

long-acting injectables360

Operationalizing Adherence: *A Practical Guide to LAI Integration in Schizophrenia Care*

MasterClass

Supported by educational grants from Alkermes, Inc.; Johnson & Johnson; and Teva Pharmaceuticals, USA, Inc.

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Disclosure

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Learning Objectives

- Analyze the evolving role of LAIs versus OAPs in schizophrenia, integrating the latest clinical guidelines, real-world outcomes, and expert consensus recommendations
- Differentiate among current LAI formulations based on their pharmacologic profiles, dosing intervals, administration requirements, and patient-centered considerations to support individualized treatment planning
- Apply effective strategies, including shared decision-making and motivational interviewing, to initiate or reintroduce LAI treatment with patients and care partners

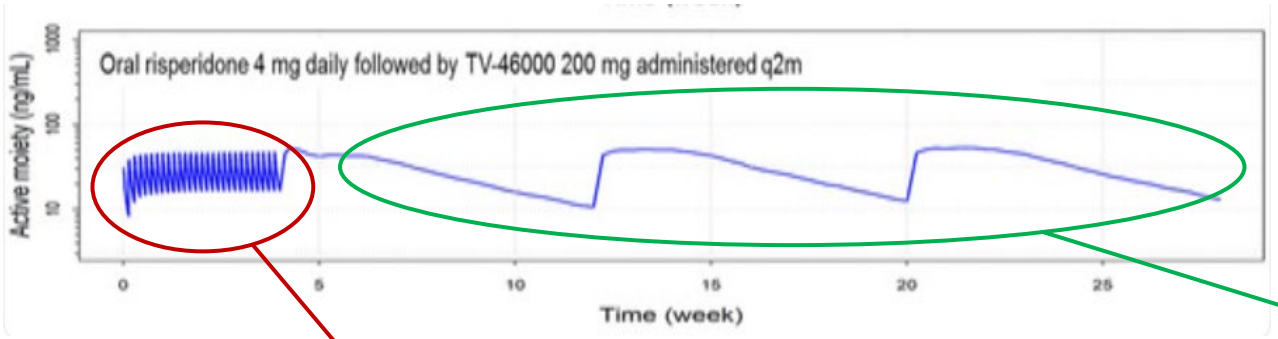
LAI Overview

Advantages of LAIs vs Oral Antipsychotics

Oral Issue One: Variable plasma concentrations	**Oral Issue Two:** 28 more opportunities for missed doses per month	**Oral Issue Three:** The primary effects of antipsychotics are on maintenance of brain tissue
Clinical Consequence: Increased opportunities for symptom relapse, with increased relapse diminishing response to treatment over time	**Clinical Consequence:** Adherence improves outcome sin schizophrenia treatment (oral non-adherence is as high as 50% in some studies)	**Clinical Consequence:** Each psychotic episode and relapse results in progressive brain changes, potentially leading to irreversible loss of cognitive function
How LAIs Help: LAIs offer consistent plasma concentrations without the opportunity for missed doses	**How LAIs Help:** Adherence is a guarantee, rather than a goal	**How LAIs Help:** LAIs help prevent unnecessary relapses, protecting against cognitive decline and further brain damage

Correll CU, Kim E, Sliwa JK, et al. Pharmacokinetic Characteristics of Long-Acting Injectable Antipsychotics for Schizophrenia: An Overview. *CNS Drugs*. 2021;35(1):39-59. doi:10.1007/s40263-020-00779-5
Brissos S, Veguilla MR, Taylor D, Balanzá-Martinez V. The role of long-acting injectable antipsychotics in schizophrenia: a critical appraisal. *Therapeutic Advances in Psychopharmacology*. 2014;4(5):198-219. doi:10.1177/2045125314540297. Emsley R. Antipsychotics and structural brain changes: could treatment adherence explain the discrepant findings? *Therapeutic Advances in Psychopharmacology*. 2023;13:20451253231195258. doi:10.1177/20451253231195258. Andreasen NC, Liu D, Ziebell S, Vora A, Ho BC. Relapse Duration, Treatment Intensity, and Brain Tissue Loss in Schizophrenia: A Prospective Longitudinal MRI Study. *AJP*. 2013;170(6):609-615. doi:10.1176/appi.ajp.2013.12050674

Pharmacokinetic Differences: LAI vs PO



Plasma concentration variability of oral (with *perfect* adherence)

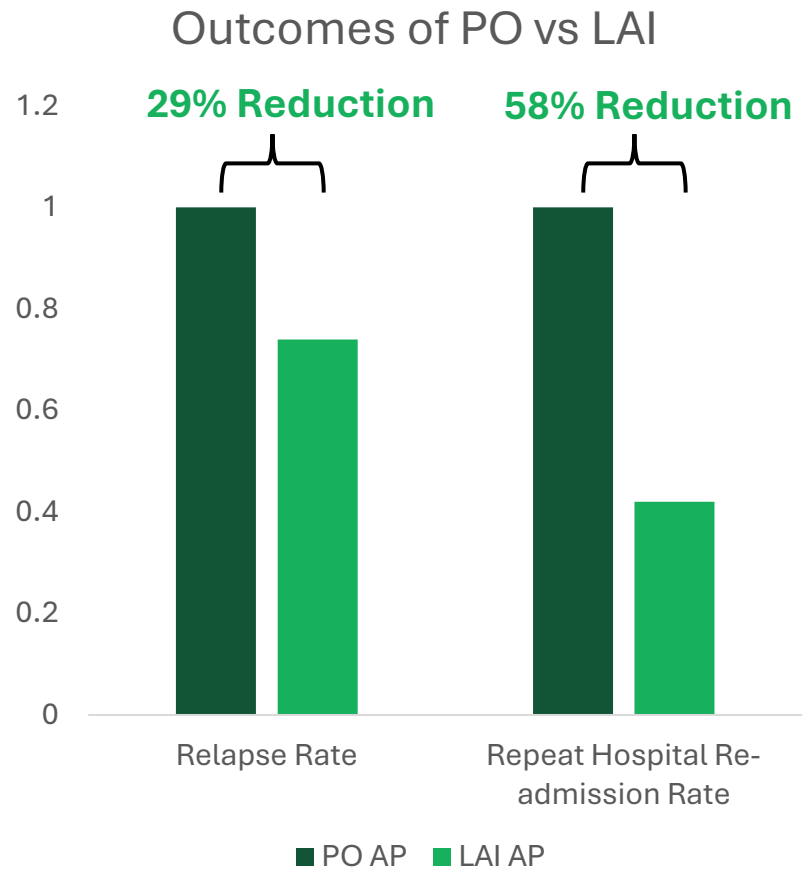
Plasma concentration variability of LAI

- Increased stability of plasma concentration
- Less opportunities for erratic plasma levels
- Greater stability = less relapse events

Perlstein I, Merenlender Wagner A, Gomeni R, et al. Population Pharmacokinetic Modeling and Simulation of TV-46000: A Long-Acting Injectable Formulation of Risperidone. *Clinical Pharm in Drug Dev*. 2022;11(7):865-877. doi:10.1002/cpdd.1078

LAIs Reduce Relapses and Hospital Re-Admission Rates

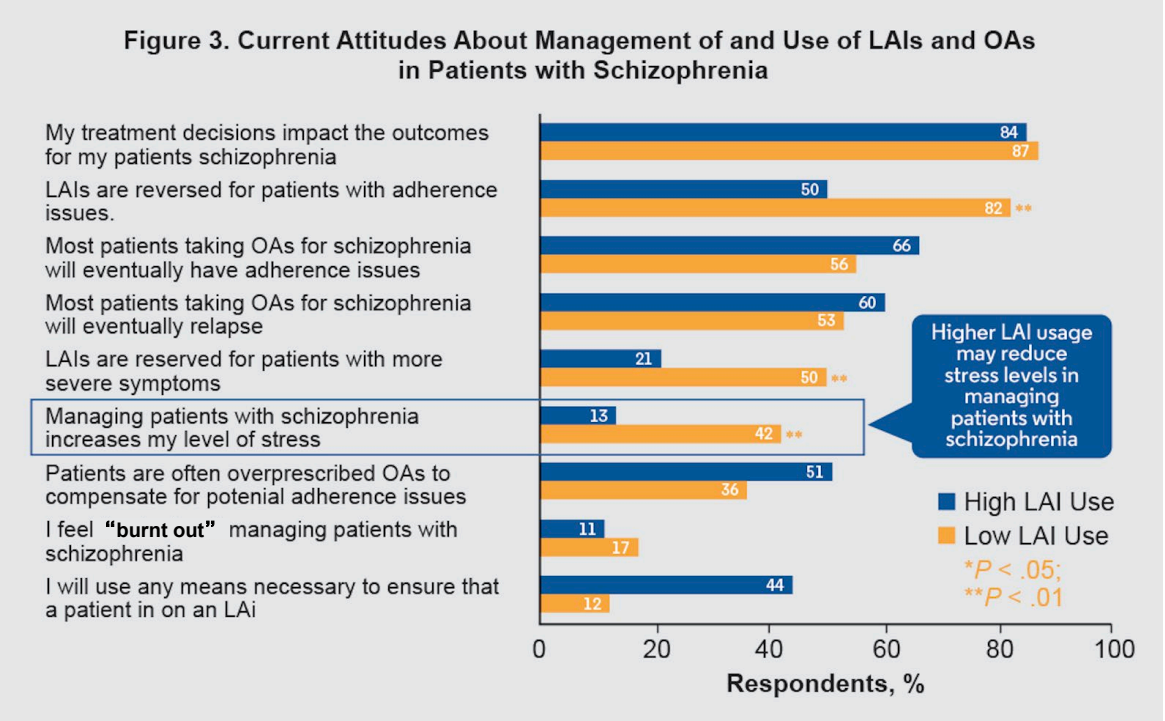
- **Study:** Within-subject data analysis of 75,274 patients (10 years)
- **Data collection:** HIRA database from South Korea (132,028 episodes)
- **Study Findings:** Real-world data from 75,274 patients showed:
  - **29%** reduction in relapse with LAIs ($p < 0.001$)
  - **58%** lower re-admission rates for repeat hospitalizations ($p < 0.001$)



