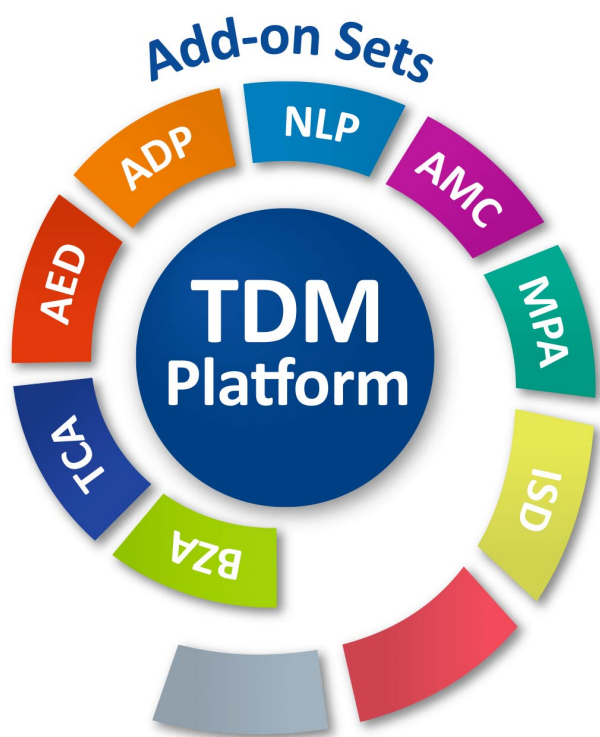# +RECIPE

Antiepileptic Drugs in Serum/Plasma

Antiepileptic Drugs

The "ClinMass® TDM Kit System is based on a universal TDM Platform (order no. MS9000), which can be used with various Add-on Sets for the Therapeutic Drug Monitoring (TDM).

The ClinMass® Add-on Set for Antiepileptic Drugs (order no. MS9200) is intended for the determination of antiepileptic drugs from human serum or plasma.

+ Identification of steady-state conditions
+ monitoring of parent compound/active metabolites

Therapeutic Drug Monitoring (TDM)

Increasing recommendation in
+ conditions with a small therapeutic range
+ optimisation of a personalised pharmaco-therapy
+ monitoring the effective therapy regime
+ detection of drug/drug interactions
+ toxicity avoidance
+ monitoring of patient's compliance

Please note:
The use of the RECIPE Kit System requires an LC system with tandem mass spectrometer (LC-MS/MS) with sufficient sensitivity and evaluation software.

Clinical Background

Epilepsy is a chronic neurological disorder, characterised by recurrent epileptic seizures. The frequency and the rhythm of seizures are hardly predictable. Therefore, seizures are not only a considerable psychological and physical burden for the patient, they may also lead to grave and even life-threatening hurts (e.g. craniocerebral injuries in case of falls). Brain damages may result in case of a hypoxia. Today, a variety of antiepileptic drugs (AEDs) with different pharmacological properties is available.

Therapeutic drug monitoring (TDM) is the clinical laboratory practice to determine drug concentrations in blood to optimise a personalised pharmacotherapy, especially in indications with a small therapeutic range. Drug interactions, efficacy, toxicity avoidance and the surveillance of compliance are typical indications where TDM is requested.

