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# Cariprazine and the Future of Mood and Psychotic Disorder Treatment

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## Introduction

Psychopharmacological advances in the field of medicine have led to treatments for the more complex psychiatric diseases like schizophrenia, bipolar disorder, and major depressive disorder (MDD). One of the latest products is cariprazine, a third-generation atypical antipsychotic with a novel molecular feature and vast therapeutic relevance. With its approval by the FDA for schizophrenia and bipolar I disorder, and more recently for treatment of MDD, cariprazine has generated a good treatment response across a broad spectrum of symptom groups, including anxiety and depression.

Mental health problems remain a huge global health issue and lead to disability and compromised quality. Traditional antipsychotics, which mainly relieve positive symptoms (including hallucinations and delusions), show limited efficacy in addressing negative and cognitive symptoms. This paper is concerned with the pharmacological and clinical use of cariprazine in decreasing the probability of misdiagnosis in psychiatric care.

## What is Cariprazine?

Cariprazine is an orally administered atypical antipsychotic classified as a dopamine D3-preferring D2/D3 receptor partial agonist. Its unique pharmacological profile distinguishes it from earlier antipsychotic agents, which primarily function as dopamine D2 receptor antagonists. Unlike these agents, cariprazine exhibits partial agonist activity at dopamine D2 and D3 receptors and serotonin 5-HT<sub>1A</sub> receptors, while acting as an antagonist at 5-HT<sub>2B</sub> receptors (Laszlovszky et al., 2021). This receptor activity contributes to its efficacy across positive, negative, and affective symptoms of psychiatric disorders.

Although Cariprazine was initially approved in 2015 for schizophrenia and bipolar I disorder, it has since expanded to include adjunctive treatment for MDD. Its distinct receptor selectivity, particularly its high affinity for the D3 receptor, has been associated with improvements in motivation, cognition, and emotional regulation (Koziej et al., 2024).

## How It Works: Mechanism of Action

The therapeutic effects of cariprazine are primarily attributed to its partial agonist activity at dopamine D3 and D2 receptors. Partial agonists function as stabilizers of dopaminergic activity, acting as antagonists in hyperdopaminergic states and agonists in hypodopaminergic conditions. This dual action allows cariprazine to effectively modulate neurotransmission in different brain pathways implicated in psychiatric disorders (Laszlovszky et al., 2021).

Cariprazine's preferential binding to D3 receptors, predominantly located in the mesolimbic system, plays a critical role in addressing negative symptoms such as anhedonia, social withdrawal, and reduced motivation. Additionally, its activity at serotonin receptors contributes to

mood stabilization and antidepressant effects, making it particularly useful in bipolar disorder and treatment-resistant depression (Pejuskovic et al., 2024).

Pharmacokinetically, cariprazine has a long half-life and produces two active metabolites, desmethyl-cariprazine and didesmethyl-cariprazine, which contribute to sustained therapeutic effects and once-daily dosing convenience (Laszlovszky et al., 2021).

## Prevalence and Clinical Relevance

Schizophrenia occurs in around 1% of the global population and is related to severe functional disability and reduced life expectancy. Bipolar disorder and major depressive disorder are widely recognized as major causes of disability. Nevertheless, people need to manage symptoms either with drug therapy (cariprazine) or without treatment. Cariprazine targets symptoms that are not frequently treated by conventional antipsychotic therapies. The benefits of the new drug are also found in clinical experiments, including its positive and negative effects on cognitive and functional recovery for people with schizophrenia (Selvan et al., 2024). Meta-analytic evidence also indicates that it is effective in treating depressive episodes related to major depressive disorder as well as bipolar disorder (Martins-Correia et al., 2024).

## Benefits and Limitations

Cariprazine offers several benefits over traditional antipsychotic drugs. There is a wide application of the drug; cariprazine is proven effective for positive, negative, and affective symptoms in schizophrenia and mood disorders. Its D3 receptor preference contributes to improved motivation, cognition, and emotional function of the patient. Compared with other atypical antipsychotics, cariprazine is associated with lower risks of weight gain, metabolic syndrome, and hyperprolactinemia (Koziej et al., 2024). Cariprazine has potential for treating bipolar depression and major depressive disorder.

