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

Gabriel Barillas, PharmD, PGY1 Community-Based Pharmacy Resident - Aurora Health Care Metro, Inc.

Satjinder Singh, PharmD, PGY1 Community-Based Pharmacy Resident - Aurora Health Care Metro, Inc.

11/04/2025

Disclosures

The planners and speakers have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Abbreviation Key

BMI: Body Mass Index

CI: Confidence Interval

CrCl: Creatinine Clearance

CYP: Cytochrome P450 Enzymes

ED: Emergency Department

EPS: Extra Pyramidal Side-Effects

FDA: Food and Drug Administration

FGA: First Generation Antipsychotic

HR: Hazard Ratio

LAI: Long-Acting Injection

PK: Pharmacokinetic

QoL: Quality of Life

QTc: Corrected QT interval

RCT: Randomized Controlled Trial

RR: Risk Ratio

SGA: Second Generation Antipsychotic

SMD: Standardized Mean Difference

Learning Objectives

At the end of this session, learners should be able to:

- Identify the available long-acting injectable (LAI) antipsychotics and how their pharmacokinetic properties influence clinical use.
- Compare long-acting injectable antipsychotics to their oral counterparts in terms of patient level outcomes.
- Recognize patient-specific factors that influence the selection and initiation of long-acting injectable antipsychotics.
- Select treatment plans for patients utilizing long-acting injectable antipsychotics.

Identify the available long-acting injectable antipsychotics and how their pharmacokinetic properties influence clinical use.

Compare long-acting injectable antipsychotics to their oral counterparts in terms of patient level outcomes.

Recognize patient-specific factors that influence the selection and initiation of long-acting injectable antipsychotics.

Select treatment plans for patients utilizing long-acting injectable antipsychotics.

- Background
- Available LAI's
- Pharmacokinetics
- Clinical Use Implications

ADVOCATE HEALTH

Disease States Treated with LAIs

- Schizophrenia
  - Affects 1% of the global population
  - Chronic disorder characterized by positive, negative, and cognitive symptoms
    - Positive: delusions, hallucinations, disorganize speech/behavior, conceptual disorganization
    - Negative: avolition and reduced expression
    - Cognitive: deficits in attention, memory, and processing speed
  - Etiology: genetics, environmental risks (prenatal complication, psychosocial stress, cannabis), neurobiological factors (dopamine and glutamate dysfunction, brain structure changes)

ADVOCATE HEALTH

Hany M, Rizvi A. Schizophrenia. In: StatPearls Publishing; 2024.

So How Can LAIs Help?

Goals of Therapy with LAIs in Schizophrenia

Primary Goals

- Enhance medication adherence
  - Missed doses-even brief gaps-significantly increase relapse and hospitalization risk.
- Maintain symptom stability
  - Continuous receptor occupancy with LAIs supports sustained control of positive and negative symptoms
- Delay disease progression
  - Preventing Relapse helps limit functional decline and loss of autonomy over time

ADVOCATE HEALTH

Correll CU et al., J Clin Psychiatry, 2021

Disease States Treated with LAIs

- Bipolar disorder
  - Lifetime prevalence is 2.4% globally
  - Chronic mood disorder with episodes of depression and mania (I) or hypomania (II)
  - Classifications: Bipolar I, Bipolar II, cyclothymic disorder, and related disorders
  - Etiology: unknown but involves genetics, neurochemical, environmental

Jain A, Mitra P. Bipolar Disorder StatPearls Publishing, 2023.

Goals of Therapy with LAIs in Bipolar Disorder

Primary Goals

- Reduce hospitalization and inpatient days
- Prevent mood relapses
  - Reduce hypo/manic recurrences
- Enhance adherence and treatment continuity
  - Benefits are seen primarily in patients maintaining full adherence to LAIs, underscoring adherence as a key therapeutic event

Bartoli F et al., Ther Adv Psychopharmacol, 2023

What are LAIs?

- Long-acting injectable antipsychotics are depot formulations that deliver medication over weeks to months
- Designed to improve adherence and reduce relapse when compared to daily oral antipsychotics
- Commonly recommended in guidelines for patients with poor adherence or frequent relapse

APA Schizophrenia Practice Guideline, 2020

Why LAIs Matter?

- Up to 50% of patients with schizophrenia discontinue oral antipsychotics within 1 year
- Nonadherence increases relapse, and hospitalizations
- Patients may experience improved quality of life and satisfaction with treatment

Kappi A, Wang T, Abu Farsakh B, Okoli CTC. J Am Psychiatr Nurses Assoc., 2025

How do LAIs Work?

- Intramuscular or subcutaneous depot injections provide sustained medication release
- Formulation technology influences absorption and duration of action
- Some injections may require oral overlap upon initiation while others achieve therapeutic levels quickly

ADVOCATE HEALTH

Toja-Camba et al., Pharmaceutics, 2021

Available LAIs

Class	Medication	Dosing Intervals	Indications
First-Generation Antipsychotics (FGA)	Haloperidol decanoate	Monthly	Schizophrenia
	Fluphenazine decanoate	Monthly	Schizophrenia
Second-Generation Antipsychotics (SGA)	Aripiprazole lauroxil (Aristada®) Aripiprazole(Abilify Astimufii®) Aripiprazole (Abilify Maintena®)	Aripiprazole lauroxil (Aristada®): Every 4 to 8 weeks depending on dosing Aripiprazole(Abilify Astimufii®): Every 2 months Aripiprazole (Abilify Maintena®): Monthly Bipolar 1, Schizophrenia	Schizophrenia: All Bipolar 1: Aripiprazole (Abilify Astimufii®)
	Olanzapine Pamoate (Zyprexa Relprev®)	Every 2 or 4 weeks (dose-dependent)	Schizophrenia
	Paliperidone palmitate (Invega Hafyera®) Paliperidone palmitate (Invega Sustenna®) Paliperidone palmitate (Invega Trinza®)	Paliperidone palmitate (Invega Hafyera®): Every 6 months Paliperidone palmitate (Invega Sustenna®): Monthly Paliperidone palmitate (Invega Trinza®): Every 3 months	Schizophrenia
	Risperidone (Risperdal Consta®) Risperidone (Perseris®)	Risperidone (Risperdal Consta®): Biweekly Risperidone (Perseris®): Monthly	Bipolar 1, Schizophrenia

Package inserts for Haldol® Decanoate, Fluphenazine Decanoate, Risperdal Consta®, Perseris®, Invega Sustenna®, Invega Trinza®, Invega Hafyera®, Abilify Maintena®, Aristada®, Asimtufii®, Zyprexa Relprevv®.

ADVOCATE HEALTH

LAIs Administered at WI/IL Advocate Health Pharmacies

- Aripiprazole
  - Abilify Maintena®
  - *Not* Abilify Aristada® or Astimufii®
- Haloperidol decanoate (Haldol® decanoate)
- Paliperidone Palmitate
  - Invega Sustenna®
  - *Not* Invega Hafyera®
- Risperidone
  - Risperdal Consta®, Uzedy®
  - *Not* Perseris®

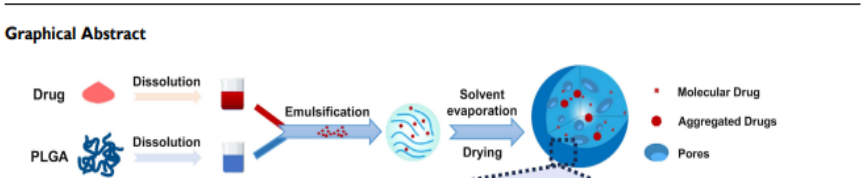
ADVOCATE HEALTH

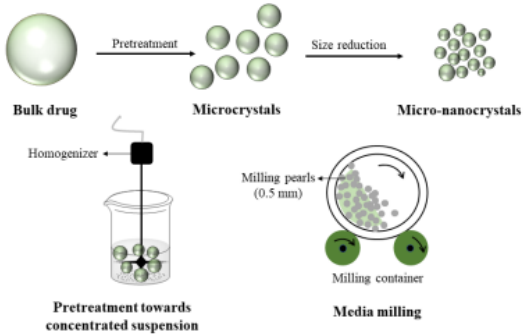
Pharmacokinetic Properties of LAIs

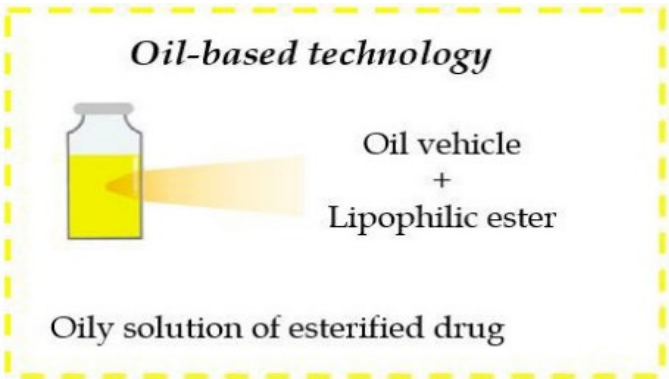
- Drug release depends on formulation technology
  - Microspheres
  - Nanocrystals
  - ATRIGEL®
  - Decanoate esters
- Absorption rate determines the oral overlap needs
- Half-life of medications often extended which allows for monthly or longer dosing
- Steady state is reached after multiple doses (vary by agent)
- The PK profile directly impacts initiation strategies, dosing intervals and adverse event management

