YOU DON'T SCARE ME: USE OF LONG-ACTING INJECTABLES IN SCHIZOPHRENIA

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Learning Objectives

• Explore the role of LAI antipsychotic medications in improving adherence in schizophrenia

• Improve clinical utilization of LAIs in the treatment of schizophrenia

• Apply evidence-based practices when initiating LAIs in the treatment of schizophrenia
Presentation Agenda

• Why We Should Care About Relapse (and Thus, Adherence to Treatment)
• Can LAI Antipsychotic Medications Help?
• How to Choose Among the LAIs
• More About the Switch From Oral to LAI
Why We Should Care About Relapse (and Thus, Adherence to Treatment)
Preventing Relapse Today: Makes a Difference for a Lifetime

• **Irreversible functional decline occurs with each relapse**

• Thus, preventing relapse is a key goal in many international clinical guidelines for schizophrenia

• “Minimizing risk of relapse in a remitted patient is a high priority, given the potential clinical, social, and vocational costs of relapse”
With Every Relapse, Patients are at Risk of Irreversible Lifetime Functional Impairment

With Every Relapse, Patients are at Risk of Irreversible Lifetime Functional Impairment

Deteriorating course, brain tissue loss, and treatment resistance with repetitive relapses after the first episode in schizophrenia

Partial Adherence in Schizophrenia Begins Early After Hospital Discharge and Worsens Over Time

Consistent Medication Treatment is Key in Preventing Relapse

- ~50% of patients who discontinue/do not take antipsychotics will relapse within 3 to 10 months\(^1,2\)
- Relapse rates are much higher in non-adherent patients\(^3\)
  - 69% of patients with poor adherence relapsed, compared to 18% of patients with good adherence (NNT=2)
  - This is a HUGE effect size!

Can LAI Antipsychotic Medications Help?
Potential Advantages of LAI Antipsychotics

- Reduces dosage deviations
- Eliminates guessing about adherence status
- Helps disentangle reasons for poor response to medication: can focus on psychosocial issues/stressors, or possibility on substance use, etc., as a cause for exacerbation of illness or relapse
- Eliminates need for the patient to remember to take a daily pill
- Enables prescribers to avoid first-pass metabolism; therefore, a better relationship between dose and blood level exists
- Results in predictable and stable plasma levels
- Eliminates abrupt loss of efficacy if dose missed
- Many patients prefer them, especially if already receiving them

LAI = long-acting injectable

LAI antipsychotics can address the guesswork about adherence status and patients often prefer them, provided that they are offered this as a choice

Real-World Studies Favor Use of LAI Antipsychotics

As study design shifts toward real-world populations, LAI formulations display significant advantages.

Mirror-image LAI Studies Do Show Reduced Risk of Hospitalization Compared With Orals

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Risk Ratio and 95% CI</th>
<th>RR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girardi et al. 2010</td>
<td></td>
<td>0.024</td>
<td>0.0091</td>
</tr>
<tr>
<td>Beauclair et al. 2005</td>
<td></td>
<td>0.092</td>
<td>0.0000</td>
</tr>
<tr>
<td>Arató &amp; Erdős 1979</td>
<td></td>
<td>0.204</td>
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<tr>
<td>Devito et al. 1978</td>
<td></td>
<td>0.281</td>
<td>0.0000</td>
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<tr>
<td>Denham &amp; Adamson 1971</td>
<td></td>
<td>0.333</td>
<td>0.0000</td>
</tr>
<tr>
<td>Morriss 1974</td>
<td></td>
<td>0.343</td>
<td>0.0000</td>
</tr>
<tr>
<td>Lam et al. 2009</td>
<td></td>
<td>0.369</td>
<td>0.0000</td>
</tr>
<tr>
<td>Lindholm 1975</td>
<td></td>
<td>0.391</td>
<td>0.0004</td>
</tr>
<tr>
<td>Peng et al. 2011</td>
<td></td>
<td>0.452</td>
<td>0.0000</td>
</tr>
<tr>
<td>Gottfries &amp; Green 1974</td>
<td></td>
<td>0.529</td>
<td>0.0046</td>
</tr>
<tr>
<td>Rosa et al. 2012</td>
<td></td>
<td>0.529</td>
<td>0.0944</td>
</tr>
<tr>
<td>Chang et al. 2012</td>
<td></td>
<td>0.557</td>
<td>0.0000</td>
</tr>
<tr>
<td>Johnson &amp; Freeman 1972</td>
<td></td>
<td>0.570</td>
<td>0.0000</td>
</tr>
<tr>
<td>Crivera et al. 2011</td>
<td></td>
<td>0.597</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ren et al. 2011</td>
<td></td>
<td>0.663</td>
<td>0.0000</td>
</tr>
<tr>
<td>Svestka et al. 1984</td>
<td></td>
<td>1.286</td>
<td>0.5694</td>
</tr>
<tr>
<td>Total (16 studies; n=4066)</td>
<td></td>
<td>0.430</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

