

**Introduction**

Lamotrigine (LAMICTAL®; GlaxoSmithKline) is an antiepileptic drug indicated as adjunctive therapy in patients ≥2 years of age who are 6 years or older with partial seizures. Lamotrigine concentrations reported in the literature range from 1.0-38.8 µg/mL. Linearity studies were performed as suggested in CLSI/NCCLS Protocol EP6-A. A 48.00 µg/mL Lamotrigine substance concentration was tested. Crossreactivity to the major metabolite ranged 1.09 to 2.91%. Crossreactivity to the minor metabolite ranged 0.02 to 0.24%. The levels of metabolites tested were well above those reported in the literature.

**Precision**

Precision was determined as described in CLSI/NCCLS Protocol EP8-A. Trained controls and three patient controls containing lamotrigine were assayed in quadruplicate twice a day for 20 days. Mean determinations of lamotrigine, standard deviation (SD) for within-run, between-day, and total coefficients of variation (% CV) were calculated. The amount of lamotrigine recovered from nominal ranged from 90.8% to 105.1%, and the mean percentage recovery was 98.2%.

**Endogenous Interference**

Endogenous interference studies were conducted using CLSI/NCCLS Protocol EP7-A1 as a guideline. Clinically high concentrations of the following potentially interfering substances in sera with known levels of lamotrigine were assayed up to 3 µg/mL and spiked along with a serum control of lamotrigine. Measurement of lamotrigine resulted in <1% error in the presence of drug compounds at the levels tested. The following compounds did not interfere with the measurement of lamotrigine at the levels tested.

**Specitivity**

A high concentration of each compound was spiked into normal human serum with known levels of lamotrigine (approximately 1-3 µg/mL) and assayed along with a serum control of lamotrigine. Measurement of lamotrigine resulted in <1% error in the presence of drug compounds at the levels tested. The following compounds did not interfere with the measurement of lamotrigine at the levels tested.

**Linearity**

Linearity studies were performed as suggested in CLSI/NCCLS Protocol EP8-A. A 48.00 µg/mL serum sample was prepared and diluted were made proportionally with human serum. Correlation studies were performed using CLSI/NCCLS Protocol EP9-A2. Results from the ARK Lamotrigine Assay along with a serum control of lamotrigine. The correlation coefficient (r²) for the assay was determined. Using Passing & Bablok (I) fit the calibration curve was as follows: y = 0.9769 x + 0.1522 (r² = 0.9999). Lower Limit of Quantitation of lamotrigine was evaluated according to CLSI/NCCLS EP7-A. A pooled serum sample was supplemented with known amounts of lamotrigine and assayed 4 times (n=4). The limits of quantitation (LOQ) was 0.75 µg/mL (4.15% CV). Analytical recovery in serum was within 10% of the nominal value from 0.50 to 30.00 µg/mL. The LOQ was 0.75 µg/mL (4.15% CV). Analytical recovery in serum was within 10% of the nominal value from 0.50 to 30.00 µg/mL. Lower Limit of Quantitation (LOQ) was 0.75 µg/mL (4.15% CV). Analytical recovery in serum was within 10% of the nominal value from 0.50 to 30.00 µg/mL. Correlation studies were performed using CLSI/NCCLS Protocol EP9-A2. Results from the ARK Lamotrigine Assay along with a serum control of lamotrigine. Measurement of lamotrigine resulted in <1% error in the presence of drug compounds at the levels tested. The following compounds did not interfere with the measurement of lamotrigine at the levels tested.

**Method Comparison**

Accuracy (trueness) was determined by adding standard concentrations of lamotrigine to human serum negative for lamotrigine. Test sample concentrations were 0.5, 1.0, 2.5, 5.0, 10.0, 20.0, 30.0, and 40.0 µg/mL. Two analytical runs of three replicates of each sample were assayed. The results of the six replicates were averaged and compared to the theoretical target concentration and the percentage recovery was calculated. The amount of lamotrigine recovered from nominal ranged from 90.8% to 105.1%, and the mean percentage recovery was 98.2%.

**Conclusion**

Performance of the ARK Lamotrigine Assay was demonstrated on the Roche/Hitachi 917 Synergy. Performance of the assay showed good precision, accuracy, specificity and linearity with excellent correlation in HPLC. The ARK lamotrigine assay, calibration and controls are provided in liquid form ready to use.

**INTENDED USE**

The ARK Lamotrigine Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of lamotrigine in human serum or plasma on automated clinical chemistry analyzers.

**ASSAY RANGE**

The range of the assay is 0.0 to 48.00 µg/mL. Results below the range is <0.0 µg/mL and results above the range is 48.00 µg/mL. The lower limit of quantitation (LOQ) is 0.75 µg/mL and above. The mean standard deviation, %CV, percentage recovery (% R), and percentage of consensus values were calculated for each sample.

**United Kingdom National External Quality Assessment Scheme**

Heath Controls (UK NEQAS: United Kingdom National External Quality Assessment Scheme, Cordis/cordis for Services Ltd, Yeovil, Brolan (Cordis) Ltd (UK), were evaluated. The samples were tested with a pool of 4 different, thrice in each run with 10% bias. The mean, standard deviation, %CV, percentage recovery (% R), and percentage of consensus values were calculated for each sample.