

Long-acting injectable (LAI) antipsychotics – How to manage patients on long-acting injectable (LAI, or depot) antipsychotics during the COVID-19 pandemic.

Please note all questions within each section are linked to each other and should be read in conjunction. Below each question is the weblink to the source of evidence to support the guidance recommendation.

Please read the following advice in combination with [national UK advice on protection/self-isolation](#).

This guidance includes information about LAI antipsychotic medications which are currently licensed in the UK (that is: Xeplion®, Trevicta®, Abilify Maintena®, Risperdal Consta®, Zypadhera®). The guidance may not be accurate for different formulations of the medications. If a different formulation is used, please refer to the manufacturer's information for further details.

Guidance for individual medications references the SmPC/IMPD for each individual medication, to inform dose and dosing interval information.

Clinical question	Guidance
Starting LAI/depot antipsychotic medications	
Can I start my patient on a LAI/depot antipsychotic? [link1]	<p>Yes, although clinicians will need to check local arrangements for administration of these injections.</p> <p>Also, consider the following general advice for all psychotropic medication:</p> <ul style="list-style-type: none"> • Careful consideration should be given to whether now is the best the time to withdraw or change patients from antidepressant, anxiolytic or antipsychotic medication. In some circumstances this may be unavoidable due to clinical need, but the clinical rationale should be carefully documented and arrangements for monitoring put in place. • For many patients it is likely that advice will be given to continue on regular medication until this can be reviewed in a face-to-face setting and the patient can be involved in shared decision making with their usual doctor or healthcare provider. This should take account of the fact that anxiety, depressive and psychotic symptoms are all likely to worsen during extreme stress and social disruption. Patients will be at increased risk of relapse or recurrence of affective and psychotic illnesses. • Advise patients to continue their current dosage until the changes in health care provision necessary during the COVID-19 pandemic have been reversed, and only then consider whether dosage reductions or withdrawal might be appropriate, in discussion with their usual doctors.
Managing patients who are already taking LAI antipsychotics	
How should I manage the schedule of LAI/depot antipsychotic administration	<ul style="list-style-type: none"> • For many patients, stopping or missing medication for a long period is likely to result in a deterioration in mental state with increased risk to themselves and others. This is also likely to affect their ability to comply with precautions around reducing COVID-19 transmission and spread.

in general for patients during the COVID-19 pandemic?

[\[link2\]](#)

[\[link16\]](#)

- Therefore, patients maintained on LAI antipsychotic medication **should stay on them if at all possible/feasible**.
- The role of long-acting injectables (LAI) is a **clinically necessary treatment** and should be continued for patients with chronic mental illness. Whilst there are some patients where it is possible to switch to an oral medication, others would be destabilised by this. Individuals with serious mental illness **are at much higher risk of morbidity and mortality even when provided continuous, stabilizing treatment; withdrawal of this treatment would likely increase their risk of physical and psychiatric decompensation**. These risks are increased during the COVID-19 pandemic due to **reduced support and access to outpatient treatment** including pharmacy services.
- **Staff may also have concerns** in administering such medication given the **close contact involved**.
- Consider **depot administration as a high transmission risk situation**.
- Staff should consider other options available including **detailed advice below on individual medications**, and **consider general actions as follows**:
 - **Increasing the dosing interval of the depot where possible**, e.g. instead of weekly or two weekly dosing, increase to four-weekly dosing.
 - Remember that a longer dosing interval does not diminish the effectiveness of the drug **as long as the overall dose remains the same**.
 - For **paliperidone monthly patients consider switching to paliperidone 3-monthly long-acting depot, where possible**.
 - Consider that all patients and staff are at risk of being carriers or to have COVID-19. Close contact situations, **such as depot administration, should be done only using personal protective equipment (PPE)** (see [here](#)). **Explain what you are doing and why and do this before meeting** the patient so as not to alarm them.

What should I do if a patient on a depot/LAI antipsychotic is self-isolating with or without symptoms of COVID-19?

[\[link1\]](#)

[\[link3\]](#)

- If the patient describes COVID-19 symptoms, and is due to have their depot/LAI administered, consult the prescriber and **consider an alternative short term treatment plan, such as deferring treatment for 2 weeks** (if currently psychologically well and risk of rapid relapse is considered to be low) **or switching to oral formulations** (see details below and refer to guidance about dosage equivalence).
- If the decision is made to defer the depot/LAI, **ensure a clear plan/risk assessment is agreed and documented regarding follow up with continued monitoring of mental and physical health, with the agreed date of when to review and next administer depot/LAI**.
- If the patient describes COVID-19 symptoms **but it is essential to administer depot/LAI, do so wearing PPE and follow [Infection Prevention and Control \(IPC\) procedures](#)**.
- In all circumstances, **ensure a clear plan is agreed and documented with the patient/carer, their care coordinator and the Consultant responsible for the patient's care** (or their deputy) regarding follow up after depot administration and monitoring of physical and mental health symptoms. **Ensure that colleagues in primary care are made aware of any changes** to pharmacological treatment.

In some cases, **it may be appropriate to switch a patient from a depot antipsychotic to an oral equivalent**. However, it is important to consider what the **risks** are:

- **Relapse or destabilisation** if the dose of oral medication is too low or if the patient has reduced adherence to the oral medicine.
- **Exacerbation of their condition** due to stress and anxiety from the switch.
- **Potential medication errors during the cross over**:
 - **Difficulties in working out equivalent doses** requiring periods of dose adjustments.
 - **Combined adverse drug reactions (ADRs) during the period of crossover** or ADRs due to the oral dose equivalent being too high.

