06 - Target ranges

Target ranges

Pharmacokinetics CHAPTER 11 Interpretation of results Is there a target range of plasma levels? If so, then plasma levels (from samples taken at the right time) will usefully guide dosing. If there is not an accepted target range, plasma levels can only indicate adherence or potential toxicity. However, if the sample is being used to check compliance, then bear in mind that a plasma level of zero indicates only that the drug has not been taken in the past several days. Plasma levels above zero may indicate erratic compliance, full compliance or even long-standing non-compliance disguised by recent taking of prescribed doses. Note also that target ranges have their limitations – patients may respond to lower levels than the quoted range and tolerate levels above the range. Also, ranges quoted by different laboratories vary sometimes widely, often without explanation. This is discussed further later. The basic rule for sample level interpretation is to act upon assay results only in conjunction with reliable clinical observation (‘treat the patient, not the level’). For example, if a patient is responding adequately to a drug but has a plasma level below the accepted target range, then the dose should not normally be increased. If a patient has intolerable adverse effects but a plasma level within the target range, then a dose decrease may be appropriate. Where a plasma level result is substantially different from previous results, a repeat sample is usually advised. Check the dose, the timing of dose and recent compliance but ensure, in particular, the correct timing of the sample, or at the very least that the timing of sampling is known. Many anomalous results are the consequence of changes in sample timing. Target ranges In psychiatry, target ranges for psychotropic drug concentrations should be treated with some caution. Establishing a range of concentrations associated with response is made difficult by the presence in trials of non-responders (who show no response whatever the blood concentration) and by the presence of placebo responders and spontaneous remitters (who respond at any blood concentration). Establishing a target range based on adverse effects is made difficult by the development of tolerance over time. Thus, most studies aimed at determining target ranges have as much ‘noise’ as ‘signal’ and results ultimately represent broad approximations. Interestingly, drug concentrations associated with response in clinical practice show a fairly close correlation to published target ranges.2 The lower quartile (25th percentile) of drug concentrations is usually close to the lower end of the target range and the upper quartile (75th percentile) is around the value of, but usually less than, the upper limit. Broadly speaking, this means that around 25% of patients respond below the target range and up to 25% tolerate blood concentrations above the target range. The simplicity of published target ranges disguises considerable complexity. For most drugs, the concentration at which therapeutic activity appears is fairly constant across a population. This is called the therapeutic threshold – above it, full effect is seen, but below it, activity is lost. A good example here is risperidone where the threshold concentration of active

moiety is 20mcg/L. Risperidone and paliperidone could reasonably be considered to have a target concentration rather than a target range of

868 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 11 concentrations. This concept of a therapeutic threshold is supported by neuroimaging studies. A concentration of 20mcg/L of active moiety is associated with a dopamine occupancy of 65–70%3 – the degree of pharmacological activity associated with response for most antipsychotics.4 Increasing dopamine occupancy above this level does not improve efficacy or likelihood of response but does make adverse effects more likely.3 Clozapine is completely different. For clozapine, the target range represents concentrations usually associated with both response and good tolerability. However, perhaps 10% of responders will improve with clozapine concentrations below the target range and as many as 20% of responders will only respond at concentrations above the target range. There is also a so-called point of futility – the concentration above which no additional responders will be uncovered. Responders to clozapine will have blood concentrations between 250 and 1000mcg/L5 – a much wider range than the accepted target range. Unlike risperidone and many other drugs, the threshold concentration is not fixed across populations. This subject is eloquently covered in much more detail in The Clinical Use of Antipsychotic Plasma Levels by Jonathan Meyer and Stephen Stahl (Cambridge University Press, 2021). Table 11.1 discusses the interpretation of sample results for various drugs. Table 11.1 Interpreting sample results for drugs with established target ranges. Drug Target range Sample timing Time to steady state Comments Amisulpride 200–320mcg/L 20–60mcg/L (elderly) Trough 3 days See text Aripiprazole 100–210mcg/L Trough 15–16 days See text Carbamazepine6–8

> 7mg/L Bipolar disorder Trough 2 weeks Carbamazepine induces its own metabolism. Time to steady state dependent on auto-induction Clozapine 350–600mcg/L Trough 2–3 days See text Lamotrigine9–11 Not established but suggest 2.5–15mg/L Trough 5 days Auto-induction is thought to occur, so time to steady state may be longer Some debate over utility of lamotrigine levels, especially in bipolar disorder. In treatment- resistant unipolar depression, plasma levels of above 12.7µmol/L (3.3mg/L) are associated with response.12,13 Toxicity may be increased above 15mg/L but is normally well tolerated Lithium14–18 0.6–1.0mmol/L (0.4mmol may be sufficient for some patients/indications; 1.0mmol/L required for mania) 12 hours 5 days post-dose Well-established target range, albeit derived from ancient data sources. A fairly recent study19 suggested 0.6mmol/L was the minimum level for a prophylactic effect

Revision #1
Created 2026-01-04 20:18:06 UTC by Omar Ayman
Updated 2026-01-04 20:18:06 UTC by Omar Ayman