

## Direct healthcare-professional communication (DHPC)

12-10-2017

### Direct Healthcare Professional Communication, Clexane (enoxaparin sodium): Updates to strength expression, dose regimens in DVT/PE, use in patients with severe renal impairment

*Neurologists, Rheumatologists, ICU, Hematologists, and clinical pharmacists.*

Dear Healthcare Professional,

Sanofi, in agreement with the Saudi Food and Drug Authority (SFDA), would like to inform you that the product information for Clexane (enoxaparin sodium) will be updated. 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 milligrams (mg) will now be expressed both in international units (IU) of anti-Xa activity and in milligrams (mg):**

**1 mg of enoxaparin sodium is equivalent to 100 IU of anti-Xa activity**

For example for the pre-filled syringes of 0.4 ml, the strength will appear as: Clexane Syringes 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 venous thromboembolism (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 (iliac vein) 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 haemodialysis 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.

Using in patients with end stage kidney disease (creatinine clearance <15 ml/min) is not recommended outside the prevention of thrombus formation in haemodialysis 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. This information will update soon in Saudi Arabia.

#### **Reporting of suspected adverse reactions**

Saudi Food and Drug Authority-Drug sector  
National Pharmacovigilance and Drug Safety Center

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Kind regards,

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