PharmFacts - Metformin ER Recall

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Did You Know…

Over the past two weeks, several companies have recalled their metformin ER formulations due to laboratory findings of certain lots containing N-nitrosodimethylamine (NDMA) above the FDA's acceptable limits.

What is NDMA? NDMA is a common contaminant found in water and foods including cured and grilled meats, dairy products and vegetables. The FDA does not expect nitrosamines to cause harm when ingested at or below the acceptable intake limit levels (such as low levels of nitrosamines that are present in foods and ingested as part of usual diets) even over a long period of time (such as a 70-year lifespan). Nitrosamine impurities may increase the risk of cancer if people are exposed to them at above-acceptable levels over long periods of time, but the FDA does not anticipate that shorter-term exposure at levels above the acceptable intake limit would lead to an increase in the risk of cancer. This is the same contaminant that led to ARB and ranitidine recalls.

What was recalled? Four companies – Apotex, Amneal, Teva, and Marksans have metformin ER recalls published on the FDA website in the past week in response to the FDA's recommendation for a voluntary recall. One other company has yet to respond. See the chart below from the FDA website – as of 6/9/20.

Date	Brand Name(s)	Product Description	Product Type	Recall Reason Description	Company Name
06/05/2020	Apotex Corp	Metformin Hydrochloride Extended-Release Tablets, USP 500mg	Drugs,	Due to detection of N-Nitrosodimethylamine (NDMA)	Apotex Corp
06/05/2020	Actavis	Metformin Hydrochloride Extended-Release Tablets, USP 500mg and 750mg	Drugs,	Due to detection of N-Nitrosodimethylamine (NDMA)	Teva Pharmaceuticals USA Inc.
06/05/2020	Time-Cap Labs, Inc.	Metformin Hydrochloride Extended-Release Tablets, USP 500mg	Drugs,	Due to detection of N-Nitrosodimethylamine (NDMA)	Marksans Pharma Limited, India
06/01/2020	Amneal	Metformin Hydrochloride Extended-Release Tablets, USP 500mg and 750mg	Drugs,	Due to detection of N-Nitrosodimethylamine (NDMA)	Amneal Pharmaceuticals LLC

What should patients do? **The FDA has stated patients should continue taking metformin ER tablets even after recalls occur, until they consult with their health care professional who can prescribe a replacement. The FDA recommends that health care professionals continue to prescribe metformin when clinically appropriate.** ***If a patient is concerned they may have received an impacted lot, they can call their pharmacy for determination and return (if needed). Express Scripts mail-order is notifying patients by letter if they received an impacted lot with instructions on how to return product and obtain a refund from manufacturer (if offered). Patients will need to order a replacement refill – this will not be proactive. Other pharmacies may be notifying patients in a similar fashion (TBD).***

What alternatives do patients have? Other manufacturers of metformin ER are still available. Pharmacies may switch patients to an alternative manufacturer if they have in stock. *Also, metformin immediate release has not been shown to have elevated NDMA – this will be an option for patients interested in switching. A discussion with their healthcare provider and a new RX would be needed.*

What can providers do? If patients are concerned they may have an impacted lot, refer them to their pharmacy. The pharmacy can tell the patient how they may obtain a new supply/contact the manufacturer for returns/refunds as appropriate. You can consider writing for metformin IR if the pharmacy does not have alternative metformin ER stock as you deem clinically appropriate. The attached document outlines how patients can contact the manufacturers directly regarding return of impacted product.

What happens next? For now, there is metformin ER available (that may change depending on whether or not additional recalls occur). The batches currently released to US market are being tested and the manufacturers have been asked to not release any containing NDMA. Patients may be switched to metformin IR as an alternative.

For more information, please see the FDA Updates and Press Announcements. https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-metformin

This communication was approved by the Duke Basic/Duke Select Ambulatory Care Pharmacy Provider Workgroup. For more information, please contact Lee Jackson at lee.jackson@dm.duke.edu