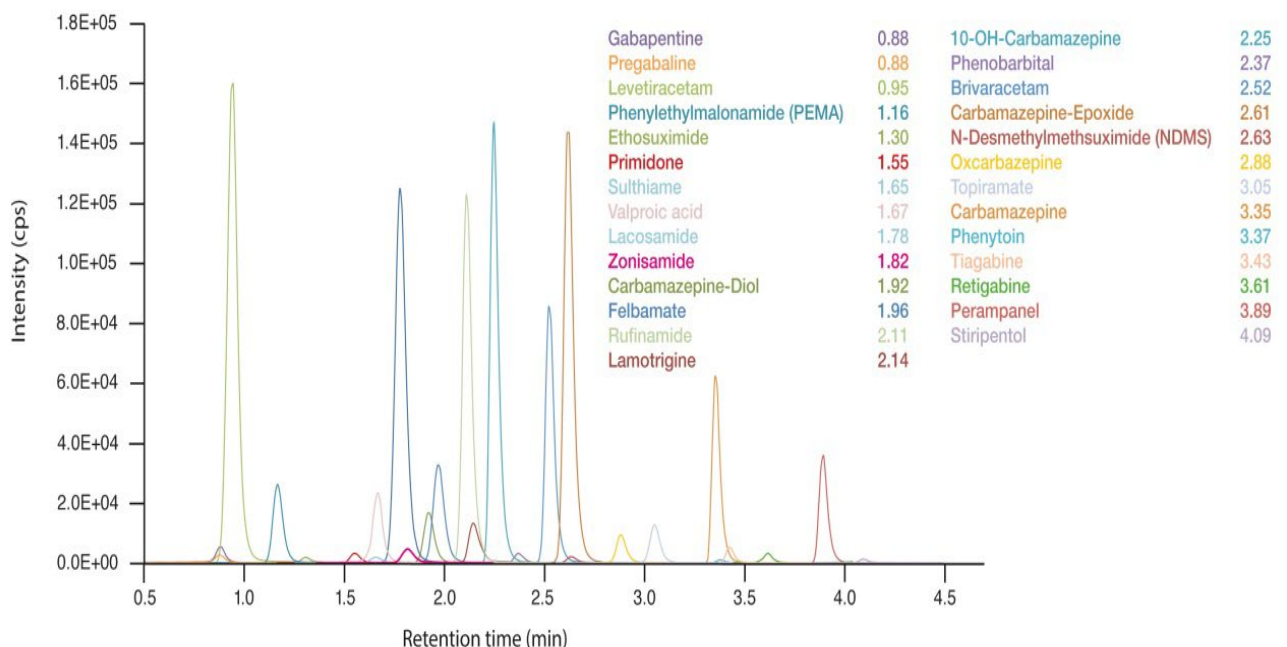**The RECIPE analytical method provides the reliable quantification of 27 AEDs.**

Compound	RT	Compound	RT
Gabapentine	0.88	10-OH-Carbamazepine	2.25
Pregabaline	0.88	Phenobarbital	2.37
Levetiracetam	0.95	Brivaracetam	2.52
Phenylethylmalonamide (PEMA)	1.16	Carbamazepine-Epoxide	2.61
Ethosuximide	1.30	N-Desmethylmethsuximide (NDMS)	2.63
Primidone	1.55	Oxcarbazepine	2.88
Sulthiame	1.65	Topiramate	3.05
Valproic acid	1.67	Carbamazepine	3.35
Lacosamide	1.78	Phenytoin	3.37
Zonisamide	1.82	Tiagabine	3.43
Carbamazepine-Diol	1.92	Retigabine	3.61
Felbamate	1.96	Perampanel	3.89
Rufinamide	2.11	Stiripentol	4.09
Lamotrigine	2.14		

Figure 1 *Chromatogram of the ClinCal® Serum Calibrator (order no. MS9213), level 2*

Method Performance

The interassay precision of the method was determined with samples at two concentration levels. The samples were prepared by different persons on eight different days and measured on several systems from different manufacturers (for data from a specific system please contact info@recipe.de). The analyte concentrations were selected according to the respective therapeutic reference range and are contained in Table 2 together with the precision results.

