

## Arriving at Long-Acting Therapy: Clinical Considerations for Injectable Antipsychotics

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### Addendum to Presentation – 3/20/26

*Participants: Please read the following before taking the enduring course*

- **Slide 15 – Available LAIs:<sup>1</sup>**
  - Uzedy® (risperidone) was not included in the original presentation due to the timing of slide development and the primary focus on LAI antipsychotics most utilized within the Advocate Health retail formulary in Wisconsin and Illinois. At the time of presentation, content primarily reflected retail formulary and administration practices. Uzedy® is currently available on Advocate Health inpatient formulary, with potential expansion to outpatient use under consideration.
  - Uzedy® (risperidone) is a second-generation atypical antipsychotic indicated for the treatment of schizophrenia in adults. It is administered as a subcutaneous injection with monthly or every 2-month dosing options, which may offer flexibility in maintenance therapy.
  
- **Slide 15 – Available LAIs & Slide 21 – Formulation: ATRIGEL® Risperidone (Perseris®)**
  - Perseris® was included in the original presentation to highlight differences in LAI formulation technology, specifically its subcutaneous delivery system and formulation characteristics. However, Perseris® is currently removed from the market due to poor financial performance and is not utilized within the Advocate Health retail formulary in Wisconsin and Illinois.
  - To improve clarity, on slide 15, Perseris® should be considered off-market. On slide 21, Perseris® should be considered primarily for formulation science discussion rather than clinical comparison.
  
- **Slide 16 – LAIs Administered at WI/IL Advocate Health Pharmacies**
  - This list reflects LAI antipsychotics that can be administered within the outpatient pharmacy setting at Advocate Health retail pharmacies in Wisconsin and Illinois, based on the current Advocate Health retail formulary.

- **Slide 25 – Oral Overlap Requirements of LAIs<sup>2</sup>**
  - For Abilify Maintena® (aripiprazole), option 1 for oral overlap should specify that initiation includes two 400 mg Abilify Maintena® injections administered at separate injection sites, in addition to a single 20 mg oral dose of aripiprazole on the same day.
- **Slide 26 – Oral Overlap Requirements of LAIs<sup>3</sup>**
  - For Aristada® (aripiprazole lauroxil), option 1 for oral overlap should specify that one dose of Aristada INITIO® 675 mg is administered intramuscularly, followed by an initial dose of Aristada® administered intramuscularly plus a single 30 mg oral dose of aripiprazole, regardless of a previous oral dose.
- **Slide 27 – Oral Overlap Requirements of LAIs<sup>4</sup>**
  - For fluphenazine, in addition to establishing tolerability with short-acting fluphenazine prior to LAI initiation, oral overlap strategies may be utilized in clinical practice. A common approach is to continue approximately 50% of the patient’s oral maintenance dose until the second injection, then discontinue, to maintain therapeutic drug levels during initiation.
- **Slide 29 – Oral Overlap Requirements of LAIs<sup>5</sup>**
  - The loading dose strategy for Invega Sustenna® (paliperidone palmitate) was not detailed in the original presentation due to time constraints and the overall scope of the CE activity.
  - For initiation, Invega Sustenna® (paliperidone palmitate) utilizes an intramuscular loading dose of 234 mg on Day 1 followed by an intramuscular dose of 156 mg on Day 8, with both injections administered in the deltoid muscle. Following initiation, monthly maintenance dosing begins. Notably, oral antipsychotic overlap is not required, which may simplify the transition from oral therapy to an LAI.
- **Slide 59 – Strategies to Address Missed Appointments**
  - Under the heading for agent selection, the first bullet that mentions considering agents with “greater grace period” flexibility should be re-worded to considering agents with dosing window flexibility.
- **Slide 62 – Metabolic Considerations<sup>1,6</sup>**
  - Because Uzedy® (risperidone) was not included in the original presentation, it was not included in the table regarding metabolic considerations. However,

Uzedy® (risperidone) does have renal considerations that should be acknowledged.

- Per the Uzedy® (risperidone) package insert, if patients have renal impairment, it is recommended to titrate with oral risperidone (up to 2 mg daily) prior to initiating treatment with Uzedy® (risperidone). Uzedy® (risperidone) was not studied in patients with renal impairment.<sup>1</sup>
- Per Lexicomp, the following recommendations should be considered for patients with renal impairment when treating with Uzedy® (risperidone):<sup>6</sup>
  - CrCl > 60 mL/min: No dose adjustment necessary.
  - CrCl 10 to ≤ 60 mL/min: Use with caution. Closely monitor for adverse effects along with therapeutic drug monitoring.
  - CrCl < 10 mL/min: Avoid use.
- **Slide 63 - CYP2D6 Considerations<sup>7</sup>**
  - Aripiprazole is a substrate of CYP2D6/3A4. The slide acknowledges that aripiprazole doses should be adjusted if patients are also taking strong CYP2D6 inhibitors, such as fluoxetine or paroxetine. Another strong CYP2D6 inhibitor that would require aripiprazole dose adjustment is bupropion.
- **Slide 64 - CYP2D6 Considerations<sup>7</sup>**
  - When considering a patient's metabolism, phenoconversion should be taken into account. Strong or moderate CYP2D6 inhibitors can make a normal or ultrarapid metabolizer function like a poor or intermediate metabolizer. Genomic testing is used to measure metabolism. The genomic testing results should not be used to select therapy but can be used to help determine how therapy may be tolerated.
- **Slide 67 – Dose Adjustments in Older Adults<sup>8</sup>**
  - The row in the table that references haloperidol decanoate should include an additional clinical cue in the last column recommending monitoring the patient's QTc interval.
- **Slide 73 – Determining the Need for Oral Overall**
  - This slide title should be adjusted to “Preparing for LAI Initiation” to better reflect the content covered.

- **Slide 82 – Restarting Therapy**

- This slide title should be adjusted to “Example of Restarting Therapy” to better reflect the content covered.
- Due to time constraints when presenting the CE activity, only Aristada® (aripiprazole lauroxil) was discussed as one example of restarting LAI therapy.
- Clinicians should refer to each LAI product’s package insert for that specific product’s recommended regimen for restarting therapy.
- In regard to restarting Aristada® (aripiprazole lauroxil), the patient’s previous maintenance LAI dose should be administered, in addition to the supplementary dose information recommended within the table.

- **References:**

1. Uzedly® [package insert]. Parsippany, NJ: Teva, Inc.; Revised 2025.
2. Abilify Maintena® [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; Revised 2023
3. Aristada® [package insert]. Waltham, MA: Alkermes, Inc.; Revised 2023.
4. Tran JT, Binger KJ, Miles TM. Assessment of oral overlap with antipsychotic long-acting injectables initiated in an inpatient setting. *Ment Health Clin.* 2023;13(3):147-151. Published 2023 Jun 28. doi:10.9740/mhc.2023.06.147
5. Invega Sustenna® [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; Revised 2023.
6. Risperidone. In: Lexi-Drugs, Lexicomp. Wolters Kluwer Health, Inc.; 2020. Updated March 19, 2026.  
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7. Nahid NA, Johnson JA. CYP2D6 pharmacogenetics and phenoconversion in personalized medicine. *Expert Opin Drug Metab Toxicol.* 2022 Nov;18(11):769-785. doi: 10.1080/17425255.2022.2160317. Epub 2023 Jan 3. PMID: 36597259; PMCID: PMC9891304.
8. Haldol® Decanoate [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; Revised 2025.