### ARIPIPRAZOLE

#### THERAPEUTICS

**Brands**
- Abilify
- Abilify Maintena
- Aristada

*see index for additional brand names*

**Generic?** Yes

**Class**
- Neuroscience-based Nomenclature: dopamine, serotonin receptor partial agonist (DS-RPA)
- Dopamine partial agonist (dopamine stabilizer, atypical antipsychotic, third-generation antipsychotic; sometimes included as a second-generation antipsychotic; also a mood stabilizer)

**Commonly Prescribed for**
*(bold for FDA approved)*
- Schizophrenia (ages 13 and older) *(Abilify, Abilify Maintena, Aristada)*
- Maintaining stability in schizophrenia
- Acute mania/mixed mania (ages 10 and older; monotherapy and adjunct)
- Bipolar maintenance (monotherapy and adjunct)
- Depression (adjunct)
- Autism-related irritability in children ages 6 to 17
- Tourette’s disorder in children ages 6 to 18
- Acute agitation associated with schizophrenia or bipolar disorder (IM)
- Bipolar depression
- Other psychotic disorders
- Behavioral disturbances in dementias
- Behavioral disturbances in children and adolescents
- Disorders associated with problems with impulse control

**How the Drug Works**
- Partial agonism at dopamine 2 receptors
- Theoretically reduces dopamine output when dopamine concentrations are high, thus improving positive symptoms and mediating antipsychotic actions
- Theoretically increases dopamine output when dopamine concentrations are low, thus improving cognitive, negative, and mood symptoms

**Actions at dopamine 3 receptors could theoretically contribute to aripiprazole’s efficacy**
- Partial agonism at 5HT1A receptors may be relevant at clinical doses
- Blockade of serotonin type 2A receptors may contribute at clinical doses to cause enhancement of dopamine release in certain brain regions, thus reducing motor side effects and possibly improving cognitive and affective symptoms
- Blockade of serotonin type 2C and 7 receptors as well as partial agonist actions at 5HT1A receptors may contribute to antidepressant actions

**How Long Until It Works**
- Psychotic and manic symptoms can improve within 1 week, but it may take several weeks for full effect on behavior as well as on cognition and affective stabilization
- Classically recommended to wait at least 4–6 weeks to determine efficacy of drug, but in practice some patients require up to 16–20 weeks to show a good response, especially on cognitive symptoms

**If It Works**
- Most often reduces positive symptoms in schizophrenia but does not eliminate them
- Can improve negative symptoms, as well as aggressive, cognitive, and affective symptoms in schizophrenia
- Most schizophrenic patients do not have a total remission of symptoms but rather a reduction of symptoms by about a third
- Perhaps 5–15% of schizophrenic patients can experience an overall improvement of greater than 50–60%, especially when receiving stable treatment for more than a year
- Such patients are considered super-responders or “awakeners” since they may be well enough to be employed, live independently, and sustain long-term relationships
- Many bipolar patients may experience a reduction of symptoms by half or more
- Continue treatment until reaching a plateau of improvement
- After reaching a satisfactory plateau, continue treatment for at least a year after first episode of psychosis
ARIPIPRAZOLE (continued)

- For second and subsequent episodes of psychosis, treatment may need to be indefinite
- Even for first episodes of psychosis, it may be preferable to continue treatment indefinitely to avoid subsequent episodes
- Treatment may not only reduce mania but also prevent recurrences of mania in bipolar disorder

If It Doesn’t Work
- Try one of the other atypical antipsychotics (risperidone, olanzapine, quetiapine, ziprasidone, paliperidone, amisulpride, asenapine, iloperidone, lurasidone)
- If two or more antipsychotic monotherapies do not work, consider clozapine
- Some patients may require treatment with a conventional antipsychotic
- If no first-line atypical antipsychotic is effective, consider higher doses or augmentation with valproate or lamotrigine
- Consider noncompliance and switch to another antipsychotic with fewer side effects or to an antipsychotic that can be given by depot injection
- Consider initiating rehabilitation and psychotherapy such as cognitive remediation
- Consider presence of concomitant drug abuse

Best Augmenting Combos for Partial Response or Treatment Resistance
- Valproic acid (valproate, divalproex, divalproex ER)
- Other mood-stabilizing anticonvulsants (carbamazepine, oxcarbazepine, lamotrigine)
- Lithium
- Benzodiazepines

