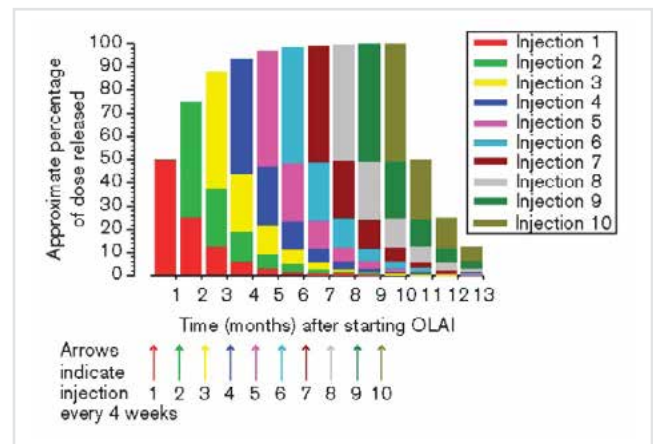


## Fact Sheet: LAI Trough Levels

Obtaining plasma levels can be helpful during antipsychotic treatment. Aside from monitoring for adherence, plasma levels allow the provider to see how the patient is metabolizing the medication and if their plasma levels are in the therapeutic range. By convention, antipsychotic plasma levels are drawn at **trough levels, once steady state has been achieved**. Steady state is achieved after 4-5 half-lives.

For oral medications, the time to draw the plasma level is fairly straightforward. Since many oral antipsychotics have an approximate half-life of 24 hours, the nadir level is 24 hours after ingestion. However, obtaining blood at the nadir level is not practical since many antipsychotics are prescribed at night. Consequently, researchers investigating the correlation of plasma levels to clinical efficacy have settled on 12 hours post-ingestion as being the trough level. (Meyer, 2021). Thus, for an oral antipsychotic with a half-life of 24 hours or less, steady state will be achieved after 5 doses and the plasma level can be drawn in the AM on the following day.

For LAIs, the trough level is **1-72 hours prior to the next injection**, but calculating the point when steady state is achieved is a little more complicated. This is because of individual variance of medication metabolism during the four phases: absorption, distribution, metabolism, and elimination. A 20% variance in the half-life of a medication like aripiprazole lauroxil could result in a +/- 10-day difference amongst different patients. **However, since adherence is no longer an issue with an LAI, we just need a general sense of the plasma levels to determine metabolism and therapeutic range. Therefore, as a general rule, at 1-72 hours prior to the FOURTH injection of an antipsychotic LAI, there will be reasonably accurate plasma levels** (see above graph from Heres, 2014 to understand why at least 3 injections are required to get close to steady state, using olanzapine LAI as an example).



If seeking to obtain trough plasma levels at true steady state, see the table below for the average half-lives and approximate durations to reach steady state for each of the commonly used antipsychotic LAIs, adapted from Heres, 2014 and Correll, 2021:

MEDICATION	SCHEDULE	HALF LIFE	STEADY STATE REACHED
fluphenazine decanoate	q2wk	7-10 days	6 weeks
haloperidol decanoate	monthly	21 days	
aripiprazole lauroxil	monthly	53.9-57.2 days	at 4th month
aripiprazole monohydrate	monthly	29.9-46.5 days	at 4th month
olanzapine pamoate	monthly	30 days	around 4th month
paliperidone palmitate 1m	monthly	25-49 days	8-9 months

It is possible to shorten the time to steady state plasma levels by using a loading schedule (Wei, 1996). Links for the loading schedule of various LAIs are provided as follows: [Fluphenazine](#); [Haloperidol](#); [Aripiprazole](#); [Paliperidone](#).

#### References

1. Alkermes Inc. Aristada Initio package insert. 2020. Walltham, MA.
2. Correll C, et al. Pharmacokinetic Characteristics of Long-Acting Injectable Antipsychotics for Schizophrenia: An Overview. *CNS Drugs*. 2021 Jan;35(1):39-59. doi: 10.1007/s40263-020-00779-5.
3. Heres S, et al. Pharmacokinetics of olanzapine long-acting injection: the clinical perspective. *Int Clin Psychopharmacol*. 2014 Nov;29(6):299-312. doi: 10.1097/YIC.0000000000000040
4. Janssen Pharmaceuticals Inc. Invega Sustenna package insert. 2019. Titusville, NJ.
5. Meyer JM, Stahl SM. The Clinical Use of Antipsychotic Plasma Levels, *Stahl's Handbooks*, Chapter 1: Sampling Times for Oral and Long-Acting Injectable Agents. Cambridge University Press; 2021
6. Otsuka America Pharmaceutical Inc. Abilify Maintena package insert. 2020. Rockville, MD.
7. Wei, F. C., et al. A practical loading dose method for converting schizophrenic patients from oral to depot haloperidol therapy. 1996. *J Clin Psychiatry*, 57:298-302.

Funding for SMI CalAdviser was made possible by the State of California Department of State Hospitals (DSH) (the Department), but does not necessarily represent the views of the Department or any of its employees except to the extent, if any, that it has formally been approved by the Department.