Psychiatry Quetiapine Assay Kit

INTENDED USE

Rx only

The Psychiatry Quetiapine Assay Kit is intended for the *in vitro* quantitative measurement of quetiapine in human serum using automated clinical chemistry analyzers. Measurements obtained are used for monitoring patient adherence to quetiapine therapy to help ensure appropriate treatment.

SUMMARY AND EXPLANATION OF THE TEST

Quetiapine (2-[2-(4-dibenzo [b,f] [1,4]thiazepin-11-yl-1-piperazinyl)-ethoxy]-ethanol is a dibenzothiazepine derivative atypical antipsychotic agent used in the treatment of schizophrenia, manic episodes associated with bipolar I disorder, and depressive episodes associated with bipolar disorder.[1]

Nonadherence to medication is well known for patients with severe mental illness.[2] While adherence to medication is critical to successful treatment outcomes, adherence is also least likely to be accurately assessed.[3,4] Measurement of quetiapine provides clinicians with objective evidence of concentrations that may be related to patient adherence.[5]

The quetiapine assay is a homogenous two reagent nanoparticle agglutination assay used for detection of quetiapine in human serum. It is based on competition between drug and drug-conjugates for binding to drug specific antibodies covalently bound to nanoparticles. The extent of particle aggregation can be followed spectrophotometrically on clinical chemistry analyzers.

REAGENTS

The kit contains sufficient reagent for 100 tests.

Psychiatry Quetiapine Assay Kit **REF** C82917	Quantity x Volume
Reagent 1 **R1** Reaction buffer that contains drug-conjugate, protein, and buffer	1 x 10.0 mL
Reagent 2 **R2** Nanoparticle reagent that contains monoclonal antibody bound to nanoparticles in a buffered solution	1 x 5.0 mL

WARNINGS AND PRECAUTIONS

- For In Vitro Diagnostic Use Only.
- For diagnostic purposes, the results should always be assessed with the patient's medical history, clinical examination and other findings.
- Exercise normal precautions required for handling all laboratory reagents.
- Follow reagent handling instructions. Improper mixing of reagents can affect assay performance.
- All components of the quetiapine assay contain less than 0.1% sodium azide. Avoid contact with skin and mucous membranes. Flush affected areas with copious amounts of water. Seek immediate medical attention if reagents are ingested or come into contact with eyes. When disposing of such reagents, always flush with large amounts of water to prevent accumulation of azide.
- The Safety Data Sheet (SDS) is available at https://www.saladax.com/bci_applications/

REAGENT HANDLING

The quetiapine assay reagents are ready to use.

Mix the reagents (R1 and R2) by gently inverting five times, avoiding the formation of bubbles then place them on the analyzer.

STORAGE AND STABILITY

Store reagents refrigerated at 2 - 8°C. Do not freeze.

When stored and handled as directed unopened reagents are stable until the expiration date on the label. Improper storage of reagents can affect assay performance.

SPECIMEN COLLECTION AND HANDLING

Serum is required. Do not use serum separator tubes.

Trough or C_{min} samples at steady state have been recommended for testing antipsychotics.[5] After one week of treatment on the same dose, collect samples before the next dose.[6]

Prepare serum within 3 days of blood collection. Blood and serum samples may be stored at room temperature or 2 - 8°C. Store serum for up to 7 days before measuring. Freeze (≤ -20°C) for longer storage. Avoid repeated freezing and thawing of samples.

PROCEDURE

Assay

To run the assay, see the instrument specific application sheet and appropriate analyzer operator's manual.

Materials Provided:

REF C82917 – Psychiatry Quetiapine Assay Kit

Materials Required – Provided Separately:

REF C82911 – Psychiatry Calibrator Kit 2

REF C82912 – Psychiatry Control Kit 2

Calibration

Perform a full calibration using the six calibrators in the Calibrator Kit 2. Verify the calibration by testing the low, medium, and high controls in the Control Kit 2.

Calibration Frequency - Calibration is recommended:

- After a reagent kit lot change,
- After performance of major instrument maintenance,
- As required following quality control procedures.

Quality Control (QC)

Each laboratory should establish its own QC procedures for the quetiapine assay kit. All quality control requirements and testing should be performed in accordance with local, state and/or federal regulations or accreditation requirements. Good laboratory practice suggests that at least two QC concentrations be tested each day patient samples are measured, and each time calibration is performed. Ensure that the quality control results meet the acceptance criteria before reporting patient results.

Specimen Dilution Procedure

Samples containing quetiapine in concentrations greater than 700 ng/mL can be diluted 1:3 (1-part sample plus two parts water) to give an upper range of 2,100 ng/mL. Refer to the instrument specific operation manual for an automatic dilution protocol (by cuvette only) of quetiapine samples with water. Alternatively, specimens out of range can be manually diluted 1:2 or 1:3 with deionized water and placed in the sample rack for analysis.

