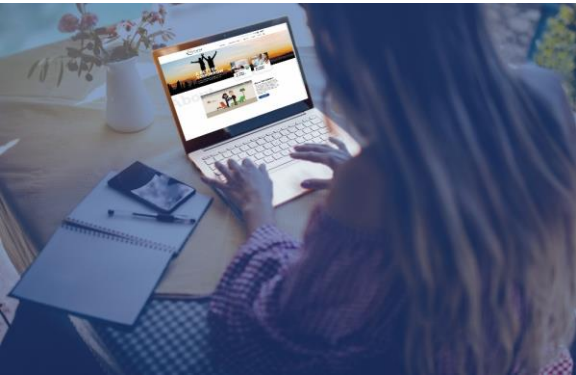


WELCOME

Clozapine & LAI Virtual Forum

August 3, 2022 | 4:00 – 4:45 pm ET

The Clozapine & LAI Virtual Forum is a peer-to-peer, interactive dialogue between psychiatrists, nurse practitioners, and other prescribing clinicians. It is informal, no registration required — just join our Zoom call and share your challenges and questions on the month's trending topic around either clozapine or LAIs.



TODAY'S TOPIC: Long-Acting Injectable (LAI) Antipsychotic Discontinuation

MODERATORS

Robert Cotes, MD

SMI Adviser Physician Expert; Emory University

Dr. Robert Cotes, MD, is an Associate Professor at Emory University School of Medicine in the Department of Psychiatry and Behavioral Sciences. He has interest in clozapine, characterizing persistent symptoms of schizophrenia, understanding cardiometabolic side effects of antipsychotic medications, and first episode psychosis.

Donna Rolin, PhD, APRN

SMI Adviser Nursing Expert; University of Texas, Austin

Dr. Donna Rolin is Clinical Associate Professor and the Director of the Psychiatric Mental Health Nurse Practitioner program at the University of Texas with experience in psychiatric nursing, including inpatient, community, forensic, and older adult settings.

Discussion Questions for Virtual Forum: Discontinuing Long-Acting Injectable Antipsychotic (LAI) Medications

- What reasons have you encountered from patients who want to discontinue LAIs?
- How have you discontinued LAIs?
 - Do you use a different method for the various LAIs?
- What types of education do you provide to patients who want to discontinue LAIs?

Long-Acting Injectable Antipsychotic Pharmacokinetics

LAI	TMAX	Apparent Half-Life
Paliperidone palmitate once monthly	13 days	25-49 days
Paliperidone palmitate every 3 months	30-33 days	Deltoid: 84-95 days Gluteal: 118-139 days
Paliperidone palmitate every 6 months		148-159 days
Risperidone microspheres	~30 days	3-6 days
Risperidone polymer	Risperidone: 4-6 h	Risperidone: 9-11 days 9-hydroxyrisperidone: 8-9 days Total active moiety: 8-9 days

Correll CU, et al. Pharmacokinetic Characteristics of Long-Acting Injectable Antipsychotics for Schizophrenia: An Overview. CNS Drugs 2021;35:39-59.

Long-Acting Injectable Antipsychotic Pharmacokinetics

LAI	TMAX	Apparent Half-Life
Fluphenazine Dec.	-	7-10 days
Haloperidol Dec.	3-9 days	21 days
Aripiprazole monohydrate	Deltoid: 4 days Gluteal: 5-7 days	29.9-46.5 days
Aripiprazole lauroxil	41 days	441 mg q4w: 57.2 days 882 mg q6w: 55.1 days 1064 mg q8w: 53.9 days
Aripiprazole lauroxil NanoCrystal Dispersion	27 (range 16-35) days 4 days with a concomitant 30 mg oral dose of aripiprazole	15-18 days
Olanzapine pamoate	2-6 days	~30 days

