

## **Class 4 Drug Alert (Caution in use): CP Pharmaceuticals - Multiparin<sup>®</sup> / Monoparin<sup>®</sup> Products (Heparin Sodium) - EL (09)A08**

Wockhardt UK has identified the presence of a very low level (0.6%) of over-sulphated chondroitin sulphate (OSCS) in the active raw material used in the manufacture of 31 batches of CP Pharmaceuticals/Wockhardt UK heparin sodium injections distributed in the UK.

A Class 4 Drug Alert (Caution in use) EL (09)A08 first issued by the MHRA on 31<sup>st</sup> March 2009 was revised on 1<sup>st</sup> April 2009.

Full details of the alert and a list of the affected batches can be found on the MHRA website: <http://www.mhra.gov.uk/Publications/Safetywarnings/Drugalerts/CON041521>

### **Answers to Anticipated Questions**

Q. What is heparin and what is it used for?

A. Heparin sodium injection is a type of medicine called an anticoagulant. It is used to stop blood clots forming within the blood vessels. Heparin Sodium is sometimes referred to as standard or unfractionated heparin.

Q. What is OSCS?

A. Over-sulphated chondroitin sulphate was identified as an adulterant of heparin sodium following the reporting of a large number of serious adverse anaphylactic reactions in the United States and elsewhere during 2008. No direct causative link was established, but the balance of evidence suggested that the presence of OSCS was responsible for at least some of the reported reactions. The proportion of OSCS in the heparin batches associated with these reports was approximately 20%.

Q. How did the OSCS get into heparin?

A. It is believed that it was deliberately introduced as an adulterant during the collection of crude heparin in certain Chinese workshops. The use of these workshops has ceased and strict controls are in place to assure the quality of crude heparin supplied to factories where it is purified to produce pharmaceutical grade heparin.

Q. What precautions are taken to ensure the absence of OSCS in Heparin?

A. During 2008, analytical methods were developed and published to detect the presence of OSCS in heparin. In August 2008, the European Monographs for heparin sodium and heparin calcium were amended to require all batches of Heparin raw materials to be tested by these methods to assure the absence of OSCS.

Q. Was OSCS found in any raw material previously used by Wockhardt UK/CP Pharmaceuticals?

A. No. All batches of heparin raw material used by Wockhardt UK/CP Pharmaceuticals from the beginning of 2006 have been tested by the methods described above and the absence of detectable levels of OSCS was confirmed.

Q. Why has OSCS now been detected in one batch of raw material used by Wockhardt UK/CP Pharmaceuticals?

A. In January 2009, a new analytical method for OSCS in heparin was published. This method is capable of detecting levels of OSCS 10 times lower than the methods used in 2008. All batches of heparin raw material used by Wockhardt UK/CP Pharmaceuticals since the beginning of 2008 have been re-tested by this new method. All batches but one have been shown to be clear. A level of 0.6% OSCS was detected in one batch.

Q. How much OSCS is in the finished products?

A. The heparin raw material is of course diluted during manufacture to produce the injections. The estimated level of OSCS in the products made from the affected batch is as follows:

25000u/ml injection contains approximately 0.075% OSCS

5000u/ml injection contains approximately 0.015% OSCS

1000u/ml injection contains approximately 0.003% OSCS

R. Why are so many finished product batches affected?

A. One batch of heparin sodium raw material provides sufficient material for the production of a large number of batches of branded and unbranded heparin injections.

Q. Are these batches being recalled?

A. No. The batches can be used subject to the cautions in the Drug Alert, and their distribution is not being restricted.

Q. Is there any patient risk?

A. There is no evidence to suggest that this very low level of OSCS is associated with the anaphylactoid reactions reported following use of batches of heparin with approximately 20% OSCS during 2008

Q. Why is this Drug Alert being issued?

A. In consultation with the MHRA, Wockhardt UK believes it is appropriate for a caution in use notice to be issued to alert healthcare professionals to what has been detected. While there is no evidence to suggest that this level of OSCS will cause any adverse patient reactions, we believe that it is sensible to take extra precautions during the administration of these batches.

Q. Why are the batches not being replaced?

A. If the affected batches were withdrawn from circulation, or their continued distribution suspended, it would lead to a potential out-of-stock situation that would have adverse clinical consequences.

Q. Will this raw material lot be used for any more batches of finished product?

A. No.

Q. How will Wockhardt UK ensure that no future batches are similarly affected?

A. All heparin raw materials used since the beginning of 2008 and all future batches of heparin raw material will be tested by the new method to assure the absence of detectable levels of OSCS.

Q. How can I identify the affected batches?

A. A list of affected batches is attached to the Drug Alert. No other batches are affected. Please note that affected batches are packed in both original branded livery as well as new unbranded packaging. The packaging of all Wockhardt heparin products distributed

in the UK has been recently changed to replace brand names with generic names, and reflect the change of company name from CP Pharmaceuticals to Wockhardt UK Ltd. These pack improvements also include the use of colour to differentiate between different product ranges and strengths, clearer and larger fonts, and minimised corporate branding.