RESULTS

The concentration result is automatically calculated from the non-linear calibration curve by the analyzer. Report results in ng/mL or nmol/L. The conversion factor from ng/mL is 2.61 x ng/mL = 1 nmol/L.

This assay should only be used in conjunction with other clinical and laboratory findings and results from this test alone should not be used to make treatment decisions.

Consider obtaining assay results before patient consultation.

If assay results are not yet available, treatment decisions should be based upon best clinical judgment at the time the patient is evaluated based on other clinical and laboratory findings.

LIMITATIONS OF THE PROCEDURE

The quetiapine assay has been validated for serum. Do not use serum separator tubes.

As with any assay utilizing mouse antibodies, the possibility exists for interference by human anti-mouse antibodies (HAMA) in the sample. Samples containing such antibodies can potentially produce erroneous quetiapine results, which are inconsistent with the patient's clinical profile.

For samples containing 100 ng/mL quetiapine, addition of amoxapine (500 ng/mL), clotiapine (100 ng/mL), loxapine (150 ng/mL) or zolpidem (5,000) caused assay biases of ≥ 19%. Elevated levels of quetiapine may be seen in patients administered amoxapine, clotiapine, loxapine or zolpidem.

EXPECTED VALUES

The therapeutic range for quetiapine in serum is not fully established. A therapeutic range from 100 to 500 ng/mL has been proposed.[5] Measured concentrations for adherent patients at steady-state are expected to be in the measuring range of the assay. Therapeutic drug monitoring of quetiapine has been recommended because of high interpatient variability, unpredictable response, and the importance of adherence for successful therapy.[5] The complexity of the clinical state, individual differences in sensitivity, and co-administered medications may contribute to different requirements for optimal quetiapine blood levels. Users should investigate the transferability of the expected values to their own patient population and if necessary, determine their own reference range. For diagnostic purposes, the test findings should always be assessed in conjunction with the patient's medical history, clinical examinations, and other findings. Clinicians should carefully monitor patients during therapy initiation and dose adjustments. It may be necessary to obtain multiple samples to determine expected variation of optimal (steady-state) concentrations for individual patients.

SPECIFIC PERFORMANCE DATA

Typical performance data for the quetiapine assay obtained on a Beckman Coulter AU480 are shown below. Results obtained in individual laboratories may differ from these data.

Precision

Within-laboratory precision and repeatability were verified throughout the measuring range according to CLSI Guideline EP05-A3.[7] Three Control Kit 2 controls, two total quetiapine spiked pools (Serum 1, 2) and two pools of clinical samples (Clinical 1, 2) were tested.

Sample	N	Mean (ng/mL)	Repeatability	Within-Laboratory
			CV	CV
Control 1	80	59	3.4%	7.4%
Control 2	80	317	1.3%	3.7%
Control 3	80	574	1.5%	3.7%
Serum 1	80	51	3.0%	7.9%
Serum 2	80	1002	1.6%	4.6%
Clinical 1	80	91	2.3%	5.6%
Clinical 2	80	506	1.7%	3.5%

Limit of Quantitation (LoQ) and Limit of Detection (LoD)

The lower limits of quantitation and detection were established using CLSI guideline EP17-A2.[8]

LoQ

The LoQ was determined with an accuracy goal at the LoQ of ≤ 35% total error (Westgard model). The LoQ of the quetiapine assay is 34 ng/mL.

LoD

The LoD is the lowest amount of analyte that can be reliably detected (≥ 95% of results greater than the limit of blank.). The LoD of the quetiapine assay is 10 ng/mL.

Measurement Range

The measurement range of the quetiapine assay is 34 – 700 ng/mL.

Specificity

Metabolism

Quetiapine is extensively metabolized by the liver. Metabolic pathways of quetiapine include sulfoxidation (quetiapine sulfoxide), N-dealkylation (N-desalkylquetiapine, O-desalkylquetiapine), and 7-hydroxylation (7-hydroxyquetiapine).[9] N-desalkylquetiapine, also known as nor-quetiapine, is quetiapine's major active metabolite.[10] Norquetiapine is further metabolized to N-desalkylquetiapine sulfoxide, 7-hydroxy-N-desalkylquetiapine and an unidentified molecule. The metabolite 7-hydroxy-N-desalkylquetiapine also has pharmacological activity.[11]

Interfering Substances

Testing of interferents was conducted according to CLSI guideline EP7-A2.[12] No significant assay bias was observed from samples with the following endogenous interferents at the given levels:

Interferent	Level	
Rheumatoid Factor	508 IU/mL	
Total Protein Matrix Effect	12.7 g/dL	127 g/L
Icteric Interference	18.32 mg/dL	313 µmol/L
Lipemic Interference	662 mg/dL	7.5 mmol/L
Hemolysate	210 mg/dL	

Specificity for the following cross-reactants was tested in the absence and presence of quetiapine at 100 and 500 ng/mL.