Kim HO, Seo GH, Lee BC. Real-world effectiveness of long-acting injections for reducing recurrent hospitalizations in patients with schizophrenia. *Ann Gen Psychiatry*. 2020;19(1):1. doi:10.1186/s12991-019-0254-2

Differences Between Clinicians Reporting High vs Low LAI Use

- The DECIDE study assessed differences among psychiatry clinicians (N=380) associated with how frequently they use LAIs for patients with schizophrenia.
- Clinicians reporting “high” LAI use (for ≥31% of patients) vs clinicians reporting “low” LAI use (for ≤14% of patients) differed across numerous measures of their experience with and attitudes towards LAIs.
  - High LAI utilizers estimated a significantly lower proportion of patients who refuse LAIs and a shorter time between LAI initiation and patient acceptance
  - In summary, high clinician utilizers of LAIs were much more confident in every area of their utilization and reported better outcomes.



The only way to gain confidence in something is to practice it.

Velligan D, et al. (2022, November 9-12). *Differences Between Archetypes of Healthcare Professionals Who Use Long-Acting Injectable Antipsychotic Agents to Treat Patients With Schizophrenia: A Survey of US-Practicing Psychiatric Clinicians (Results From the DECIDE Survey)* [Poster Presentation]. NEI Congress, Colorado Springs, CO.

Patient Attitudes About LAIs Are Often Positive

Survey in France: Patients (N=206) with schizophrenia with ≥ 3 months treatment with an LAI antipsychotic, injections were the favored dosage form

67%

said they **felt better having received an injectable treatment** than they felt before

51%

considered injectable therapy to be **more effective than other medications**

49%

reported that injectable treatment could **impact positively on their plans and aspirations**

Caroli F, et al. *Patient Prefer Adherence*. 2011;5:165-171.

Barriers to Wider Adoption of LAIs

HCP Concerns



- Misconceptions
  - Misbelief that LAIs are solely for non-adherent patients
  - Limits proactive discussions about LAIs for wider patient groups
- Lack of Training
  - HCPs may feel unprepared to recommend, educate on, and administer LAIs

Patient Concerns

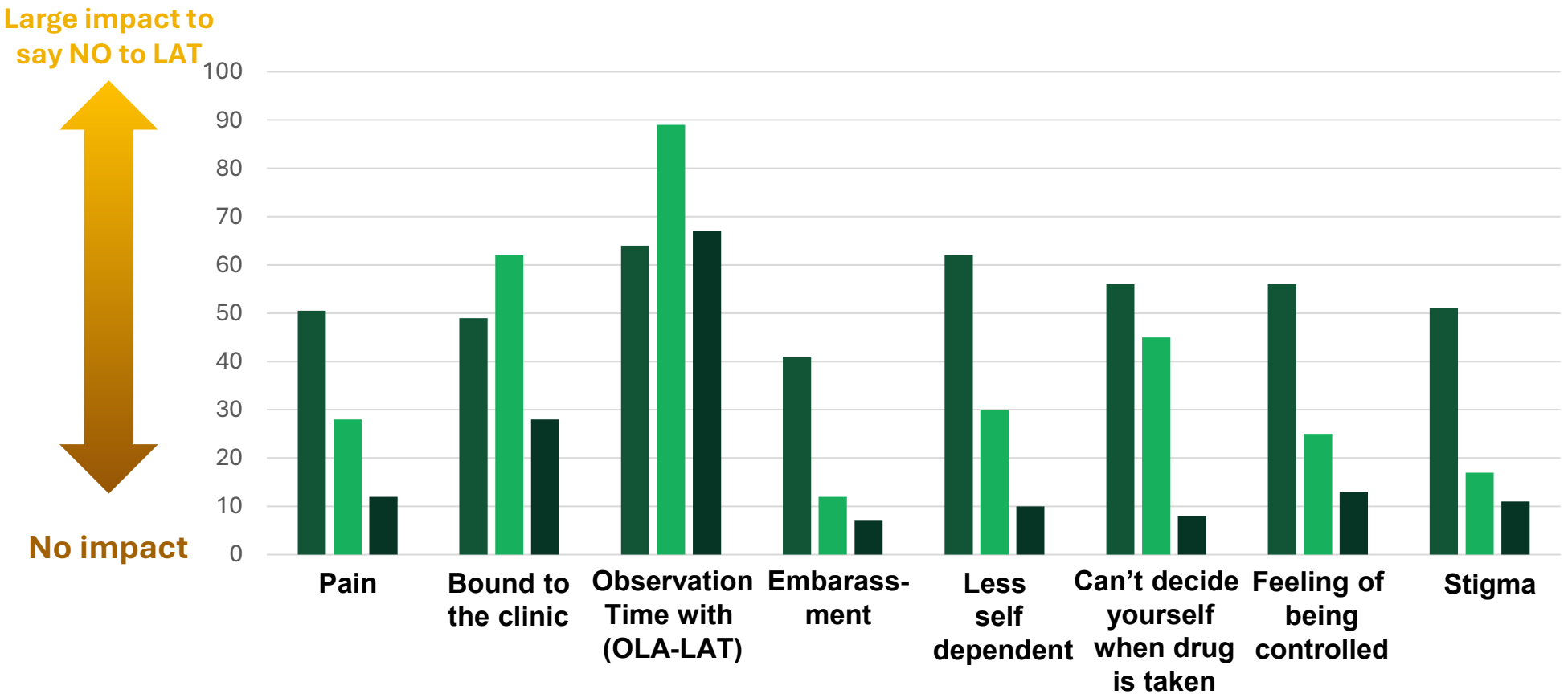


- Needle-related anxiety
  - Significant psychological barrier to acceptance
- Lack of awareness
  - Patients may be unaware of the long-term benefits and improved outcomes
  - They may even be unaware that LAIs exist at all

41–59% of HCPs acknowledge that LAIs are underutilized

Schwartz S, et al. Attitudes and perceptions about the use of long-acting injectable antipsychotics among behavioral health practitioners. *Mental Health Clinician*. 2022;12(4):232-240. doi: 10.9740/mhc.2022.08.232. Robinson DG, et al. Focused Ethnographic Examination of Barriers to Use of Long-Acting Injectable Antipsychotics. *PS*. 2020;71(4):337-342. doi: 10.1176/appi.ps.201900236

Clinician Assumptions of Patient Concerns Regarding LAIs May Be Inaccurate



Cross-sectional study using semi-structured interviews to assess patient and HCP perceptions of LAIs (164 patients, 63 physicians/nurses) in a psychiatry catchment area in Stockholm, Sweden.

- Doctors' or nurses' **beliefs** (n=63)
- Patients' **concern** (pt on oral) (n=101)
- Patients' **experience** (pt on LAT) (n=63)

OLA = olanzapine; LAT = long-acting treatment.
Cahling L, et al. *BJ Psych Bull*. 2017;41(5):254-259.

Promoting Patient-Centered Care

(With the DECIDE Framework)

Define the Problem



Patients are struggling with adherence to daily oral treatments for schizophrenia, leading to inconsistent symptom control and high risk of relapse.

Explore the Options



Present LAIs as a treatment option, emphasizing their benefits, including reduced burden from daily dosing and lower risk of relapse.

Consider Patient Preferences and Values



Allow patients to share their concerns about injections or treatment goals, ensuring these perspectives are respected.

Identify the Best Options



Collaboratively decide if an LAI is the best choice given the patient's needs, focusing on improving mental health outcomes and day-to-day convenience.

Develop a Care Plan



Set up a timeline for initiating an LAI, including a discussion of the first injection, follow-up schedules, and a plan for addressing side effects or concerns.

Evaluate and Monitor Treatment



Schedule regular follow-ups to assess side effects, symptom control, and satisfaction with treatment outcomes.

Guo KL. DECIDE: A Decision-Making Model for More Effective Decision Making by Health Care Managers. *Health Care Manag*. 2020;39(3):133-141. doi: 10.1097/HCM.0000000000000299

APA and Guideline Recommendations

- **APA 2020**:
  - APA suggests (2B) that patients receive treatment with a **long-acting injectable antipsychotic** medication **if they prefer such treatment** or if they have a **history of poor or uncertain adherence**.
  - This guideline statement should be implemented in the context of a person-centered treatment plan that includes evidence-based nonpharmacological and pharmacological treatments for schizophrenia.

- **NICE 2014**
  - Consider offering **depot/long-acting injectable antipsychotic medication** to people with psychosis or schizophrenia:
    - **who would prefer such** treatment after an acute episode
    - **where avoiding covert non-adherence** (either intentional or unintentional) to antipsychotic medication **is a clinical priority** within the treatment plan.

