**Introduction:**

Amitryptilline is a tricyclic antideprepressant drug which acts by preventing serotonin and noradrenaline from being reabsorbed back into the nerve cells in the brain. Thus, the effect of the released noradrenaline and serotonin are prolonged which minimises depressive state.

**Indications:** Commonly used in treatment of depression, neuropathic pain, chronic pain, obsessive compulsive disorder, anxiety and panic disorder. Other possible uses may include migraine prophylaxis, treatment of attention deficit/ hyperactivity disorder (ADHD), nocturnal enuresis, adjunctive therapy for smoking cessation.

**Pharmacodynamics/kinetics**

Amitryptillene is rapidly absorbed following ingestion of therapeutic dosages and reach peak concentrations within 2-8 hrs.

Distribution: Vd: 18-22L/kg, Crosses placenta; enters breast milk

Protein binding: 90%-97%

Metabolism: Hepatic to Nortriptyline (active), hydroxy and conjugated derivatives; may be impaired in the elderly; significant 1st pass effect.

Half-life elimination: Adults: 9-27 hours (average: 15 hours)

Time to peak, serum: ~4 hours

Excretion: Urine (18% as unchanged drug); feces (small amounts)

**Therapeutic and toxic levels:**

Therapeutic levels: 100-250 ng/ml (SI: 360-900nMol/L)

Toxic levels: >0.5 mcg/ml. Plasma levels do not always correlate with clinical effectiveness.

**Assay Parameters:**

Sample:

1 mL serum or plasma (0.5 mL minimum)

Container:

One 7ml plain red (min 3ml), or lavender (EDTA), pink (K2EDTA), green (sodium heparin), or gray (sodium fluoride/potassium oxalate)

Collection:

Specimens should be drawn at steady state, after the third maintenance dose. Serum or plasma should be separated from cells as soon as possible and refrigerated.

Trough: Collect 30 minutes prior to next dose. If dosing by the older conventional regimen, peak levels are drawn 30 minutes following completion of 30-minute infusion or 1 hour following initiation of infusion or I.M. injection.

Storage Instructions:

Refrigerate. For prolonged transport, separate serum or plasma from cells and freeze within 1 hour of collection.

**Analytical methods:**

Commercial reagent-based techniques represent the primary methodology for the analysis of amikacin such as serum high performance liquid chromatography (HPLC).

**HPLC:**

Because results will vary depending on whether the assay is done on whole blood or serum/plasma, and on the method and cyclosporine antibody employed (monospecific or polyspecific), it is best for a given patient's specimens to be analyzed at a single laboratory to eliminate as many assay-dependent variables as possible. If switching of laboratories is unavoidable, it is advisable to have a few specimens run in parallel in the second laboratory prior to changing. HPLC is a preferred method as it measures parent drug and is independent of metabolite interferences.

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**Conclusion:**

The unpredictable relationship between dose and Amitriptylene concentration, its narrow therapeutic index and the presence of numerous clinically significant drug interactions support the need to individualize and maintain therapy using TDM.

**References:**

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