Cariprazine has many upsides, but there are some risks. The side effects typically include akathisia, insomnia, and nausea, which can also contribute to patient adherence (Martins-Correia et al., 2024). Due to its long half-life, dose adjustments may take several weeks to achieve full therapeutic effects. As a new medication, there may not be a lot of access to cariprazine, and therefore, many patients do not benefit, depending on treatment coverage and regional access to the medication.

## Real-World Applications

Functional effects of cariprazine are appreciated and are highly effective in schizophrenia or bipolar disorder, and adjunctive treatments for treatment-resistant depression. Cariprazine has also shown promising performance in addressing depressive symptoms like anhedonia and

fatigue, where individual treatment is personalized (Pejuskovic et al., 2024).

## Advancements and Future Directions

Developments and future directions for cariprazine indicate that there is evidence of its promising therapeutic effect in various psychiatric disorders, pediatric populations, substance use disorders, and cognitive impairment. Future studies aim to determine its safety and performance in real-world settings and comparative effectiveness with other current third-generation antipsychotics. Further investigation of dopamine D3 receptor-targeted drugs with specific drug targets for schizophrenia is being undertaken to better address complex psychiatric diseases, which may be further developed in the future.

## Mismedicine and Cariprazine

The concept of Mismedicine, coined by Dr. Pooya Beigi, refers to medical practices that result in harm, inefficiency, or failure to meet the standard of care. In psychiatry, Mismedicine may occur through inappropriate medication selection, delayed diagnosis, or inadequate treatment of symptom domains such as negative or cognitive symptoms.

Cariprazine has the potential to reduce Mismedicine by providing a targeted and evidence-based treatment option for patients with complex psychiatric conditions. Its ability to address unmet therapeutic needs, particularly in negative symptoms and treatment-resistant depression, supports more precise and effective clinical decision-making. However, improper dosing, insufficient monitoring of side effects, or limited access to the medication may still contribute to Mismedicine if not carefully managed.

## Conclusion

Cariprazine represents a significant advancement in the treatment of psychiatric disorders, offering a novel pharmacological approach that addresses both psychotic and affective symptoms. Its unique D3-preferring partial agonist activity contributes to improvements in negative symptoms, cognitive function, and mood regulation, distinguishing it from traditional antipsychotic medications. While its favourable safety profile and broad therapeutic applications make it a valuable treatment option, careful consideration of side effects and accessibility remains essential. Future research should focus on long-term outcomes and personalized treatment strategies to optimize its clinical utility and further reduce the risk of Mismedicine in psychiatric care.

## What makes cariprazine different from other antipsychotics?

Cariprazine is a dopamine D3-preferring D2/D3 partial agonist, meaning it stabilizes dopamine activity rather than fully blocking it. Its high affinity for D3 receptors helps improve negative symptoms, motivation, and cognitive function more effectively than many traditional antipsychotics.

### What conditions is cariprazine approved to treat?

Cariprazine is approved for the treatment of schizophrenia, bipolar I disorder (including manic and depressive episodes), and as an adjunctive therapy for major depressive disorder in adults.

### How does cariprazine help with negative symptoms of schizophrenia?

Negative symptoms are linked to low dopamine activity in certain brain regions. Because cariprazine acts as a partial agonist, especially at D3 receptors, it can enhance dopaminergic signalling where it is deficient, improving symptoms like anhedonia, avolition, and social withdrawal.

### What are the main benefits and limitations of cariprazine?

Benefits include broad-spectrum efficacy, lower metabolic risk compared to many atypical antipsychotics, and effectiveness in mood disorders. Limitations include side effects such as akathisia and insomnia, as well as delayed steady-state levels due to its long half-life.

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