

Brexpiprazole and Cariprazine: Clinical Pearl

Background	<p>Pharmacology for the treatment of schizophrenia involved agents that target neurotransmitter receptors. The main target of antipsychotics is to block dopamine receptors.</p> <ul style="list-style-type: none"> • First-generation antipsychotics (FGAs), like haloperidol, fluphenazine, etc. have a greater action on dopamine receptors. <ul style="list-style-type: none"> • These medications are also associated with an increase in EPS. • Some of the less potent FGAs and second-generation antipsychotics (SGAs) like risperidone, olanzapine, etc., have mixed receptor targeting may have additional actions on histamine, cholinergic, and adrenergic receptors. <ul style="list-style-type: none"> • Aripiprazole (Abilify) is a common second-generation antipsychotic that may be used for adjunct treatment of schizophrenia or depression. • Aripiprazole exerts its effects through partial antagonism of the dopamine receptor. Just recently, similar agents, brexpiprazole and cariprazine have been added to the market. • With a similar mechanism of action to aripiprazole, it's important to understand the key differences between these agents. 			
Mechanism of Action	<ul style="list-style-type: none"> • Aripiprazole- Partial agonist at 5-HT_{1A} and D₂ receptors, and antagonist at 5-HT_{2A} • Brexpiprazole- Higher affinity (10-fold) 5-HT_{1A} and 5-HT_{2A} than for D₂ receptors. • Cariprazine- Higher affinity for dopamine D₃ receptors over D₂. The benefits of this receptor binding are unknown but are thought to be pro-cognitive. 			
	Indication	Aripiprazole (ABILIFY)	Brexpiprazole (REXULTI)	Cariprazine (VRAYLAR)
	Serotonin	+++	+++	++
	Dopamine D2	+++	++	++
	Dopamine D3	+++		+++
	Histamine	+		+
	Adrenergic	+		+
	Cholinergic			
Indications	<p>All three medications are approved for the treatment of schizophrenia. Aripiprazole & brexpiprazole- also approved for major depressive disorder Aripiprazole & cariprazine-also approved for the treatment of manic or mixed episodes associated with bipolar type 1.</p>			
Contraindications	History of hypersensitivity			
Black box warnings	Increased mortality in elderly patients with dementia-related psychosis, suicidal thoughts and behaviors.			
Starting Doses	Indication	Aripiprazole (ABILIFY)	Brexpiprazole (REXULTI)	Cariprazine (VRAYLAR)
	Schizophrenia	10-15 mg/day Max=30 mg/day	1 mg /day Max=4 mg/day	1.5 mg/day
	Major Depressive Disorder	2-5 mg/day Max=15 mg/day	0.5-1 mg/day Max=3 mg/day	n/a
	Adults with bipolar mania	15 mg/day (10mg if adjunct to Lithium or valproate) Max=30 mg/day	n/a	1.5 mg/day Recommended= 3-6mg/day
Elimination half-life	Brexpiprazole		Cariprazine	
	91 hours (86 hours for metabolite)		2-4 days (1-3 weeks for active metabolite)	
Adverse effects	<ul style="list-style-type: none"> • BBW- increased mortality in elderly patients with dementia-related psychosis, suicidal thoughts and behaviors <p>Comparing S/E to the other SGA's</p>			

	Drug	EPS	QTc	Sedation	DM	Lipids
	Risperidone	Yes	Low	Low	Low/Moderate	Low
	Olanzapine	Yes	Low	Moderate	High	High
	Brexpiprazole	Yes	Very Low	Low	Low	Low
	Cariprazine	Yes	Very Low	Low	Low	Very Low
	Clozapine	No	Low	High	High	High
Effectiveness	<ul style="list-style-type: none"> When comparing to aripiprazole, both brexpiprazole and cariprazine showed similar effectiveness in reducing both positive and negative symptoms. However, no head-to-head trial has been performed to address superiority. Brexpiprazole: When compared to placebo, brexpiprazole was reported to have a significant decrease in positive and negative symptoms of schizophrenia. Cariprazine: In clinical trials, for the treatment of schizophrenia cariprazine was shown to be superior at reducing both positive and negative symptoms when compared to risperidone and aripiprazole. 					
Administration	Can be given with or without food					
Formulations	Brexpiprazole-tablet (can be crushed) Cariprazine-capsule					
Place in therapy	Third-line agent					

Case 1: KM is a 34 y/o male that has a history of schizophrenia. He is currently takes olanzapine and this new medicine called REXULTI that his outpatient psychiatrist started. You notice that he has been pretty sedated over the past couple days. You remember listening to an amazing clinical pearl the other week on this medication but forgot the side effects of REXULTI.

- What is the generic name of REXULTI?
 - Carpirazine
 - Aripiprazole
 - Brexpiprazole
- True or false: You would expect REXULTI to have more sedative effects than olanzapine.
- You see a medication order for brexpiprazole or cariprazine has been put in, but has not been verified by pharmacy. What should you do?
 - Confirm with the patient that this is a home medication
 - Call the pharmacy and ask them to verify the medication
 - Call the pharmacy and let them know if the patient has their own medication in the hospital
 - Do nothing
 - A&C
- The doctor wants to try Vraylar instead, would you expect an increase risk of EPS with Vraylar than with olanzapine?
 - Yes
 - No
- Which of the following is TRUE ?
 - Vraylar has a higher affinity for D3 receptors than Rexulti
 - Vraylar is indicated for schizophrenia and bipolar disorder
 - Vraylar is superior to Rexulti in treating schizophrenia
 - A&B