234 - Dosing

Dosing

Schizophrenia and related psychoses CHAPTER 1 ■ ■Echocardiogram if clinically indicated. ■ ■Consider work-up for BEN where baseline neutrophil counts are low (see section on clozapine, neutropenia and lithium in this chapter). Genetic testing for BEN is also available (see section on clozapine: genetic testing for clozapine treatment in this chapter). Mandatory blood monitoring and registration ■ ■Register with the relevant monitoring service. ■ ■Perform baseline blood tests (white cell and differential counts) before starting clozapine. ■ ■Further blood testing continues weekly for the first 18 weeks and then every 2 weeks for the remainder of the year. After that, the blood monitoring is usually done monthly. ■ ■Inform the patient's GP. Dosing Starting clozapine in the community requires a slow and flexible titration schedule. Prior antipsychotics should be slowly discontinued during the titration phase (depots can usually be stopped at the start of titration). Clozapine can, of course, cause marked postural hypotension. The initial monitoring is partly aimed at detecting and managing this, partly at ensuring sedative effects are manageable. There are two approaches to giving the first dose of clozapine in the community. One is to give the first dose in the morning in clinic and then monitor the patient for postural hypotension for at least 1 hour. If the dose is well tolerated, the patient is then allowed home with a dose to take before going to bed. The second approach involves giving the patient the first dose to take immediately before bed, thereby avoiding the need for close physical monitoring immediately after administration. All initiations should take place early in the week (e.g. on a Monday) so that adequate staffing and monitoring are assured. Unless there are significant concerns regarding tolerability (e.g. postural hypotension), the 1-hour monitoring for morning doses in clinic can be omitted. Previous guidelines2,3 recommended physical observations on 5 days/week during weeks one and two of community clozapine initiations, followed by 3 days/week for weeks three and four. A 2023 study showed that this frequency can be reduced when using a slower titration schedule.4 Example titration schedules for these two protocols are shown in Table 1.55. These dose increase schedules are examples and may need to be adjusted based on tolerability and target dose. Additional reviews may be necessary to manage adverse effects. The low-frequency monitoring (on the left of the table) is suitable for most patients and even lower frequency of monitoring may be feasible in some patients (e.g. re-titration of clozapine where the patient tolerated it well previously). The standard monitoring frequency is recommended for patients who may be more sensitive to adverse effects (e.g. female non-smokers) or who may struggle to adhere to frequent dose adjustments. The two protocols do not differ in the frequency of physical monitoring after week four (i.e. both reduce to once a week). As with in-patient initiation, estimating the target dose for each individual patient is recommended before starting clozapine. This gives some idea of the likely duration of the titration schedule. Genetic testing appears to be the most accurate method of

predicting an effective dose.5

238 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 Table 1.55 Suggested titration regimens for initiation of clozapine in the community. Day Low-frequency monitoring Morning dose (mg) Evening dose (mg) Standard- frequency monitoring Morning dose (mg) Evening dose (mg) Approximate percentage dose of previous antipsychotic Mon #* 6.25 Mon #* 6.25 6.25 2 Tue 12.5 Tue # 6.25 12.5 Wed # 6.25 12.5 Wed # 12.5 12.5 Thu 6.25 Thu # 12.5 5 Fri # 12.5 Fri # 25 Sat 12.5 Sat 25 Sun 12.5 37.5 Sun 50 Mon #* 37.5 Mon #* 50 9 Tue 50 Tue # 50 Wed # 62.5 Wed # 50 Thu 75 Thu # 75 Fri # 37.5 Fri # 75 Sat 37.5 Sat 75 Sun 37.5 87.5 Sun 75 Mon #* 87.5 Mon #* 100 16 Tue 100 Tue 100 Wed 125 Wed # 125 Thu # 125 Thu 125 Fri 125 Fri # 150 Sat 125 Sat 150 Sun 150 Sun 150 Mon #* 150 Mon #* 175 23 Tue 150 Tue 175 Wed 150 Wed 200 Thu # 150 Thu # 200 Fri 150 Fri 225 Sat 150 Sat 225 Sun 175 Sun 225 Further increments should be 25–50mg/day (generally 25mg/day) until target dose is reached (use plasma levels). Beware of sudden increase in plasma levels due to saturation of first-pass metabolism (watch for increase in sedation/other adverse effects). # Face-to-face assessments including physical observations (sitting and standing blood pressure, heart rate, oxygen saturation, temperature and respiratory rate), adverse effect and mental state review, actively manage adverse effects (e.g. behavioural advice, slow clozapine titration or reduce dose of other antipsychotic, start adjunctive treatments – see sections on clozapine adverse effects in this chapter). * Full blood count; also consider C-reactive protein, CK, troponin, beta-natriuretic peptide.

Revision #1
Created 2026-01-04 20:13:21 UTC by Omar Ayman
Updated 2026-01-04 20:13:21 UTC by Omar Ayman