Canada: Health Canada updates Canadians on estimates of health risks for recalled valsartan drugs containing NDMA

Health Canada announces the results of its review of potential long-term health effects involving valsartan drugs that were found to contain the impurity N-nitrosodimethylamine (NDMA). Health Canada scientists have assessed the available data to determine the potential increased risk of developing cancer, to help put the risk into context for Canadians.

Based primarily on animal studies, NDMA is classified as a probable human carcinogen. This means that exposure over the long term could increase the risk of cancer. We are all exposed to low levels of NDMA. NDMA can be found in some foods (such as meats, dairy products and vegetables) and in drinking water. It is not expected to cause harm when ingested in very low levels.

Health Canada believes that NDMA was introduced to the affected valsartan drugs as a result of a change in manufacturing processes at Zhejiang Huahai Pharmaceuticals (the manufacturer of the valsartan ingredient) in 2012. The longest time affected products were on the Canadian market was approximately three years.

The amounts of NDMA present in the valsartan active ingredient varied, but on average were higher than levels that are considered reasonably safe, which is why the valsartan products were recalled. Health Canada has derived estimates of the possible increased cancer risk using internationally accepted methods and information available to the Department at this time. It is important to keep in mind that the actual health risk varies from person to person, and depends on factors including daily dose, how long the affected valsartan was taken, and the actual level of NDMA present in the finished product.

For patients taking the highest dose of valsartan (320 mg) containing 60 ppm NDMA per tablet once daily for three years, Health Canada estimates that the potential increased risk of cancer over a lifetime could be 1 additional case of cancer for every 11,600 people taking the product. For patients taking the lowest valsartan dose (40 mg) containing 60 ppm NDMA per tablet once daily for three years, Health Canada estimates that the potential increased risk of cancer over a lifetime could be 1 additional case for every 93,400 people taking the product. To put these estimates into a broader context, nearly 1 in 2 Canadians is expected to develop cancer during their lifetime.

Health Canada is working closely with international partners to share information and coordinate efforts on inspections, risk assessments and public communications. Notably, Health Canada's estimated potential increased cancer risk is lower than those reported by the United States (US) Food and Drug Administration (FDA) and the European Medicines Agency (EMA) because the contaminated valsartan products were on the Canadian market for a shorter period of time, compared to the exposure timelines used in the assessments communicated by the FDA and EMA. Health Canada will take action should any new safety issue be identified and will continue to keep Canadians updated.

Please refer to the following website in Health Canada for details:
http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2018/67734a-eng.php

In Hong Kong, there are 83 registered pharmaceutical products containing valsartan, and all products are prescription-only medicines.

A public announcement was issued on 6 Jul 2018 on the issue, and letters to inform local healthcare professionals of the latest development, including the affected products, recommendations on drug use and possible risk, were issued by the Department of Health (DH) on 6 Jul 2018, 9 Jul 2018, 25 Jul 2018 and 3 Aug 2018. Related news was also previously issued by various overseas drug regulatory authorities, and was posted on the Drug Office website since 6 Jul 2018, with the latest update posted on 1 Sep 2018.

In summary, there are four manufacturers, namely Zhejiang Huahai, Zhejiang Tianyu and Zhuhai Rundu in China and Hetero Labs Limited in India, reported to have detection of trace amounts of NDMA in the valsartan Active Pharmaceutical Ingredient (API) by various overseas drug regulatory authorities.

The DH contacted the certificate holders of all registered valsartan products to follow up on the local impact regarding valsartan API produced by the above mentioned manufacturers.

For API produced by Zhejiang Huahai, there are 5 affected products marketed in Hong Kong. DH instructed the certificate holders to recall all the products from the market as a precautionary measure on 6 Jul 2018, and DH noted that all the recalls have been completed. The affected products are:

Product	Hong Kong Registration Number	Registration certificate holder
Valtensin 160mg tablets	HK-61786	Actavis Hong Kong Limited
Valtensin 80mg tablets	HK-61787	Actavis Hong Kong Limited
Valtensin HCT tablets 160/12.5mg	HK-61784	Actavis Hong Kong Limited
Valtensin HCT tablets 80/12.5mg	HK-61785	Actavis Hong Kong Limited
Valsartan Stada 80mg tablets	HK-60794	Hong Kong Medical Supplies Ltd

For API produced by Zhejiang Tianyu, amongst the registered pharmaceutical products containing valsartan, there is only one product namely Retoni Tablets 80mg (HK-65604) registered by Swiss Pharmaceutical Co Limited (Swiss Pharmaceutical) which has used API produced by Zhejiang Tianyu and is available in the local market. As confirmed with Swiss Pharmaceutical, the API was tested by the Taiwan Food and Drug Administration (TFDA) and the company has not received any notice from the TFDA for NDMA contamination. The DH collected samples of Retoni tablets for analysis and no NDMA was detected.

For API produced by Zhuhai Rundu and Hetero Labs Limited, the certificate holders confirmed that the valsartan products available in local market are not manufactured using API produced by Zhuhai Rundu or Hetero Labs Limited.

So far, the DH has not received any adverse reactions related to the above products affected by the recall.

Patients who are taking the above products should not stop taking the medicines, but should seek advice from their healthcare professionals as soon as possible for proper arrangement.

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