number (637) of exposed pregnancies indicate no additional risk of tinzaparin on pregnancy or on the health of the foetus / new-born child. No transplacental passage was demonstrated in two (2) clinical studies. Data from sequential pharmacokinetic monitoring in 55 pregnancies suggest that pharmacokinetic properties of tinzaparin do not differ from the non-pregnant state.
Tinzaparin is not recommended for use in pregnant women with prosthetic heart valves.
Caution should be exercised when prescribing tinzaparin to pregnant women.
There are no data available concerning lactation.

For vials only:
Cases of "Gasping Syndrome" have occurred in premature infants when large amounts of benzyl alcohol have been administered (99-404 mg/Kg/day). Despite the low content of benzyl alcohol in the vials (10 mg per ml), as it may cross the placenta the use of **innohep®** formulations containing benzyl alcohol is not recommended during pregnancy.

Incompatibilities
innohep® is compatible with isotonic sodium chloride (9 mg/ml) or isotonic glucose (50 mg/ml). It should not be admixed with other infusion fluids.

Storage condition
Do not store above 30°C.

Shelf life
Vials: 2 years.
Syringes: 3 years.

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