LAI = long-acting injectable antipsychotic; CI = confidence interval; AP = antipsychotic; RR = risk ratio.

LAI Options in the United States

- First-generation antipsychotics (all are in sesame seed oil)
  - Haloperidol decanoate
  - Fluphenazine decanoate

- Second-generation antipsychotics (all IM formulations are water-based)
  - Risperidone- or paliperidone-containing formulations
    - Risperidone microspheres
    - Risperidone subcutaneous LAI
    - Paliperidone palmitate monthly
    - Paliperidone palmitate every 3 months
  - Aripiprazole-containing formulations
    - Aripiprazole monohydrate
    - Aripiprazole lauroxil
  - Olanzapine pamoate
How to Choose Among the LAIs?
Amenities of Care

• How often are the injections administered?
• What is the needle gauge?
• What is the injection volume?
• Is there a choice of injection site?
• Does this product require reconstitution?
• Is oral supplementation required?
• Does this product need refrigeration?
• Are there any special requirements for observation?
• Are there any important drug-drug interactions, and can they be remedied?
• Missed doses: What is the “grace period?”
• Is reimbursement an issue if used “off-label?”
Who Gives the Injections?

- Prescriber?
- Another member of the care staff?
- The PCP office down the hall?
- Pharmacist at the pharmacy?
FGA LAIs in More Detail

• **Haloperidol decanoate**
  • Approved for use in the USA in 1986; among inpatients in New York state, the average dose is 135 mg administered monthly (maximum approved dose is 450 mg/4 weeks)
  • Available as 50 and 100 mg/ml in 1- and 5-ml ampules/vials, 21G needles used; do not exceed 3 ml injection volume
  • No oral supplementation; no refrigeration needed

• **Fluphenazine decanoate (IM or sc)**
  • Fluphenazine enanthate was approved for marketing in 1967 and in 1972, fluphenazine decanoate replaced it as it has a longer half-life; among inpatients in New York state, the average dose is ~38 mg administered every 2 weeks (maximum approved dose is 100 mg/2 weeks)
  • Available as 25 mg/ml 5-ml vials, 21G needles used
  • No oral supplementation; no refrigeration needed
### What’s Different Among the Risperidone- or Paliperidone-Containing LAIs?

