

The United States: FDA posts laboratory analysis of NDMA levels in recalled valsartan products

The US Food and Drug Administration (FDA) continues to investigate the presence of impurities in valsartan products and other angiotensin II receptor blockers (ARBs) used to treat high blood pressure and heart failure. FDA recently identified the impurities N-Nitrosodimethylamine (NDMA) and N-Nitrosodiethylamine (NDEA) in certain valsartan products. FDA is posting its test results showing NDMA levels in recalled valsartan products. FDA will also post test results and an assessment of the cancer risk from NDEA when they are available.

The table below shows the NDMA test results for the recalled valsartan products. The analyses reflect average levels of NDMA present in a single tablet based on the strength of the tested drug product within the lots tested, which are identified in the table. Some of products listed below may have been repackaged by other companies as noted in FDA's list of valsartan products under recall. For reference, consuming up to 0.096 micrograms of NDMA per day is considered reasonably safe for human ingestion based on lifetime exposure.

FDA previously estimated that if 8,000 people took the highest valsartan dose (320 mg) containing NDMA from the recalled batches daily for four years, there may be one additional case of cancer over the lifetimes of the 8,000 people. That estimate was based on the highest daily dose, however many people may have taken lower doses, and therefore their risks would theoretically be less. FDA expects the actual cancer risk to most consumers to be lower than our estimate.

Company	Product (tablets)	Lots Tested	NDMA level (mcg/tablet)
Hetero Labs Ltd	Valsartan 320mg	VLS18049, VLS18051, VLS18050	0.3-0.4
Prinston Pharmaceutical	Valsartan 320mg/HCTZ 25mg	611B18025, 611B18026, 611B18027	13-20
Prinston Pharmaceutical	Valsartan 320mg	344B18027, 344B18028, 344B18029	15-16
Teva Pharmaceuticals	Valsartan 320mg	1240425A, 1247282M,	8-17

		1263943A	
Teva Pharmaceuticals	Valsartan 320mg/HCTZ 25mg	1217576M, 1217577M, 1217578M	7-10
Torrent Pharmaceuticals	Amlodipine 10mg/Valsartan 320 mg/HCTZ 25mg	BBX2E001, BBX2E002, BBX2E003	10-12
Torrent Pharmaceuticals	Amlodipine 10mg/Valsartan 320 mg	BV77E001, BV77E002, BV77E003	5-9
Torrent Pharmaceuticals	Valsartan 320mg	BV48D001, BV48D002	0.5-0.6

Please refer to the following website in FDA for details:

<https://www.fda.gov/Drugs/DrugSafety/ucm622717.htm>

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

Regarding impurities in valsartan, a public announcement was issued on 6 Jul 2018, and letters to inform local healthcare professionals were issued by the Department of Health (DH) on 6 Jul 2018, 9 Jul 2018, 25 Jul 2018 and 3 Aug 2018. Related news for the detection of impurities in sartan-containing products 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 3 Oct 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 (HK-61786, HK-61787, HK-61784, HK-61785 and HK-60794) marketed in Hong Kong. The DH instructed the certificate holders to recall all the products from the market as a precautionary measure on 6 Jul 2018, and the DH noted that all the recalls have been completed.

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 of the above products related to the presence of NDMA. The DH will keep vigilant on any further updates on the matter issued by overseas regulatory authorities.

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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