FDA, Scientific Gap Analysis: Polymeric In Situ Depot Products
Markowicz-Piasecka M, et al., Pharmaceutics, 2023
Shi et al., Pharmaceutics, 2022
Wang et al., Int J Nanomedicine, 2024

Formulation Technology Drives PK





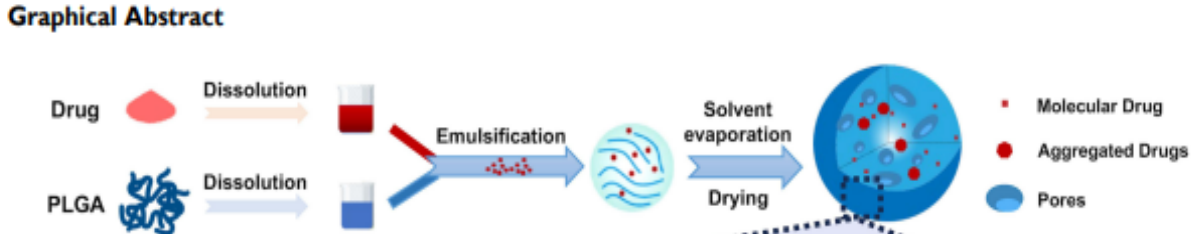


FDA, Scientific Gap Analysis: Polymeric In Situ Depot Products
Markowicz-Piasecka M, et al., *Pharmaceutics.* 2023
Shi et al., Pharmaceutics, 2022
Wang et al., Int J Nanomedicine, 2024

ADVOCATE HEALTH

Formulation: Microspheres Risperidone (Risperdal Consta®)

- Drug is embedded in polymer beads
- Emulsification + Solvent drying forms the beads
- Pores in beads slowly erode, controlling the release over time
- Requires oral overlap until steady state
- Expected time to onset: ~3 weeks

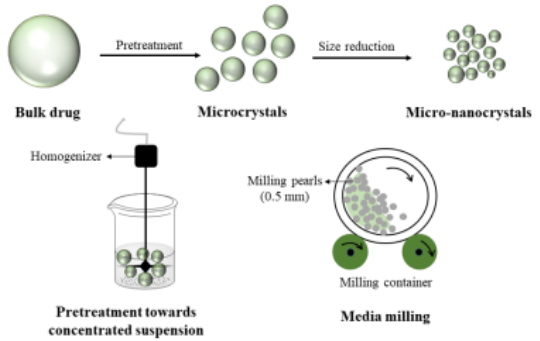


ADVOCATE HEALTH

Wang et al., Int J Nanomedicine, 2024

Formulation: Nanocrystals (Paliperidone)

- Drug crystalized, then wet-milled into nano-sized particles
- Increased surface area→ faster dissolution and stable release
- Rapid therapeutic levels→ no oral overlap needed
- Used in paliperidone products with different intervals (monthly to every 6 months)
- Onset: Begins on day one and continues up to four months.



ADVOCATE HEALTH

Shi et al., Pharmaceutics, 2022

Formulation: ATRIGEL® Risperidone (Perseris®)

- Risperidone dissolved in liquid polymer + solvent system
- After injection→ solvent exchanges with bodily fluids → polymer solidifies into depot
- Depot slowly biodegrades, releasing drug
- Provides rapid onset and sustained exposure
- Onset: Within days to weeks

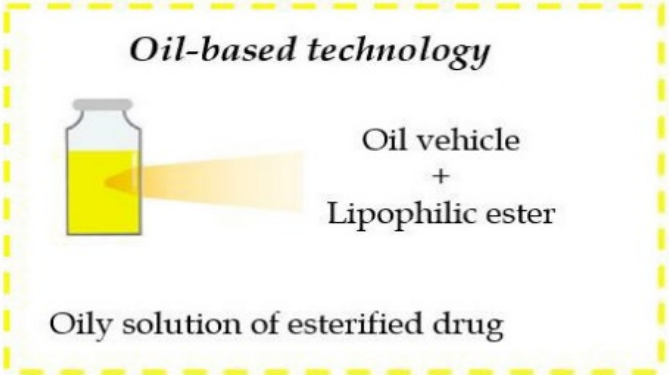
Figure 1. Schematic view of the ATRIGEL drug delivery technology

ADVOCATE HEALTH

FDA, Scientific Gap Analysis: Polymeric In Situ Depot Products

Formulation: Esterification (Decanoates: Fluphenazine, Haloperidol)

- Drug chemically linked to fatty acid (decanoate)
- Makes drug lipophilic→ suspended in oil vehicle
- Once injected, depot forms; ester bond hydrolyzed back into active drug
- Provides monthly release profile
- Onset: ~ 6 days for both decanoates



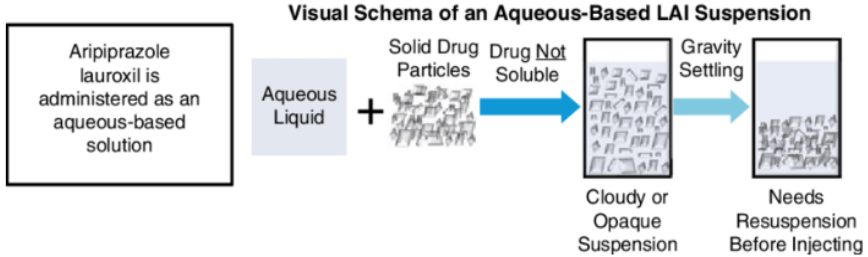
ADVOCATE HEALTH

Markowicz-Piasecka M, et al., Pharmaceutics, 2023

Formulation: Aqueous Suspension & Lyophilized Powder (Aripiprazole)

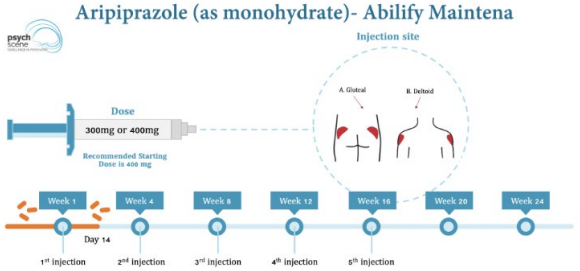
Aripiprazole lauroxil (Abilify Aristada®)

- Formulation: Aqueous-based suspension with solid drug particles
- Appearance: Cloudy/opaque suspension



Aripiprazole (Abilify Maintena®)

- Formulation: Lyophilized powder for reconstitution→ prolonged release suspension
- Appearance: Milky/opaque after reconstitution



ADVOCATE HEALTH

Jain R et al., CNS Spectr, 2020
Psych Scene Hub. Psychopharmacology of aripiprazole LAIs. 2021. Updated 2025

Summary of LAI Pharmacokinetics

Drug	Formulation	Half-Life	Dosing Interval	Expected Onset
Haloperidol Decanoate	Decanoate Ester	~3 weeks	Monthly	~6 days
Fluphenazine Decanoate	Decanoate Ester	1-3 weeks	Every 2-4 weeks	~6 days
Aripiprazole (Aristada®)	Nanosuspension	29-54 days	Monthly	Initio dosing: ~4 days No Initio dosing: ~3 weeks
Aripiprazole (Abilify Maintena®)	Monohydrate Suspension	29-46 days	Monthly	~14 days
Olanzapine pamoate (Relprevv®)	Salt Suspension	30 days	Every 2-4 weeks	~7 days
Paliperidone palmitate (Invega Sustenna®)	Nanocrystals	25-49 days	Every 4 weeks	~1 day
Paliperidone palmitate (Invega Trinza®)	Nanocrystals	84-95 days	Every 3 months	~1 day
Risperidone (Risperidal Consta®)	Microspheres	3-6 days	Every 2 weeks	~3 weeks

