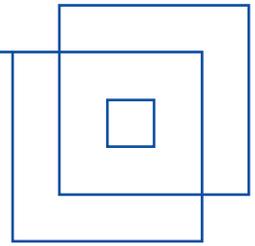


LAI ANTIPSYCHOTICS

FREQUENTLY ASKED QUESTIONS



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- **Who should receive LAIs** (long acting injectable antipsychotics)?
- **Which antipsychotics are available** in long acting formulations in the United States?
- **What are the potential advantages** of LAIs?
- **What are the potential disadvantages** of LAIs?
- **Are there different side effect profiles** for long acting injectable antipsychotics compared to their oral antipsychotic equivalents?
- **How do I switch patients from an oral antipsychotic** to a long acting formulation?
- **How do I switch patients from one** long acting antipsychotic agent to another?
- **How do I switch patients from a long acting antipsychotic agent** to an oral antipsychotic agent?
- **What are the recommended** starting doses?

q: Who should receive LAIs?

A. Consider LAIs with these points in mind:

- Everyone appropriate for daily oral antipsychotic therapy is appropriate for long acting formulations.
 - This includes first episode psychosis patients and those in recovery on oral medications. (For these groups, the goal of considering long acting formulations is to keep people well.)
- Only offering long acting formulations after relapse due to non-adherence reinforces false beliefs and stigmatizes LAIs as “only for sicker people.”
- Medication non-compliance is a common reality in all aspects of medicine, not only in psychiatry.

q: Which antipsychotics are available in long acting formulations in the US?

A. These antipsychotics are available as LAIs:

- aripiprazole monohydrate
- aripiprazole lauroxil
- fluphenazine decanoate
- haloperidol decanoate
- olanzapine pamoate
- paliperidone palmitate
- risperidone microspheres

q: What are the potential advantages of LAIs?

A. The potential advantages are:

- You know definitively whether or not your patient is taking the medication
- Patients don't need to remember to take medication every day
- Reduced relapse frequency and reduced re-hospitalization rates
- Allows you to know if relapse is caused by lack of response to medication or to poor adherence
- Eliminates the risk of patients taking the wrong dose of medication
- Avoidance of first-pass metabolism — better relationship between dose and blood level of drug
- Plasma concentrations will be more stable with LAIs than with oral medications
- Lower and less frequent peak plasma level — reduced side effects

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q: What are the potential disadvantages of LAIs?

A. The potential disadvantages are:

- Slow dose titration
- Longer time to achieve steady state levels
- Less flexibility of dose adjustment
- Delayed disappearance of distressing and/or severe side effects
- Pain at the injection site can occur, and leakage into the subcutaneous tissue and/or the skin may cause irritation and lesions (especially for the decanoate injectables)
- Burden of travel to outpatient clinics or home visits by community nurses for their administration
- Risperidone long-acting injectable needs refrigeration, which may be cumbersome in some latitudes
- Perception of stigma

q: Are there different side effect profiles for long acting injectable antipsychotics compared to their oral antipsychotic equivalents?

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A. In general, side effect profiles are the same:

- A brief trial of oral antipsychotic equivalent prior to administering the long acting injectable formulation establishes side effect tolerability.
- Plasma concentrations are often more stable and peak at lower levels with long acting vs. oral.
- Injection site reactions include pain, bleeding, nodules (oil based formulations), and skin thickening.

There is no evidence to indicate the risk of Neuroleptic Malignant Syndrome is greater with long acting antipsychotics compared to their oral formulation equivalents. That being said, a history of NMS is generally considered a contraindication to treatment with an LAI. NMS caused by an LAI may be more serious than when occurring with oral antipsychotics because plasma and central nervous system antipsychotic levels will remain high for weeks with an LAI.

A post-injection delirium/sedation syndrome exists for olanzapine pamoate which is rarely seen but unique here. Olanzapine pamoate crystals are insoluble in muscle, but rapidly dissolve in blood. The theorized mechanism is damaged blood vessels during injection with leakage of blood into the injection site.

q: How do I switch patients from one long acting antipsychotic agent to another?

A. Substitute the new LAI for the previous one at a planned injection appointment.

- This essentially results in the equivalent of a cross-taper oral antipsychotic medication switch.
- Due to kinetics of LAIs, there's low risk of rebound psychosis or withdrawal emergent dyskinesias.
- Previous plasma levels will fall, with a corresponding slow rise to a steady state of the new agent.

q: How do I switch patients from oral antipsychotics to long acting formulations?

A. Planning a switch to a first generation antipsychotic LAI should include considering:

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- Expected time to steady state of the LAI
- Period before it will achieve minimally effective plasma level

For second generation agents:

- Risperidone requires oral antipsychotic supplementation for the first 3 weeks after first injection.
- Aripiprazole lauroxil requires supplementation for the first 21 days after initial injection.
- Requires oral supplementation with oral aripiprazole for the first 14 days after initial injection.
- For paliperidone palmitate monthly, oral supplementation can be gradually discontinued after administering the injection. Paliperidone palmitate every 3 months should be started following paliperidone palmitate monthly, not oral paliperidone.
- For olanzapine pamoate, oral supplementation can be gradually discontinued after the injection.

q: How do I switch patients from long acting to oral antipsychotic agents?