Cross-reactivity

Cross-reactivity was tested according to CLSI guideline EP7-A2.[12] The following compounds did not interfere with the quetiapine assay: assay bias was ≤ 8%.

Compound	Tested at (ng/mL)	Compound	Tested at (ng/mL)
Acetaminophen	200,000	Acetazolamide	60,000
Acetylsalicylic acid	500,000	Albuterol	1,000
Alendronate sodium	1,000	Alpha - tocopherol	40,000
Alprazolam	2,000	Amantadine Hydrochloride	10,000
Amikacin sulfate	100,000	Amiloride HCl dihydrate	500
Amisulpride	400	Amitriptyline	1,000
Amlodipine besylate	100	S (+)-amphetamine	1,000
Amoxicillin	80,000	Aripiprazole	500
L-ascorbic acid	60,000	Asenapine	500
Atomoxetine	5,000	Atorvastatin calcium	600
Baclofen	3,000	Benztropine	400
Betamethasone	100	Biotin	300
Biperiden	100	Blonanserin	100
Brexpiprazole	1,000	Bromperidol	100
Budesonide	50	Bupropion	3,000
Buspirone	200	Caffeine	60,000
Calcium carbonate	300,000	Cannabidiol	100
Cannabinol	100	Carbamazepine	30,000
Cariprazine	50	L-Carnosine	50,000
Cefalexin	200,000	Celecoxib	1,000
Cetirizine dihydrochloride	3,500	8-chloro-theophylline	3,000

Compound	Tested at (ng/mL)	Compound	Tested at (ng/mL)
Chlorpromazine HCl	2,500	Cimetidine	20,000
Ciprofloxacin	10,000	Citalopram HBr	750
Clindamycin	50,000	Clonazepam	150
Clotrimazole	50	Clozapine	1,000
Codeine	2,000	Cortisol	300
(-)-Cotinine	2,000	Cyclosporin A	9,000
Desloratadine	600	Desvenlafaxine	400
Dextro-methorphan	1,000	Diazepam	6,000
Diphenhydramine HCl	6,000	Divalproex Sodium	50,000
Docosahexaenoic acid ethyl ester	150,000	Donepezil	50,000
Doxycycline HCl	35,000	Droperidol	100
D-Serine	100,000	Duloxetine	200
Erythromycin	60,000	Escitalopram	100
Eszopiclone	200	Ethanol	4,000,000
Famotidine	600	Fenofibrate	50,000
Fentanyl	600	Fluoxetine HCl	4,000
Fluticasone propionate	1	Fluvoxamine	2,000
Folic acid	15	Furosemide	60,000
Galantamine	100	Gentamicin sulfate	30,000
Glyburide	2,000	Haloperidol	1,000
Heparin sodium salt	50 U/mL	Hydro-chlorothiazide	6,000

Compound	Tested at (ng/mL)	Compound	Tested at (ng/mL)
Hyoscine (Scopolamine HBr)	100	Ibuprofen	500,000
Iloperidone	10	Imipramine	700
Indinavir sulfate	400	Lactulose	10,000
Lamivudine	2000	Lamotrigine	15,000
Lansoprazole	1,000	Lisinopril dihydrate	350
Lithium carbonate	250,000	Lorazepam	1,000
Lovastatin	500	Lurasidone	100
Meclizine dihydrochloride	500	Metformin	40,000
Methotrimeprazine	200	Methylphenidate HCl	350
Metoclopramide HCl	500	Metoprolol tartrate	5,000
Metronidazole	120,000	Midazolam	1,000
Milnacipran	10,000	Mirtazapine	300
Mometasone furoate	50	Morphine	500
Naltrexone	50	Naproxen sodium	500,000
Nateglinide	20,000	Nefazodone HCl	3,500
Nicotinic acid	20,000	Nordiazepam	5,000
Nortriptyline	1,000	Olanzapine	300
Omeprazole	6,000	Oxazepam	5,000
Oxcarbazepine	35,000	Oxycodone	500
Paliperidone	60	Pantothenic acid	150
Paroxetine	1,000	Penicillin V	6,000
Perazine	1,000	Perlapine	150
Perphenazine	100	Phenobarbital	50,000
Phentermine	500	Phenytoin	50,000
Pimozide	20	Pipamperone dihydrochloride	400