Data from manufacturer package inserts (Risperdal Consta, Invega Sustenna, Invega Trinza, Abilify Maintena, Aristada, Zyprexa Relprevv, Haldol Decanoate, Fluphenazine Decanoate, 2025)

ADVOCATE HEALTH

Oral Overlap Requirements of LAIs

Requires Oral Overlap

- Aripiprazole (Abilify Maintena®)
  - Fourteen day overlap
  - Option 1: Abilify Maintena® 400mg + single dose aripiprazole 20 mg
  - Option 2: Abilify Maintena® 400mg + 14 day concurrent use with oral aripiprazole or current oral antipsychotic

ADVOCATE HEALTH

Abilify Maintena [package insert]

Oral Overlap Requirements of LAIs

Requires Oral Overlap

- Aripiprazole Lauroxil (Aristada®)
  - Option 1: 1 dose Aristrada INITIO® 675 mg (injection), followed by initial dose of Aristada® (injection) + single dose oral aripiprazole
    - May receive second injection same day as Aristada® or up to 10 days after INITIO® loading dose
  - Option 2: After first injection of Aristrada®, take oral aripiprazole for 21 days

ADVOCATE HEALTH

Aristada [package insert]

Oral Overlap Requirements of LAIs

Requires Oral Overlap

- Fluphenazine
  - Establish tolerability using short-acting fluphenazine prior to initiating LAI

Fluphenazine decanoate [package insert]

Oral Overlap Requirements of LAIs

Requires Oral Overlap

- Risperidone (Risperdal Consta®)
  - Three week oral overlap

Risperdal Consta [package insert]

Oral Overlap Requirements of LAIs

No Overlap Required

- Haloperidol Deconoate (Haldol®)
- Olanzapine pamoate (Zyprexa Relprevv®)
- Paliperidone palmitate (Invega Sustenna®
- Paliperidone palmitate (Invega Trinza®)
- Risperidone (Uzedy®)

Data from manufacturer package inserts (Haldol Decanoate, Invega Sustenna, Invega Trinza, Zyprexa Relprevv, Risperdal Uzedy)

ADVOCATE HEALTH

Clinical Implications of PK

- Initiation
  - Oral overlap depends how quickly therapeutic levels are achieved
  - Tolerability testing with oral formulation
- Dosing Intervals
  - Long half-lives support extended dosing
- Steady State & Monitoring
  - True steady state may take months
  - Clinical response shouldn't be judged too early
  - Early side effects may persist longer due to extended half-life

Assessment Question 1

Which long-acting formulation uses polymer beads that delay drug release, requiring an oral overlap period?

A. ATRIGEL®
B. Esterification
C. Microspheres
D. Nanocrystals

Identify the available long-acting injectable antipsychotics and how their pharmacokinetic properties influence clinical use.

Compare long-acting injectable antipsychotics to their oral counterparts in terms of patient level outcomes.

Recognize patient-specific factors that influence the selection and initiation of long-acting injectable antipsychotics.

Select treatment plans for patients utilizing long-acting injectable antipsychotics.

- Improved Adherence with LAIs
- Hospitalizations and ED Admissions
- Healthcare Utilizations and Costs
- Quality of Life (QoL) Improvements
- LAIs and Their PK Properties for Clinical Use

Improved Adherence with LAIs

- Systematic review and meta-analysis of 137 studies, n = 397,319
  - Design: 32 randomized controlled trials (RCT), 65 cohort studies, 40 pre-post studies
  - Primary outcome: hospitalizations and relapse
    - RCTs: RR 0.88 (95% CI 0.79 - 0.99)
    - Cohort: RR 0.92 (0.88 - 0.98)
    - Pre-post: RR 0.44 (0.39 - 0.51)

ADVOCATE HEALTH

Kishimoto et al., The Lancet Psychiatry, 2025

Improved Adherence with LAIs (cont.)

- Limitations:
  - Adverse event reporting is unclear or incomplete
  - Not all studies used the same antipsychotics for both LAI and oral forms
    - Limits direct comparisons and introduces variability in efficacy
  - Heterogeneity – varied across studies and subgroup analysis was used to explore benefits
    - Subgroup analysis: 25 of 37 subgroups showed no significant difference which indicates a robust study overall

ADVOCATE HEALTH

Kishimoto et al., The Lancet Psychiatry, 2025

Takeaway Message

- Despite limitations, LAIs show consistent advantages in preventing relapse and hospitalization
- Findings support clinical use of LAIs to improve long-term outcomes in patients with schizophrenia

ADVOCATE HEALTH

Kishimoto et al., The Lancet Psychiatry, 2025

Hospitalizations and ED Admissions

- Mirror-image study on LAI effectiveness
  - Objective: evaluate real word effectiveness of LAI's in schizophrenia in reducing psychiatric hospitalizations, duration of hospitalizations, and psychiatric ED admissions
  - Design: mirror-image study, France 2015-2016
  - Population: 12,373 patients with schizophrenia
  - Compared 1 year on oral dosage form to 1 year post-LAI initiation

ADVOCATE HEALTH

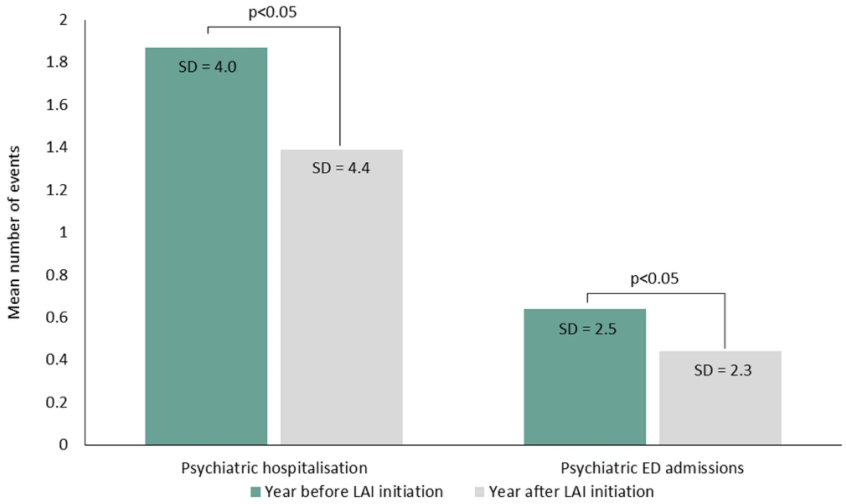
Boyer et al., Molecular Psychiatry, 2023

Hospitalizations and ED Admissions (cont.)

- Standardized mean differences (SMD) for one year before with oral antipsychotics and one year after LAI initiation
- LAI initiation reduced
  - Psychiatric hospitalizations (SMD = -0.19)
  - Duration of hospitalization (SMD = -0.26)
  - Psychiatric ED admissions (SMD = -0.12)

Fig. 2

From: Real-world effectiveness of long-acting injectable antipsychotic treatments in a nationwide cohort of 12,373 patients with schizophrenia-spectrum disorders



Healthcare utilization relating to psychiatric care one year before LAI initiation (during oral AP treatment) and one year after LAI initiation.

ADVOCATE HEALTH

Boyer et al., Molecular Psychiatry, 2023

Hospitalizations and ED Admissions (cont.)

- Limitations
  - Effects of involuntary commitment
  - No adjustment for confounders – social determinants of health, illness severity
  - Generalizability issues due to location of study
  - Clozapine not analyzed separately

Takeaway Message

- LAIs improve outcomes in non-compliant schizophrenia patients by reducing the number of psychiatric hospitalizations and emergency visits.

ADVOCATE HEALTH

Boyer et al., Molecular Psychiatry, 2023

Healthcare Utilizations and Costs

- One-year retrospective mirror-image study in China
- Utilized once-monthly paliperidone palmitate (Invega Sustenna®)
- Switched 72 patients from oral antipsychotic to Invega Sustenna®
- Primary focus: investigate impact of Invega Sustenna® on treatment patterns, healthcare resource use, and economic outcomes related to schizophrenia treatment

ADVOCATE HEALTH

Zhou et al., Frontier in Psychiatry, 2024

Healthcare Utilizations and Costs (cont.)

