

Long-Acting Injectable Antipsychotics: A Summary for Prescribers

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This article summarizes the most clinically relevant features of long-acting injectable antipsychotics (LAIs, previously known as depot antipsychotics). We discuss general concepts as well as key prescribing facts of individual agents.

The guide also includes two new formulations: aripiprazole lauroxil (Aristada) and 3-month paliperidone palmitate (Invega Trinza).

Clinical questions answered

Castillo and Stroup [2] reviewed the effectiveness of LAIs and addressed the following questions:

Who should receive LAIs?

Consider LAIs for patients with recent-onset schizophrenia and those with risk factors for medication non-adherence: history of non-adherence, severe symptoms, comorbid substance use, cognitive impairment, ambivalence or negative attitudes towards medications, and poor insight.

Are the newer LAIs more effective?

The effectiveness of newer LAIs (aripiprazole, olanzapine, paliperidone and risperidone) and older LAIs (haloperidol, fluphenazine, flupenthixol) is similar.

Practical considerations

Abilify Mantenna

- *Aripiprazole monohydrate requires a period of overlap of 2 weeks with oral aripiprazole.*
- *Available as a lyophilized powder which needs to be reconstituted.*

[See full prescribing information \(PDF\)](#)

Aristada

- *Aripiprazole lauroxil requires a period of overlap of 3 weeks with oral aripiprazole.*
- *Available as a prefilled syringe that does not require reconstitution.*

[See full prescribing information \(PDF\)](#)

Zyprexa Relprevv

- Olanzapine pamoate does not need overlap with oral olanzapine.
- It has a small risk of post-injection syndrome (0.07% of injections):
 - Symptoms include sedation, confusion, agitation, anxiety, aggressiveness, dizziness, ataxia and extrapyramidal symptoms
 - This risk limits use olanzapine pamoate use
 - After injection, the patient must be monitored for three hours by a healthcare professional
 - In the US, prescribers who administer Zyprexa Relprevv must enroll in a national registry that documents the incidence of this adverse effect

[See full prescribing information \(PDF\)](#)

Invega Sustenna

- Paliperidone palmitate does not need overlap with oral paliperidone.
- Requires two separate loading dose injections during the first week.

[See full prescribing information \(PDF\)](#)

Invega Trinza

- The 3-month paliperidone palmitate (PPM-3) formulation can only be used if the patient has been receiving 1-month paliperidone palmitate injections for at least 4 months.
- It is administered 4 times a year, providing the longest interval of any approved LAI.

[See full prescribing information \(PDF\)](#)

Risperdal Consta

- Risperidone microspheres requires a period of overlap of 3 weeks with oral risperidone.
- It has a 2-week dosing interval.

[See full prescribing information \(PDF\)](#)

Advantages and disadvantages of long-acting antipsychotics

Brissos and colleagues [1] reviewed the role of long-acting injectables in schizophrenia. They summarized the key advantages and disadvantages of LAIs in clinical practice.

Potential advantages	Potential disadvantages
<ul style="list-style-type: none">• <i>Early identification of non-adherence</i>• <i>Providing a mechanism for monitoring adherence with injections</i>• <i>No need to remember to take medication every day</i>• <i>Regular interactions between patient and medical staff</i>• <i>Reduced relapse frequency and rehospitalization rates</i>• <i>Clear attribution of the cause of relapse or non-response, discriminating between non-adherence or lack of response</i>• <i>Reduce the risk of accidental or deliberated overdose</i>• <i>Treating patients with more stable plasma concentrations than oral medications</i>• <i>Avoidance of first-pass metabolism - better relationship between dose and blood level of drug</i>• <i>Lower and less frequent peak plasma level - reduced side effects</i>	<ul style="list-style-type: none">• <i>Slow dose titration</i>• <i>Longer time to achieve steady state levels</i>• <i>Less flexibility of dose adjustment</i>• <i>Delayed disappearance of distressing and/or severe side effects</i>• <i>Pain at the injection site can occur, and leakage into the subcutaneous tissue and/or the skin may cause irritation and lesions (especially for oily long-acting injectable)</i>• <i>Burden of frequent travel to outpatient clinics or home visits by community nurses for their administration</i>• <i>Risperidone long-acting injectable needs refrigeration, which may be cumbersome in some latitudes</i>• <i>Perception of stigma</i>



Tables summarizing individual agents

First-generation antipsychotics available as long-acting injectable medications

Drug	Starting dose (mg)	Maintenance dose (mg)
Haloperidol decanoate	50	50–200 every 3–4 weeks
Fluphenazine decanoate	12.5	12.5 - 50 every 2–3 weeks
Flupenthixol decanoate	20	50–300 every 2–4 weeks
Zuclopenthixol decanoate	100	200–500 every 1–4 weeks

Second-generation antipsychotics available as long-acting injectable medications

Drug (Brand name)	Manufacturer	Formulations	Injection interval	Comments
Aripiprazole monohydrate (Abilify Mantenna)	Otsuka/ Lundbeck	300,400 mg vials, prefilled syringes	400 mg once/month	Requires a period of 2 weeks of overlap with oral aripiprazole.
Aripiprazole lauroxil (Aristada)	Alkermes	441, 662, 882 mg prefilled syringes	441–882 mg once/month 882 mg q 6 weeks	The 882 mg dose can be administered every 6 weeks. Requires a period of 3 weeks of overlap with oral aripiprazole.
Olanzapine pamoate (Zyprexa Relprevv)	Lilly	210, 300, 405 mg vials	150–300 mg q2 weeks 300–405 mg once/month	Requires monitoring post injection (3 hours)
Paliperidone palmitate (Invega Sustenna, Xeplion)	Janssen	39,78,117,156 or 234 mg prefilled syringes	117 mg once/month	Oral supplementation not necessary.
Paliperidone palmitate (Invega Trinza)	Janssen	273, 410, 546, 819 mg prefilled syringes	410 mg q3 months	Use in patients already treated with Invega Sustenna
Risperidone microspheres (Risperdal Consta)	Janssen	12.5, 25, 37.5 or 50 mg vials	25 mg q2 weeks	Requires a period of 3 weeks of overlap with oral risperidone



References

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