Compound	Tested at (ng/mL)	Compound	Tested at (ng/mL)
Potassium EDTA	1000	Pravastatin sodium	150
Prednisolone	3,000	Pregabalin	5,000
Procyclidine	1,000	Promethazine	1,200
R,R-(-)-pseudoephedrine	10,000	S,S-(+)-pseudoephedrine	10,000
Pyridoxine HCl	100	Quinidine	12,000
Raloxifene	50	Ranitidine	6,000
Retinol	4,000	Riboflavin	200
Rifampicin	65,000	Risperidone	60
Rosuvastatin calcium	50	Salicylic acid	500,000
Sarcosine	1,000	Sertindole	50
Sertraline hydrochloride	600	Simvastatin	30
Sodium benzoate	400,000	Sodium fluoride	150
Spironolactone	600	Sulfamethoxazole	400,000
Sulpiride	50,000	Temazepam	5,000
Theophylline	40,000	Thiamine HCl	50
Topiramate	10,000	Trazodone HCl	6,000
Triamcinolone acetonide	10	Triamterene	9,000
Triazolam	40	Valproic acid	500,000
Vancomycin HCl	100,000	Varenicline	50
Venlafaxine HCl	400	Vitamin B12	50
Vitamin D2	40	Vitamin K1	50
Warfarin	10,000	Ziprasidone	200
Zonisamide	40,000	Zopiclone	100
Zuclopenthixol	250		

Recovery

The recovery of total quetiapine was assessed in the 3 controls, two spiked serum pools and two clinical pools measured for the EP05-A3 precision performance study. The percent recovery was determined by dividing the mean measured concentration of each sample by the expected concentration of quetiapine. The mean percent recoveries were all within 78% to 105%.

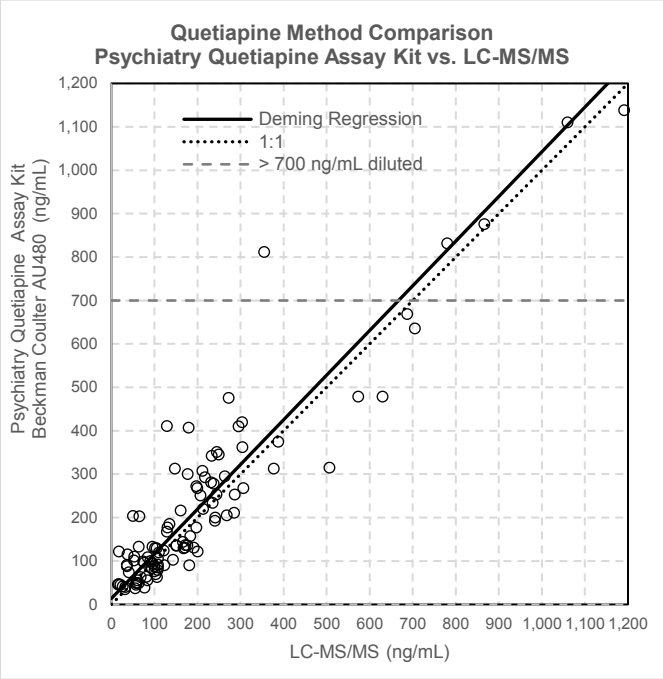
Linearity

The linearity of the quetiapine assay was verified according to CLSI guideline EP6-A.[13] Eleven linearity samples covering the measuring range were prepared in human serum spiked with quetiapine. Deviation from linearity (n=5) was ≤ 12%. The assay was linear across the measuring range from 34 – 700 ng/mL.

Method Comparison

Results of the quetiapine assay were compared to a validated LC-MS/MS according to CLSI guideline EP09-A3.[14] Deming regression analysis was performed with 103 patient samples. Patient samples above the test range of the quetiapine assay kit were diluted as described under Specimen Dilution Procedure. Results are shown for one lot.

Deming Regression Statistics Psychiatry Quetiapine Assay vs. LC-MS/MS	
Slope	1.03
Intercept	13.55
Correlation Coefficient (R)	0.92
N	103
Concentration Range (LC-MS/MS)	16 – 1192 ng/mL



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SYMBOLS USED

IVD	*in vitro* Diagnostic Device		Consult Instructions for Use
REF	Catalog Number		Use By
LOT	Batch Code		Temperature Limitation
	Manufacturer	**Rx only**	For Prescription Use Only
R1 R2	Reagent 1 Reagent 2	 (N) x	Gently invert reagents (R1 and R2) N number of times prior to use
CE	CE mark	EC REP	Authorized Representative in the European Community
Made in USA	Made in USA	UK CA	UK Mark

For technical assistance:

Contact the Customer Technical Support Center at 1-800-854-3633 (USA & Canada).

In other countries, please contact your local Beckman Coulter representative.

ADDITIONAL INFORMATION

For more detailed information on AU Systems, refer to the appropriate system manual. Since Beckman Coulter does not manufacture the reagent or perform quality control or other tests on individual lots, Beckman Coulter cannot be responsible for the quality of the data obtained which is caused by performance of the reagent, any variation between lots of reagent, or protocol changes by the manufacturer.

SHIPPING DAMAGE

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