Clinical utilization outcomes

- Decreased hospitalizations, ER visits, and direct medical costs (all with $p < 0.001$)
- In patients with ≥1 hospitalization prior to LAI switch:
  - >90% reduction in hospitalizations, hospital days, and costs ($p < 0.001$)

Economic outcomes

- Pharmacy costs increased 222% ($p < 0.001$)
  - Invega Sustenna®= 88% of total pharmacy cost
- Total costs increased by 16% overall ($p < 0.001$)

ADVOCATE HEALTH

Zhou et al., Frontier in Psychiatry, 2024

Healthcare Utilizations and Costs (cont.)

- Limitations
  - Short follow-up (1 year)
  - Conducted at a single site
    - Small sample size
  - Cost analysis is limited to direct costs, not indirect costs such as productivity and caregiver costs

Zhou et al., Frontier in Psychiatry, 2024

ADVOCATE HEALTH

Takeaway Message

- Switching from oral antipsychotics to Invega Sustenna® reduced hospitalization, emergency visits, and overall healthcare resources.
  - However this comes at the expensive of higher costs of the LAI, which may limit its adoption within institutions

ADVOCATE HEALTH

Zhou et al., Frontier in Psychiatry, 2024

Quality of Life Improvements

- Systematic review of 111 studies investigating antipsychotics effectiveness on quality of life (QoL) improvements
  - Compared: dosage forms (oral, depot, LAI), generations (first, second, third), and patient characteristics
  - Results:
    - QoL often a secondary outcome in most trials
    - Second generation antipsychotics showed better QoL improvements vs first generation
    - LAI's showed more stable QoL

ADVOCATE HEALTH

Sampogna et al., Brain Sci, 2023

Quality of Life Improvements (cont.)

- Limitations
  - QoL not usually a primary endpoint which leads to less robust data
  - More than half of the studies recruited patients from outpatient settings which typically have less severe illness than inpatient
  - Different tools used to measure QoL: Clinical Global Impression-Severity, World Health Organization Quality of Life , Social and Occupational Functioning Assessment Scale, Quality of Life Scale
  - QoL is a complex construct that may not be accounted for in assessment and may not be influenced by treatment
    - Social context, support systems, and clinical factors (e.g. severity of negative symptoms, cognition)

ADVOCATE HEALTH

Sampogna et al., Brain Sci, 2023

Takeaway Message

- Second generation LAIs are associated with more stable and improved QoL for patients with schizophrenia.
- However, QoL is not prioritized in clinical trials by manufactures despite it being a key factor in treatment selection.
- Holistic views of patients are necessary in patients with behavior disorders such as schizophrenia.

ADVOCATE HEALTH

Sampogna et al., Brain Sci, 2023

LAIs and Their PK Properties for Clinical Use

Outcome	Oral Antipsychotics	LAI Antipsychotics
Adherence/Persistence	High rates of non-adherence due to pill burden, stigma and side effects	Improved adherence and persistence; reduced relapse risk
Hospitalization/ED Use	Higher relapse-related admissions and ED visits	Reduced hospitalization and ED visits after LAI initiation
Healthcare Utilization/Cost	Lower drug acquisition cost but higher overall healthcare costs (driven by hospital use)	Higher drug acquisition cost but reduced total cost through fewer admissions
Quality of Life / Functioning	Variable; Adherence challenges often limit benefit	Improved stability, functioning, and patient reported QoL

Boyer et al., Molecular Psychiatry, 2023
Kishimoto et al., The Lancet Psychiatry, 2025
Sampogna et al., Brain Sci, 2023
Zhou et al., Frontier in Psychiatry, 2024

Assessment Question 2

Which of the following best summarizes the patient-level benefits of LAI antipsychotics compared to oral antipsychotics based on current evidence?

A. LAIs are associated with increased pharmacy costs but reduced hospitalizations, relapse rates, and more stable quality of life.
B. LAIs show no significant difference in relapse or hospitalization rates compared to oral antipsychotics.
C. LAIs are only beneficial for patients with severe schizophrenia in inpatient settings.
D. LAIs consistently outperform oral antipsychotics in all clinical and economic outcomes across all patient populations.

Identify the available long-acting injectable antipsychotics and how their pharmacokinetic properties influence clinical use.

Compare long-acting injectable antipsychotics to their oral counterparts in terms of patient level outcomes.

Recognize patient-specific factors that influence the selection and initiation of long-acting injectable antipsychotics.

Select treatment plans for patients utilizing long-acting injectable antipsychotics.

- Relapse History
- Missed Doses and Appointments
- Metabolism Considerations
- Patient Characteristics
- Administration Factors

Real-World Effectiveness of LAIs vs Orals in Medicare Patients with Schizophrenia

- Design: Retrospective, Medicare cohort
- Population: Adults 18 or older with schizophrenia
- Intervention: LAI vs oral antipsychotics
- Primary Outcomes:
  - Treatment discontinuation
  - Treatment failure (hospitalization, switch or death)

ADVOCATE HEALTH

Li P et al., Adv Ther, 2025

Outcomes

- Discontinuation
  - Oral risperidone: Reference group
  - LAI risperidone: Hazard Ratio (HR) 0.43 (95% CI 0.19-0.67, $p < 0.05$)
  - Other LAIs: HR 0.55 (95%CI 0.35-0.75, $p < 0.05$)

- Treatment Failure
  - Oral risperidone: reference group
  - LAI risperidone: HR 0.69 (95% CI 0.53-0.85 $p < 0.05$)
  - Other LAIs: HR 0.72 (95% CI 0.60-0.84, $p < 0.05$)

- Takeaway
  - LAIs significantly reduced treatment discontinuation and failure compared with oral risperidone demonstrating improved persistence and effectiveness in real world use

ADVOCATE HEALTH

Li P et al., Adv Ther, 2025

Real-World Effectiveness of LAIs vs Orals in Medicare Patients

Outcome	Oral Risperidone (Reference)	LAI Risperidone HR (95% CI)	Other LAIs HR (95% CI)
Discontinuation	1.0	0.43 (0.19-0.67)	0.55 (0.35-0.75)
Treatment Failure	1.0	0.69 (0.53-0.85)	0.72 (0.60-0.84)

ADVOCATE HEALTH

Li P et al., Adv Ther, 2025

Delayed or Skipped Doses

- Missed oral doses
  - Most common reason for relapse
- LAIs improve adherence by reducing daily pill burden
- LAI selection depends on
  - Injection frequency
  - Flexibility of missed dose window
    - Some LAIs have grace periods, while others may require a re-initiation protocol
- Patients with history of missed doses may benefit from longer interval LAI

ADVOCATE HEALTH

Manchado Perero S et al., Front Psychiatry, 2025

Missed Appointments as a Patient-Specific Factor

- Missed injection visits are common in real-world practice
- Risk factors: transportation issues, unstable housing, stigma, limited insight, competing priorities
- Consequences for missed doses:
  - Decreased adherence
  - Increased relapse risk
  - Increased ED visits and hospitalizations