Tests
Before starting an atypical antipsychotic
- Weigh all patients and track BMI during treatment
- Get baseline personal and family history of diabetes, obesity, dyslipidemia, hypertension, and cardiovascular disease
- Get waist circumference (at umbilicus), blood pressure, fasting plasma glucose, and fasting lipid profile
- Determine if the patient is

- overweight (BMI 25.0–29.9)
- obese (BMI ≥30)
- has pre-diabetes (fasting plasma glucose 100–125 mg/dL)
- has diabetes (fasting plasma glucose >126 mg/dL)
- has hypertension (BP >140/90 mm Hg)
- has dyslipidemia (increased total cholesterol, LDL cholesterol, and triglycerides; decreased HDL cholesterol)
- Treat or refer such patients for treatment, including nutrition and weight management, physical activity counseling, smoking cessation, and medical management

Monitoring after starting an atypical antipsychotic
- BMI monthly for 3 months, then quarterly
- Consider monitoring fasting triglycerides monthly for several months in patients at high risk for metabolic complications and when initiating or switching antipsychotics
- Blood pressure, fasting plasma glucose, fasting lipids within 3 months and then annually, but earlier and more frequently for patients with diabetes or who have gained >5% of initial weight
- Treat or refer for treatment and consider switching to another atypical antipsychotic for patients who become overweight, obese, pre-diabetic, diabetic, hypertensive, or dyslipidemic while receiving an atypical antipsychotic
- Even in patients without known diabetes, be vigilant for the rare but life-threatening onset of diabetic ketoacidosis, which always requires immediate treatment, by monitoring for the rapid onset of polyuria, polydipsia, weight loss, nausea, vomiting, dehydration, rapid respiration, weakness and clouding of sensorium, even coma
- Patients with low white blood cell count (WBC) or history of drug-induced leukopenia/neutropenia should have complete blood count (CBC) monitored frequently during the first few months and aripiprazole should be discontinued at the first sign of decline of WBC in the absence of other causative factors
SIDE EFFECTS

How Drug Causes Side Effects
- By blocking alpha 1 adrenergic receptors, it can cause dizziness, sedation, and hypotension
- Partial agonist actions at dopamine 2 receptors in the striatum can cause motor side effects, such as akathisia
- Partial agonist actions at dopamine 2 receptors can also cause nausea, occasional vomiting, and activating side effects

Mechanism of any possible weight gain is unknown; weight gain is not common with aripiprazole and may thus have a different mechanism from atypical antipsychotics for which weight gain is common or problematic

Mechanism of any possible increased incidence of diabetes or dyslipidemia is unknown; early experience suggests these complications are not clearly associated with aripiprazole and if present may therefore have a different mechanism from that of atypical antipsychotics associated with an increased incidence of diabetes and dyslipidemia

Notable Side Effects
- Dizziness, insomnia, akathisia, activation
- Nausea, vomiting
- Orthostatic hypotension, occasionally during initial dosing
- Constipation
- Headache, asthenia, sedation
- Theoretical risk of tardive dyskinesia

Life-Threatening or Dangerous Side Effects
- Rare impulse control problems
- Rare neuroleptic malignant syndrome (much reduced risk compared to conventional antipsychotics)
- Rare seizures
- Increased risk of death and cerebrovascular events in elderly patients with dementia-related psychosis

Weight Gain
- Reported in a few patients, especially those with low BMIs, but not expected

DOSING AND USE

Usual Dosage Range
- 15–30 mg/day for schizophrenia and mania
- 2–10 mg/day for augmenting SSRIs/SNRIs in depression
- 5–15 mg/day for autism
- 5–20 mg/day for Tourette’s disorder
- 300–400 mg/4 weeks (LAI Maintena; see Aripiprazole Depot Formulations after Pearls for dosing and use)
- 441 mg, 662 mg, or 882 mg administered monthly or 882 mg administered every 6 weeks (LAI Aristada; see Aripiprazole Depot Formulations after Pearls for dosing and use)

Dosage Forms
- Tablet 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg
- Orally disintegrating tablet 10 mg, 15 mg
• Oral solution 1 mg/mL  
• Injection 9.75 mg/1.3 mL  
• Depot (Maintena) 300 mg, 400 mg  
• Depot (Aristada) 441 mg, 662 mg, 882 mg

