NAME OF THE MEDICINAL PRODUCT: innohep 8.000 IU anti-Xa/0.4 ml, solution for injection - innohep 10.000 IU anti-Xa/0.5 ml, solution for injection - innohep 12.000 IU anti-Xa/0.6 ml, solution for injection - innohep 14.000 IU anti-Xa/0.7 ml, solution for injection - innohep 16.000 IU anti-Xa/0.8 ml, solution for injection - innohep 18.000 IU anti-Xa/0.9 ml, solution for injection. **QUALITATIVE AND QUANTITATIVE COMPOSITION:** innohep 8.000 IU anti-Xa/0.4 ml, solution for injection - innohep 10.000 IU. anti-Xa/0.5 ml, solution for injection - innohep 12.000 IU anti-Xa/0.6 ml, solution for injection - innohep 14.000 IU anti-Xa/0.7 ml, solution for injection - innohep 16.000 IU anti-Xa/0.8 ml, solution for injection - innohep 18.000 IU anti-Xa/0.9 ml, solution for injection. Excipients with known effect: Sodium metabisulfite (1.83 mg/ml) and sodium (in total < 23 mg/dose). **PHARMACEUTICAL FORM:** Solution for injection, pre-filled syringes. 1 ml syringe holding a colourless or straw-coloured liquid, free from turbidity and from matter that deposits on standing. **THERAPEUTIC INDICATIONS:** Treatment of venous thrombosis and thromboembolic disease including deep vein thrombosis and pulmonary embolus in adults. Extended treatment of venous thromboembolism and prevention of recurrences in adult patients with active cancer. For some patients with pulmonary embolism (e.g. those with severe haemodynamic instability) alternative treatment, such as surgery or thrombolysis, may be indicated. **POSOLOGY AND METHOD OF ADMINISTRATION:** Posology: *Treatment in adults:* 175 anti-Xa IU/kg body weight given subcutaneously once daily for at least 6 days and until adequate oral anticoagulation is established. *Extended treatment in adult patients with active cancer:* 175 anti-Xa IU/kg body weight given subcutaneously once daily for a recommended treatment period of 6 months. The benefit of continued anticoagulation treatment beyond 6 months should be evaluated. *Neuraxial anaesthesia:* Treatment doses of innohep (175 IU/kg) are contraindicated in patients who receive neuraxial anaesthesia, see section 4.3. If neuraxial anaesthesia is planned, innohep should be discontinued at least 24 hours before the procedure is performed. innohep should not be resumed until at least 4-6 hours after the use of spinal anaesthesia or after the catheter has been removed. *Interchangeability:* For interchangeability with other LMWHs, see section 4.4 of SmPC. *Paediatric population:* The safety and efficacy of innohep in children below 18 years have not yet been established. Currently available data are described in section 5.2, but no recommendation on a posology can be made. *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 treatment can be initiated with anti-Xa monitoring, if the benefit outweighs the risk (see section 4.4: Renal impairment os SmPC). In this situation, the dose of innohep should be adjusted, if necessary, based on anti-factor Xa activity. If the anti-factor Xa level is below or above the desired range, the dose of innohep should be increased or reduced respectively, and the anti-factor Xa measurement should be repeated after 3-4 new doses. This dose adjustment should be repeated until the desired anti-factor Xa level is achieved. For guidance, mean levels between 4 and 6 hours after administration in healthy volunteers and patients without severe renal insufficiency have been between 0.5 and 1.5 IU/anti-factor Xa IU/ml. Anti-factor Xa activity determinations were by a chromogenic assay. *Elderly:* innohep should be used in the elderly in standard doses. Precaution is recommended in the treatment of elderly patients with renal impairment. If renal impairment is suspected, see section 4.2: Renal impairment and section 4.4: Renal impairment of SmPC. 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 by storage but is still suitable. Administration is by subcutaneous injection. 