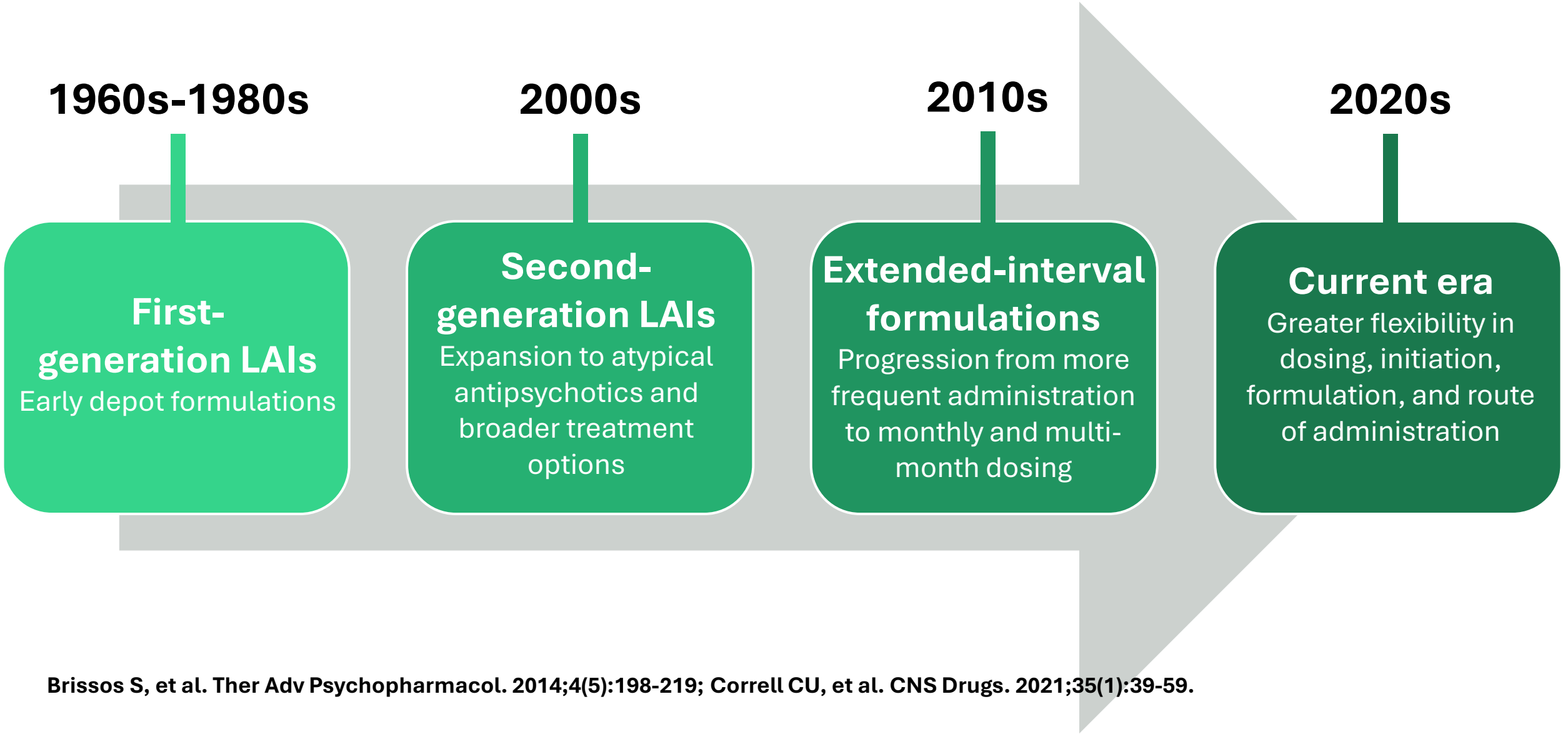
- **BAP 2020:**
  - Patients should be **offered the option of depot/long-acting injectable antipsychotic** medication for maintenance treatment, **given the evidence of lower risk of relapse**.

Consistent themes across guidelines emphasize LAIs for adherence, relapse prevention, and patient preference.

American Psychiatric Association, ed. *The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia*. Third edition. American Psychiatric Association; 2021.Barnes TR, Drake R, Paton C, et al. Evidence-based guidelines for the pharmacological treatment of schizophrenia: Updated recommendations from the British Association for Psychopharmacology. *J Psychopharmacol*. 2020;34(1):3-78. doi: 10.1177/0269881119889296. Recommendations | Psychosis and schizophrenia in adults: prevention and management | Guidance | NICE. February 12, 2014. Accessed March 15, 2025. https://www.nice.org.uk/guidance/cg178/chapter/Recommendations#promoting-recovery-and-possible-future-care

Updates on Recently Approved and Investigational LAIs for Schizophrenia

How Did We Get Here? The Evolution of LAIs



Brissos S, et al. Ther Adv Psychopharmacol. 2014;4(5):198-219; Correll CU, et al. CNS Drugs. 2021;35(1):39-59.

Recent Advances in the LAI Landscape

1	**Longer dosing intervals**	Monthly → every 2 months → longer-interval options
2	**Simplified initiation**	Less reliance on prolonged oral supplementation or complex loading strategies
3	**New delivery approaches**	Expansion beyond traditional IM depot formulations, including newer SC technologies
4	**Broader treatment options**	More molecules and investigational formulations entering the LAI space

Recently Approved and Emerging LAIs

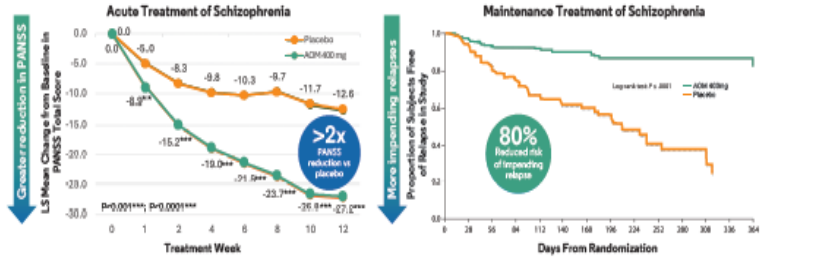
- Recently Approved
  - **2021**: 6-month paliperidone palmitate (first twice-yearly injection)
  - **2023**: 2-month aripiprazole 960mg
  - **2023**: risperidone SC
- Emerging
  - Once-monthly olanzapine SC (NDA under review as of February 2026)

US Food and Drug Administration. *INVEGA HAFYERA (paliperidone palmitate) extended-release injectable suspension: prescribing information;* ABILIFY ASIMTUFII (aripiprazole) extended-release injectable suspension: approval package; *UZEDY (risperidone) extended-release injectable suspension, for subcutaneous use: prescribing information*. Accessed August 7, 2026; Teva Pharmaceuticals. U.S. Food and Drug Administration accepts Teva's New Drug Application for olanzapine extended-release injectable suspension (TEV-'749) for the once-monthly treatment of schizophrenia in adults. Published February 20, 2026. Accessed August 7, 2026

Summary of Characteristics and Clinical Trial Data for Aripiprazole-Based LAIs

Author: Craig Chepke, MD, DFAPA

Aripiprazole Once Monthly in Schizophrenia Clinical Data[1-3]

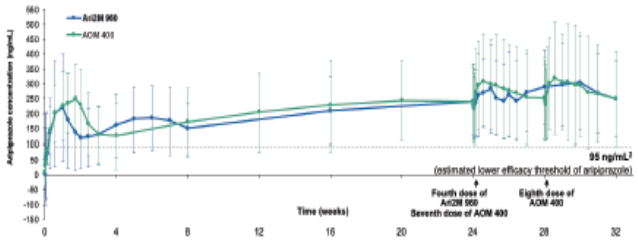


Aripiprazole-naive patients were given 10 mg oral tablets daily for 3 days to assess tolerability

Aripiprazole Monohydrate demonstrated efficacy as both acute and long-term maintenance treatment of schizophrenia

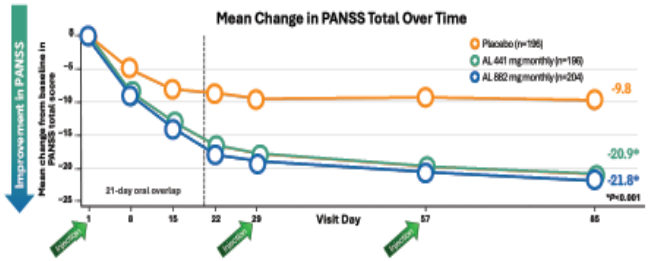
Discontinuation due to AE
AOM vs. Placebo
4.2% vs. 7.6% in 12 wk study
7.1% vs. 13.4% in 52 wk study

Mean Aripiprazole Plasma Concentrations with Ari2M 960 Remained Above 95 ng/mL During the Entire Study Period[4,5]



Mean aripiprazole plasma concentrations delivered by Ari2M were found to be comparable to those from AOM and also remained above the minimum efficacy threshold of 95 ng/mL during the entire study period.