<table>
<thead>
<tr>
<th></th>
<th>Risperidone Subcutaneous</th>
<th>Risperidone Microspheres</th>
<th>Paliperidone Palmitate Monthly</th>
<th>Paliperidone Palmitate Every 3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brand Name (US)</strong></td>
<td>Perseris™</td>
<td>Risperdal Consta®</td>
<td>Invega® Sustenna®</td>
<td>Invega Trinza®</td>
</tr>
<tr>
<td><strong>Year Approved</strong></td>
<td>2018</td>
<td>2003</td>
<td>2009</td>
<td>2015</td>
</tr>
<tr>
<td><strong>Active Moiety</strong></td>
<td>Risperidone and paliperidone</td>
<td>Risperidone and paliperidone</td>
<td>Paliperidone</td>
<td>Paliperidone</td>
</tr>
<tr>
<td><strong>Approved Indications (All Adult)</strong></td>
<td>Schizophrenia</td>
<td>Schizophrenia; bipolar I disorder maintenance treatment (monotherapy or adjunctive to lithium or valproate)</td>
<td>Schizophrenia; schizoaffective disorder (monotherapy or adjunctive to mood stabilizers or antidepressants)</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td><strong>Dosage Forms/Strengths</strong></td>
<td>Syringe kits: 90 mg, 120 mg</td>
<td>Vial kits: 12.5 mg, 25 mg, 37.5 mg, 50 mg</td>
<td>Injectable suspension: 39 mg, 78 mg, 117 mg, 156 mg, 234 mg</td>
<td>Injectable suspension: 273 mg, 410 mg, 546 mg, 819 mg</td>
</tr>
<tr>
<td><strong>Requires Adding Diluent/Liquid</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Injection Type</strong></td>
<td>Subcutaneous</td>
<td>Intramuscular</td>
<td>Intramuscular</td>
<td>Intramuscular</td>
</tr>
<tr>
<td><strong>Injection Sites</strong></td>
<td>Abdomen</td>
<td>Deltoid or gluteal muscle</td>
<td>Deltoid or gluteal muscle</td>
<td>Deltoid or gluteal muscle</td>
</tr>
<tr>
<td><strong>Needle Gauge and Length</strong></td>
<td>18G and 5/8-inch</td>
<td>20G and 2-inch, 21G and 1-inch</td>
<td>22G and 1.5-inch, 23G and 1-inch</td>
<td>22G and 1 or 1.5-inch</td>
</tr>
<tr>
<td><strong>Injection Volume</strong></td>
<td>0.6 mL (90 mg), 0.8 mL (120 mg)</td>
<td>Approximately 2 mL</td>
<td>156 mg/mL; range 0.25 mL (39 mg) to 1.5 mL (234 mg)</td>
<td>312 mg/mL; range 0.9 mL (273 mg) to 2.6 mL (819 mg)</td>
</tr>
<tr>
<td><strong>Injection Interval</strong></td>
<td>4 weeks</td>
<td>2 weeks</td>
<td>4 weeks</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

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### What’s Different Among the Risperidone- or Paliperidone-Containing LAIs? (cont’d)

<table>
<thead>
<tr>
<th></th>
<th>Risperidone Subcutaneous</th>
<th>Risperidone Microspheres</th>
<th>Paliperidone Palmitate Monthly</th>
<th>Paliperidone Palmitate Every 3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brand Name (US)</strong></td>
<td>Perseris™</td>
<td>Risperdal Consta®</td>
<td>Invega® Sustenna®</td>
<td>Invega Trinza®</td>
</tr>
<tr>
<td><strong>Starting Dose</strong></td>
<td>90 or 120 mg</td>
<td>25 mg</td>
<td>234 mg day 1 and 156 mg day 8 (deltoid)</td>
<td>After treatment with 1-month paliperidone palmitate for at least 4 months: 273 mg, 410 mg, 546 mg, 819 mg (3.5 × the last dose of the once monthly formulation)</td>
</tr>
<tr>
<td><strong>Maintenance Dose</strong></td>
<td>90 or 120 mg</td>
<td>25 mg, maximum 50 mg/2 weeks</td>
<td>117 mg, range 39–234 mg/4 weeks</td>
<td>Same as above</td>
</tr>
<tr>
<td><strong>Half-Life</strong></td>
<td>9–11 days</td>
<td>3–6 days</td>
<td>25–49 days</td>
<td>84–95 days (deltoid), 118–139 days (gluteal)</td>
</tr>
<tr>
<td><strong>Oral Supplementation?</strong></td>
<td>No</td>
<td>21 days after the initial injection and after any change in dose</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Stored Refrigerated?</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

What’s Different Among the Long-Acting IM Aripiprazole-Containing Formulations?

