Information Exchange System

Drug Alert No. 129

Contaminated Dextromethorphan active pharmaceutical ingredient

Background

On 24 January 2013 WHO Drug Alert number 126 was published following the discovery in Pakistan of two types of locally produced cough syrups containing the contaminated active pharmaceutical ingredient (API) Dextromethorphan.

This led to the death of approximately 50 persons in Pakistan, all with a history of drug addiction, who had been abusing dextromethorphan containing syrups for many years without any reported unexpected adverse reactions.

The subsequent investigation identified that both manufacturers in Pakistan were obtaining Dextromethorphan API from Konduskar Laboratories in India.

Full laboratory testing of the Dextromethorphan showed that it was contaminated with Levomethorphan, the enantiomer of Dextromethorphan, which is a potent opioid analgesic internationally controlled under schedule 1 of the single convention on Narcotic Drugs 1961.

In January 2013, as a result of this incident, the Indian Regulatory authorities suspended the manufacture, distribution, sale or use of Dextromethorphan by Konduskar Laboratories.

The WHO Drug Alert number 126 called on all countries to increase vigilance for Dextromethorphan in general, and specifically if it had been obtained from Konduskar Laboratories, to ensure that the API met all required quality specifications.

Update

On the 26 September 2013 WHO HQ were notified of suspected drug intoxications involving 11 paediatric patients in Paraguay. All of the patients were experiencing influenza-like symptoms and had consumed medical products produced by a local manufacturer (INDUFAR C.S.I.A.) containing Dextromethorphan. The children were aged between 2-9 years and serious adverse reactions included altered consciousness, cyanosis, respiratory distress, and seizures. The onset of symptoms occurred between 2-7 hours of ingesting the Dextromethorphan. Since then the number of patients experiencing adverse reactions has risen to 44 confirmed cases, and ranging in age from 5 months to 48 years. There has been one fatality that may be linked to this event.

The Paraguayan Ministry of Health has issued warnings concerning the medicines thought to be connected to this incident.
Investigations by the Paraguayan authorities indicated the source of the API Dextromethorphan, to be Konduskar Laboratories, India. The batch number of the Dextromethorphan API manufactured by Konduskar and used by the Paraguayan manufacturer was the same as one of the contaminated batches found in Pakistan. However, the Paraguayan manufacturer appears to have ordered the API from Konduskar in 2012, prior to the events in Pakistan.

According to the local manufacturer in Paraguay none of the products have been exported, however it could possibly be available in neighbouring countries through local traders and travellers.

WHO requests extra vigilance for the API Dextromethorphan in general, and in particular that originating from Konduskar Laboratories, and strongly advises that extreme caution should be exercised by importing countries and manufacturers in determining that it is carefully tested for the presence of the contaminant Levomethorphan, and meets the recognized specifications.

Samples of contaminated Dextromethorphan API from the original Pakistan incident have been analysed at the request of WHO and revealed limits of Levomethorphan varying between 9.5%-22.6%. All of the samples tested so far in both incidents have failed to comply with the requirements for the specific optical rotation as specified in the monograph for Dextromethorphan hydrobromide published in *The International Pharmacopeia* (see http://apps.who.int/phint/en/p/about/).

For any further information concerning this Alert, or if you have imported Dextromethorphan from Konduskar Laboratories, India please contact rapidalert@who.int.