12-Week Acute Efficacy of Aripiprazole Lauroxil[6,7]



Both doses were significantly better than placebo at day 85

>2x PANSS reduction versus placebo

Tolerability was established in Aripiprazole-naive patients with 5 mg daily for 2 days

Pain with first injection 3% to 4% (placebo 2%) and ≤1% with later injections
Akathisia with first injection 10% to 12% (placebo 4%) and ≤1% with later injections

Discontinuation due to AE: Placebo (17.9%), AL 441 (6.8%), AL 882 (2.9%)

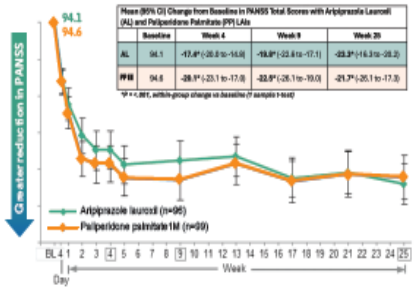
Initiating Aripiprazole Lauroxil[6,8]

Two Options For Initiation
- 21 days of oral aripiprazole overlap
- 1-day initiation regimen

1-day regimen:
30 mg PO aripiprazole + AL nanocrystal injection + maintenance dose of AL
Either regimen gives relevant concentrations within 4 days (but not until day 11 if the 30 mg oral dose not given)

Deltoid (21G)/gluteal (20G)
2.4 mL injection volume
No refrigeration required

Aripiprazole Lauroxil and Paliperidone Palmitate: INitiation Effectiveness (ALPINE) Study[9]



The 25-week phase 3b ALPINE trial evaluated the efficacy and safety of 2-month aripiprazole lauroxil and 1-month paliperidone palmitate in acutely symptomatic patients with schizophrenia (N=200).

Please note: This was an Active Controlled Study.

Both LAIs significantly reduced symptoms of schizophrenia at week 4 (primary endpoint), week 9, and week 25

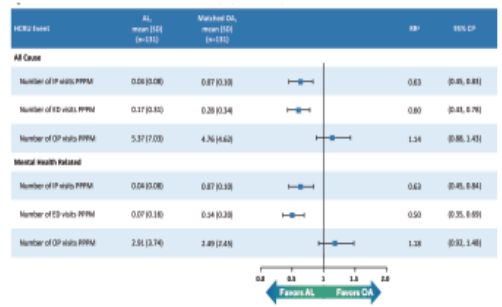
Both LAIs were well-tolerated, with largely mild-to-moderate AEs

Most common AEs, in order, were: injection site pain; increased weight; akathisia

Overview of the Currently Available Long-Acting Formulations of Aripiprazole[10-14]

	Aripiprazole Monohydrate Once Monthly	Aripiprazole Monohydrate 2-Month	Aripiprazole Lauroxil
Brand name (US)	Abilify Maintena®	Abilify Asmtufii®	Aristada® (and Aristada Initio®)
Year Approved	2013	2023	2015 (2018 NCD)
Approved Indications	Schizophrenia, Maintenance Monotherapy of Bipolar I Disorder	Schizophrenia, Maintenance Monotherapy of Bipolar I Disorder	Schizophrenia
Injection Sites	Deltoid or gluteal	Gluteal	Deltoid (441 mg and NCD 675 mg) or gluteal (all doses)
Needle Gauge and Length	21 G, 2-inch; 22 G, 1.5-inch; 23 G, 1-inch	21 G, 1-inch; 22 G, 1.5-inch	20 G, 1.5-inch or 2-inch; 21 G, 1.5-inch or 2-inch
Injection Volumes	0.8 ml (160 mg), 1 ml (200 mg), 1.5 ml (300 mg), 2 mL (400 mg)	2.4 mL (720 mg), 3.2 mL (960 mg)	441 mg (1.6 mL), 662 mg (2.4 mL), 882 mg (3.2 mL), 1064 mg (3.9 mL); NCD 675 mg (2.4 mL)
Injection Intervals	Every 4 weeks	Every 8 weeks	Once at initiation (NCD 675 mg), Q4 weeks (441, 662, 882 mg), Q6 weeks (882 mg), Q8 weeks (1064 mg)
Starting Dose	400 mg	960 mg	441, 662, 882, or 1064 mg
Maintenance Doses	300 or 400 mg (adjust for CYP2D6 or CYP3A4 inhibitors; cannot give with CYP3A4 inducers)	720 or 960 mg; (adjust for CYP2D6 or CYP3A4 inhibitors; cannot give with CYP3A4 inducers)	441, 662, 882, or 1064 mg (adjust for CYP2D6 or CYP3A4 modulators)
Half-life	29.9 days (300 mg); 46.5 days (400 mg)	29.4 days	53.9–57.2 days; 15–18 days (NCD)
Oral Supplementation	1 day with the 2 injection start regimen with AOM 400 mg, otherwise 14 days	1 day with the 2 injection start regimen with AOM 400 mg, otherwise 14 days	1 day with NCD 675 mg, otherwise 21 days
Reconstitution	Yes, but dual-chamber syringe available for 300 and 400 mg doses	No	No
Refrigeration	No	No	No

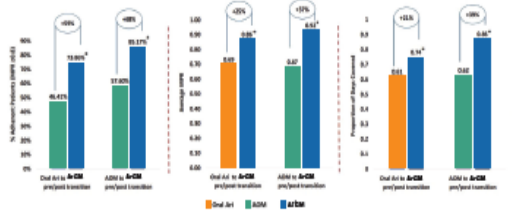
Initiating AL vs OA Is Associated With Reduced Odds of All-Cause Inpatient and Emergency Department Visits[15]



Compared with matched oral aripiprazole, aripiprazole lauroxil was associated with significantly fewer all-cause and mental health-related inpatient and emergency department visits per patient per month for individuals early in schizophrenia treatment. Outpatient visit rates were similar between groups.

Overall, AL favored lower acute care utilization without increasing outpatient use.

Transition to Aripiprazole 2-Month Is Associated With Significant Improvements in Treatment Adherence[16]



Adherence Improved Post-Index
- Oral Ari + Ari2M
  - Adherence (MPR ≥0.8) + 59% (p=0.0005)
  - MPR + 25% (p<0.0001)
  - PDC + 21% (p<0.0001)
- AOM + Ari2M
  - Adherence (MPR ≥0.8) + 48% (p<0.0001)
  - MPR + 37% (p<0.0001)
  - PDC + 39% (p<0.0001)

Six months after switching from oral aripiprazole or AOM to aripiprazole 2-month (Ari 2M), patients with schizophrenia showed statistically significant improvements in adherence, with higher proportions achieving MPR ≥0.8 and increases in both MPR and proportion of days covered.

Practical Take-Aways

- Aripiprazole-based LAIs have shown robust efficacy in acute treatment of schizophrenia. Additionally, AOM has a trial demonstrating maintenance efficacy in schizophrenia.
- Aripiprazole-based LAIs generally have low rates of discontinuation due to AEs.
- Aripiprazole-based LAIs are available in durations between 1 and 2 months and have options for single day initiations

PANSS=Positive and Negative Syndrome Scale; AOM=Aripiprazole Once-Monthly; AE=adverse event; Ari2M=ARISTADA 960=aripiprazole 2-month ready-to-use 960 mg; SD=Standard Deviation; AL=Aripiprazole Lauroxil; D/C=discontinuation; NCD=NanoCrystal Dispersion; CYP = Cytochrome P450; G = Gauge; mg = Milligram; ml = Milliliter; NCD Initiation regimen = A single 30 mg dose and initial injection of nano-crystal formulation (Aristada Initio®) can substitute for 21-day oral aripiprazole supplementation 1. Abilify Maintena (aripiprazole) [package insert]. Rockville, MD: Otsuka Pharmaceuticals; 2020. 2. Kane, JM, et al. J Clin Psychiatry 73.5 (2012): 1339. 3. Kane, JM, et al. J Clin Psychiatry 76.11 (2014): 1547. 4. Harlin et al. CNS Drugs 2005;19(4):337-360; 5. Wand et al. Clin Pharmacol Ther Dev 2022;11(2):150-164. 6. Aristada (aripiprazole lauroxil) [package insert]. Akermes, plc. Waltham, MA. 2020. 7. Meltzer HY et al. J Clin Psych. 76.8 (2015):1085-1090. 8. Jain R, et al. CNS spectrums. 25.3 (2020): 325-330. 9. Weiden PJ, et al. J Clin Psych. 83(3) (2020): 6953. 10. Otsuka America Pharmaceutical Inc. ABILIFY MAINTENA® (aripiprazole) Prescribing Information. Accessed 04/18/2024, https://www.otsuka-us.com/sites/g/files/qhldwo6761/files/media/static/Abilify-M-PI.pdf 11. Otsuka America Pharmaceutical Inc. ABILIFY ASIMTUFII® (aripiprazole) Prescribing Information. https://otsuka-us.com/sites/g/files/qhldwo8366/files/media/static/Abilify-Asimtufii-PI.pdf 12. Akermes I, Aristada TM (aripiprazole lauroxil). Prescribing Information. Accessed 24 April, 2024, https://www.aristada.com/downloadables/ARISTADA-PI.pdf 13. Wang Y, Harlin M, Larsen F, et al. Population Pharmacokinetics and Dosing Simulations for Aripiprazole 2-Month Ready-to-Use Long-Acting Injectable in Adult Patients With Schizophrenia or Bipolar I Disorder. Clin Pharmacol Drug Dev. Apr 11 2024;doi:10.1002/cpdd.1397 14. Chepke, Craig, Peter J. Weiden, and Leslie Citrome. "Pharmacokinetic evaluation of aripiprazole monohydrate as a once every 2-months long-acting injectable antipsychotic for schizophrenia." Expert Opinion on Drug Metabolism & Toxicology 21.9 (2025): 1043-1047. 15. Kane JM, et al. Treatment patterns and healthcare resource utilization of patients early in schizophrenia illness initiating aripiprazole lauroxil versus oral aripiprazole: a retrospective claims-based study. Poster presented at Psych Congress 2025; September 17–21, 2025; San Diego, CA. 16. Hansen K, et al. Real-world impact of transitioning from oral or once-monthly injectable aripiprazole to a 2-month ready-to-use aripiprazole formulation on adherence and healthcare utilization in US adults diagnosed with schizophrenia. Poster presented at Psych Congress 2025; September 17–21, 2025; San Diego, CA.