Manchado Perero S et al., Front Psychiatry, 2025

ADVOCATE HEALTH

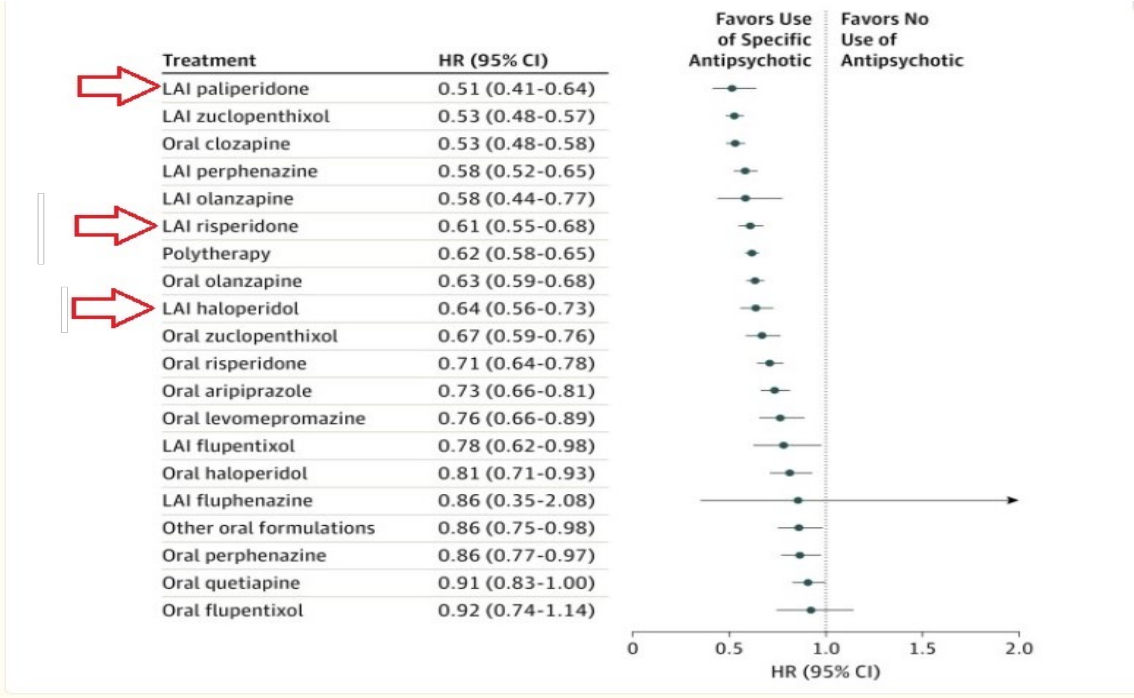
Missed Doses & Risk of Relapse

- Missed doses/appointments = strong predictor of relapse and hospitalization
- Real-world data
  - 29,823 patients with schizophrenia, 5.7-year follow-up
  - Paliperidone LAI: HR 0.51 (95% CI 0.41-0.64, p<0.001)
  - Risperidone LAI: HR 0.61 (0.55-0.68)
  - Haloperidol LAI HR 0.78 (0.72-0.84)

ADVOCATE HEALTH

Tiihonen J et al., JAMA Psychiatry, 2017

LAIs vs Oral Antipsychotics on Risk of Hospitalization



Treatment	HR (95% CI)
LAI paliperidone	0.51 (0.41-0.64)
LAI zuclopenthixol	0.53 (0.48-0.57)
Oral clozapine	0.53 (0.48-0.58)
LAI perphenazine	0.58 (0.52-0.65)
LAI olanzapine	0.58 (0.44-0.77)
LAI risperidone	0.61 (0.55-0.68)
Polytherapy	0.62 (0.58-0.65)
Oral olanzapine	0.63 (0.59-0.68)
LAI haloperidol	0.64 (0.56-0.73)
Oral zuclopenthixol	0.67 (0.59-0.76)
Oral risperidone	0.71 (0.64-0.78)
Oral aripiprazole	0.73 (0.66-0.81)
Oral levomepromazine	0.76 (0.66-0.89)
LAI flupentixol	0.78 (0.62-0.98)
Oral haloperidol	0.81 (0.71-0.93)
LAI fluphenazine	0.86 (0.35-2.08)
Other oral formulations	0.86 (0.75-0.98)
Oral perphenazine	0.86 (0.77-0.97)
Oral quetiapine	0.91 (0.83-1.00)
Oral flupentixol	0.92 (0.74-1.14)

Tiihonen J et al., JAMA Psychiatry, 2017

Strategies to Address Missed Appointments

- Agent Selection
  - Consider agents with "greater grace period" flexibility
  - Longer-interval LAI may reduce visit burden
- Pharmacist Role
  - Identify high-risk patients and implement solutions
  - Reminder calls, align injections with prescription refills or other clinic visits

ADVOCATE HEALTH

Correll CU et al., J Clin Psychiatry, 2021

Renal Considerations for LAIs

- Some LAIs rely on renal elimination
- Impaired renal function leads to:
  - Slow clearance of medication
  - Increase risk for adverse effects
- Dose adjustments or avoidance may be needed in moderate-to-severe impairment
- Clinical takeaway: Always assess renal function before selecting an LAI

Invega Sustenna [package insert]

Hepatic Metabolism

- Most SGA LAIs undergo hepatic metabolism via CYP450 enzymes (CYP2D6, CYP3A4)
- FGA LAIs also rely on hepatic metabolism
- Drug interactions
  - Strong CYP inhibitors may increase exposure; strong inducers may lower efficacy
- Clinical pearls: Adjust dose if persistent coadministration is unavoidable, otherwise monitor closely or consider alternatives

ADVOCATE HEALTH

Gao Y et al., Front Pharmacol, 2023

Metabolic Considerations

Medication	Clearance Pathway	CYP Enzymes	Renal Consideration
Aripiprazole	Hepatic Metabolism	CYP2D6, 3A4	No adjustment needed
Haloperidol	Hepatic Metabolism	CYP2D6, 3A4	No adjustment needed
Paliperidone	Primarily renal elimination	Minimal CYP involvement	Reduce dose if Creatinine Clearance (CrCl) 50-80 mL/min; Avoid if CrCl < 50 mL/min
Risperidone	Hepatic→ active metabolite is paliperidone	CYP2D6, 3A4	Slower clearance in renal impairment Consta®: Consider 12.5mg every 2 to 4 weeks

CYP2D6 Considerations

- Aripiprazole
  - Substrate of CYP2D6/3A4
  - Poor metabolizers have higher drug exposure and should be initiated at a lower dose
  - Adjust dose if on strong CYP2D6 inhibitors (fluoxetine, paroxetine)
- Haloperidol
  - CYP2D6/3A4 metabolism
  - Poor metabolizers may have increased plasma concentrations
  - Manage clinically with monitoring/adjustment
- Paliperidone palmitate
  - No CYP considerations
- Risperidone
  - CYP2D6 metabolizes to active metabolite (paliperidone)
  - Poor metabolizers increase risperidone levels and lower starting dose may be warranted

ADVOCATE HEALTH

Package inserts for (Haldol® Abilify Maintena®, Aristada®, Asimtufii®, Risperdal Consta®, Perseris®)

CYP2D6 Considerations

- How to identify metabolizer status
  - Genetic testing
    - CYPD2D6 pharmacogenomic assays – not routine everywhere
  - Clinical clues
    - Unexpected side effects→ possible poor metabolizer
    - Reduced efficacy/early relapse → possible rapid metabolizer

- Clinical Pearl
  - In practice, CYP2D6 status is rarely tested upfront – dose adjustments are usually guided by clinical response and drug-drug interactions

ADVOCATE HEALTH

Toja-Camba FJ et al., Prog Neuropsychopharmacol Biol Psychiatry, 2024

Geriatric Population

- Increased sensitivity to extrapyramidal symptoms, orthostasis and sedation
- Age related renal decline
  - Impacts paliperidone clearance
- Prefer lower doses, slower titration
- Monitor cognition, fall risk

AGS Beers Criteria® J Am Geriatr Soc, 2023

ADVOCATE HEALTH

Beers Criteria

- Beers Criteria
  - All antipsychotics (oral, injectable) are listed as potentially inappropriate in older adults with dementia due to increased risk of stroke, cognitive decline and mortality
  - Avoid except in FDA approved indications
  - No LAI-specific exclusion, but risks apply across formulations

Antipsychotics, first- (typical) and second- (atypical) generation Aripiprazole Haloperidol Olanzapine Quetiapine Risperidone Others[d]	Increased risk of stroke and greater rate of cognitive decline and mortality in persons with dementia. Additional evidence suggests an association of increased risk between antipsychotic medication and mortality independent of dementia.	Avoid, except in FDA-approved indications such as schizophrenia, bipolar disorder, Parkinson disease psychosis (see Table 3), adjunctive treatment of major depressive disorder, or for short-term use as an antiemetic.

ADVOCATE HEALTH

AGS Beers Criteria® J Am Geriatr Soc, 2023

Dose Adjustments in Older Adults

LAI	Geriatric Consideration	Clinical Cue
Aripiprazole Maintena®	Start at 300 mg (instead of 400 mg)	Monitor sedation/akathisia
Haloperidol decanoate	Start at lower end of the conversion range (10 times the daily oral dose)	Monitor extra pyramidal side-effects (EPS), cognitive effects
Paliperidone Sustenna®	Use lower initiation dose (78 mg) if renal decline present	Monitor QTc; metabolic effects
Risperidone Consta®	Consider 12.5 mg every 2 weeks (instead of 25 mg)	Orthostasis, EPS more likely

Data from manufacturer package inserts (Abilify Maintena® [Otsuka, 2025]; Risperdal Consta® [Janssen, 2025]; Invega Sustenna® [Janssen, 2025]; Haldol Decanoate® [Janssen, 2025]).

ADVOCATE HEALTH

The Role of Pharmacists in Long-Acting Injectable Antipsychotics

- All LAI antipsychotics must be administered by a healthcare professional
- Access & Barriers
  - LAI use remains low (6.5% in Canada vs 15-80% internationally)
  - Patients face barriers including transportation, limited availability of prescribers and stigma
- Pharmacist Impact
  - Accessible (community-based, extended hours)
  - Trusted relationships with patients on complex medications
  - Can address adherence gaps and improve continuity

ADVOCATE HEALTH

Murphy et al., Pharmacy (Basel), 2023

Injection Site Considerations-Deltoid vs Gluteal?