<table>
<thead>
<tr>
<th></th>
<th>Aripiprazole Monohydrate</th>
<th>Aripiprazole Lauroxil</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brand name (US)</strong></td>
<td>Abilify Maintena®</td>
<td>Aristada® (and Aristada Initio®)</td>
</tr>
<tr>
<td><strong>Year Approved</strong></td>
<td>2013</td>
<td>2015 (2018)</td>
</tr>
<tr>
<td><strong>Other Indications</strong></td>
<td>Bipolar disorder</td>
<td>No</td>
</tr>
<tr>
<td><strong>Injection Sites</strong></td>
<td>Deltoid or gluteal</td>
<td>Deltoid (441 mg dose and NCD 675 mg dose*) or gluteal (all doses)</td>
</tr>
<tr>
<td><strong>Needle Gauge</strong></td>
<td>21G, 22G, or 23G</td>
<td>20G or 21G</td>
</tr>
<tr>
<td><strong>Injection Volume</strong></td>
<td>2 mL (400 mg)</td>
<td>1.6 to 3.9 mL</td>
</tr>
<tr>
<td><strong>Injection Interval</strong></td>
<td>Every 4 weeks</td>
<td>Every 4 weeks (all doses), every 6 weeks (882 mg), or every 2 months (1064 mg)</td>
</tr>
<tr>
<td><strong>Starting Dose</strong></td>
<td>400 mg</td>
<td>441, 662, 882, or 1064 mg</td>
</tr>
<tr>
<td><strong>Maintenance Dose</strong></td>
<td>300 or 400 mg (adjust for CYP2D6 or CYP3A4 inhibitors; can’t give with CYP3A4 inducers)</td>
<td>441, 662, 882, or 1064 mg (adjust for CYP2D6 or CYP3A4 modulators)</td>
</tr>
<tr>
<td><strong>Half-Life</strong></td>
<td>29.9 days (300 mg), 46.5 days (400 mg)</td>
<td>53.9–57.2 days; 15–18 days (NCD formulation)</td>
</tr>
<tr>
<td><strong>Oral Supplementation</strong></td>
<td>Yes (14 days)</td>
<td>1 day with NCD 675 mg*, otherwise 21 days</td>
</tr>
<tr>
<td><strong>Reconstitution</strong></td>
<td>Yes, but dual-chamber syringe available</td>
<td>No</td>
</tr>
<tr>
<td><strong>Refrigeration</strong></td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

*NCD = a single 30 mg pill and initial injection of nano-crystal formulation (Aristada Initio®) can substitute for 21-day oral aripiprazole supplementation.

What About Olanzapine Pamoate?

• OLAI is a crystalline salt of olanzapine and pamoic acid in water, approved in 2009 for schizophrenia; no other approved indications

• Efficacy was established in two double-blind, randomized clinical trials of OLAI for the treatment of **acute** schizophrenia and for the **maintenance** of response

• Therapeutic OLAI dosages are 150 mg every 2 weeks, 210 mg every 2 weeks, 300 mg every 2 weeks or every 4 weeks, and 405 mg every 4 weeks

• Gluteal injection only, 19G needle, 1–2.7 mL volume, reconstitution required, stored at room temperature, no oral supplementation but higher dose at start

• OLAI has essentially the same general tolerability as that of oral olanzapine; however, with the depot there is the additional risk of **post-injection delirium sedation syndrome** occurring at a rate of 0.07% of injections, requiring a risk-management plan that includes **observing the patient for 3 hours after each injection**

OLAI = olanzapine pamoate.

A. Is the patient demonstrating adequate efficacy and tolerability on oral fluphenazine, haloperidol, risperidone, paliperidone, olanzapine, or aripiprazole?

• Offer and switch to the corresponding LAI formulation
• For patients receiving oral risperidone, consider paliperidone palmitate instead of risperidone microspheres because of convenience
  • No requirement for oral Rx upon initiation
  • Less frequent injections, eventually q3months
  • Supplied in prefilled syringes
  • Smaller needle bore, lower injection volume
  • No requirement for refrigeration

Updated from Citrome L. Expert Rev Neurother 2017;17:1029-43.
B. What is the downside to fluphenazine or haloperidol? What is the downside to olanzapine LAI?

- For patients receiving oral fluphenazine or haloperidol, concomitant oral anticholinergics for the management of motoric adverse effects are problematic – especially because anticholinergic agents can interfere with memory and other cognitive functions.
  - Exposure to benztropine or other anticholinergics can also increase the risk of developing tardive dyskinesia, and can make existing tardive dyskinesia worse.

- For patients receiving oral olanzapine, olanzapine pamoate will require close monitoring.

Updated from Citrome L. Expert Rev Neurother 2017;17:1029-43.
C. What do we need to know about aripiprazole?

• For patients receiving oral aripiprazole there are two competing formulations of LAI aripiprazole in the US—aripiprazole monohydrate and aripiprazole lauroxil; they have differing doses and injection intervals, as well as initiation strategies.

Updated from Citrome L. Expert Rev Neurother 2017;17:1029-43.
D. Is the patient being treated acutely and avoiding/minimizing oral Rx is desired?

