— we help people achieve healthy skin

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Important Product Information Update for Healthcare Professionals (HCP)

Update to the Prescribing Information for innohep® 10,000 IU/ml (tinzaparin sodium) Vial and Syringes

	Product / strength	Product authorisation number	Active substance
10,000 IU/mL Vial (for SC injection)	innohep® 10,000 IU/ml solution for injection	PA 0046/060/002	Tinzaparin sodium
10,000 IU/ml Syringes (for SC injection)	innohep® 2,500 IU in 0.25 ml, solution for injection	PA 0046/060/008	
	innohep® 3,500 IU in 0.35 ml, solution for injection	PA 0046/060/009	
	innohep® 4,500 IU in 0.45 ml, solution for injection	PA 0046/060/007	

Dear Healthcare Professional

LEO Pharma would like to inform you of the following:

The Summary of Product Characteristics (SmPCs) for innohep® 10,000 IU/ml Vial and Syringes have been updated following a European Union (EU) harmonisation work-sharing procedure. This update was as a result of a review by the EU Co-ordination Group for Mutual Recognition and Decentralised Procedures (CMDh) in 2014, when significant differences in section 4.1 (Therapeutic indications) and section 4.2 (Posology and Method of Administration) of the SmPCs across the EU were noted.

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Please note that this communication only highlights the changes to the product information in relation to the EU harmonisation procedure. HCPs should refer to the updated SmPCs and PILs for full prescribing information, which are available at www.hpra.ie and www.medicines.ie.

Summary of significant changes to the SmPCs

Section 4.1, Therapeutic indications

The prophylaxis indication has been amended to:

Prophylaxis of venous thromboembolism in adult patients undergoing surgery, particularly orthopaedic, general or oncological surgery.

Prophylaxis of venous thromboembolism in non-surgical adult patients immobilised due to acute medical illness including: acute heart failure, acute respiratory failure, severe infections, active cancer, as well as exacerbation of rheumatic diseases.

Section 4.2, Posology and Method of Administration

The following wording (in italics) has been amended to the posology for surgical patients:

Prophylaxis of thromboembolic events in adults:
Administration is by subcutaneous injection.

Surgical patients at moderate risk of thromboembolic events:
3,500 anti-Xa IU given SC 2 hours before surgery and then once daily *for as long as the patient is considered to be at risk of VTE.*

Surgical patients at high risk of thromboembolic events e.g. undergoing orthopaedic or cancer surgery:
4,500 anti-Xa IU given SC 12 hours before surgery and then once daily *for as long as the patient is considered to be at risk of VTE.*

Non-surgical patients immobilised due to acute medical illness:
3,500 anti-Xa IU given SC once daily in patients at moderate risk of VTE, or
4,500 anti-Xa IU given SC once daily in patients at high risk of VTE.
Administration should continue for as long as the patient is considered to be at risk of VTE.

The following section on Neuraxial anaesthesia has been added to the Posology section:

Neuraxial anaesthesia

Caution is advised when performing neuraxial anaesthesia or lumbar puncture in patients receiving prophylactic doses of innohep, see section 4.4: Neuraxial anaesthesia. If neuraxial anaesthesia is planned, a minimum delay of 12 hours should be allowed between the last prophylactic dose and the needle or catheter placement. innohep should not be resumed until at least 4-6 hours after the use of spinal anaesthesia or after the catheter has been removed. Thus, the 2 hours preoperative initiation of thromboprophylaxis with innohep is not compatible with neuraxial anaesthesia.

The Posology section on haemodialysis has been amended (significant changes in italics):

Haemodialysis *and haemofiltration in adults*:

Duration of 4 hours or less:

A bolus injection of 2,000 to 2,500 anti-Xa IU at the start of dialysis.

Duration of more than 4 hours:

A bolus injection of 2,500 anti-Xa IU at the start of dialysis/filtration, followed by 750 anti-Xa IU/hour as a continuous infusion.

Dose adjustment:

If necessary, the bolus dose may be increased or decreased *gradually in increments of 500 anti-Xa IU* until a satisfactory response is obtained. *The usual dose is within 2,000 - 4,500 anti-Xa IU*.

If case of concomitant transfusion of blood or concentrated red corpuscles, an extra bolus injection of 500 - 1,000 anti-Xa IU can be administered.

The section on renal impairment has been amended to:

Renal impairment

If renal impairment is suspected, renal function should be assessed using a formula based on serum creatinine to estimate creatinine clearance level.

Use in patients with a creatinine clearance level < 30 ml/minute is not recommended, as dosage in this population has not been established. Available evidence demonstrates no accumulation in patients with creatinine clearance levels down to 20 ml/min. When required in these patients, innohep administration can be initiated with anti-Xa monitoring, if the benefit outweighs the risk (see section 4.4: Renal impairment).

The following section on Weight has been added to section 4.2:

Weight
For patients with very low or very high body weight, 50 anti-Xa IU per kg body weight once daily, may be considered as an alternative to fixed dosing. For surgical patients, the first dose is given SC 2 hours before surgery. The administration should continue once daily for as long as the patient is considered to be at risk of VTE.

The section on Method of Administration has been amended to:

Method of administration

Parenteral products should be inspected visually prior to administration. Do not use if cloudiness or precipitate is observed. The liquid may turn yellow during storage but is still useable.

Administration is by subcutaneous injection when given as prophylaxis of thromboembolic events in adults. This can be done in abdominal skin, the outer side of the thigh, lower back, upper leg or upper arm. Do not inject in the area around the navel, near scars or in wounds.

For abdominal injections, the patient should be in a supine position, alternating the injections between the left and right side. The air-bubble within the syringe should not be removed. During the injection, the skin should be held in a fold.

For haemodialysis, the dose of innohep should be given into the arterial side of the dialyser or intravenously. The dialyser can be primed by flushing with 500–1,000 ml isotonic sodium chloride (9 mg/ml) containing 5,000 anti-Xa IU innohep per litre.

Section 4.4, Special warnings and precautions for use

The section on renal impairment has been amended to:

Renal impairment
Use in patients with a creatinine clearance level < 30 ml/minute is not recommended, as dosage in this population has not been established. Available evidence demonstrates no accumulation in patients with creatinine clearance levels down to 20 ml/minute. When required in these patients, innohep administration can be used cautiously with anti-Xa monitoring, if the benefit outweighs the risk (see section 4.2). Although anti-Xa monitoring remains a poor predictor of haemorrhage risk, it is the most appropriate measure of the pharmacodynamic effects of innohep.

The following section on interchangeability has been added:

Interchangeability
Low molecular weight heparins should not be used interchangeably because of differences in pharmacokinetics and biological activities. Switching to an alternative low molecular weight heparin, especially during extended use, must be exercised with particular caution and specific dosing instructions for each proprietary product must be followed.

Please ensure that all relevant staff are made aware of the content of this letter and that the information is communicated to all relevant HCPs within your hospital, as appropriate.

The communication of this information has been agreed with the Health Products Regulatory Authority (HPRA).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

Adverse events should also be reported to LEO Pharma by calling +353 1 4908924 or e-mail medical-info.ie@leo-pharma.com. If you have any questions, please contact LEO Medical Information by calling +353 1 4908924 or e-mail medical-info.ie@leo-pharma.com.

Yours sincerely

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