Example: Risperidone/Paliperidone Products

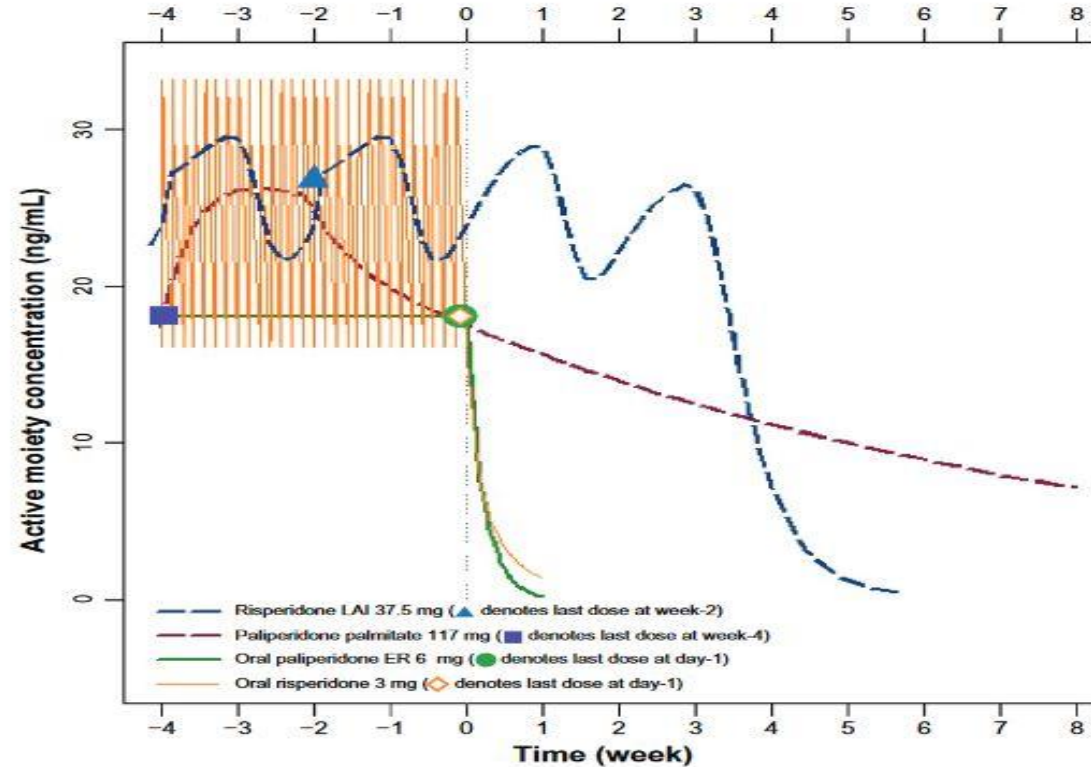


Figure 1 Active moiety concentrations following complete treatment discontinuation (week 0 denotes administration time of next scheduled dose, which was missed).
Notes: Within a few days of oral risperidone or oral paliperidone ER discontinuation, there was a substantial decrease in the concentration of the active moiety. Two weeks following the last injection of risperidone LAI, the concentration of the active moiety continued to approximate the steady-state concentration for approximately 3–4 weeks due to the delay in release (3-week lag time between last injection and last release phase). After this lag phase, there was a subsequent and rapid decline of the concentration of the active moiety, with near zero concentrations reached by week 5. As compared with the other formulations, discontinuation of paliperidone palmitate exhibited the slowest decline of the concentration of the active moiety with levels of approximately 7 ng/mL at week 8.
Abbreviations: ER, extended-release; LAI, long-acting injection.

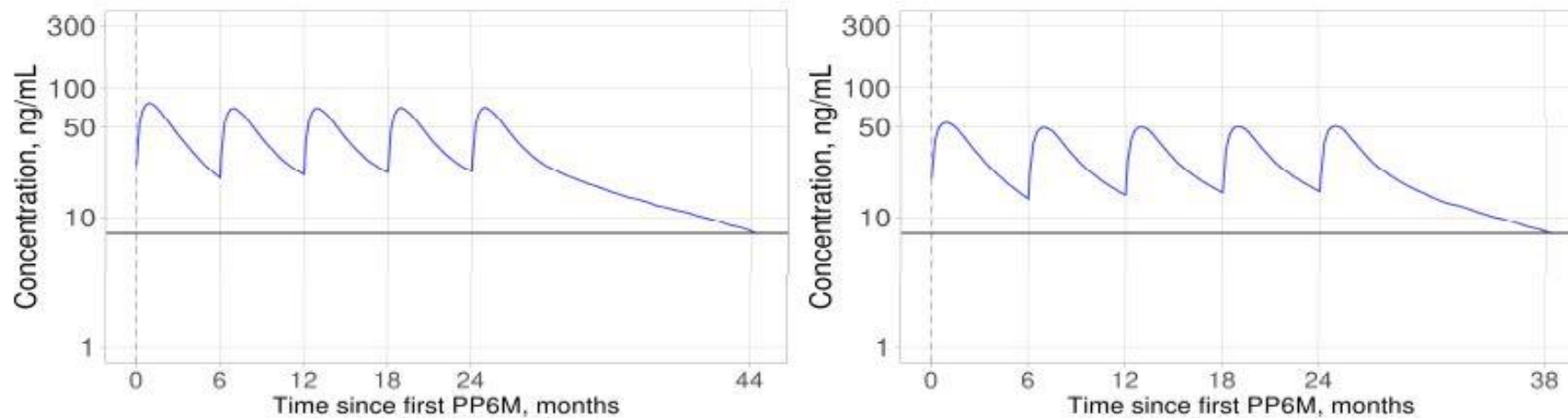
Samtani MN, et al. Management of antipsychotic treatment discontinuation and interruptions using model-based simulations. Clin Pharmacol 2012;4:25-40.

