Clexane Syringes 100mg/ml Solution for Injection PA540/97/1
Clexane Forte Syringes 150mg/ml Solution for Injection PA540/97/2
(enoxaparin sodium)
Updates to strength expression, dose regimens in DVT/PE, use in patients with severe renal impairment

21st April 2017

Dear Healthcare professional,

Sanofi-Aventis Ireland Ltd., T/A SANOFI, in agreement with the European Medicines Agency and the Health Products Regulatory Authority would like to inform you that, following completion of a Europe-wide review, the product information for Clexane (enoxaparin sodium) and associated names has been harmonised in all European Union (EU) countries. Strength expression, dose regimens in deep vein thrombosis (DVT)/pulmonary embolism (PE) and use in patients with severe renal impairment are updated as follows:

Summary

- **Enoxaparin strength, previously expressed in mg/ml, will now be expressed both in international units (IU) of anti-Xa activity and in milligram (mg): One mg of enoxaparin sodium is equivalent to 100 IU anti-Xa activity.**

  For example for the pre-filled syringes of 0.4 mL, the strength will appear as: Clexane 4,000 IU (40 mg)/0.4 mL solution for injection.

- **The dosage in treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) has been clarified as follows:**

  Enoxaparin sodium can be administered subcutaneously:
  - **either as a once daily injection of 150 IU/kg (1.5 mg/kg):** used in uncomplicated patients with low risk of VTE recurrence.
  - **or as twice daily injections of 100 IU/kg (1 mg/kg):** used in all other patients such as those with obesity, with symptomatic PE, cancer, recurrent VTE or proximal (vena iliaca) thrombosis.

  The regimen should be selected by the physician based on an individual assessment including evaluation of the thromboembolic risk and the bleeding risk.

- **Use in patients with end stage kidney disease (creatinine clearance <15 ml/min) is not recommended outside the prevention of thrombus formation in dialysis patients.**

Background on the safety concern
Important discrepancies existed between EU member states in the way enoxaparin strength was expressed in the product denomination and throughout the product information, the approved dosage regimen in DVT/PE and use in severe renal impairment.

Expressing strength both in IU and mg provides Healthcare Professionals clarity about enoxaparin doses regardless of which style they are familiar with, and will avoid medication error leading to risk of thrombosis or major bleeding.

A once daily 150 IU/kg (1.5 mg/kg) or a twice daily 100 IU/kg (1 mg/kg) regimen or both regimens were approved in the member states for the treatment of DVT/PE. Whilst keeping mention of the two dose regimens, these have been harmonised by strengthening recommendations about the populations in which the possible regimens should be used.

A contraindication in patients with severe renal impairment (creatinine clearance < 30 ml/min) that existed in some EU member states was removed from the product information (as needed), however, use in patients with end stage kidney disease (creatinine clearance <15 ml/min) is not recommended outside the prevention of thrombus formation in dialysis patients due to lack of data in this population.

For patients with severe renal impairment (creatinine clearance [15-30] ml/min) the following dose adjustment is recommended:

Indication	**Dosing regimen**
Prophylaxis of venous thromboembolic disease	2,000 IU (20 mg) SC once daily
Treatment of DVT and PE	100 IU/kg (1 mg/kg) body weight SC once daily
Treatment of unstable angina and Non ST-segment elevation myocardial infarction	100 IU/kg (1 mg/kg) body weight SC once daily
Treatment of acute ST-segment elevation myocardial infarction (patients under 75)	1 x 3,000 IU (30 mg) IV bolus plus 100 IU/kg (1 mg/kg) body weight SC and then 100 IU/kg (1 mg/kg) body weight SC every 24 hours
Treatment of acute ST-segment elevation myocardial infarction (patients over 75)	No IV initial bolus, 100 IU/kg (1 mg/kg) body weight SC and then 100 IU/kg (1 mg/kg) body weight SC every 24 hours

Further Information
Enoxaparin is a low molecular weight heparin.

On 15 December 2016, the Committee for Medicinal Products for Human Use (CHMP) at the European Medicines Agency (EMA) adopted the European labelling harmonisation for efficacy and safety information of Clexane and associated names.

Further information can be found on the Health Products Regulatory Authority website www.hpra.ie or www.medicines.ie

Call for reporting

Please continue to report any suspected adverse drug reactions (ADRs) to the Pharmacovigilance Section of the Health Products Regulatory Authority using the on-line reporting function on the HPRA website (www.hpra.ie) or alternatively by contacting the HPRA at 01 676 4971 or medsafety@hpra.ie

Adverse reactions should also be reported to Sanofi by telephone on 01 403 5600 or via email to IEPharmacovigilance@sanofi.com

Company contact point
For further information on Clexane please contact:

Sanofi Ireland Ltd.,
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Citywest Business Campus
Dublin 24
Telephone: 01 403 5600
Email: IEmedinfo@sanofi.com

We remain at your disposal for any further information you may need.

Yours sincerely

Liz Bergin

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