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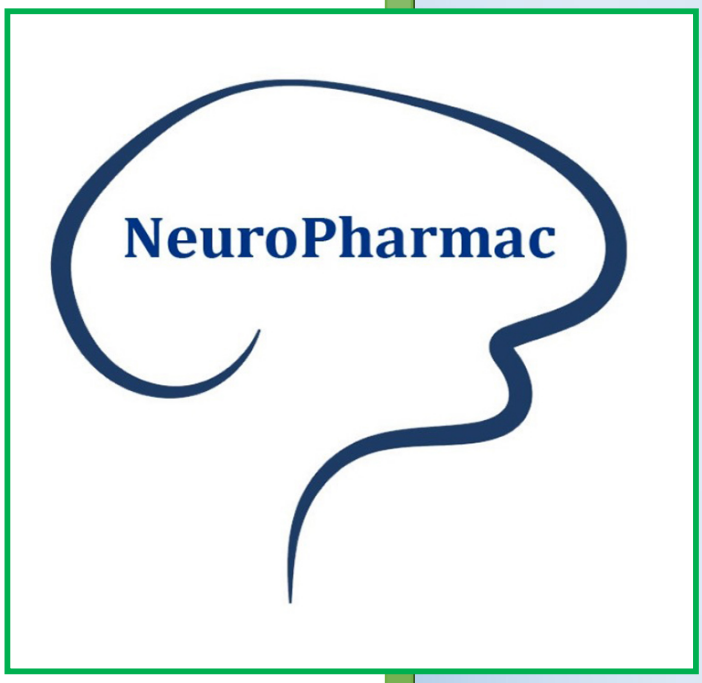


**Top Pharma companies not following current good manufacturing processes: Angiotensin II receptor blockers with carcinogenic impurities: A threat to global public health**

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Review

# Top Pharma companies not following current good manufacturing processes: Angiotensin II receptor blockers with carcinogenic impurities: A threat to global public health

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**ABSTRACT**

Angiotensin II receptor blockers (ARBs) are the first-line treatment in the management of hypertension used worldwide. Examples of ARBs include the drugs valsartan, losartan, irbesartan, candesartan, eprosartan, olmesartan, and telmisartan. Beginning in June 2018, FDA learned that some generic versions of the prescription drug valsartan contained unexpected impurities that posed a safety concern. The impurities in ARB medications, N-Nitrosodimethylamine (NDMA) and N-Nitrosodiethylamine (NDEA) are probable human carcinogens (cancer-causing), and N-Nitroso-N-methyl-4-aminobutyric acid (NMBA) is a potential human carcinogen. Most medicines found to contain these impurities above the interim acceptable intake limits have been recalled and are no longer available in the U.S. market. FDA recalled ARBs with carcinogenic impurity, the big question is that, what about the consumers who ate carcinogenic impured medicines by paying to pharma companies? FDA should take necessary action to prevent a threat to global public health.

**Keywords:** Angiotensin II receptor blockers, Valsartan, Losartan, Carcinogenic impurities

**Teva/Actavis, Prinston/Solco, Aurobindo, Torrent, Mylan, Hetero/Camber, Vivimed, Macleods, ScieGen top pharmaceutical companies with revenue greater than $10 billion? Not able to follow the current good manufacturing processes and validation protocol for the manufacture of medicines?**

## FDA warns Mylan for CGMP deviations

On 13/11/2019, the U.S. Food and Drug Administration posted a warning letter to Mylan Pharmaceuticals, Inc. in Chodavaram Village, Vizianagaram, Andhra Pradesh, India. Mylan manufactures valsartan active pharmaceutical ingredient (API) and has been one subject of an ongoing global investigation into nitrosamine impurities in angiotensin II receptor blockers (ARBs) such as valsartan, losartan and irbesartan.

The warning letter outlines several current good manufacturing practice (CGMP) deviations at this Mylan facility, including failure to have adequate written procedures for the receipt, identification and handling of raw materials and failure to adequately clean equipment and utensils. Failure to correct these deviations may result in further action by the FDA. The warning letter is another result of the FDA's ongoing investigation.

FDA reminds patients taking recalled ARBs to continue taking their current medicine until their pharmacist provides a replacement or their doctor prescribes a different medication that treats the same condition.

The U.S. Food and Drug Administration (FDA) inspected drug manufacturing facility, Mylan Laboratories Limited, Unit 8, FEI 3002785310, at G. Chodavaram Village, Vizianagaram, Andhra Pradesh, India, from May 27 to June 5, 2019.

During FDA's inspection, FDA investigators observed specific deviations including, but not limited to, the following.

1. Failure to have adequate written procedures for the receipt, identification, testing and handling of raw materials.

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2. Failure to clean equipment and utensils to prevent contamination or carry-over of a material that would alter the quality of the API beyond the official or other established specifications.

## FDA warns Torrent for CGMP violation

On 15/10/2019, the U.S. Food and Drug Administration posted a warning letter to Torrent Pharmaceuticals in Ahmedabad, Gujarat, India. Torrent manufactures losartan potassium tablets and has been one subject of an ongoing global investigation into nitrosamine impurities in angiotensin II receptor blockers (ARBs) such as valsartan, losartan and irbesartan.

The U.S. Food and Drug Administration (FDA) inspected drug manufacturing facility, Torrent Pharmaceuticals Limited, FEI 3005029956, at Ahmedabad-Mehsana Highway, Taluka-Kadi, Indrad, Gujarat from April 8 to 16, 2019.

During FDA's inspection, FDA investigators observed specific violations and deviations including, but not limited to, the following.

1. Failed to follow written procedures for production and process control designed to assure that the drug products you manufacture have the identity, strength, quality, and purity they purport or are represented to possess.
2. Failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed.

## How did the impurities get into the ARBs?

FDA's ongoing investigation has determined that these impurities may be generated when specific chemicals and reaction conditions are present in the manufacturing process of the starting materials, intermediates or finished active pharmaceutical ingredient (API).

As per the US FDA, the presence of these impurities in other processes may also be caused when current good manufacturing processes (CGMPs) are not appropriately followed.

## How many ARBs recalled by FDA?

1,159 ARBs with other combinations recalled by FDA till 23/09/2019.

## Which Pharma companies involved in the recall of the FDA?

Teva/Actavis & Prinston/Solco, Aurobindo Pharma USA, Torrent Pharma, Mylan Pharma, Hetero/Camber, Vivimed, Macleods Pharmaceuticals, ScieGen Pharmaceuticals

## Summary

These are the top pharmaceutical companies with revenue greater than $10 billion and not able to follow the current good manufacturing processes and validation protocol for the manufacture of medicines? The warning letter issued by FDA to Mylan Pharma indicates the failure to clean the equipment and utensil used for the manufacturing of the medicine process. Is it clearly indicating that Pharma companies playing with people's lives worldwide and interested in money-making protocol instead of validation protocol?

FDA recalled ARBs with carcinogenic impurity, the big question is that, what about the consumers who ate carcinogenic impured medicines by paying to pharma companies? FDA should take necessary action to prevent a threat to global public health.

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