A. To minimize adverse effects of dual therapy, don't start the oral prior to the date of the next injection.

- When the LAI is discontinued, over a number of months the plasma levels will fall, while the new oral antipsychotic builds to a steady state.
- While it may take weeks to months for the LAI to wash out of the system, most oral antipsychotics achieve steady state within 5 to 10 days.
- If the oral is instigated immediately after the last depot injection, there will be active effects from both medications for a period. Having two agents may result in an increased side effect burden.
- Combined therapy has little evidence to support it – to minimize adverse effects of dual therapy during a switch, do not start the oral antipsychotic prior to the date of the next scheduled injection.

Q: What are the recommended starting doses?

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|------------------------------------|---|
| A. aripiprazole monohydrate | <ul style="list-style-type: none">• Dose is 400mg monthly (not before 26 days after previous injection).• If adverse reactions, consider reducing dosage to 300mg monthly. |
| aripiprazole monohydrate | <ul style="list-style-type: none">• Dose is 400mg monthly (not before 26 days after previous injection).• If adverse reactions, consider reducing dosage to 300mg monthly. |
| aripiprazole lauroxil | <ul style="list-style-type: none">• Dosing depends on the daily oral dose of aripiprazole.• The 441mg dose per month is equivalent to 10mg oral dose daily.• The 662mg dose per month is equivalent to 15mg oral dose daily.• The 882mg dose per month is equivalent to ≥ 20mg oral dose daily. |
| fluphenazine decanoate | <ul style="list-style-type: none">• A dose of 12.5 – 25mg (0.5 – 1mL) may be given to initiate therapy.• Subsequent injections and the dosage interval are determined in accordance with the patient's response.• Fluphenazine hydrochloride 20mg daily is equivalent to 25mg (1mL) of fluphenazine decanoate injection every 3 weeks.• This represents an approximate conversion ratio of 12.5mg (0.5mL) of decanoate every 3 weeks for every 10mg of fluphenazine hydrochloride daily.• A single dose has been found to be effective for patients for 4-6 weeks in maintenance therapy. <p style="text-align: right;">BACK TO TOP</p> |
| haloperidol decanoate | <ul style="list-style-type: none">• Haloperidol decanoate comes in 50mg and 100mg doses. The preferred approach to determining the minimum effective dose is to begin with lower initial doses and to adjust upward as needed.• For patients previously maintained on low doses of antipsychotics (e.g. up to the equivalent of 10 mg/day of oral haloperidol), it is recommended that the initial dose of haloperidol decanoate be 10-15 times the previous daily dose in oral haldol equivalents.• In patients previously maintained on higher doses of antipsychotics for whom a low dose approach risks recurrence of psychiatric decompensation and in patients whose long-term use of haloperidol has resulted in a tolerance to the drug, 20 times the previous daily dose in oral haloperidol equivalents should be considered for initial conversion, with downward titration on succeeding injections.• The initial dose of haloperidol decanoate should not exceed 100mg regardless of previous antipsychotic dose requirements. If conversion requires more than 100mg of haloperidol as an initial dose, that dose should be administered in two injections, i.e. a maximum of 100mg initially followed by the balance in 3-7 days. |

olanzapine pamoate

- Olanzapine pamoate is available in doses of 210mg/2wk, 300mg/2wk, and 405mg/4wk.
- An oral olanzapine dose of 10mg/day corresponds to 210mg/2 weeks or 405mg/4 weeks (changed to 150mg/2 weeks or 300mg/4 weeks after 8 weeks).
- An oral dose of 15mg/day corresponds to 300mg/2weeks (changed to 210mg/2weeks or 405mg/4 weeks after 8 weeks)
- An oral dose of 20mg/day corresponds to 300mg/2 weeks (same dose in maintenance).

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paliperidone palmitate (monthly)

- To initiate, inject 234mg day 1, followed by 156mg day 8, followed by first maintenance dose five weeks after first injection.
- Maintenance doses are 39-234mg/month with recommended maintenance dose of 117mg monthly.
- Dosing options are 39mg, 78mg, 117mg, 156mg, or 234mg.
- Oral dose of 3mg daily corresponds to 39-78mg monthly.
- Oral dose of 6mg daily corresponds to 117mg monthly.
- Oral dose of 12mg daily corresponds to 234mg monthly.

paliperidone palmitate (every 3 months)

- Dosing options include 273mg, 410mg, 546mg, or 819mg.
- Transition to every 3 months — paliperidone palmitate should follow treatment with monthly paliperidone palmitate.
- 78mg monthly corresponds to 273mg every 3 months.
- 117mg monthly corresponds to 410mg every 3 months.
- 156mg monthly corresponds to 546mg every 3 months.
- 234mg monthly corresponds to 819mg every 3 months.

risperidone long acting injectable

- Dosing options include 12.5mg, 25mg, 37.5mg, and 50mg.
- The recommended dose is 25mg every 2 weeks.
- Although dose response for effectiveness has not been established, some patients not responding to 25mg may benefit from a higher dose of 37.5mg or 50mg.
- The maximum dose should not exceed 50mg every 2 weeks.

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