How to Dose – Oral and Acute IM  
• Schizophrenia, mania: initial approved recommendation is 10–15 mg/day; maximum approved dose 30 mg/day  
• Depression (adjunct): initial dose 2–5 mg/day; can increase by 5 mg/day at intervals of no less than 1 week; maximum dose 15 mg/day  
• Autism: initial dose 2 mg/day; can increase by 5 mg/day at intervals of no less than 1 week; maximum dose 15 mg/day  
• Tourette’s disorder (patients weighing less than 50 kg): initial dose 2 mg/day; after 2 days increase to 5 mg/day; after 1 additional week can increase to 10 mg/day if needed  
• Tourette’s disorder (patients weighing more than 50 kg): initial dose 2 mg/day; after 2 days increase to 5 mg/day; after 5 additional days can increase to 10 mg/day; can increase by 5 mg/day at intervals of no less than 1 week; maximum dose 20 mg/day  
• Agitation: 9.75 mg/1.3 ml; maximum 30 mg/day  
• Depot: must initiate oral aripiprazole first; after tolerability is established can administer initial injection along with an overlapping 14-day (Maintena) or 21-day (Aristada) dosing of oral aripiprazole; initial and maintenance doses are described under dosing tips below  
• Oral solution: solution doses can be substituted for tablet doses on a mg-per-mg basis up to 25 mg; patients receiving 30-mg tablet should receive 25-mg solution

Dosing Tips – Oral

✽ For some, less may be more: frequently, patients not acutely psychotic may need to be dosed lower (e.g., 2.5–10 mg/day) in order to avoid akathisia and activation and for maximum tolerability

✽ For others, more may be more: rarely, patients may need to be dosed higher than 30 mg/day for optimum efficacy  
• Consider administering 1–5 mg as the oral solution for children and adolescents, as well as for adults very sensitive to side effects

✽ Although studies suggest patients switching to aripiprazole from another antipsychotic can do well with rapid switch or with cross-titration, clinical experience suggests many patients may do best by adding either an intermediate or full dose of aripiprazole to the maintenance dose of the first antipsychotic for at least several days and possibly as long as 3 or 4 weeks prior to slow down-titration of the first antipsychotic. See also the Switching section below, after Pearls

• Rather than raise the dose above these levels in acutely agitated patients requiring acute antipsychotic actions, consider augmentation with a benzodiazepine or conventional antipsychotic, either orally or intramuscularly

• Rather than raise the dose above these levels in partial responders, consider augmentation with a mood-stabilizing anticonvulsant, such as valproate or lamotrigine

• Children and elderly should generally be dosed at the lower end of the dosage spectrum

• Due to its very long half-life, aripiprazole will take longer to reach steady state when initiating dosing, and longer to wash out when stopping dosing, than other atypical antipsychotics

• Treatment should be suspended if absolute neutrophil count falls below 1,000/mm³

Overdose  
• No fatalities have been reported; sedation, vomiting

Long-Term Use  
• Approved to delay relapse in long-term treatment of schizophrenia

• Approved for long-term maintenance in bipolar disorder

• Often used for long-term maintenance in various behavioral disorders

Habit Forming  
• No

How to Stop  
• See Switching section of individual agents for how to stop aripiprazole
Do Not Use

- If there is a proven allergy to aripiprazole

**Pharmacokinetics**

- Metabolized primarily by CYP450 2D6 and CYP450 3A4
- Mean elimination half-life 75 hours (aripiprazole) and 94 hours (major metabolite dehydro-aripiprazole)
- Food does not affect absorption

**Drug Interactions**

- Ketaconazole and possibly other CYP450 3A4 inhibitors such as nefazodone, fluvoxamine, and fluoxetine may increase plasma levels of aripiprazole
- Carbamazepine and possibly other inducers of CYP450 3A4 may decrease plasma levels of aripiprazole
- Quinidine and possibly other inhibitors of CYP450 2D6 such as paroxetine, fluoxetine, and duloxetine may increase plasma levels of aripiprazole
- Aripiprazole may enhance the effects of antihypertensive drugs
- Aripiprazole may antagonize levodopa, dopamine agonists

**Other Warnings/Precautions**

- There have been reports of problems with impulse control in patients taking aripiprazole, including compulsive gambling, shopping, binge eating, and sexual activity; use caution when prescribing to patients at high risk for impulse-control problems (e.g., patients with bipolar disorder, impulsive personality, obsessive-compulsive disorder, substance use disorders) and monitor all patients for emergence of these symptoms; dose should be lowered or discontinued if impulse-control problems manifest
- Use with caution in patients with conditions that predispose to hypotension (dehydration, overheating)
- Dysphagia has been associated with antipsychotic use, and aripiprazole should be used cautiously in patients at risk for aspiration pneumonia