Example: Invega Hafyera™

DISCONTINUATION FOLLOWING MULTIPLE DOSES

Paliperidone concentrations ≥ 7.5 ng/mL were maintained for 14 to 20 months after discontinuation of INVEGA HAFYERA 1,092 and 1,560 mg, see Figure: Predicted Plasma Concentrations After Discontinuation of INVEGA HAFYERA 1,092 and 1,560 mg at Steady State.² A 7.5 ng/mL paliperidone concentration is associated with a 60% D₂-receptor occupancy.³ A central D₂-receptor occupancy of 60 to 80% is generally thought to be required for antipsychotic efficacy.⁴

Predicted Plasma Concentrations After Discontinuation of INVEGA HAFYERA 1,092 and 1,560 mg at Steady State²



Abbreviation: PP6M, paliperidone palmitate 6-month formulation.

The blue solid line represents the median paliperidone concentration. The black horizontal line at 7.5 ng/mL = 60% D₂-receptor occupancy. The left panel is for the high dose (INVEGA HAFYERA 1,560 mg), the right panels are for the moderate dose (INVEGA HAFYERA 1,092 mg) level.

Therapeutic Drug Monitoring

Antipsychotic	Therapeutic threshold (ng/ml)
Aripiprazole	110
Fluphenazine	1.0
Haloperidol	2.0
Olanzapine	23
Paliperidone	20
Risperidone (active moiety)	15

Meyer J and Stahl S. The Clinical Use of Antipsychotic Plasma Levels. PP.372-3



Missed LAI Dose Windows Resource

Guidance for specific LAIs

Abilify Maintena (aripiprazole monohydrate monthly LAI):

- Abilify Maintena doses should be administered not earlier than 26 days after the last injection.
- If the second or third doses are missed, Abilify Maintena should be administered not later than 5 weeks after the last injection.
- If the fourth or subsequent doses are missed, Abilify Maintena should be administered not later than 6 weeks after the last injection.
- References: [Lexicomp](#); [Prescribers Digital Reference](#)

Aristada (aripiprazole lauroxil monthly, every 6 week, or 2-month LAI):

- The recommended ARISTADA dosing interval is monthly for the 441 mg, 662 mg and 882 mg doses, every 6 weeks for the 882 mg dose, or every 2 months for the 1064 mg dose and should be maintained.
- In the event of early dosing, an Aristada injection should not be given earlier than 14 days after the previous injection.
 - Reference: [Aristada Prescribing Information](#)
- In the event of missed dose, an Aristada injection should be administered not later than the following:
 - Monthly 441 mg not later than 6 weeks after the last injection;
 - Monthly 662mg or 882 mg not later than 8 weeks after the last injection;
 - 882 mg every 6 weeks, not later than 8 weeks after the last injection;
 - 1064 mg every 2 months, not later than 10 weeks after the last injection.
 - References: [Aristada USPI](#); [Lexicomp](#); [Prescribers Digital Reference](#)

Haldol Decanoate (haloperidol monthly LAI):

- If the second or third doses are missed, Haldol Decanoate should be administered not later than 5 weeks after the last injection.
- If the fourth or subsequent doses are missed, Haldol Decanoate should be administered not later than 8 weeks after the last injection.
- References:
 - American Psychiatric Association. (2021). [The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. 3rd edition.](#)
 - [Lexicomp](#); [Prescribers Digital Reference](#)

FEEDBACK

Please help us improve the Clozapine & LAI Virtual Forum by completing this survey:
<http://smiadviser.org/forumfeedback>



Pre-submit Cases

www.smiadviser.org/vfcases

UPCOMING VIRTUAL FORUM

Clozapine topic TBA

Wednesday, September 7 @4-4:45pm ET

For additional questions and resources – join the Clozapine and LAI Centers of Excellence Exchange Community

- www.smiadviser.org/cloz_lai_signup