

## The Determination of N-Nitroso Labetalol (NDSRI) in Labetalol using a sensitive Sciex 5500 LC-MS/MS Instrument

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### Abstract:

N-Nitroso Labetalol, a potential genotoxic impurity formed through nitrosation of the manage blood pressure drug Labetalol, has recently gained regulatory attention due to the broader risk of nitrosamine contamination in pharmaceutical products. This study aims to quantify N-Nitroso labetalol in Labetalol drug substance and finished dosage forms using a sensitive and selective analytical method. A liquid chromatography–mass spectrometry (LC-MS/MS) procedure was developed and validated in accordance with ICH guidelines to ensure accuracy, precision, specificity, and robustness at trace-level detection. Sample preparation conditions were optimized to prevent in-situ nitrosation. The method demonstrated a limit of detection in the low ng/g range, enabling reliable assessment of nitrosamine levels relative to the acceptable intake limits recommended by regulatory authorities. Results from multiple parameters showed that N-Nitroso Labetalol. The validated method provides a reliable tool for routine testing and supports risk-based evaluation of nitrosamine impurities in Labetalol products.

In 2018, alerts surfaced that some sartan medicines carried trace amounts of the cancer-linked nitrosamines NDMA (N-nitroso-dimethylamine) and NDEA (N-nitrosodiethylamine). Since then, those contaminants have also been found in other drugs—most notably metformin and ranitidine, prompting the European Medicines Agency (EMA) to launch a deep dive into the manufacturing process. Key findings point to certain catalysts, reagents, and amine nitrogen combinations in the production line as the usual culprits. While a recall of some medications in Croatia didn't cut off access to metformin or sartans, ranitidine was voluntarily withdrawn across the EU (including Croatia). The temporary shortage was quickly mitigated by switching to alternative drugs. The EMA is scrutinizing how these nitrosamines get into drugs, and regulators are working hard to keep the market safe while ensuring patients have continuous access to essential medicines. Labetalol is a prescription Blood pressure regulator drug. It's used to manage the blood flow and maintain the blood pressure in the vessels.

### Keywords:

Labetalol, N-Nitroso Labetalol, NDSRI, Method development and Validation.