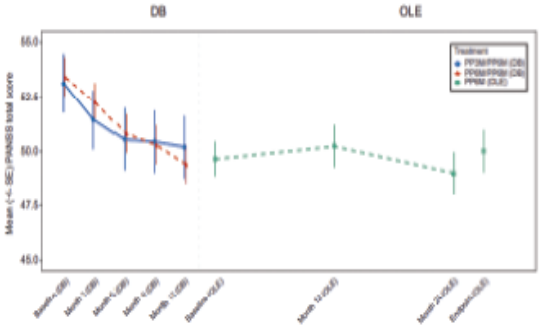
Summary of Characteristics and Clinical Trial Data for Paliperidone-Based LAIs

Author: Craig Chepke, MD, DFAPA

Acute and Long-Term Results of Longer Duration Paliperidone Palmitate 6-Month[1,2]

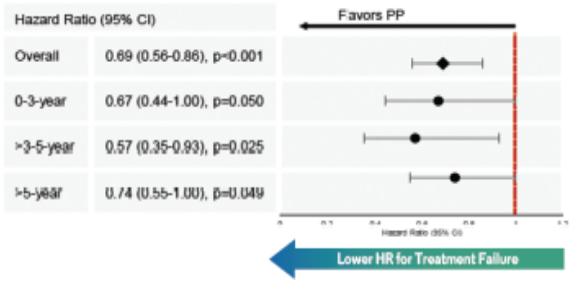
Paliperidone palmitate 6-month (PP6M) was shown to be noninferior to the 3-month formulation (PP3M) in a 1-year double-blind (DB) phase 3 trial. Participants completing that trial without relapse were enrolled in a 2-year open-label extension (OLE). In those who completed this OLE (N=154):

- **No new safety concerns were identified**
- **Clinical and functional improvements measured with the PANSS, CGI-S, and PSP during the DB trial were maintained over the 2 years of the OLE**
- **Over 2 years, the rate of relapse was low (3.9%)**

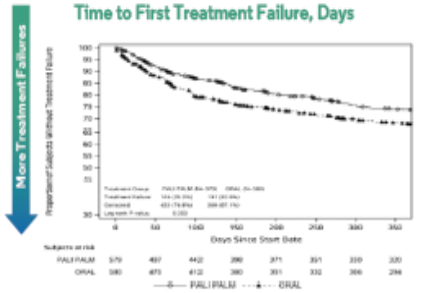


Time to Treatment Failure with Paliperidone Palmitate vs. Oral Antipsychotics in Patients with Schizophrenia with Varying Durations[3]

Hazard Ratio of Time to First Treatment Failure By Duration of Illness



Time to First Treatment Failure, Days



Integrated Patient-Level Post Hoc Analysis of the PRIDE and PROSIPAL studies

DREaM Suggests Multiple Potential Advantages of LAI Use in Recent-Onset Schizophrenia[4,5]

For the primary endpoint, there was a trend toward significance for PP compared to OAP in the EDP period (p=0.080, NNT=6)

If the use of oral supplementation was excluded, PP significantly reduced the risk of modified TF compared to OAP over the 18-month EDP in a post-hoc analysis.

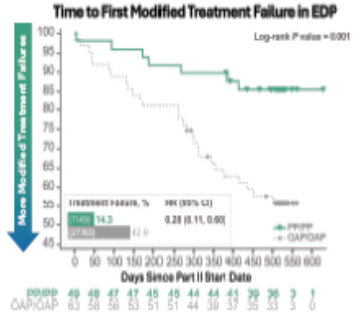
An MRI component of the study showed that frontal lobe intracortical myelin volume was preserved in those treated with PP, but decreased significantly for those on OAPs during part II (9 mos)

Safety results were consistent with the known safety profile of PP in adults with schizophrenia

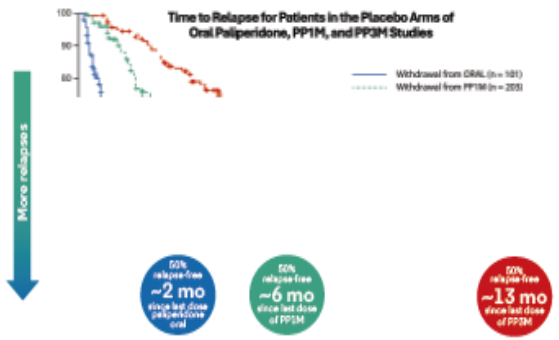
72% reduction in risk of modified TF

NNT=3

Time to First Modified Treatment Failure in EDP



Longer Duration LAIs May Better Protect People Even After Discontinuation[6]



This post hoc analysis includes data from stable participants taking oral paliperidone, PP1M, and PP3M randomized to the double-blind placebo arms of each respective study

Relapse risk was:
56% lower for discontinuing PP1M vs. oral paliperidone (P≤0.001)
79% lower for discontinuing PP3M vs. oral paliperidone (P≤0.001)

52% lower for discontinuing PP3M vs. PP1M (P≤0.001)

Overview of the Currently Available Long-Acting Formulations of Paliperidone[7-9]

Formulation (Manufacturer)	Paliperidone Palmitate 1-Month (Janssen)	Paliperidone Palmitate 1-Month (Luye)	Paliperidone Palmitate 3-Month (Janssen)	Paliperidone Palmitate 6-Month (Janssen)
Brand Name (US)	INVEGA SUSTENNA	ERZOFRI	INVEGA TRINZA	INVEGA HAFYERA
Year Approved	2009	2024	2015	2021
Approved Indications	Schizophrenia, Schizoaffective Disorder	Schizophrenia, Schizoaffective Disorder	Schizophrenia (after adequate treatment with PP1M for 4 months)	Schizophrenia (after adequate treatment with PP1M for months or with PP3M for one 3-month cycle)
Injection Type/Site	IM, Deltoid or Gluteal	IM, Deltoid or Gluteal	IM, Deltoid or Gluteal	IM, Gluteal
Needle Gauge and Length	22-23 gauge, 1-1.5 inches	22-23 gauge, 1-1.5 inches	22 gauge, 1-1.5 inches	20 gauge, 1.5 inch
Injection Volume	0.25-1.5 mL (based on dose)	0.25-2.25 mL (based on dose)	0.875-2.625 mL	3.5 mL (1,092 mg), 5 mL (1,560 mg)
Injection Intervals	Monthly	Monthly	Every 3 months	Every 6 months
Doses Available	39 mg, 78 mg, 117 mg, 156 mg, 234 mg	39 mg, 78 mg, 117 mg, 156 mg, 234 mg, 351 mg	273 mg, 410 mg, 546 mg, 819 mg	1,092 mg, 1,560 mg
Reconstitution Required	No. Pre-filled syringe. Shake before use.	No. Pre-filled syringe. Shake before use.	No. Pre-filled syringe. Shake before use.	No. Pre-filled syringe. Shake before use.
Refrigeration Required	No	No	No	No
Initiation Dosing Required	Yes; 234 mg on day 1, 156 mg on day 8	Yes, single injection of 351 mg initiation dose, IM	Yes; 4 months of PP1M	Yes; 4 months of PP1M or 1 cycle of PP3M

Practical Take-Aways

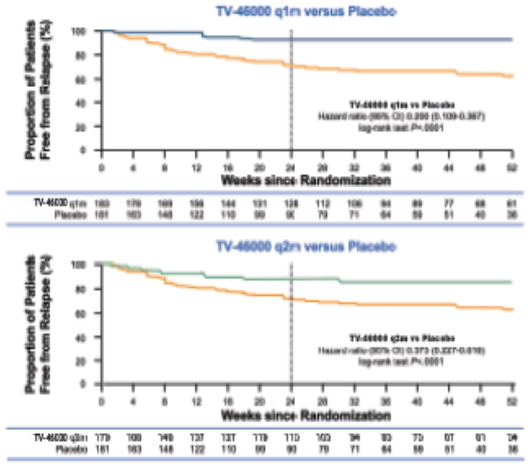
- The rate of relapse for Paliperidone Palmitate 6-Month after two years of open label treatment is 3.9%.
- Post-hoc analyses suggest that individuals with schizophrenia in the early-phase of the illness taking PP may have a longer time to treatment failure compared to those taking oral antipsychotics.
- Post-hoc analyses suggest that LAIs may better protect against relapse for a period of time after discontinuation than oral antipsychotics and that longer duration LAIs may have an advantage over shorter duration LAIs.

