

Analysis of Antimycotics in Serum / Plasma Using RECIPE® ClinMass® TDM Kit with Fully Automated Sample Preparation LC/MS/MS System

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Background

Antimycotics (antifungal drugs, antifungals) are a class of drugs that are used for the treatment and prophylaxis of fungal infections. For all compounds of clinical use therapeutic drug monitoring (TDM) is recommended to monitor the variability of pharmacokinetics of antifungal agents in patients with life-threatening fungal infections. LC-MS/MS has become an essential tool for monitoring drug concentrations samples of human origin. However, it is not suited for effective routine work because of the manual sample preparation at laboratories. Shimadzu CLAM (Clinical Laboratory Automated sample preparation Module for LCMS) in front of the LC-MS/MS system provides a fully automated sample preparation with a fast and high-precision analytical workflow. To demonstrate that the automated sample preparation provides reliable and reproducible results with minimal variation a method verification procedure was evaluated according to the CLSI Guidelines EP06-A, EP15-A3, EP17-A2.

Methods

For the analytical verification, a Shimadzu CLAM-2040 coupled with a Nexera X3 UHPLC system and a LCMS-8060 triple quadrupole mass spectrometer was used. Human serum samples spiked with eight widely used antimycotic compounds (5-fluorocytosine, fluconazole, isavuconazole, itraconazole, ketoconazole, hydroxy-itraconazole, Posaconazole and voriconazole) were subjected to published verification procedures using the ClinMass® TDM Platform (order no. MS9000) in combination with the ClinMass® Add-on Set for Antimycotics in Serum /Plasma (order no. MS9600) (RECIPE®, Germany).

Results

The trueness was determined by two different quality control (QC) samples in a single analysis sequence. The precision in CV% and deviation from the target in % Bias (N=4) of each compound was excellent (CV<7.3%, Bias<10.5%). The intraassay precision (N=8) for each level was low (CV<3,6%). Several dilutions of the Calibrator Set showed good linearity, including LLOQ, of each compound ($R^2 > 0.998$).

Conclusions

The ClinMass® TDM Kit System for Antimycotics in Serum /Plasma (order no. MS9000 and MS9600) was successfully verified on the CLAM-2040 with the analytical system LCMS-8060 from Shimadzu. All 8 analytes: 5-fluorocytosine, fluconazole, isavuconazole, itraconazole, ketoconazole, hydroxy-itraconazole, Posaconazole and voriconazole passed the acceptance criteria for accuracy (trueness, precision) and linearity. The lower limit of quantification (LLOQ) was below published clinical reference ranges.

Key words:

TDM, Antimycotics, Automation, LCMSMS, Kit, IVD