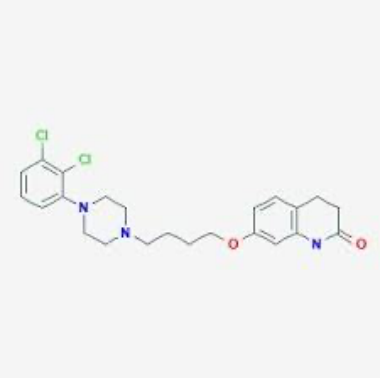
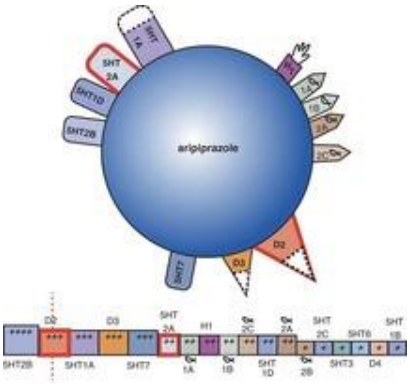
# Aripiprazole (Abilify®)






**Mechanism of action**: Targets multiple receptors, and acts as partial agonist at dopamine and serotonin receptors. D2 partial agonist (decreases activity in mesolithic pathway, while increasing activity in mesocortical pathway), Partial agonist of 5HT1A, antagonist at 5HT2A.

**FDA-approved uses**: Bipolar disorder (acute mania and bipolar maintenance, ages 10+), Schizophrenia (ages 13+), Tourette Disorder/tics (ages 6+), Irritability in children with autism (ages 6+), Adjunct agent in major depressive disorder (adults)

**Off-label uses**: Adjunct agent in obsessive compulsive disorder, behavioral problems in adults with dementia (though has black-box warning), borderline personality disorder (limited evidence), anxiety (limited evidence)

**Dosing and formulation**: For adults, with schizophrenia: 10-30mg daily. Bipolar mania: 15-30mg daily. Adjunct to antidepressant treatment: 2-15mg daily (start 2-5mg daily, and be mindful of drug interaction). For irritability with autism, 2-15mg daily. For children and adolescents, start at lower doses, such as 2mg/day.

Comes in tablet, disintegrating tablet, oral solution, 4 week long acting injectable (for adults) and 2 month long acting injectable (for adults only). Tablets come in 2mg, 5mg, 10mg, 15mg, 20mg and 30mg.

CYP2D6 inhibitors (like Paroxetine, Fluoxetine) or CYP3A4 inhibitors (like Ketoconazole) can raise Aripiprazole concentration significantly, while inducers of CYP3A4 (like Carbamazepine) can decrease levels.

No dosage adjustments needed for renal or hepatic impairment. Has ability to cross placenta and to be found in breastmilk.

**Time to peak**: 3-5 hours after oral dose. Can be taken with or without food.
**Duration of clinical action**: Half life 75 hours (in adults); 94 hours for metabolite dehydro-aripiprazole

**Steady state**: 14 days with oral dosing (based on 15mg and 30mg trials)
99% protein bound

**Metabolism/Elimination**:
Substrate of CYP2D6, CYP3A4
Inhibits CYP2D6
Eliminated in urine and feces

**Side effects**:
*Frequent/bothersome*: **weight gain**, headache, constipation, nausea/vomiting, **akathisia**, tiredness, lightheadedness, lipid abnormalities.

May also cause EPS (though less risk than typical antipsychotics, with children being at greater risk).
Some reports of increased impulsive behaviors (gambling, sexual behaviors, binge eating, shopping)

*Rare but serious*: Neuroleptic Malignant Syndrome (NMS), agranulocytosis, seizures, SIADH

**Monitoring**: baseline height, weight, waist circumference, blood pressure, fasting glucose/HgA1c, fasting lipids, electrolytes, EKG (if concern for QTc prolongation).

**Special considerations**:

- less likely to cause QTc prolongation as compared to other antipsychotics
- less likely to cause prolactin elevation
- while often used with SSRIs for augmentation of major depressive disorder, need to be mindful of CYP interactions which can increase Aripiprazole levels several times. So start with small dose if introducing Aripiprazole to someone on a CYP2D6 inhibiting SSRI
- monitor for EPS, as children more likely than adults to have this side effect
- monitor for SIADH or hyponatremia (especially in older adults)
- Take akathisia seriously if it develops, as there have been reports of suicide in patients who become distressed due to this side effect. Can lower dose or change antipsychotic, or treat with beta-adrenergic antagonist like Propranolol.

References:

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