**Renal Impairment**

- Dose adjustment not necessary

**Hepatic Impairment**

- Dose adjustment not necessary

**Cardiac Impairment**

- Use in patients with cardiac impairment has not been studied, so use with caution because of risk of orthostatic hypotension

**Elderly**

- Dose adjustment generally not necessary, but some elderly patients may tolerate lower doses better
- Although atypical antipsychotics are commonly used for behavioral disturbances in dementia, no agent has been approved for treatment of elderly patients with dementia-related psychosis
- Elderly patients with dementia-related psychosis treated with atypical antipsychotics are at an increased risk of death compared to placebo, and also have an increased risk of cerebrovascular events

**Children and Adolescents**

- Approved for use in schizophrenia (ages 13 and older), manic/mixed episodes (ages 10 and older), irritability associated with autism (ages 6–17), and treatment of Tourette’s disorder (ages 6–18)
- Clinical experience and early data suggest aripiprazole may be safe and effective for behavioral disturbances in children and adolescents, especially at lower doses
- Children and adolescents using aripiprazole may need to be monitored more often than adults and may tolerate lower doses better
- May be more risk of weight gain in children than in adults
**Potential Advantages**

- Patients concerned about gaining weight and patients who are already obese or overweight
- Patients with diabetes
- Patients with dyslipidemia (especially elevated triglycerides)
- Patients requiring rapid onset of antipsychotic action without dosage titration
- Patients who wish to avoid sedation

**Potential Disadvantages**

- Patients in whom sedation is desired
- May be more difficult to dose for children, elderly, or “off-label” uses

**Primary Target Symptoms**

- Positive symptoms of psychosis
- Negative symptoms of psychosis
- Cognitive symptoms
- Unstable mood and depression
- Aggressive symptoms

**Pearls**

- Approved as an adjunct treatment for depression (e.g., to SSRIs, SNRIs)
- May work better in 2–10 mg/day range than at higher doses for augmenting SSRIs/SNRIs in treatment-resistant unipolar depression
- Frequently used for bipolar depression as augmenting agent to lithium, valproate and/or lamotrigine
- Well accepted in clinical practice when wanting to avoid weight gain because less weight gain than most other antipsychotics
- Well accepted in clinical practice when wanting to avoid sedation because less sedation than most other antipsychotics at all doses
- Can even be activating, which can be reduced by lowering the dose or starting at a lower dose
- If sedation is desired, a benzodiazepine can be added short-term at the initiation of treatment until symptoms of agitation and insomnia are stabilized or intermittently as needed
- May not have diabetes or dyslipidemia risk, but monitoring is still indicated
- Anecdotal reports of utility in treatment-resistant cases of psychosis

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**Pregnancy**

- Effective June 30, 2015, the US FDA requires changes to the content and format of pregnancy and lactation information in prescription drug labels, including the elimination of the pregnancy letter categories; the Pregnancy and Lactation Labeling Rule ( PLLR or final rule) applies only to prescription drugs and will be phased in gradually for drugs approved on or after June 30, 2001
- Controlled studies have not been conducted in pregnant women
- There is a risk of abnormal muscle movements and withdrawal symptoms in newborns whose mothers took an antipsychotic during the third trimester; symptoms may include agitation, abnormally increased or decreased muscle tone, tremor, sleepiness, severe difficulty breathing, and difficulty feeding
- In animal studies, aripiprazole demonstrated developmental toxicity, including possible teratogenic effects, at doses higher than the maximum recommended human dose
- Psychotic symptoms may worsen during pregnancy and some form of treatment may be necessary
- Aripiprazole may be preferable to anticonvulsant mood stabilizers if treatment is required during pregnancy

**Breast Feeding**

- Some drug is found in mother’s breast milk
- Recommended either to discontinue drug or bottle feed
- Infants of women who choose to breast feed while on aripiprazole should be monitored for possible adverse effects

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**THE ART OF PSYCHOPHARMACOLOGY**

