

REVIEWER'S REPORT

Manuscript No.: IJAR-52081

Date: 05-06-2025

Title: Brexpiprazole augmentation on mirtazapine for treatment-resistant depression in an elderly patient

Recommendation:

Accept as it is.....**YES**.....
 Accept after minor revision.....
 Accept after major revision
 Do not accept (*Reasons below*)

Rating	Excel.	Good	Fair	Poor
Originality		√		
Techn. Quality		√		
Clarity		√		
Significance			√	

Reviewer's Name: Dr Aamina

Reviewer's Decision about Paper: **Recommended for Publication.**

Comments (*Use additional pages, if required*)

Reviewer's Comment / Report

1. Relevance and Significance

The manuscript addresses a clinically significant and challenging issue: treatment-resistant depression (TRD) in the elderly. The elderly population poses unique therapeutic concerns due to polypharmacy, pharmacokinetic variability, and increased vulnerability to side effects. Highlighting brexpiprazole augmentation in this demographic is both relevant and timely, as real-world data on such combination strategies remain limited.

2. Abstract

The abstract concisely outlines the clinical background, patient presentation, therapeutic approach, and outcome. It effectively introduces the rationale for combining brexpiprazole with

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mirtazapine and presents the clinical benefit observed. The summary successfully conveys the case's contribution to understanding pharmacological strategies in geriatric TRD, highlighting pharmacodynamic complementarity and favorable tolerability.

3. Introduction

The introduction provides a clear definition of TRD and contextualizes its prevalence and complexity, particularly in elderly patients. The cited prevalence rates and reference to standard pharmacologic and non-pharmacologic treatments establish a strong foundation. The discussion of brexpiprazole's pharmacological profile is accurate and clinically meaningful, emphasizing its role as an adjunctive treatment option with a favorable side effect profile.

4. Case Relevance and Clinical Context

Although the full clinical case details are not provided in the excerpt, the summary sufficiently outlines key elements: an elderly patient with recent-onset MDD, partial response to mirtazapine, and significant improvement upon brexpiprazole augmentation. The presentation of core symptoms—paranoid delusions, insomnia, weight loss, and social withdrawal—demonstrates the severity of the depressive episode and supports the classification as TRD. The use of brexpiprazole is appropriate in this context, and the observed response adds weight to its clinical utility in geriatric psychiatry.

5. Pharmacological Justification

The pharmacodynamic discussion of brexpiprazole is well-grounded in current psychopharmacological understanding. The description of its partial agonism at dopamine D2 and serotonin 5-HT_{1A} receptors, as well as antagonism at 5-HT_{2A} and α _{1B} receptors, underscores its potential benefit in modulating depressive symptoms while maintaining a favorable safety profile—particularly important in elderly patients.

6. Clarity and Structure

The structure of the document is logical and well-organized. The transition from defining TRD to discussing therapeutic approaches and finally introducing the specific case of brexpiprazole augmentation is coherent. The language is clear, and the clinical terminology is used appropriately, making the report accessible to both clinicians and researchers in psychiatry and geriatric medicine.

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7. Scholarly Merit

The case supports existing evidence on the efficacy of brexpiprazole in TRD while providing specific insight into its utility in older adults. The inclusion of current statistics and literature references lends credibility to the background discussion. The topic adds to the body of literature advocating for individualized pharmacological strategies in difficult-to-treat depressive cases, particularly within aging populations.

Verdict:

A well-conceived and clinically informative case study that contributes meaningfully to the literature on pharmacological management of treatment-resistant depression in the elderly. The documentation of brexpiprazole's efficacy and tolerability in combination with mirtazapine is particularly relevant for clinicians managing complex depressive presentations in geriatric patients.