DREaM=Disease Recovery Evaluation and Modification; EDP=Extended Disease Progression; PP=Paliperidone Palmitate; OAP=Oral Antipsychotic; TF=Treatment Failure; MRI=Magnetic Resonance Imaging; 1M=once monthly, 3M=every 3 months, IM=Intramuscular 1. Nitjarian D, et al. Int J Neuropsychopharmacol. 2022 March 1; 25(3):238–251. 2. Nitjarian D, et al. Int J Neuropsychopharmacol. 2023 Aug 29; 26(8):537–544. 3. Sajatovic, M. et al. Poster 24 presented at 2024 Psych Congress Elevate, May 30 – June 2 | Las Vegas, NV 4. Alphs L, et al. Schizophrenia Research 243 (2022): 86-97. 5. Tohiver TA, et al. Schizophrenia Research 255 (2023): 195-202. 6. Weiden, P.J, et al. Journal of Clinical Psychiatry 78.7 (2017): 17256. 7. INVEGA SUSTENNA (Paliperidone Palmitate) Package Insert: U.S. Food and Drug Administration (FDA). (2017). Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022264s023lbl.pdf 8. INVEGA TRINZA (Paliperidone Palmitate) Package Insert: Janssen Pharmaceutica's. (2023). Available at https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/INVEGA+TRINZA-pi.pdf. 9. INVEGA HAFYERA (Paliperidone Palmitate) Package Insert: Janssen Pharmaceutica's. (2024). Available at https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/INVEGA+HAFYERA-pi.pdf.

Summary of Characteristics and Clinical Trial Data for Risperidone-Based LAIs

Author: Craig Chepke, MD, DFAPA

Risperidone SC Polymer 1-2 Month (TV-46000) in Prevention of Impending Relapse[1]



Primary Endpoint: Time to Impending Relapse Compared to Placebo*

Time to impending relapse was prolonged by
5.0 times with Q1M and **2.7 times with Q2M,**

Risk of impending relapse was reduced by
80% with Q1M and **62.5% with Q2M**

**Impending relapse was operationalized as meeting at least one of four criteria, including (1) hospitalization due to worsening of psychotic symptoms, (2) suicidality as assessed by CGI-SS, (3) violent behavior, and (4) clinically significant increases from baseline or high scores on specific items of the PANSS and CGI-I (see article for more details).*

TV-46000 q1m
TV-46000 q2m
Placebo

Adverse Event Data for TV-46000[1,2]

	Placebo-Controlled Efficacy Study		Long-Term Randomized DB Safety Study	
	Injection Site Pain	Discontinuation due to any AE	Injection Site Pain	Discontinuation due to any AE
TV-46000 q1m	9 (5%)	21 (11%)	9 (5%)	3 (2%)
TV-46000 q2m	12 (7%)	14 (8%)	7 (4%)	5 (3%)
Placebo	11 (6%)	10 (6%)	N/A	N/A

Available Risperidone-Based LAIs

Risperidone microspheres [Consta]
2 weeks, 21 day oral overlap

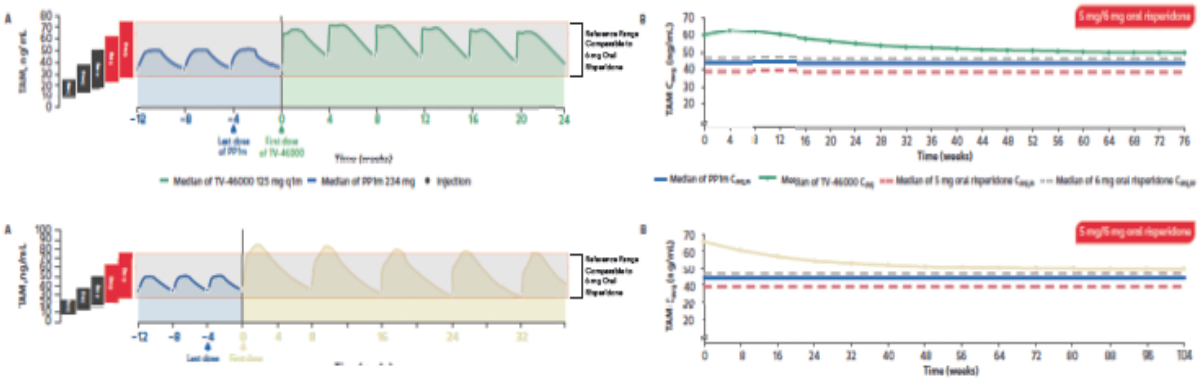
Risperidone ISM [Risvan]
1 month, no oral overlap

Risperidone Polymer [Uzedy]
1 month and 2 month
no oral overlap

Intramuscular

Subcutaneous

Switching Patients with Schizophrenia from Intramuscular Paliperidone Palmitate Once Monthly to Subcutaneous TV-46000[3]



Overview of the Available Long-Acting Formulations of Risperidone[5-7]

Formulation (manufacturer)	Risperidone IM 2 week (Janssen)	Risperidone SC Polymer 1-2 Month (Teva)	Risperidone ISM (Rovi)
Brand Name (US)	Risperdal Consta®	Uzedy®	Risvan®
Year Approved	2003	2023	2024
Approved Indications	Schizophrenia, maintenance of Bipolar I Disorder (monotherapy or adjunct to lithium/valproate)	Schizophrenia, maintenance of Bipolar I Disorder (monotherapy or adjunct to lithium/valproate)	Schizophrenia
Injection Type/Site	IM, deltoid, gluteal	SC, abdomen, upper arm	IM, deltoid, gluteal
Needle Gauge and Length	21 G, 1-inch deltoid; 20 G 2-inch gluteal	21 G, ½-inch	21 G, 1-inch deltoid; 20 G, 2-inch gluteal
Injection Volume	2 mL (all doses)	0.14 mL – 0.7 mL depending on dose	0.55 mL (75 mg), 0.73 mL (100 mg)
Injection Intervals	2 weeks	1 month (BP1, SZ), 2 months (SZ)	1 month
Doses Available	12.5, 25, 37.5, 50 mg (There is no dose equivalency with oral risperidone documented in product labeling)*	50 mg, 75 mg 100 mg, 125 mg, 150 mg, 200 mg, 250 mg (equivalent to oral risperidone 2 mg to 5 mg/day)	75 mg, 100 mg (equivalent to oral risperidone 3 mg and 4 mg/day, respectively
Oral Supplementation	21 days	None	None
Reconstitution Required	Yes (combine the powder in the vial with the diluent provided in the syringe)	No reconstitution required; ready to use after whipping the prefilled syringe 3 times	Yes (place the Solvent Syringe on top of the Powder Syringe [to prevent powder spillage] and connect the syringes and push back and forth for 50 cycles)
Length of time it can be kept at room temperature rather than refrigerated	7 days	90 days	NA – always stored at room temperature

Practical Take-Aways

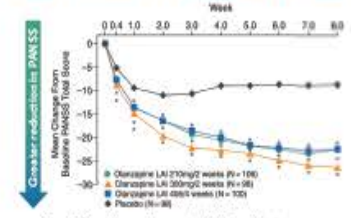
- Several risperidone-based LAIs have been approved in the past several years, each of which has a longer injection interval and shorter required oral overlap during initiation, or none at all.
- Risperidone microspheres (21 days overlap) and Risperidone SC Polymer 1-2 Month are commercially available in the U.S. currently. Additionally, an older 1-month SC risperidone polymer LAI was discontinued from the market in 2024.
- Risperidone SC Polymer 1-2 Month increased time to impending relapse for both injection frequencies, and demonstrated safety and tolerability in short and long-term trials.

BP1 = Bipolar 1; SZ = Schizophrenia; IM = Intramuscular; SC = Subcutaneous; RCT = Randomized controlled trial. 1. Kane JM, et al. *Lancet Psychiatry*. 2023 Nov 1;10(12):934-43 2. Kane JM, et al., CNS Drugs (2024) 38:625–636 3. Poster 161 Presented at the Annual Psych Congress; October 29–November 2, 2024; Boston, MA 4. Risperdal Consta (risperidone). Package Insert. Janssen Pharmaceuticals; 2023 Feb. Available from https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/020272Orig1s083,020588Orig1s071,021444Orig1s057,021346Orig1s061lbl.pdf 5. Rykindo (risperidone). Package Insert. Shandong Luye Pharmaceutical Co; 2023 Jun [cited 2024 Apr 27]. Available from https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/ 212849s000lbl.pdf 6. Risvan (risperidone). Package Insert. Rovi S.A; 2024 [cited 2024 Apr 27]. Available from https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/214635s003lbl.pdf 7. Uzedy (risperidone) extended-release injectable suspension. Package Insert. Parsippany (NJ): Teva Neuroscience, Inc; 2023 [cited 2024 Apr 27]. Available from https://www.uzedyhcp.com/ globalassets/uzedy/prescribing-information.pdf

Summary of Characteristics and Clinical Trial Data for Olanzapine-Based LAIs

Author: Craig Chepke, MD, DFAPA

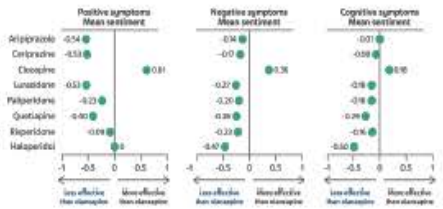
Acute Efficacy of IM Olanzapine Pamoate[1,2]



*p <.05 type III sum of squares (analysis of variance).