**Potential Advantages**

- Some cases of psychosis and bipolar disorder refractory to treatment with other antipsychotics
• Has a very favorable tolerability profile in clinical practice
• Favorable tolerability profile leading to “off-label” uses for many indications other than schizophrenia (e.g., bipolar II disorder, including hypomanic, mixed, rapid cycling, and depressed phases; treatment-resistant depression; anxiety disorders)
• A short-acting intramuscular formulation is available as well as long-acting depot
• Lacks D1 antagonist, anticholinergic, and antihistamine properties, which may explain relative lack of sedation or cognitive side effects in most patients
• High affinity of aripiprazole for D2 receptors means that combining with other D2 antagonist antipsychotics could reverse their actions and thus often makes sense not to combine with other antipsychotics
• An exception to this is in case of hyperprolactinemia or galactorrhea, when administration of even low dose (1–5 mg) can reverse the hyperprolactinemia/galactorrhea of other antipsychotics, also proving that aripiprazole interferes with the D2 actions of other antipsychotics
• Abilify Maintena (depot) may be particularly well suited to early-onset psychosis/first-episode psychosis to reduce rehospitalizations and to enhance adherence with relatively low side effect burden

### DEPOT FORMULATIONS

<table>
<thead>
<tr>
<th>Monohydrate (Maintena)</th>
<th>Lauroxil (Aristada)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>Water</td>
</tr>
<tr>
<td>Tmax</td>
<td>6.5–7.1 days</td>
</tr>
<tr>
<td></td>
<td>44.1–50.0 days</td>
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<tr>
<td>T1/2 with multiple dosing</td>
<td>29.9–46.5 days</td>
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<tr>
<td></td>
<td>29.2–34.9 days</td>
</tr>
<tr>
<td>Time to reach steady state</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>4 monthly injections</td>
</tr>
<tr>
<td>Able to be loaded</td>
<td>No</td>
</tr>
<tr>
<td>Dosing schedule (maintenance)</td>
<td>4 weeks</td>
</tr>
<tr>
<td></td>
<td>4–6 weeks</td>
</tr>
<tr>
<td>Injection site</td>
<td>Intramuscular gluteal</td>
</tr>
<tr>
<td></td>
<td>Intramuscular injection in deltoid (441 mg dose only) or gluteal (441, 662, or 882 mg)</td>
</tr>
<tr>
<td>Needle gauge</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>20 or 21</td>
</tr>
<tr>
<td>Dosage forms</td>
<td>300 mg, 400 mg</td>
</tr>
<tr>
<td></td>
<td>441 mg, 662 mg, 882 mg</td>
</tr>
<tr>
<td>Injection volume</td>
<td>200 mg/mL; range 0.8 mL (160 mg)–2 mL (400 mg)</td>
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<tr>
<td></td>
<td>441 mg/1.6 mL; 662 mg/2.4 mL; 882 mg/3.2 mL</td>
</tr>
</tbody>
</table>

### Usual Dosage Range
- 300–400 mg/4 weeks (monohydrate Maintena)
- 441 mg, 662 mg, or 882 mg administered monthly or 882 mg administered every 6 weeks (lauroxil Aristada)

### How to Dose
- Not recommended for patients who have not first demonstrated tolerability to oral aripiprazole (in clinical trials, 2 oral or short-acting IM doses are generally used to establish tolerability)
- Loading is not possible, necessitating oral coverage for 14 days (Maintena) or 21 days (Aristada)
- Conversion from oral to Maintena: administer initial 400 mg injection along with an overlapping 14-day dosing of oral aripiprazole
- Conversion from oral to Aristada: administer initial injection (441 mg, 662 mg, or 882 mg) along with an overlapping 21-day dosing of oral aripiprazole
Dosing Tips

- With LAIs, the absorption rate constant is slower than the elimination rate constant, thus resulting in “flip-flop” kinetics—i.e., time to steady-state is a function of absorption rate, while concentration at steady-state is a function of elimination rate.
- The rate-limiting step for plasma drug levels for LAIs is not drug metabolism, but rather slow absorption from the injection site.
- In general, 5 half-lives of any medication are needed to achieve 97% of steady-state levels.
- The long half-lives of depot antipsychotics mean that one must either adequately load the dose (if possible) or provide oral supplementation.
- The failure to adequately load the dose leads either to prolonged cross-titration from oral antipsychotic or to sub-therapeutic antipsychotic plasma levels for weeks or months in patients who are not receiving (or adhering to) oral supplementation.
- Because plasma antipsychotic levels increase gradually over time, dose requirements may ultimately decrease from initial; obtaining periodic plasma levels can be beneficial to prevent unnecessary plasma level creep.
- The time to get a blood level for patients receiving LAI is the morning of the day they will receive their next injection.
- Advantages: refrigeration not required; option of 6-week injections with Aristada.
- Disadvantages: both formulations require oral coverage.
- Downward dose adjustment is needed for poor CYP450 2D6 metabolizers and patients taking strong CYP450 2D6 or 3A4 inhibitors; avoid use with strong CYP450 3A4 inducers, as this can lead to sub-therapeutic plasma levels.