• Consider LAI antipsychotics that do not require oral supplementation and where the clinical trials have demonstrated acute efficacy—paliperidone palmitate or olanzapine pamoate, and possibly aripiprazole lauroxil/NCD

• A new subcutaneous long-acting injectable formulation of risperidone is also now available, administered monthly with no oral supplementation required, and efficacy established with acute use
  • Dosage equivalents are 3 mg/d oral = 90 mg sc, 4 mg/d oral = 120 mg sc

Updated from Citrome L. Expert Rev Neurother 2017;17:1029-43.
E. Are weight gain and metabolic adverse effects a concern for this individual patient?

• Consider an aripiprazole LAI, paliperidone palmitate, risperidone subcutaneous long-acting injectable, and risperidone microspheres among the second-generation LAI antipsychotics; avoid olanzapine pamoate

• Can possibly consider the first-generation LAI antipsychotics as well

Updated from Citrome L. Expert Rev Neurother 2017;17:1029-43.
F. Are prolactin-related adverse effects a clinical concern for this individual patient?

- Consider an aripiprazole LAI
- Avoid paliperidone palmitate, risperidone microspheres, risperidone subcutaneous long-acting injectable, or the first-generation LAI antipsychotics

Updated from Citrome L. Expert Rev Neurother 2017;17:1029-43.
G. Is acquisition cost the primary concern?

• The first-generation LAI antipsychotics may be the only option available but using concomitant oral anticholinergics for the management of motoric adverse effects add complexity and can interfere with memory; overall health care costs are not always lower!

• There are sometimes shortages of first-generation LAI antipsychotics

• *Patient-assistance programs* should be considered for outpatients who are not covered to receive second-generation LAI options

Updated from Citrome L. Expert Rev Neurother 2017;17:1029-43.
More About the Switch From Oral to LAI
Back to Basics: The Pharmacokinetics of Switching to an LAI

LAI therapies and Flip-Flop Kinetics

Oral Antipsychotic

LAI Antipsychotic

Avoiding Sub-Therapeutic Plasma Levels

Loading

Oral Supplementation

First Things First: Get a Plasma Level

- For patients on twice/day dosing, make sure they hold the morning dose until the AM trough is obtained.
- Levels may fluctuate up to 30% in adherent patients.
- Greater fluctuations likely reflect nonadherence or kinetic issues.

How to Dose Haloperidol Decanoate: Initiation

- Loading dose = 10 times the oral daily dose, weekly for the first 3 weeks
- Can discontinue oral immediately
- Some patients may require oral coverage for the first week
- Steady state is achieved after 4 weeks

How to Dose Haloperidol Decanoate: Maintenance

• Maintenance dose = 20 times the oral daily dose, every 4 weeks

• Maintenance dose should start two weeks after last loading injection

• Single-injection volumes greater than 300 mg are not tolerated

  • For patients who require higher doses, give the monthly dose as split injections every 2 weeks

### Risperidone Microspheres: Predicting the Appropriate Long-Acting Dose

<table>
<thead>
<tr>
<th>Dose of Risperidone Microspheres</th>
<th>Active Moiety (Risperidone + 9-OH Risperidone) Plasma Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12 Wk Study $^1$</td>
</tr>
<tr>
<td>25 mg</td>
<td>18.7 ± 9.23</td>
</tr>
<tr>
<td>50 mg</td>
<td>35.5 ± 18.7</td>
</tr>
<tr>
<td>75 mg</td>
<td>44.7 ± 20.6</td>
</tr>
<tr>
<td>100 mg</td>
<td>--</td>
</tr>
</tbody>
</table>

Risperidone + 9-OH Risperidone = 7 x oral dose
35 ng/mL = 7 x 5 mg oral = ~50 mg LAI

How to Dose Risperidone Microspheres: Initiation and Maintenance

- Lag time to active release requires oral coverage
- Steady state achieved

Recommended therapeutic range:
- Cannot be loaded
- Oral coverage for 21–28 days
- Dose titration should occur at intervals of >4 weeks
- If a dose is missed by 2 or more weeks, oral coverage for 3 weeks may be necessary
- Usual maintenance dose: 12.5–50 mg/2 weeks
- >8 mg/day oral = more than one injection

New Risperidone sc 1-Month Formulation

How to Dose Risperidone sc 1-Month: Initiation and Maintenance

• No oral supplementation or loading necessary
• Two absorption peaks
  • 4–6 hours after injection
  • 10–14 days after injection
• Administer subcutaneously in the abdomen
• Do not administer more than one dose (90 mg or 120 mg) per month