All 3 doses of IM olanzapine demonstrated statistically significant reductions in PANSS total score; however, adoption was substantially low due to the risk of PDSS.

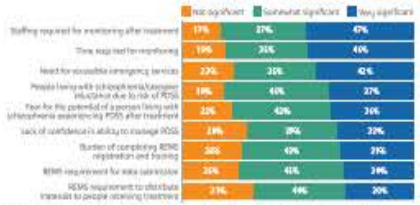
Clinician Perceptions of Olanzapine Efficacy[1,2]



Besides clozapine, no antipsychotic was felt to be more efficacious than olanzapine on any of the 3 core domains of schizophrenia.

Clinician Perspectives on Barriers to IM LAI Olanzapine Treatment

Survey on Olanzapine Needs and Attitudes Research (SONAR) Study[3]

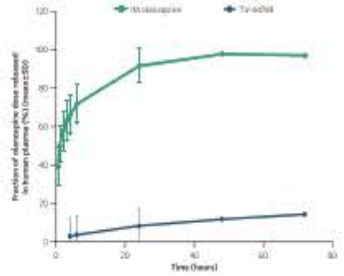


Clinicians were asked "How significant are each of the following barriers to your ability to utilize the currently available IM olanzapine Relprevv long-acting injectable olanzapine for your adult patients with schizophrenia?"

Among respondents, 76% indicated that concern about PDSS limits use of IM LAI olanzapine pamoate, and absence of PDSS would likely increase utilization.

Operational demands, including staffing needs (47%), post-injection monitoring time (46%), and access to emergency services (42%), were identified as the primary factors limiting use of IM olanzapine pamoate LAI.

SC Olanzapine LAI Has Slower Release than IM In Vitro[4]

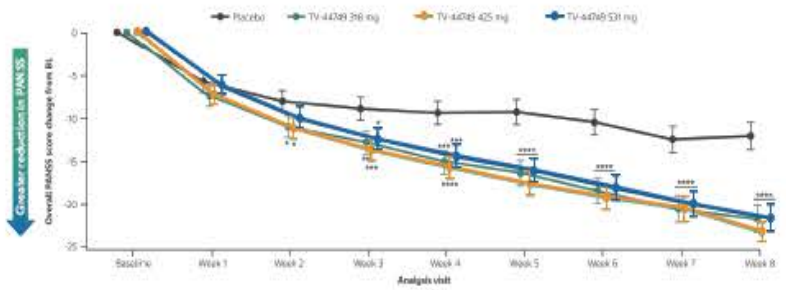


IM LAI olanzapine exhibited rapid and complete release within 24 hours, whereas TV-44749 rapidly forms a solid depot, entrapping olanzapine particles and preventing a burst of olanzapine in the plasma.

No suspected or reported cases of PDSS were present in any clinical trials following 3470 injections of TV-44749.

Acute Efficacy of SC Olanzapine (Week 8)

SOLARIS Trial[5]

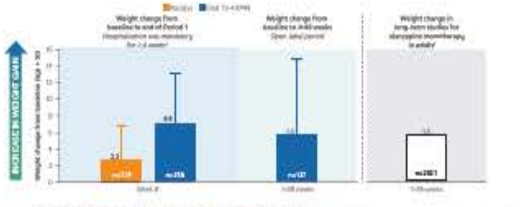


TV-44749 demonstrated clinically meaningful and statistically significant reductions in the PANSS total score from baseline to Week 8 compared with placebo across all dosing groups.

Statistical significance versus placebo was reached at week 2 for the 318 mg and 425 mg doses and at week 3 for 531 mg (all P≤0.05)

Short-Term Safety and Tolerability of SC Olanzapine

SOLARIS Trial[5]



n, (%)	Period 1	Integrated trial periods
	Placebo	TV-44749
Patients with at least 1 metabolic AE	17 (10%)	106 (39%)	253 (42%)
Weight abnormalities	15 (9%)	173 (35%)	221 (37%)
Weight increase	15 (9%)	171 (35%)	220 (36%)
Waist circumference increase	1 (<1%)	11 (2%)	11 (2%)
Glucose abnormalities	2 (1%)	21 (4%)	39 (6%)
Glycosylated hemoglobin increase	0	4 (<1%)	15 (2%)
Blood glucose increase	2 (1%)	7 (1%)	14 (2%)
Diabetes mellitus	0	5 (1%)	7 (1%)
Lipids abnormalities	2 (1%)	10 (4%)	30 (5%)
Metabolic syndrome	1 (<1%)	7 (1%)	9 (1%)
Blood triglycerides increase	1 (<1%)	3 (<1%)	7 (1%)
Hypertriglyceridemia	0	4 (<1%)	8 (1%)

Participants are counted only once in each preferred term category, and only once in each category.

Weight gain and metabolic changes over the long-term were comparable to other olanzapine formulations.

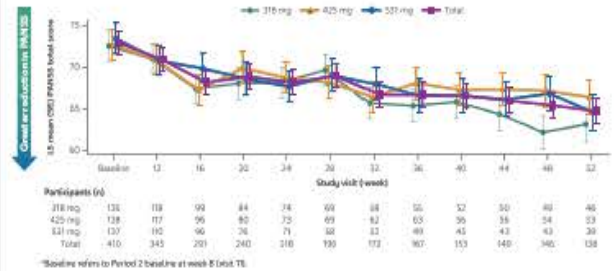
39% of participants treated with TV-44749 experienced at least 1 metabolic AE. Across all trial periods, weight abnormalities were present in 37% of participants.

Long-Term Effectiveness and Safety of SC Olanzapine

SOLARIS Trial[5]

The systemic safety profile of TV-44749 is consistent with other olanzapine formulations, with no suspected or confirmed PDSS events

The most commonly reported treatment-emergent AEs (≥5% incidence in TV-44749 total group) were weight increase (36%) and certain injection-site reactions (ISRs)



*Baseline refers to Period 2 baseline at week 8 (visit 19).

All TV-44749 doses exhibited long-term, continuous symptom improvement and maintenance of clinical effectiveness in Period 2 of the SOLARIS trial

Practical Take-Aways

- Despite its robust efficacy, safety concerns related to PDSS have limited the clinical use of IM olanzapine pamoate LAI.
- TV-44749 is an investigational subcutaneous olanzapine LAI with doses of 318 mg, 425 mg, or 531 mg, which are comparable to daily oral olanzapine doses of 10 mg, 15 mg, and 20 mg.
- Efficacy, safety, and tolerability of TV-44749 are comparable to IM LAI; however, there were no cases of PDSS reported in 3470 injections.

SD = Standard deviation; BL = Baseline; LS = Least squares; SE = Standard error; AE = adverse event; SC = subcutaneous; IM = Intramuscular; PDSS = Post-Injection Delirium/Sedation Syndrome; and PANSS = Positive and Negative Syndrome Scale; 1. Hansen R, et al. Clinician Perspectives on the Efficacy and Safety/Tolerability of Olanzapine Compared With Other Antipsychotics: Results From the SONAR (Survey on Olanzapine Needs and Attitudes Research) Study. Poster presented at: 9th Annual Psych Congress (Elevate); May 28–31, 2025; Las Vegas, NV.; 2. Laurello, John, et al. "An 8-week, double-blind, randomized, placebo-controlled study of olanzapine long-acting injection in acutely ill patients with schizophrenia." Journal of Clinical Psychiatry 69.5 (2008): 790-799.; 3. Hansen R, et al. Clinician perspectives on long-acting injectable olanzapine treatment barriers and unmet needs from the SONAR (Survey on Olanzapine Needs and Attitudes Research) study. Poster presented at: Psych Congress 2025; September 17–21, 2025; San Diego, CA.; 4. Correll CU, et al. Olanzapine for extended-release injectable suspension (TV-44749) for subcutaneous use is designed for sustained efficacy and to eliminate the risk of post-injection delirium/sedation syndrome: in vitro and clinical data. Poster presented at: 9th Annual Psych Congress (Elevate); May 28–31, 2025; Las Vegas, NV.; 5. Correll CU, Shulman K, Bar-Nur T, et al. Evaluating long-term weight gain and other metabolic changes with subcutaneous long-acting injectable olanzapine (TV-44749) in adults with schizophrenia: results from the phase 3 SOLARIS trial. Poster presented at: Psych Congress 2025; September 17–21, 2025; San Diego, CA.; 6. Correll CU, et al. Long-term effectiveness with subcutaneous long-acting injectable olanzapine (TV-44749) in adults with schizophrenia: results from up to 48 weeks open-label treatment in the phase 3 SOLARIS trial. Poster presented at: Psych Congress 2025; September 17–21, 2025; San Diego, CA; 7. Correll CU, et al. Long-term safety of subcutaneous long-acting injectable olanzapine (TV-44749) in schizophrenia: results from the phase 3 SOLARIS trial. Poster presented at: Psych Congress 2025; September 17–21, 2025; San Diego, CA.