### Maintena

<table>
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<th>Adjusted dose for patients taking 400 mg</th>
<th>Adjusted dose for patients taking 300 mg</th>
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<tr>
<td>Poor 2D6 metabolizers</td>
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<tr>
<td>Patients taking strong 2D6 OR 3A4 inhibitors</td>
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<td>200 mg</td>
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<tr>
<td>Poor 2D6 metabolizers taking concomitant 3A4 inhibitors</td>
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<td>Patients taking 2D6 AND 3A4 inhibitors</td>
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<tr>
<td>Patients taking 3A4 inducers</td>
<td>Avoid</td>
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</table>

### Aristada

<table>
<thead>
<tr>
<th></th>
<th>Adjusted dose for patients taking 441 mg</th>
<th>Adjusted dose for patients taking 662 mg</th>
<th>Adjusted dose for patients taking 882 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor 2D6 metabolizers</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Patients taking strong 2D6 OR 3A4 inhibitors</td>
<td>N/A</td>
<td>441 mg</td>
<td>662 mg</td>
</tr>
<tr>
<td>Poor 2D6 metabolizers taking concomitant 3A4 inhibitors</td>
<td>N/A</td>
<td>441 mg</td>
<td>441 mg</td>
</tr>
<tr>
<td>Patients taking 2D6 AND 3A4 inhibitors</td>
<td>N/A</td>
<td>Avoid</td>
<td>Avoid</td>
</tr>
<tr>
<td>Patients taking 3A4 inducers</td>
<td>662 mg</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Switching from Oral Antipsychotics to Aripiprazole Depot Formulations

Aripiprazole Monohydrate Kinetics

Concomitant oral aripiprazole 10mg/day x 14 days*

![Graph showing aripiprazole concentration over time for different doses: 200 mg (n=4), 300 mg (n=8), 400 mg (n=12).] (Time in weeks: 0, 4, 8, 12, 16, 20, 24, 28)

Steady State Aripiprazole Lauroxil Levels With 441 mg

![Graph showing predicted aripiprazole steady state levels over time for gluteal and deltoid injections.] (Time in days: 0, 7, 14, 21, 28)

- Discontinuation of oral antipsychotic can begin following oral coverage of 14 days (Maintena) or 21 days (Aristada)
- How to discontinue oral formulations
  - Down-titration is not required for: amisulpride, aripiprazole, brexpiprazole, cariprazine, paliperidone ER
  - 1-week down-titration is required for: iloperidone, lurasidone, risperidone, ziprasidone
  - 3–4-week down-titration is required for: asenapine, olanzapine, quetiapine
  - 4+-week down-titration is required for: clozapine

- For patients taking benzodiazepine or anticholinergic medication, this can be continued during cross-titration to help alleviate side effects such as insomnia, agitation, and/or psychosis. Once the patient is stable on LAI, these can be tapered one at a time as appropriate.
Switching from Oral Antipsychotics to Aripiprazole

- It is advisable to begin aripiprazole at an intermediate dose and build the dose rapidly over 3–7 days.
- Clinical experience has shown that asenapine, quetiapine, and olanzapine should be tapered off slowly over a period of 3–4 weeks, to allow patients to readapt to the withdrawal of blocking cholinergic, histaminergic, and alpha-1 receptors.
- Clozapine should always be tapered off slowly, over a period of 4 weeks or more.

* Benzodiazepine or anticholinergic medication can be administered during cross-titration to help alleviate side effects such as insomnia, agitation, and/or psychosis.

Citrome L. Adjunctive aripiprazole, olanzapine, or quetiapine for major depressive disorder: an analysis of number needed to treat, number needed to harm, and likelihood to be helped or harmed. Postgrad Med 2010;122(4):39–48.