Paliperidone Palmitate Formulations: Comparative Pharmacokinetics

1-Month Formulation
Estimated Single-Dose Kinetics

3-Month Formulation
Estimated Single-Dose Kinetics

recommended therapeutic range

recommended therapeutic range

Paliperidone Palmitate, 1-Month: Initiation and Maintenance

• Initiation dose must be in deltoid muscle (28% greater absorption than gluteal)

<table>
<thead>
<tr>
<th>Oral Dose</th>
<th>~Equivalent 1-Month Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mg</td>
<td>39–78 mg</td>
</tr>
<tr>
<td>6 mg</td>
<td>117 mg</td>
</tr>
<tr>
<td>9 mg</td>
<td>156 mg</td>
</tr>
<tr>
<td>12 mg</td>
<td>234 mg</td>
</tr>
</tbody>
</table>

Switching from LAI: give first maintenance dose in place of next-scheduled depot injection

Paliperidone Palmitate, 3-Month: Initiation and Maintenance

<table>
<thead>
<tr>
<th>1-Month Dose</th>
<th>3-Month Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>78 mg</td>
<td>273 mg</td>
</tr>
<tr>
<td>117 mg</td>
<td>410 mg</td>
</tr>
<tr>
<td>156 mg</td>
<td>546 mg</td>
</tr>
<tr>
<td>234 mg</td>
<td>819 mg</td>
</tr>
</tbody>
</table>

Olanzapine Pamoate: Initiation and Maintenance

- Requires 3-hour post-injection monitoring due to rare risk of post-injection delirium from vascular breach
- Loading for 8 weeks
- Specific dosage based on previous oral dose

<table>
<thead>
<tr>
<th>Daily Oral Olanzapine Dose</th>
<th>LAI Dose: First 8 Weeks</th>
<th>LAI Dose: After 8 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg</td>
<td>210 mg/2 weeks OR 405 mg/4 weeks</td>
<td>150 mg/2 weeks OR 300 mg/4 weeks</td>
</tr>
<tr>
<td>15 mg</td>
<td>300 mg/2 weeks</td>
<td>210 mg/2 weeks OR 405 mg/4 weeks</td>
</tr>
<tr>
<td>20 mg</td>
<td>300 mg/2 weeks</td>
<td>300 mg/2 weeks</td>
</tr>
</tbody>
</table>

Aripiprazole Monohydrate: Initiation and Maintenance

- Oral supplementation for first 14 days
- Maintenance dose:
  - 300–400 mg/4 weeks
  - 400 mg injection = 20 mg oral

Aripiprazole Lauroxil: Initiation, Option 1 (Oral Supplementation)

- Dissolves slowly
- Maximum concentration at 44–50 days
- Oral supplementation for first 21 days

Aripiprazole Lauroxil: Initiation, Option 2 (Single-Dose Initiation Injection)

- 675-mg single-dose injection of a nano crystal formulation plus a single day of 30 mg oral replaces 21 days of oral supplementation
- First maintenance injection: same day as single-dose injection or up to 10 days later
- Avoid injecting both the single-dose and maintenance-dose into the same deltoid or gluteal muscle

# Aripiprazole Lauroxil: Dosing Equivalence

<table>
<thead>
<tr>
<th>Oral Aripiprazole Dose</th>
<th>Lauroxil Dose</th>
<th>Intramuscular Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg per day</td>
<td>441 mg per month</td>
<td>Deltoid or Gluteal</td>
</tr>
</tbody>
</table>
| 15 mg per day               | 662 mg per month  
882 mg every 6 weeks  
1064 mg every 2 months | Gluteal                           |
| 20 mg or higher per day     | 882 mg per month                 | Gluteal             |

Maintenance Treatment With an LAI: Periodically Obtain Plasma Levels if Available
Summary

• Preventing relapse is a priority
• Preventing relapse requires adherence
• LAIs offer most schizophrenia patients their best chance at stability
• Kinetics determine which agents can be loaded and the appropriate loading strategies to achieve levels comparable to the desired oral equivalents
• Failure to adequately load the dose or provide oral supplementation can lead to subtherapeutic antipsychotic plasma levels for weeks or months