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 supine position, alternating the injections between 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. Doses are administered in 1.000 IU increments facilitated by the 0.05 ml graduations on the syringes. The calculated dose, based on the patient's body weight, should therefore be rounded up or down as appropriate. If necessary, any excess volume should be expelled, to achieve the appropriate dosage before SC injection. *Guide to appropriate dosages for different body weights* – 175 IU/kg body weight subcutaneously once daily. 20.000 IU/ml in graduated syringes: 32-37 kg, 6.000 IU/0.30 ml – 38-42 kg, 7.000 IU/0.35 ml – 43-48 kg, 8.000 IU/0.40 ml – 49-54 kg, 9.000 IU/0.45 ml – 55-59 kg, 10.000 IU/0.50 ml – 60-65 kg, 11.000 IU/0.55 ml – 66-71 kg, 12.000 IU/0.60 ml – 72-77 kg, 13.000 IU/0.65 ml – 78-82 kg, 14.000 IU/0.70 ml – 83-88 kg, 15.000 IU/0.75 ml – 89-94 kg, 16.000 IU/0.80 ml – 95-99 kg, 17.000 IU/0.85 ml – 100-105 kg, 18.000 IU/0.90 ml – For patients weighing <32 kg or >105 kg, the same calculation as above should be used to establish the appropriate dose/volume. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of SmPC. Current or history of immune-mediated heparin-induced thrombocytopenia (type II) (see section 4.4 of SmPC). Active major haemorrhage or conditions predisposing to major haemorrhage. Major haemorrhage is defined as fulfilling any one of these three criteria: a) occurs in a critical area or organ (e.g. intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, intra-uterine or intramuscular with compartment syndrome), b) causes a fall in haemoglobin level of 20 g/l (1.24 mmol/l) or more, or c) leads to transfusion of two or more units of whole blood or red blood cells. Septic endocarditis. Treatment doses of innohep (175 IU/kg) are contraindicated in patients who receive neuraxial anaesthesia. If neuraxial anaesthesia is planned, innohep should be discontinued at least 24 hours before the procedure is performed. innohep should not be resumed until at least 4-6 hours after the use of spinal anaesthesia or after the catheter has been removed. Patients should be closely monitored for signs and symptoms of neurological injury. **UNDESIRABLE EFFECTS:** The most frequently reported undesirable effects are haemorrhage events, anaemia secondary to haemorrhage and injection site reactions. Haemorrhage may present in any organ and have different degrees of severity. Complications may occur particularly when high doses are administered. Although major haemorrhages are uncommon, death or permanent disability has been reported in some cases. Immune-mediated heparin-induced thrombocytopenia (type II) largely manifests within 5 to 14 days of receiving the first dose. Furthermore, a rapid-onset form has been described in patients previously exposed to heparin. Immune-mediated heparin-induced thrombocytopenia (type II) may be associated with arterial and venous thrombosis. innohep must be discontinued in all cases of immune-mediated heparin-induced thrombocytopenia (see section 4.4 of SmPC). In rare cases, innohep may cause hyperkalaemia due to hypoaldosteronism. Patients at risk include those with diabetes mellitus or renal impairment (see section 4.4 of SmPC). Serious allergic reactions may sometimes occur. These include rare cases of skin necrosis, toxic skin eruption (e.g. Stevens-Johnson syndrome), angioedema and anaphylaxis. Treatment should be promptly discontinued at the slightest suspicion of such severe reactions. The estimation of the frequency of undesirable effects is based on a pooled analysis of data from clinical studies and from spontaneous reporting. Undesirable effects are listed by MedDRA SOC and the individual undesirable effects are listed starting with the most frequently reported. Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness. Very common: ≥1/10; Common: ≥1/100 and < 1/10; Uncommon: ≥1/1.000 and <1/100; Rare: ≥1/10.000 and <1/1.000, Very rare: <1/10.000. Blood and lymphatic system disorders: Common (≥1/100 and <1/10): Anaemia (incl. haemoglobin decreased); Uncommon (≥1/1.000 and <1/100): Thrombocytopenia (type I) (incl. platelet count decreased); Rare (≥1/10.000 and <1/1.000): Heparin-induced thrombocytopenia (type II) Thrombocytosis. Immune system disorders: Uncommon (≥1/1.000 and <1/100): Hypersensitivity; Rare (≥1/10.000 and <1/1.000): Anaphylactic reaction. Metabolism and nutrition disorders: Rare (≥1/10.000 and <1/1.000): Hyperkalaemia. Vascular disorders: Common (≥1/100 and <1/10): Haemorrhage, Haematoma; Uncommon (≥1/1.000 and <1/100): Bruising, ecchymosis and purpura. Hepatobiliary disorders: Uncommon (≥1/1.000 and <1/100): Hepatic enzyme increased (incl. increased transaminases, ALT, AST and GGT). Skin and subcutaneous tissue disorders: Uncommon (≥1/1.000 and <1/100): Dermatitis (incl. dermatitis allergic and bullous), Rash, Pruritus; Rare (≥1/10.000 and <1/1.000): Toxic skin eruption (including Stevens-Johnson syndrome), Skin necrosis, Angioedema, Urticaria. Musculoskeletal and connective tissue disorders: Rare (≥1/10.000 and <1/1.000): Osteoporosis (in connection with long-term treatment). Reproductive system and breast disorders: Rare (≥1/10.000 and <1/1.000): Priapism. General disorders and administration site conditions: Common (≥1/100 and < 1/10): Injection site reaction (incl. injection site haematoma, haemorrhage, pain, pruritus, nodule, erythema and extravasation). Patients with cancer on extended treatment: In a trial of patients with cancer on extended (6 months) treatment with the overall frequency of adverse reactions was comparable to that seen in other patients treated with Patients with cancer generally have an increased risk of haemorrhage, which is further influenced by older age, comorbidities, surgical interventions and concomitant medications. Thus, as expected, the incidence of haemorrhagic events was higher than previously observed in short-term use, and similar to the rates seen with extended use of anticoagulants in patients with cancer. Paediatric population: Limited information derived from one study and postmarketing data indicates that the pattern of adverse reactions in children and adolescents is comparable to that in adults. 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 via Federaal agentschap voor geneesmiddelen en gezondheidsproducten, Afdeling Vigilantie, EUROSTATION II, Victor Hortaplein, 40/ 40, B-1060 Brussel - Website: www.fagg.be - e-mail: adversedrugreactions@fagg-afmps.be en in Luxemburg via Direction de la Santé – Division de la Pharmacie et des Médicaments, Villa Louvigny – Allée Marconi, L-2120 Luxembourg – Site internet: http://www.ms.public.lu/fr/activites/pharmacie-medicament/index.html **MARKETING AUTHORISATION HOLDER:** LEO Pharma N.V./S.A., Duwijckstraat 17, B-2500 - Lier, Tel: 03/740 78 68, e-mail: leo-pharma.be@leo-pharma.com **MARKETING AUTHORISATION NUMBER(S):** innohep 8.000 IU anti-Xa/0.4 ml: BE473235 - innohep 10.000 IU anti-Xa/0.5 ml: BE184326 - innohep 12.000 IU anti-Xa/0.6 ml: BE473244 - innohep 14.000 IU anti-Xa/0.7 ml: BE184317 - innohep 16.000 IU anti-Xa/0.8 ml: BE473253 - innohep 18.000 IU anti-Xa/0.9 ml: BE184301 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:** innohep 8.000 IU anti-Xa/0,4 ml: First MA 27 april 2015 - innohep 10.000 IU anti-Xa/0,5 ml: First MA 10 juni 1997, Renewal 3 november 2003 - innohep 12.000 IU anti-Xa/0,6 ml: First MA 27 april 2015 - innohep 14.000 IU anti-Xa/0,7 ml: First MA 10 juni 1997, Renewal 3 november 2003 - innohep 16.000 IU anti-Xa/0,8 ml: First MA 27 april 2015 - innohep 18.000 IU anti-Xa/0,9 ml: First MA 10 juni 1997, Renewal 3 november 2003. Medication on prescription. **DATE OF REVISION OF THE TEXT:** Date of revision of the SmPC: October 2016 - Date of approval of the SmPC: 09/2016

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1. Report on needle size investigation - performed by 3DCT, May 2017