



Department of

**Health, Social Services
and Public Safety**

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From The Chief Pharmaceutical Officer
Dr Norman Morrow

For Action: Directors of Pharmaceutical Services of the Boards & CSA
Directors of Pharmaceutical Services of HSC Trusts
Regional Quality Improvement Authority

Our reference: PHC/06/08
Date: 9th June 2008

DRUG ALERT

MEDICINES – CAUTION IN USE

Dear Healthcare Professional

Enoxaparin Sodium (Clexane) pre-filled syringes **Supply update and advice to prescribers on shortage of 150mg syringes and use in pregnancy**

Further to the drug alerts issued by the Department on 24 April (PHC/04/08) and 12 May (PHC/05/08) concerning enoxaparin (Clexane) pre-filled syringes contaminated with over-sulphated-chondroitin sulphate (OSCS), this provides an update on the supply situation and clinical advice.

Advice to prescribers

- There is no evidence of any specific risks to pregnant women or the developing foetus from exposure to the levels of OSCS found in some enoxaparin batches. However, on a purely precautionary basis, we are recommending that, wherever possible, use of affected batches should be avoided in pregnant women (see attached letter from Sanofi Aventis for details of unaffected batches).
- Prescribers should continue to avoid administering enoxaparin via the intravenous (off-label) or arterial line routes.
- In order to address a temporary shortage of 150mg pre-filled syringes, prescribers should consider using enoxaparin multi-dose vials, a combination of lower dose strengths of pre-filled syringes or a suitable alternative product. Adequate training should be provided to those patients who self-inject, to prevent administration error, particularly if syringes with different strengths are supplied.

Background to advice

On 24 April, the MHRA advised that some batches of the low molecular weight heparin enoxaparin sodium with low levels of the contaminant OSCS had been distributed in the UK in recent months. UK supplies of other low molecular weight heparin products and unfractionated heparin have not been affected.

As there was no evidence of any adverse effects associated with this low level of OSCS, and as recall of affected batches may have led to supply shortages thereby putting patient health at risk, the Commission on Human Medicines (CHM) recommended the continued supply of affected batches. However, purely as a precautionary measure, CHM advised that intravenous (off label) and arterial administration of enoxaparin should be avoided to minimise any theoretical risk of severe reactions.

These batches have been supplied in the UK and across Europe for several months and there remains no evidence of adverse effects associated with this low level of OSCS.

European review

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has now conducted a full review of the general issue of contamination of heparin products with OSCS. The CHMP position has been published on the EMA website (www.emea.europa.eu).

In relation to supply of affected enoxaparin sodium, the CHMP advice reaffirms the earlier advice of CHM; i.e. that affected batches should continue to be released to avoid national supply shortages and that intravascular administration should be avoided. The CHMP was reassured that widespread use of these batches within Europe has revealed no specific safety risks.

Although there is no evidence of any specific risks to pregnant women or the developing foetus, on a purely precautionary basis, the CHMP, has recommended that wherever possible use of affected batches should be avoided in pregnant women. This advice is supported by the CHM.

For pregnant patients requiring enoxaparin, prescribers or those administering or supplying the product, are advised to contact Sanofi Aventis Medical Information (Tel: 0800 281973) who will confirm which specific batches are free from OSCS. If OSCS-free product is not available locally, Sanofi Aventis will arrange for direct supply of OSCS-free product (see attachment for further details).

The CHMP has also outlined a coordinated approach to investigate the root cause of the OSCS contamination in order to avoid such contamination occurring in the future. The MHRA fully supports this approach.

Supply situation in the UK and clinical advice

It should be noted that there will shortly be a supply shortage of the 150mg syringes for approximately 6 weeks. If the 150mg syringes are unavailable, prescribers should consider using enoxaparin multi-dose vials, a combination of lower dose strengths of pre-filled syringes or a suitable alternative product.

The measures outlined in this notice will remain in place until all pre-filled syringes in the UK supply chain are OSCS-free – this is expected to be for the next 2 to 3 months.

Prescribers are reminded that not all available batches of enoxaparin pre-filled syringes contain OSCS and that no batches of the multi-dose vials have been affected by the contamination.

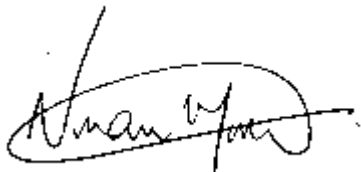
Advice from Sanofi Aventis

Sanofi Aventis are distributing a letter to Healthcare Professionals containing specific advice on batches of uncontaminated 40mg syringes for pregnant patients and recommendations for administration of 150mg doses. A copy is attached to this letter. Recipients are requested to forward both communications to listed recipients.

Area Boards/RQIA should bring this information to the attention of private hospitals/clinics registered with them, Out of Hours Centres and any other relevant care facilities.

The Central Services Agency is asked to bring this information to the attention of Community Pharmacists and Dispensing Doctors and GP's directly.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Norman Morrow', enclosed within a large, loopy oval flourish.

DR NORMAN MORROW
Chief Pharmaceutical Officer

For information:

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