

225 - Summary of alternatives to clozapine

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Schizophrenia and related psychoses CHAPTER 1 Summary of alternatives to clozapine Table 1.54 provides a summary of alternatives to clozapine in refractory schizophrenia. Table 1.54 Summary of alternatives to clozapine in refractory schizophrenia. Treatment Examples Comments Strength of evidence Monotherapy using non-clozapine antipsychotics in standard or high doses Aripiprazole 15–30mg daily Olanzapine 25–60mg daily Evidence of efficacy for any antipsychotic other than clozapine in refractory schizophrenia is controversial. Some data suggest efficacy for olanzapine above licensed doses but at the risk of metabolic adverse effects. Weak + Non-clozapine antipsychotic polypharmacy Amisulpride + olanzapine, quetiapine + amisulpride, aripiprazole + olanzapine, and various other combinations Polypharmacy is common in clinical practice. Evidence from controlled studies limited but open studies and real-world data suggest some effectiveness. Burden of adverse effects is increased. Weak + Anti-inflammatory agents as adjuncts to antipsychotics N-acetylcysteine, NSAIDs, minocycline, oestrogens, aspirin, omega-3 fatty acids A heterogeneous group of medicinal agents with inflammatory properties have been tried as adjuncts. Possible benefits in negative and cognitive symptoms but sample sizes have been small. Very weak ± NMDA receptor modulators as adjuncts Memantine, glycine, D-serine and sarcosine Rarely used in clinical practice. May have some benefit in negative symptoms. Very weak ± Treatment Comments Transcranial magnetic stimulation^{95,96} Conflicting results Ursodeoxycholic acid⁹⁷ Single case reports Valproate⁹⁸ Doubtful effect but may be useful where there is a clear affective component Yokukansan (+ antipsychotic)⁹⁹ Japanese herbal medicine, partial agonist at D2 and 5HT1A, antagonist at 5HT2A and glutamate receptors. Potential small benefit in excitement/hostility symptoms. Another 12-week double-blind placebo-controlled RCT showed modest symptomatic improvement.¹⁰⁰ Ziprasidone 80–160mg/day^{101–103} Two good RCTs. One¹⁰³ suggests superior efficacy to chlorpromazine in refractory schizophrenia, the other¹⁰¹ suggests equivalence to clozapine in subjects with treatment intolerance/resistance. Disappointing results in practice. Supratherapeutic doses offer no advantage.¹⁰⁴ Zotepine 300mg/day⁺¹⁰⁵ One study showed that some patients do not deteriorate when switched from clozapine to zotepine CGI, Clinical Global Impression; LAI, long-acting injection; NMDA, N-methyl-D-aspartate; PANSS, Positive and Negative Syndrome Scale; TRS, treatment-resistant schizophrenia; VTE, venous thromboembolism. Table 1.53 (Continued) (Continued)

Revision #1

Created 2026-01-04 20:13:18 UTC by Omar Ayman

Updated 2026-01-04 20:13:18 UTC by Omar Ayman