Feature	Deltoid	Gluteal
Drug Levels	Reaches higher blood levels early (~20 to 30% faster than gluteal) leading to a faster onset	Slower absorption; drug levels rise more gradually
Patient Comfort	Easier access, less clothing removal, many patients prefer	May cause less local tenderness/pain
Feasibility in Clinic/Pharmacy	Fits workflow better (quicker, easier, positioning, more privacy)	Less practical in outpatient settings; requires more space/positioning

Rossenu S, Cleton A, Hough D, et al., Clin Pharmacol Drug Dev., 2015
Quiroz JA, Rusch S, Thyssen A, Palumbo JM, Kushner S. Innov Clin Neurosci., 2011

ADVOCATE HEALTH

Assessment Question 3

GS is a 29-year-old male with schizophrenia who has experienced multiple hospitalizations due to psychotic relapses. He has a history of non-adherence to oral risperidone and lives with his supportive parents. His labs are currently within normal limits, BMI is 28 kg/m², and he has no significant medical comorbidities. He expresses frustration with daily oral medications and is interested in transitioning to a LAI antipsychotic.

If GS were to develop moderate renal impairment (e.g., eGFR < 50 mL/min/1.73m²), which of the following LAI antipsychotics would be least appropriate due to its primary route of elimination?

A. Aripiprazole

B. Haloperidol Decanoate

C. Olanzapine Pamoate

D. Paliperidone Palmitate

Identify the available long-acting injectable antipsychotics and how their pharmacokinetic properties influence clinical use.

Compare long-acting injectable antipsychotics to their oral counterparts in terms of patient level outcomes.

Recognize patient-specific factors that influence the selection and initiation of long-acting injectable antipsychotics.

Select treatment plans for patients utilizing long-acting injectable antipsychotics.

- First Time LAI Use (New Start)
- Switching From Oral to LAI
- Restarting Therapy
- Treatment failure
- Switching Between LAI Formulation

Determining the Need for Oral Overlap

- Confirm oral tolerability before injection
- Check agent specific initiation regimen and time to therapeutic levels
- Use oral overlap if LAI has delayed release or no rapid loading option
- Patient specific factors may push providers towards overlap or different LAI choices
  - Patient adherence, history of relapse, renal/hepatic impairment

ADVOCATE HEALTH

Throneberry AR et al., Frontiers, 2025

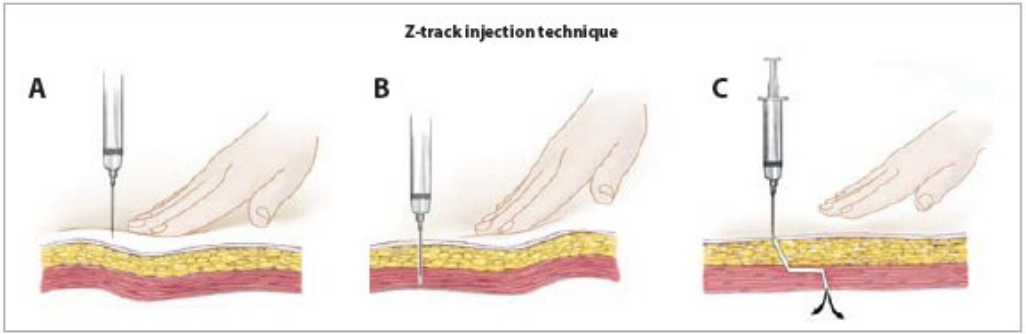
Assess Tolerability Prior to LAI Initiation

- 2 weeks to assess tolerability
  - Aripiprazole (Aristada®, Abilify Maintena®)
- No timeline given to assess tolerability
  - Olanzapine Pamoate (Zyprexa Relprevv®), Paliperidone (Sustenna®, Trinza®, Hafyera®), Risperdal (Consta®,Perseris®)
- No guideline/manufacturer recommendations: fluphenazine decanoate, haloperidol decanoate

Abilify Maintena [package insert]
Aristada [package insert]

Pearls for Administering

- Injection site
  - Lumping at the site of injection
  - Injection site reaction – most common side effect is pain
  - Ventrogluteal preferred over dorsogluteal to avoid sciatic nerve
  - Deltoid often preferred by patients
- Rotate injection sites to reduce lipohypertrophy
  - Z-track injection method for haloperidol



Zolezzi et al., Neuropsychiatric Dis Treat, 2021
https://www.western.vaems.org/drug-shortages-and-info/1000-emergency-protocol-benadryl-shortage

ADVOCATE HEALTH

Points for Providers

- Monitoring:
  - Metabolic monitoring (see table)
  - Movement disorders every clinic visits: Abnormal Involuntary Movement Scale (AIMS)
  - Agranulocytosis after first initiation, then annually
    - Absolute neutrophil count (discontinue if ANC < 1000 cells/μL)
  - Prolonged QTc after initiation in patients with family history or known risk for QT prolongation

	Baseline	4 Weeks	8 Weeks	12 Weeks	6 Months	Annually
Weight/body mass index[b]	X	X	X	X	X	X
Fasting plasma glucose/hemoglobin A1c[c]	X			X	X	X
Lipids	X			X	X	X
Blood pressure	X			X	X	X

DeJongh B., Ment Health Clin, 2021
Zolezzi et al., Neuropsychiatric Dis Treat, 2021

ADVOCATE HEALTH

Points for Providers

- Boxed warning on antipsychotics: increased risk of death in older adults with dementia-related psychosis
- Olanzapine pamoate (Zyprexa Relprevv®) has a 3 hour post-injection monitoring for delirium/sedation risk

DeJongh B., Ment Health Clin, 2021
Zolezzi et al., Neuropsychiatric Dis Treat, 2021

ADVOCATE HEALTH

Points for Patients

- Benefits of LAI
- Medication coverage
- Adherence and follow-up
- Discuss side effects
  - Movement disorders, anticholinergic side effects, sedation, metabolic changes (weight, lipids), prolactin elevation

Side Effect Profile

	Sedation	EPS	Anticholinergic	Orthostasis	Weight Gain	Prolactin
Aripiprazole	+	+/++	+	+	+	+
Fluphenazine	+	++++	+	+	+	++++
Haloperidol	+	++++	+	+	+	++++
Olanzapine	++	++	++	++	++++	+
Paliperidone	+	++	+	+	++	++++
Risperidone	+	++	+	++	++	++++

ADVOCATE HEALTH

DiPiro et al., McGraw-Hill, 2020

Switching from Oral to LAI

- Assess adherence and clinical stability on oral therapy
  - Confirm symptom control
  - Assess side effects: anaphylaxis, movement disorders (tremors, stiffness), metabolic disorder (weight gain, cholesterol, increase in blood glucose), drowsiness
- Conversion strategy
  - Direct switch or overlap option
  - Tapering option

ADVOCATE HEALTH

Keks N et al., J. Australian Prescriber, 2019

Restarting Therapy

- No guidelines or package insert information for restarting for: haloperidol decanoate, fluphenazine decanoate, olanzapine pamoate (Zyprexa Relprevv®), risperidone (Risperdal Consta® & Risperdal Perseris®)
- Please refer to package insert for restarting therapy information

Restarting Therapy

- Aripiprazole lauroxil (Aristada®)

Dose of patient's last Aristada® injection	Length of time since last injection		
441 mg	≤ 6 weeks	> 6 and ≤ 7 weeks	>7 weeks
662 mg	≤ 8 weeks	**> 8 and ≤ 12 weeks**	>12 weeks
882 mg	≤ 8 weeks	> 8 and ≤ 12 weeks	>12 weeks
1064 mg	≥ 10 weeks	> 10 and ≤ 12 weeks	>12 weeks
Dosage and administration for re-initiation of Aristada®	No supplementation required	Supplement with a single dose of Aristada Initio®	Re-initiate with a single dose of Aristada® Initio and single dose of oral aripiprazole 30 mg

ADVOCATE HEALTH

Aristada [package insert]

Treatment Failures

- Assessing failure can fall into 3 categories
  - Treatment resistance:
    - Three treatment periods in 5 years with antipsychotics with at least 2 different chemical classes
    - No period of good functioning within the preceding 5 years
  - Pseudo-resistance: lack of response to treatment not attributed to pharmacological inefficiency, but depending on modifiable and non-modifiable factors such as non-adherence
  - Non-adherence: some or none of the prescribed medication is taken