Regulatory Update: Since this poster was developed, once-monthly subcutaneous olanzapine extended-release injectable suspension received FDA approval on October 8, 2026, for schizophrenia in adults. Approval details can be found here: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=219007

Recent Research Updates on the Potential Advantages and Perceptions of LAIs

Author: Craig Chepke, MD, DFAPA

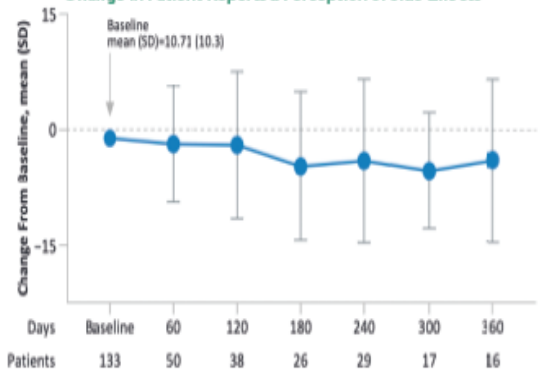
Observational Study of Long-Acting Injectables in Schizophrenia[2]

Change in CGI-S (Overall Illness Severity)



*No statistical comparisons were conducted. All cohorts have low numbers at all time points. Presented data are observed cases.
CGI-S, Clinical Global Impression-Severity

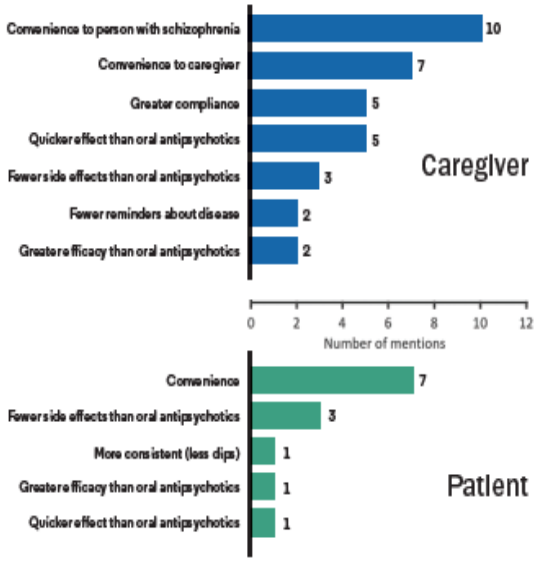
Change in Patient-Reported Perception of Side Effects



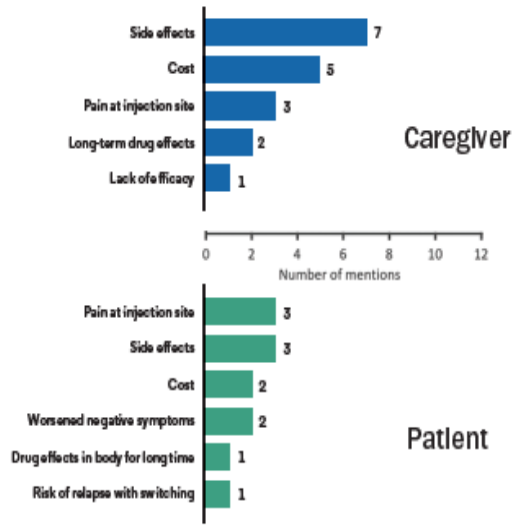
†Assessed via the Glasgow Antipsychotic Side-effect Scale. Total score (0–66) can be interpreted continuously or as 0–12=absent or mild, 22–42=moderate, ≥43=severe. No statistical comparisons were conducted. All cohorts have low numbers at all time points. Presented data are observed cases.

Among patients receiving LAIs in mostly community, outpatient settings, most patients showed stability in symptoms and overall illness severity.

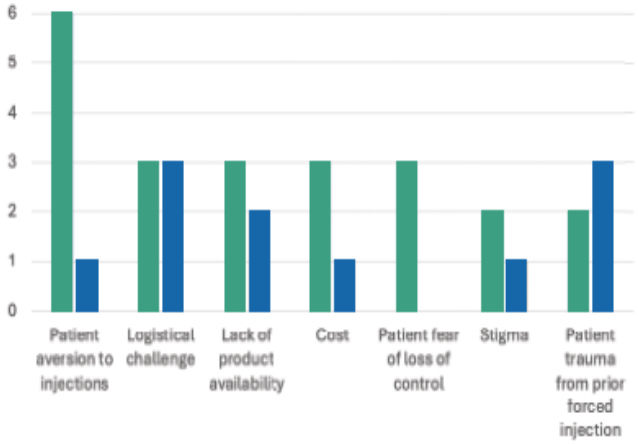
Caregiver- and Patient-Reported Advantages of LAIs[3,4]



Caregiver- and Patient-Reported Concerns of LAIs[3,4]



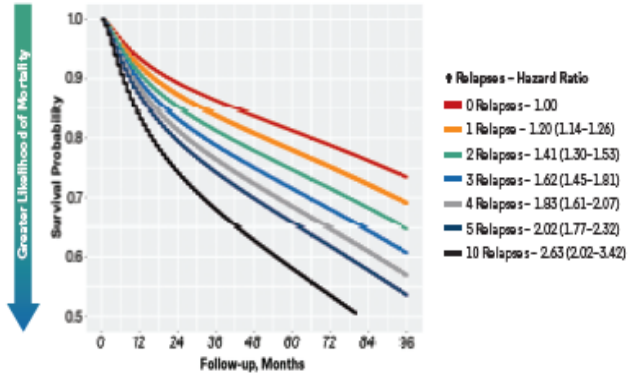
Provider Perceived Barriers to LAI Use[5,6]



Patient aversion to injections was the most common barrier to LAI use reported by **PSYCHIATRISTS**.

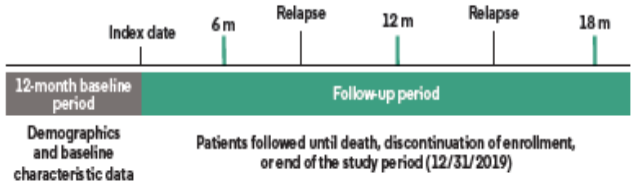
Negative patient experiences from prior forced injection and logistical challenges were the most common barriers to LAI use reported by **NURSES**.

Predicted Mortality By Number of Relapses[1]



For the first 5 relapses, each subsequent relapse increases all-cause mortality hazard by approximately 20%.

Exposure/covariate evaluation points
(covariates evaluated using 6 month period prior to each point)



Practical Take-Aways

- An observational study of LAIs in schizophrenia suggests that both illness severity and rates of side effects remain stable over a one year period.
- Patients, caregivers and providers may have different perceptions of the advantages and barriers to initiating LAIs. Specifically, providers may overestimate patient aversion to LAIs compared to patient and caregiver reports.
- Increasing numbers of relapses may increase the all-cause mortality in patients with relatively stable schizophrenia. LAIs have the opportunity to reduce this risk because they have been demonstrated to prolong time to relapse.

1. Correll, C. et al. Poster 42 presented at 2024 Psych Congress, October 29-November 2; Boston, MA 2. Strand, L. et al., Poster 163 presented at 2023 Psych Congress, September 6-10; Nashville, TN 3. Franzenburg, K. et al., Poster 20 presented at 2023 Psych Congress Elevate, May 30– June 2; Las Vegas, NV 4. Franzenburg, K. et al., Poster 48 presented at 2023 Psych Congress Elevate, May 30 – June 2; Las Vegas, NV 5. Franzenburg, K. et al., Poster 18 presented at 2023 Psych Congress Elevate, May 30– June 2; Las Vegas, NV 6. Franzenburg, K. et al., Poster 39 presented at 2023 Psych Congress Elevate, May 30 – June 2; Las Vegas, NV

Summary and Telehealth Demonstration

Using Telemedicine for LAIs



Telehealth Visit 💻

Telehealth prescriber orders LAI 🖊️

Collaborate with Pharmacy/ Pharmacist or other site for LAI injection plan 🤝



The primary difference is operational.

Key Takeaway: build a reliable network of care

- ***Pharmacies***
- ***PCPs offices***
- ***CMHCs***

Haider B, et al. *Neuropsychiatr Dis Treat*. 2023;19:623-634. Best Practices for Prescribing Long-Acting Injectable Medications Via Telehealth. HMP Global Learning Network. September 30, 2024. Accessed March 15, 2025. https://www.hmpgloballearningnetwork.com/site/pcn/videos/best-practices-prescribing-long-acting-injectable-medications-telehealth.

Three-Talk Model for Shared Decision-Making

DECISION TALK

Collaboratively finalize the treatment decision, ensuring that patients feel **validated** and confident about their choice, while reaffirming their role in the decision-making process.

TEAM TALK

Build **collaboration and respect** by empowering patients, identifying their priorities, and fostering an environment where their autonomy and concerns are acknowledged during the decision-making process.

OPTION TALK

Provide a balanced overview of treatment choices, utilizing **numerical data** and discussing both positive and negative aspects of options, including the choice of "no treatment" when appropriate.



Raleigh, M. F., Nelson, M. D., & Nguyen, D. R. (2022). Shared decision-making: Guidelines from the National Institute for Health and Care Excellence. *American Family Physician*, *106*(2), 205-207.

Example Video:
Initiating LAI Treatment Plans via Telemedicine

Practical Take-Aways

- LAIs have certain advantages over oral antipsychotics, and longer-duration LAIs may extend these advantages.
- LAIs should be offered with a shared decision-making approach and by leading with the potential benefits an individual could obtain rather than the route of administration.
- Patient concerns, such as fear of needle pain, embarrassment about gluteal injections, or others, should be acknowledged and explored rather than dismissed.