Analyte	Concentration [mg/l]		Intraassay Precision [%]		Interassay Precision [%]	
	Level		Level		Level	
	I	II	I	II	I	II
10-OH-Carbamazepine	2.80	42.9	2.3	3.1	8.3	2.9
Brivaracetam	0.300	4.25	1.7	2.9	4.6	5.9
Carbamazepine	2.66	16.4	2.1	2.0	4.8	5.7
Carbamazepine-Diol	0.889	5.20	1.8	1.7	10.3	10.6
Carbamazepine-Epoxide	1.40	8.27	1.5	2.3	11.6	10.7
Ethosuximide	19.0	93.6	3.2	3.8	5.9	5.8
Felbamate	19.6	45.8	2.1	2.0	5.0	9.2
Gabapentine	1.87	27.8	5.2	2.7	8.4	3.2
Lacosamide	3.91	11.2	0.8	2.2	5.0	4.0
Lamotrigine	2.92	13.9	1.2	2.6	5.9	2.7
Levetiracetam	9.54	23.5	0.7	1.9	5.1	7.2
NDMS	9.48	53.6	3.3	1.3	9.0	7.9
Oxcarbazepine	1.43	5.97	6.6	4.4	8.8	9.8
PEMA	4.63	25.7	2.2	1.8	3.4	4.5
Perampanel	0.0974	1.46	2.8	3.2	9.1	8.5
Phenobarbital	9.17	53.0	2.1	1.5	4.4	4.6
Phenytoine	1.94	28.3	3.5	6.6	4.2	3.3
Pregabaline	1.83	6.16	1.6	2.2	8.8	5.0
Primidone	4.39	25.1	4.5	2.2	2.2	5.5
Retigabine	0.514	0.969	1.2	2.4	4.3	5.1
Rufinamide	3.11	47.4	2.1	4.0	8.3	6.1
Stiripentol	3.85	10.9	2.3	2.9	7.6	9.3
Sulthiame	0.946	12.7	4.5	3.6	8.3	5.9
Tiagabine	47.0	132	1.6	2.2	6.7	6.9
Topiramate	2.79	8.93	1.5	2.6	8.7	7.5
Valproic acid	21.3	125	2.4	1.2	5.0	7.7
Zonisamide	9.49	21.7	2.4	1.7	6.8	7.8

Table 2. Method Performance/Precision data

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Reference ranges

The following reference ranges are taken from the „ Consensus Guidelines for Therapeutic Drug Monitoring in Neuropsychopharmacology: Update 2017"

Analyte	Therapeutic Range [mg/l]	Laboratory Alert Level[†] [mg/l]
Brivaracetam	0.5–0.9	1.8
Oxcarbazepine plus 10-OH-Carbamazepine	10–35	40
Carbamazepine	Mood stabilizing drug: 4–10 Anticonvulsant: 4–12	Mood stabilizing drug: 20 Anticonvulsant: 20
Carbamazepine-Diol	n.a.	n.a.
Carbamazepine-Epoxide	n.a.	n.a.
Ethosuximide	40–100	120
Felbamate	30–80	100
Gabapentine	2–20	25
Lacosamide	1–10	20
Lamotrigine	Mood stabilizing drug: 1–6 Anticonvulsant: 3–15	Mood stabilizing drug: 20 Anticonvulsant: 20
Levetiracetam	10–40	50
Methsuximid plus NDMS	10–40	45
PEMA	n.a.	n.a.
Perampanel	0.18–0.98	1
Phenobarbital	10–40	50
Phenytoin	10–20	25
Pregabaline	Anticonvulsant: 2–5 Anxiolytic: 2–5	Anticonvulsant: 10 Anxiolytic: 10
Primidone	5–10	25
Retigabine	0.45–0.90	1.8
Rufinamide	5–30	40
Stiripentol	1–10	15
Sulthiame	2–8	12
Tiagabine	0.02–0.2	0.3
Topiramate	2–10	16
Valproic acid	Mood stabilizing drug: 50–100 Anticonvulsant: 50–100	Mood stabilizing drug: 120 Anticonvulsant: 120
Zonisamide	10–40	40

Table 3: Reference ranges n.a.: not available; [†]at values above the „Alert level" the physician in charge should be informed immediately

The indicated reference ranges are taken from thoroughly selected and current scientific literature. Their actuality corresponds to the printing date of this document. Please note that these ranges do not reflect any recommendations by the manufacturer of this product, but may be used as a guideline for the assessment of the reference range by the clinical laboratory.

Conclusion

The RECIPE 200 TDM Kit

- ✓ **improves the individual therapeutic regimen for the patient**

- ✓ **adopts fast growing medical need by regular addition of new drug classes**

- ✓ **is validated, no new validation is necessary**

- ✓ **offers you a flexible expansion of the add-on sets**

+RECIPE

Chemicals + Instruments GmbH
Dessauerstr. 3
80992 München

Mail: info@recipe.de