SHERI SPIRT

PSYCHIATRY

16 East 96th Street, Unit 1A

New York, N.Y. 10128

(212) 595 6901

[SSDR18@aol.com](mailto:SSDR18@aol.com)

CARIPRAZINE

* A dopamine D3 and D2 partial agonist with preferential binding to D3 receptors
* D3 is preferentially expressed in areas of the brain associated with motivation and reward-related behavior.
* Partial agonist at 5-HT1A which is a mechanism thought to enhance the neurochemical and behavioral effects of SSRIs.

Side Effects

* Akathesia, EPS
* No QTc prolongation or significant weight gain
* Small increases in prolactin

2-4.5mg./d showed superior efficacy to placebo in treating depression as measure on MADRS total score.

**Adverse Effects**

**>10% (Schizophrenia)**

Extrapyramidal symptoms, all (24-33%)

Parkinsonism (13-18%)

Headache (9-18%)

Akathisia (9-14%)

Insomnia (11-13%)

**>10% (Bipolar Disorder)**

Extrapyramidal symptoms, all (41-45%)

Parkinsonism (21-26%)

Akathisia (20-21%)

Headache (13-14%)

Nausea (11-13%)

Constipation (6-11%)

**1-10% (Schizophrenia)**

Constipation (6-10%)

Somnolence (5-10%)

Nausea (5-8%)

Abdominal pain (3-7%)

Restlessness (4-6%)

Anxiety (3-6%)

Toothache (3-6%)

Hypertension (2-6%)

Dyspepsia (4-5%)

Vomiting (4-5%)

Dizziness (3-5%)

Agitation (3-5%)

Diarrhea (1-5%)

Pain in extremity (2-4%)

Cough (1-4%)

Tachycardia (2-3%)

Increased weight (2-3%)

Decreased appetite (1-3%)

Dry mouth (1-3%)

Fatigue (1-3%)

Increased CPK (1-3%)

Musculoskeletal stiffness (1-3%)

Back pain (1-3%)

Dystonia (2%)

Tachycardia (1-2%)

Arthralgia (1-2%)

Increased LFTs (1-2%)

Nasopharyngitis (1-2%)

Urinary tract infections (1-2%)

## Pharmacology

### Mechanism of Action

Precise mechanism by which cariprazine works for schizophrenia or bipolar disorder is unknown

Efficacy could be mediated through a combination of partial agonist activity at central dopamine (D2) and serotonin 5-HT1A receptors

Forms 2 major metabolites, desmethyl cariprazine (DCAR) and didesmethyl cariprazine (DDCAR), that have in vitro receptor binding profiles similar to the parent drug

### Absorption

Peak plasma time: 3-6 hr (cariprazine)

Mean concentrations of DCAR and DDCAR are ~30% and 400%, respectively, of cariprazine concentrations by the end of 12-week treatment

### Distribution

Protein bound: 91-97% (parent drug and metabolites)

### Metabolism

Active metabolites: Desmethyl cariprazine (DCAR) and didesmethyl cariprazine (DDCAR) are pharmacologically equipotent to cariprazine

Extensively metabolized by CYP3A4 to DCAR

Metabolized to a lesser extent by CYP2D6 to DCAR and DDCAR

DDCAR is metabolized by CYP3A4 to a hydroxylated metabolite

#### INTERACTIONS Contraindicated (22)

* bosentan
* carbamazepine
* dabrafenib
* dexamethasone
* efavirenz
* enzalutamide
* eslicarbazepine acetate
* etravirine
* fosphenytoin
* lumacaftor/ivacaftor
* mitotane
* nafcillin
* nevirapine
* oxcarbazepine
* pentobarbital
* phenobarbital
* phenytoin
* primidone
* rifabutin
* rifampin
* rifapentine
* st john's wort

### Elimination

Half-life: 2-4 days (cariprazine); 1-3 weeks (DDCAR)

Excretion: 21% urine (1.2% unchanged)

### Contraindications

History of hypersensitivity to cariprazine

Hypersensitivity reactions have ranged from rash, pruritus, urticaria, and events suggestive of angioedema (eg, swollen, tongue, lip swelling, face edema, pharyngeal edema, facial swelling)

### Cautions

Antipsychotic drugs increase the all-cause risk of death in elderly patients with dementia-related psychosis; a higher incidence of stroke and TIA, including fatal stroke, was also observed (see Black Box Warnings)

Neuroleptic malignant syndrome reported; monitor for hyperpyrexia, muscle rigidity, delirium, and autonomic instability; other signs include increased CPK, myoglobinuria (rhabdomyolysis), and acute renal failure

Tardive dyskinesia, a potentially irreversible, involuntary, dyskinetic movement syndrome, may develop in patients treated with antipsychotics

Adverse effects may first appear several weeks after initiating treatment, as drug and metabolite levels accumulate; monitor for extrapyramidal symptoms or akathisia

Metabolic changes associated with atypical antipsychotics include hyperglycemia, diabetes mellitus, dyslipidemia, and weight gain; extreme hyperglycemia associated with ketoacidosis or hyperosmolar coma or death have been reported with atypical antipsychotics

Leukopenia and neutropenia reported with cariprazine; agranulocytosis (including fatal cases) reported with other atypical antipsychotics

May cause orthostatic hypotension and syncope; caution in patients vulnerable to hypotension (eg, elderly, dehydration, hypovolemia, concomitant antihypertensive drugs, cardiovascular or cerebrovascular disease)

May cause seizures; risk is greatest with history of seizures or conditions that lower seizure threshold

May cause cognitive and motor impairment Body temperature dysregulation reported; may disrupt ability to reduce core body temperature; caution with strenuous exercise, exposure to extreme heat, dehydration, and coadministration with anticholinergic medications

Esophageal dysmotility and aspiration reported with antipsychotic drug use

Coadministration with CYP3A4 inhibitors requires dosage adjustment; not recommended with concomitant CYP3A4 inducers