

EPA 2025

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**PARTIAL ACTIVITY**  
**FULL IMPACT**  
INNOVATIONS  
IN SCHIZOPHRENIA  
TREATMENT



# **Bridging mechanisms and outcomes:** Insights into symptom management

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# Unmet Needs in Schizophrenia – Beyond Positive Symptoms

## Current challenges:

- Many patients continue to struggle with **negative** and **cognitive** symptoms despite treatment
- These symptoms contribute to **functional disability**, poor quality of life, and **low treatment satisfaction**

**Clinical insight:** Treatment needs to go beyond symptom control and address **individualized patient profiles** using dimensional approaches

# Negative Symptoms – The Core Challenge

**Negative symptoms** (affective flattening, alogia, anhedonia, asociality, and avolition) are:

- Often **primary** (intrinsic to schizophrenia) or **secondary** (due to EPS, depression, substance use etc)
- Not well addressed by many antipsychotics

**Cariprazine** shows **efficacy** in improving negative symptoms:

- Superior to placebo and even **outperformed risperidone** in head-to-head comparisons

# Cognitive Deficits – A Forgotten Target

**Cognitive impairment** affects 80%+ of patients with schizophrenia

- Strong predictor of functional outcomes and independence
- Associated with **D3 receptor function** in the prefrontal cortex and hippocampus

**Cariprazine** shows significant **cognitive improvement** over placebo and risperidone



# Dual Disorders – The D3 Opportunity

**Substance addiction** affect up to **48%** of schizophrenia patients

- Linked to **impulse dyscontrol, relapse**, and poor long-term outcomes
- **D3 receptors** are heavily involved in **reward, drug-seeking, and sensitization**

**Cariprazine**, with its high D3 affinity, may reduce **cravings** and improve control in these complex cases

**Takeaway:** TGAs, especially cariprazine, represent a **new pharmacological tool** in treating dual disorder patients; they are recommended as first-line treatments by a recent guideline

# Clinical Takeaways – Why D3 & Partial Agonism Matter

- **Partial agonists** (ARI, BREX, CAR) differ in receptor profiles, dosing, half-life, and clinical outcomes
- **Cariprazine**: high D3 preference → most promising for:
  - Negative symptoms
  - Cognitive deficit
  - Dual disorders (SUD)
- Early and tailored intervention may improve **long-term outcomes** and **quality of life**
- Final thought: mechanism matters – personalise based on **MoA**!