ADVOCATE HEALTH

Abdellati K et al., Front Neurosci, 2020

Reducing Treatment Failures

- Drivers of non-adherence
  - Younger age, poor illness insight, substance misuse, severe positive symptoms (paranoia, hostility), negative attitude about medications
- Protective factors
  - Positive patient/family attitudes toward medication
  - Family/social involvement and support
  - Better illness insight
- Interventions to reduce treatment failure
  - Family therapy
  - Psychoeducation
  - Motivational interviewing and trauma informed care
  - Reminders on taking medication
  - Close monitoring for higher risk groups (younger patients, active cannabis use)

ADVOCATE HEALTH

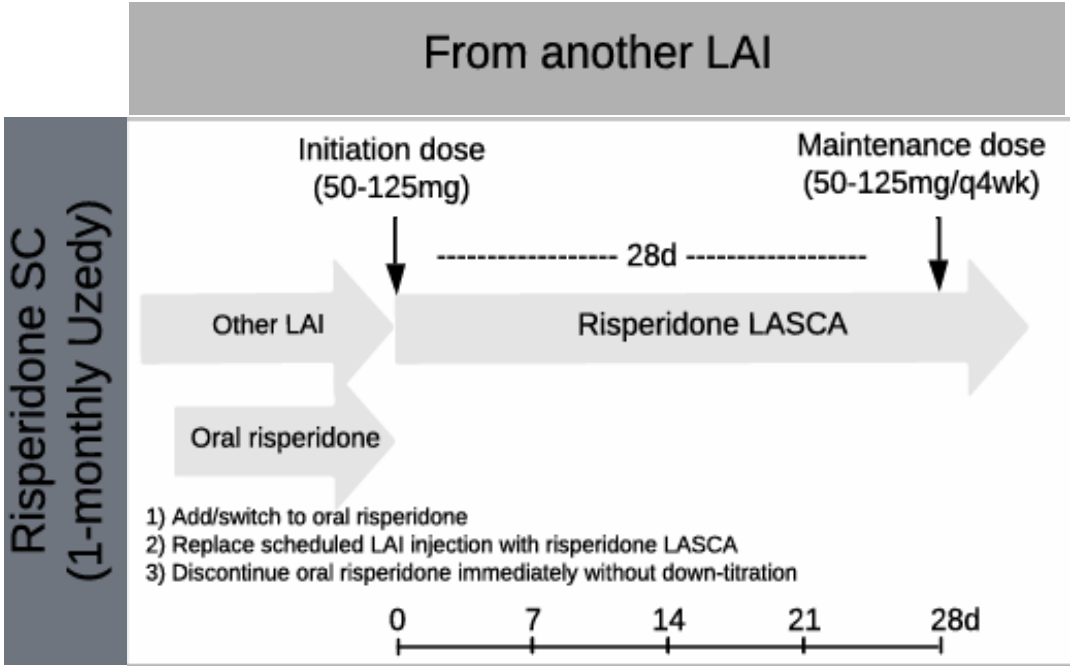
Abdellati K et al., Front Neurosci, 2020

Switching Between LAI Formulations

- Limited research as switching between LAI's is not part of the FDA approval process
- Switching is based off pharmacological properties of the drug and the clinical experience
- Before switching ensure
  - The initial antipsychotic medication has been optimized
  - Patient has been treated for an adequate amount of time
  - Patient is adherent to the therapy
- The new drug should be determined based on the reason for the switch: adverse effects, dosing regimen, patient/provider preference
- Not recommended to have a drug-free period when switching due to the risk of relapse
- Direct switch for oral: stop first drug and start second drug next day
- Cross titration for oral: taper first medication, while introducing second

Keks N et.al., Australian Prescriber, 2019
Højlund M et al., Expert Opin Pharmacother, 2023

Switching Between LAIs



ADVOCATE HEALTH

Højlund M, Correll CU, *Expert Opin Pharmacother,* 2023

Assessment Question 4

GS is a 29-year-old male with schizophrenia who has experienced multiple hospitalizations due to psychotic relapses. He has a history of non-adherence to oral risperidone and lives with his supportive parents. His labs are currently within normal limits, BMI is 28 kg/m², and he has no significant medical comorbidities. He expresses frustration with daily oral medications and is interested in transitioning to a LAI antipsychotic.

Which of the following treatment approaches best addresses GS's clinical needs and supports long-term adherence?

A. Initiate haloperidol decanoate and recommend switching injection sites monthly to reduce lipohypertrophy.

B. Begin oral risperidone to assess tolerability, initiate risperidone (Risperdal Consta®) with oral overlap, and involve family in adherence support and psychoeducation.

C. Start olanzapine (Zyprexa Relprevv®) and monitor GS for 3 hours post-injection to assess sedation risk.

D. Continue oral risperidone while implementing motivational interviewing and family-based therapy to improve adherence before considering LAI.

Conclusions

1. LAI antipsychotics are depot formulations used to improve adherence and outcomes in conditions such as bipolar disorder and schizophrenia by providing sustained drug release, reducing relapse, and requiring specific PK considerations, formulation technologies, and oral overlap protocols for optimal therapeutic effect.
2. LAI antipsychotics have shown to improve adherence, reduce hospitalizations and emergency visits, lower healthcare costs, and enhance quality of life for patients with schizophrenia.
3. LAI antipsychotics reduce treatment discontinuation and hospitalization risk, while addressing challenges like missed doses, metabolic, and PK considerations, organ function, geriatric dosing, and the critical role of pharmacists in optimizing therapy.
4. Most guidance on initiating and restarting LAI antipsychotics is found in the package insert; transitioning between LAI therapies often requires careful planning, including oral overlap for tolerability assessment and a thorough understanding of each agent’s PK to ensure a safe and effective switch.

References

1. Kappi A, Wang T, Abu Farsakh B, Okoli CTC. *J Am Psychiatr Nurses Assoc.* 2025;31(2):138-164. doi:10.1177/10783903241279605

2. Hany M, Rizvi A. Schizophrenia. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; February 23, 2024.

3. Correll CU, Citrome L, Haddad PM, et al. The Use of Long-Acting Injectable Antipsychotics in Schizophrenia: Evaluating the Evidence. *J Clin Psychiatry*. 2016;77(suppl 3):1-24. doi:10.4088/JCP.15032su1

4. Jain A, Mitra P. Bipolar Disorder. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; February 20, 2023.

5. Bartoli F, Cavaleri D, Nasti C, et al. Long-acting injectable antipsychotics for the treatment of bipolar disorder: evidence from mirror-image studies. *Ther Adv Psychopharmacol*. 2023;13:20451253231163682. Published 2023 Mar 25. doi:10.1177/20451253231163682

6. Fluphenazine Decanoate [package insert]. Bristol, TN: West-Ward Pharmaceuticals; Revised 2022.

7. Risperdal Consta® [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; Revised 2023.

8. Perseris® [package insert]. North Chesterfield, VA: Indivior, Inc.; Revised 2023.

9. Invega Sustenna® [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; Revised 2023.

10. Invega Trinza® [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; Revised 2023.

11. Invega Hafyera® [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; Revised 2023.

12. Abilify Maintena® [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; Revised 2023.

13. Aristada® [package insert]. Waltham, MA: Alkermes, Inc.; Revised 2023.

ADVOCATE HEALTH

References

14.Wang M, Wang S, Zhang C, et al. Microstructure Formation and Characterization of Long-Acting Injectable Microspheres: The Gateway to Fully Controlled Drug Release Pattern. *Int J Nanomedicine*. 2024;19:1571-1595. Published 2024 Feb 19. doi:10.2147/IJN.S445269

15.Shi J, Wang D, Tian Y, et al. Comparison of Paliperidone Palmitate from Different Crystallization Processes and Effect on Formulations In Vitro and In Vivo. *Pharmaceutics*. 2022;14(5):1094. Published 2022 May 20. doi:10.3390/pharmaceutics14051094

16.FDA. Scientific Gap Analysis of Polymeric In Situ Forming Depot Products for the Development of GDUFA Research Projects. FDA Science Forum; 2021. [Accessed Sep 17, 2024]. https://www.fda.gov/science-research/fda-science-forum/scientific-gap-analysis-polymeric-situ-forming-depot-products-development-gdufa-research-projects

