



MEDSAFE

NEW ZEALAND MEDICINES
AND MEDICAL DEVICES
SAFETY AUTHORITY

A BUSINESS UNIT OF
THE MINISTRY OF HEALTH

www.medsafe.govt.nz

Dear [insert Doctor's name or "Pharmacist"]

22 July 2008

Advice from Medsafe

Caution advised in use of medicines and medical devices containing heparin and low molecular weight heparin

Key points:

- ***Detectable levels of over-sulphated chondroitin sulphate (OSCS) have not been found in medicines containing heparin or low molecular weight heparins supplied in New Zealand.***
- ***Because of the limitations of the available test methods, the presence of low levels of OSCS in products cannot be completely excluded.***
- ***There has been no increase in adverse reaction reports in New Zealand for medicines containing heparin or low molecular weight heparins.***
- ***Two types of medical device have been found to contain heparin contaminated with OSCS. These are:***
 - ***an oxygenator used in cardiac surgery, where alternative products should be used if possible***
 - ***blood collection containers, where use of the products has been allowed where OSCS levels are below 6%.***
- ***Healthcare practitioners are asked to be alert for, and to promptly report, any adverse reactions occurring in patients exposed to medicines or medical devices containing heparin or low molecular weight heparins.***

General

Early this year the United States Food and Drug Administration (FDA) advised of serious adverse reactions in the USA associated with the intravenous use of certain brands of heparin injections. Further investigation identified that a contaminant, *over-sulphated chondroitin sulphate* (OSCS), was responsible for these adverse reactions.

The reactions were severe in some cases and were typically immunoallergic in nature (anaphylactic type reactions). By mid-April 2008, approximately 81 deaths had been reported as associated with intravenous heparin containing high levels of OSCS.

As a result of the FDA reports, Medsafe immediately conducted a review of products available in New Zealand and issued advice to key stakeholders. Investigation of the problem has been ongoing, and this letter summarises the situation to date.

Medicines

All medicines containing heparin or low molecular weight heparins¹ supplied in New Zealand have been tested. In all cases, OSCS has been reported as 'not detected'. The limitations of the test method mean that OSCS levels below 1% will not be detected. Consequently, the presence of a low level of OSCS in products supplied in New Zealand cannot be completely excluded.

An analysis conducted by Medsafe, and endorsed by its expert advisory group, supports the conclusions of medicines regulators in Europe and the United States that it is safe to use products where OSCS has not been detected. International data demonstrate that there has been no increase in adverse reactions reported worldwide for heparin or low molecular weight heparin-containing medicines in which the presence of OSCS was 'not detected'. This is supported by New Zealand data which confirm there has been no increase in the reporting of adverse reactions to heparin or low molecular weight heparins in New Zealand in 2008.

Medical devices

Information so far indicates that only one medical device used in direct patient contact that utilises heparin contaminated with OSCS has been supplied in New Zealand. Users of this device, the Medtronic Trillium Oxygenator (used in cardiac surgery), have been informed of the need to use this device with caution and only where an alternative product is unavailable. Medtronic advises that it will be approximately two months before uncontaminated stock of the Trillium Oxygenator will be available.

Some blood sample containers have also been found to contain heparin contaminated with OSCS. Medsafe is satisfied that the presence of OSCS at levels less than 6% will not affect blood test results. Laboratories and other organisations using these products have been advised to be alert to the possibility of unusual test results when these tubes are used and to re-test if necessary.

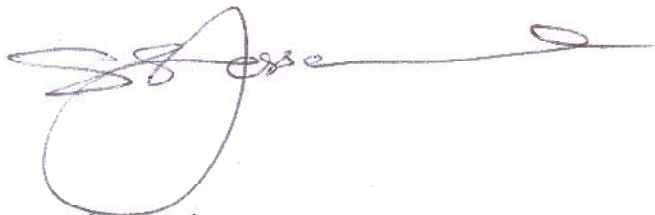
¹ This includes batches of Clexane recalled in Australia where samples of the heparin used in the manufacture of some batches of enoxaparin (the active ingredient in Clexane) were found to contain OSCS. Testing of the enoxaparin in these batches for OSCS was negative.

Reporting of adverse reactions

Health practitioners should remain alert to the possibility of adverse events and should **promptly** report any adverse reactions appearing to be associated with **medicines** or **medical devices** containing heparin or low molecular weight heparin.

- Reports of adverse reactions to **medicines** should be sent to the New Zealand Pharmacovigilance Centre / Centre for Adverse Reactions Monitoring (CARM):
<http://www.medsafe.govt.nz/profs/adverse/reactions.asp>
- Reports relating to **medical devices** should be made using the Medical Device Incident Reporting Form which can be found at:
<http://www.medsafe.govt.nz/downloads/device.doc>

Yours sincerely

A handwritten signature in blue ink, appearing to read 'Stewart Jessamine', with a long horizontal flourish extending to the right.

Stewart Jessamine
Group Manager Medsafe