dehydration and acute kidney injury are present. Near-therapeutic serum lithium levels do not exclude clinically significant neurotoxicity. Early review of psychotropic medication and renal function is essential to prevent delayed diagnosis and avoidable morbidity.

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Improving Outcomes Best Practices for Pregabalin Withdrawal Management in Hospitals

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Aims: Pregabalin dependence and overuse are a major problem, with individuals often taking doses well above the licensed daily maximum of 600mg. Users frequently combine it with other substances, raising the risk of respiratory depression. The lack of guidance on managing withdrawal from high doses poses a significant challenge in hospital settings. Failure to treat acute withdrawal can lead to severe side effects, including seizures, and may result in patients prematurely discharging themselves.

This abstract reviews the limited guidance on assessing and treating pregabalin withdrawal in hospital settings, proposing a structured, evidence-based approach. Our hypothesis is that this approach can safely mitigate withdrawal symptoms and improve patient outcomes.

Methods: The assessment should include evaluating dependence severity and screening for co-existing substance use or mental health disorders. Clinicians should also review clinical notes for previous admissions and, with patient consent, speak with family members for insight into the patient's drug use. Contacting the local addiction service is important, especially if the patient is on opioid substitute treatment. Point of Care Testing for pregabalin and other drugs can be used, with a positive result supporting a decision to prescribe.

Results: When prescribing pregabalin, the reported dose and objective signs of withdrawal are key. For a reported daily dose of 300-600mg, prescribe 100mg three times daily. For doses over 600mg, an initial dose of 150mg three times daily is recommended, increasing to a maximum of 200mg three times daily if withdrawal persists. Due to common polysubstance use, prescribing diazepam 5mg four times daily is also often required.

Conclusion: Managing high-dose pregabalin withdrawal requires a cautious approach. Patients must be observed for sedation or respiratory depression. Referral to a Mental Health Liaison Service is crucial for advice on tapering and continuity of care. This approach facilitates safer withdrawal and improved outcomes.

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Expanding the Antipsychotic Arsenal: Drug Discovery for Schizophrenia via Virtual Screening and Ligand Optimization of FDA-Approved Drugs

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Aims: Schizophrenia affects 0.43% of global adults, with an estimated annual excess economic burden of $343.2 billion in the United States alone. The schizophrenia drug ecosystem is characterized by significant heterogeneity in patient responses, warranting continual drug discovery efforts to improve outcomes for patients responding suboptimally to existing treatments. Given the centrality of dopamine D2 receptor (DRD2) antagonism in current treatments, this study focused on (i) identifying strong DRD2 binders among Food and Drug Administration (FDA)-approved drugs as repurposing candidates and (ii) generating optimized variants of known antipsychotics as novel drug candidates.

Methods: We developed a computational drug discovery pipeline to score potential drug candidates based on DRD2 receptor binding affinity. Molecular docking scores were calculated by dockstring, a Python wrapper for AutoDock Vina, that automatically finds the best binding pose and returns its binding affinity to the receptor. Virtual screening was performed on:

1. ~1,600 FDA-approved drugs, with emphasis placed on central nervous system-active drugs known to permeate the blood-brain barrier.
2. 450 variant ligands of six reference antipsychotics (haloperidol, trifluoperazine, fluphenazine, chlorpromazine, thioridazine, and risperidone), generated using SwissSimilarity.

A molecular weight threshold of 500 Da was applied to exclude large ligands, consistent with Lipinski's Rule of 5 for oral bioavailability. Candidates achieving high binding affinity (≤-9.5 kcal/mol) were further evaluated against existing literature.

Results: Among FDA-approved drugs, risperidone achieved the lowest docking score and therefore the best binding affinity (-11.9 kcal/mol), validating our pipeline by recapitulating a known antipsychotic. Several candidates with high predicted binding affinities (≤-9.5 kcal/mol) were identified, with two of particular interest:

- Dolasetron. Other serotonin 5-HT3 receptor antagonists, especially ondansetron, have improved schizophrenic symptoms in previous studies, making this a promising line of investigation.
- Trazodone. A population-based cohort study published last year offered evidence that trazodone reduced risk of re-hospitalisation for delirium in older patients as compared to other antipsychotics.

Ligand optimization yielded 4 distinct molecules with superior binding affinities relative to their parent compounds. The best-performing variant achieved -13.6 kcal/mol (risperidone-derived), while the largest improvement was observed for thioridazine (-12.7 kcal/mol versus -8.5 kcal/mol original).

Conclusion: An automated DRD2-focused docking workflow can recover known antipsychotics, surface plausible repurposing candidates, and propose optimized variants with improved predicted binding. While these computational hits require further ADMET