17.Markowicz-Piasecka M, Kubisiak M, Asendrych-Wicik K, et al. Long-Acting Injectable Antipsychotics-A Review on Formulation and In Vitro Dissolution. *Pharmaceutics*. 2023;16(1):28. Published 2023 Dec 24. doi:10.3390/pharmaceutics16010028

18.Jain R, Meyer J, Wehr A, Rege B, von Moltke L, Weiden PJ. Size matters: the importance of particle size in a newly developed injectable formulation for the treatment of schizophrenia. *CNS Spectr*. 2020;25(3):323-330. doi:10.1017/S1092852919000816

19.Psych Scene Hub. Psychopharmacology and Clinical Application of Aripiprazole Long Acting Injections – Review of Abilify Maintena & Aristada. PsychSceneHub. Published September 21, 2021. Last updated January 13, 2025. Accessed [Sep 27 , 2025]. https://www.fda.gov/science-research/fda-science-forum/scientific-gap-analysis-polymeric-situ-forming-depot-products-development-gdufa-research-projects

20.Kishimoto T, Hagi K, Kurokawa S, Kane JM, Correll CU. Long-acting injectable versus oral antipsychotics for the maintenance treatment of schizophrenia: a systematic review and comparative meta-analysis of randomised, cohort, and pre–post studies. The Lancet Psychiatry. 2021;8(5):387-404. doi:https://doi.org/10.1016/s2215-0366(21)00039-0

21.Boyer L, Falissard B, Nuss P, et al. Real-world effectiveness of long-acting injectable antipsychotic treatments in a nationwide cohort of 12,373 patients with schizophrenia-spectrum disorders. Molecular Psychiatry. 2023;28:1-8. doi:https://doi.org/10.1038/s41380-023-02175-z

22.Zhou Y, Chen B, Huang Y. Healthcare utilization and economics evaluation of paliperidone palmitate once-monthly in schizophrenia: a one-year, real-world, and retrospective mirror image study in China. Front Psychiatry. 2024;15:1415275. Published 2024 Sep 4. doi:10.3389/fpsyt.2024.1415275

23.Sampogna G, Di Vincenzo M, Giuliani L, et al. A Systematic Review on the Effectiveness of Antipsychotic Drugs on the Quality of Life of Patients with Schizophrenia. Brain Sci. 2023;13(11):1577. Published 2023 Nov 10. doi:10.3390/brainsci13111577

ADVOCATE HEALTH

References

24.Li P, Geng Z, Benson C, Patel C, Doshi JA. Real-World Effectiveness of Long-Acting Injectable and Oral Antipsychotic Agents in US Medicare Patients with Schizophrenia. Adv Ther. 2025;42(2):1251-1264. doi:10.1007/s12325-024-03075-6

25.Manchado Perero S, Rodríguez Lorente A, García-Pérez A, et al. Long-term effectiveness, adherence and safety of twice-yearly paliperidone-palmitate long acting-injectable in patients with schizophrenia in Europe: 2-year mirror-image data from the paliperdone-2 per year study (P2Y). Front Psychiatry. 2025;16:1540213. Published 2025 Mar 4. doi:10.3389/fpsyt.2025.1540213

26.Tiihonen J, Mittendorfer-Rutz E, Majak M, et al. Real-World Effectiveness of Antipsychotic Treatments in a Nationwide Cohort of 29 823 Patients With Schizophrenia. JAMA Psychiatry. 2017;74(7):686-693. doi:10.1001/jamapsychiatry.2017.1322

27.Correll CU, Citrome L, Haddad PM, et al. The Use of Long-Acting Injectable Antipsychotics in Schizophrenia: Evaluating the Evidence. J Clin Psychiatry. 2016;77(suppl 3):1-24. doi:10.4088/JCP.15032su1

28.Gao Y, Wu C, Zhai X, et al. Aripiprazole-induced liver injury: a spontaneous reporting database study. Front Pharmacol. 2023;14:1226386. Published 2023 Aug 24. doi:10.3389/fphar.2023.1226386

29.Toja-Camba FJ, Vidal GH, Vidal-Millares M, et al. Role of CYP2D6 and CYP3A4 polymorphisms on aripiprazole and dehydroaripiprazole concentrations in patients undergoing long-acting treatment. Prog Neuropsychopharmacol Biol Psychiatry. 2024;135:111134. doi:10.1016/j.pnpbp.2024.111134

30.By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023;71(7):2052-2081. doi:10.1111/jgs.18372

31.Murphy AL, Suh S, Gillis L, Morrison J, Gardner DM. Pharmacist Administration of Long-Acting Injectable Antipsychotics to Community-Dwelling Patients: A Scoping Review. Pharmacy (Basel). 2023;11(2):45. Published 2023 Feb 27. doi:10.3390/pharmacy11020045

ADVOCATE HEALTH

References

32.Rossenu S, Cleton A, Hough D, et al. Pharmacokinetic profile after multiple deltoid or gluteal intramuscular injections of paliperidone palmitate in patients with schizophrenia. Clin Pharmacol Drug Dev. 2015;4(4):270-278. doi:10.1002/cpdd.144

33.Quiroz JA, Rusch S, Thyssen A, Palumbo JM, Kushner S. Deltoid injections of risperidone long-acting injectable in patients with schizophrenia. Innov Clin Neurosci. 2011;8(6):20-28.

34.Throneberry AR, Burk BG, Pruett BS. Optimizing long-acting injectable antipsychotic safety and care continuity through documentation best practices. Frontiers in Psychiatry. 2025;16. doi:https://doi.org/10.3389/fpsyt.2025.1659290

35.VandenBerg AM. An update on recently approved long-acting injectable second-generation antipsychotics: Knowns and unknowns regarding their use. Mental Health Clinician. 2022;12(5):270-281. doi:https://doi.org/10.9740/mhc.2022.10.270

36.Zolezzi M, Abouelhassan R, Eltorki Y, Haddad PM, Noorizadeh M. Long-Acting Injectable Antipsychotics: A Systematic Review of Their Non-Systemic Adverse Effect Profile. Neuropsychiatr Dis Treat. 2021;17:1917-1926. Published 2021 Jun 14. doi:10.2147/NDT.S309768

37.DeJongh BM. Clinical pearls for the monitoring and treatment of antipsychotic induced metabolic syndrome. Ment Health Clin. 2021;11(6):311-319. Published 2021 Nov 8. doi:10.9740/mhc.2021.11.311

38.Krishna A, Goicochea S, Shah R, Stamper B, Harrell G, Turner A. A Comprehensive Guide to Long-Acting Injectable Antipsychotics for Primary Care Clinicians. The Journal of the American Board of Family Medicine. 2024;37(4):773-783. doi:https://doi.org/10.3122/jabfm.2022.220425r2

39.Dipiro JT, Yee GC, Posey ML, Haines ST, Nolin TD, Ellingrod V. Pharmacotherapy a Pathophysiologic Approach. Mcgraw-Hill Education Llc., C; 2020.

40.Aprile SF, Rodolico A, Di Francesco A, et al. Oral versus long-acting injectable antipsychotics in schizophrenia spectrum disorders: A systematic review of patients' subjective experiences. Psychiatry Research. 2025;348:116460. doi:https://doi.org/10.1016/j.psychres.2025.116460

ADVOCATE HEALTH

References

41. Keks N, Schwartz D, Hope J. Stopping and switching antipsychotic drugs. Aust Prescr. 2019;42(5):152-157. doi:10.18773/austprescr.2019.052

42. El Abdellati K, De Picker L, Morrens M. Antipsychotic Treatment Failure: A Systematic Review on Risk Factors and Interventions for Treatment Adherence in Psychosis. Front Neurosci. 2020;14:531763. Published 2020 Oct 9. doi:10.3389/fnins.2020.531763

43. Højlund M, Correll CU. Switching to long-acting injectable antipsychotics: pharmacological considerations and practical approaches. Expert Opin Pharmacother. 2023;24(13):1463-1489. doi:10.1080/14656566.2023.2228686

ADVOCATE HEALTH

Questions?

- Gabriel Barillas, PharmD, PGY1 Community-Based Pharmacy Resident - Aurora Health Care Metro, Inc.
  - Gabriel.Barillas@aah.org
- Satjinder Singh, PharmD, PGY1 Community-Based Pharmacy Resident - Aurora Health Care Metro, Inc.
  - Satjinder.Singh@aah.org

CE Learning Platform
https://ce.advocatehealth.org

Remember to create/update your profile on the CE platform, complete an evaluation, then claim credit

ADVOCATE HEALTH