Alternatively, **you may consider changing to a depot with a longer dosing frequency, if appropriate** (see details below for individual medications).

Where patients' depots or LAIs are switched or dosing intervals changed, they should be reviewed at least one week after the change to monitor for any adverse effects or any signs of emerging symptoms or relapse. Reviews can be carried out over the phone where appropriate.

Are there any other considerations?

Are patients treated with antipsychotic depots or LAIs at greater risk of COVID-19?

[\[link4\]](#)

No specific guidance.

However, those patients who are taking LAIs/depots may be at increased risk because of **associated health problems**. Psychosis and associated antipsychotic medication (especially longer term) are **associated with increased rates of obesity, heart disease, and respiratory disease (including smoking)**. These conditions are associated with an increased risk of severe illness from coronavirus (COVID-19).

General advice for patients/carers on managing medications and prescriptions during COVID-19

[\[link18\]](#)

In the UK, PHE advises patients as follows:

- Keep taking your medications.
- You might be able to order repeat prescriptions by phone, or online using an app or website if your doctor's surgery offers this.
- Ask your pharmacy about getting your medication delivered or think about who you could ask to collect it for you if you are self-isolating or shielding. The NHS website has more information about [getting prescriptions for someone else](#) and [checking if you have to pay for prescriptions](#).
- Continue to order your repeat prescriptions in your usual timeframe. There is no need to order for a longer duration or larger quantities.
- Your GP practice (or clinical team) may move your prescriptions to repeat dispensing arrangements, so you only have to contact your pharmacy to get a repeat of your medicine rather than your practice.
- Be careful about buying medication online. You should only buy from registered pharmacies. You can check if a pharmacy is registered on the [General Pharmaceutical Council website](#).
- You can contact [NHS 111](#) in England if you're worried about accessing medication.

How to manage individual medications

(Guidance for individual medications references the SmPC/IMPd for each individual medication, to inform dose and dosing interval information)

Paliperidone one monthly injection (PP1M)

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[\[link6\]](#)

[\[link19\]](#)

Paliperidone (PP1M) should be given once monthly on the same date each month.

How far can I extend the length of time between injections?

Monthly paliperidone injections can be given 7 days before or after the 1-month time point.

Where paliperidone monthly injection is delayed ensure the patient receives the correct number of injections over the course of a year. To achieve this:

- If there is a delay to the day of administration for a single month, try to revert to the original administration date the following month.
- For example, if an injection is given on 1st January, then delayed and given on 8th February, you should then attempt to regain the normal date and give again on 1st March.

What should I do if my patient misses a dose?

- **<6 weeks since last injection:** give previously stabilised dose as soon as possible, followed by injections at monthly intervals.

- **>6 weeks to 6 months since last injection:** if usual monthly dose is 50-100mg, give usual dose in deltoid as soon as possible. Repeat this dose (50mg - 100mg) a week later (day 8), then resume monthly schedule. If usual monthly dose is 150mg, give 100mg in the deltoid followed by 100mg in the deltoid a week later, then resume usual stabilised dose (150mg) monthly.

How do I switch my patient to oral medication?

Consider whether oral paliperidone is available locally. If not, you may need to switch to oral risperidone or another oral antipsychotic depending on previous tolerability. Start the oral antipsychotic when the next PP1M dose is due but titrate slowly as significant paliperidone levels can persist for up to six months.

Consider Paliperidone 3 monthly (PP3M) as an alternative for patients who are stable and have had 6 months of Paliperidone (PP1M).

Paliperidone 3 monthly should be **initiated in place of the next scheduled dose** of 1-monthly paliperidone palmitate injectable (\pm 7 days). The Paliperidone 3 monthly dose should be based on the previous 1-monthly paliperidone dose **using a 3.5-fold higher dose**.

Paliperidone 3 monthly injection (PP3M)

[\[link7\]](#)

Paliperidone (PP3M) should be given every three months on the same date of the month.

How far can I extend the length of time between injections?

3-monthly paliperidone injections can be given **14 days before or after the 3-month time point**.

What should I do if my patient misses a dose?

- **3½ months up to 4 months:** administer the usual dose as soon as possible and resume 3-monthly schedule.
- **4 months to 9 months:** follow re-initiation regimen set out in the manufacturer's literature. This involves day 1 and day 8 deltoid injections using the 1-monthly paliperidone formulation (PP1M). The dose of PP1M that should be used is determined by the original PP3M dose that the patient had been on. One month after this second dose was given, resume the previous 3-monthly formulation (PP3M).
- **More than 9 months:** Re-initiate treatment with 1-monthly paliperidone palmitate injectable as described in the prescribing information for that product. PP3M can then be resumed after the patient has been adequately treated with 1-monthly paliperidone palmitate injectable preferably for four months or more.

How do I switch my patient to oral medication?

Consider whether oral paliperidone is available locally. If not, you may need to switch to oral risperidone or another oral antipsychotic depending on previous tolerability. Start the oral antipsychotic when the next PP3M dose is due but titrate slowly – start at half target dose or less and increase the dose every 4-6 weeks with a view to reaching the target clinical dose 6 months after the last injection.

Aripiprazole long acting injection

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[\[link9\]](#)

Aripiprazole LAI should be given once monthly as a single injection, no sooner than 26 days after the previous injection.

What should I do if my patient misses a dose?

If 2nd or 3rd monthly dose is missed and time since last injection is:

- **> 4 weeks and < 5 weeks:** administer dose as soon as possible and resume monthly schedule.
- **> 5 weeks:** give oral aripiprazole for 14 days with the next administered injection.

If 4th or subsequent doses are missed and time since last injection is:

- **> 4 weeks and < 6 weeks:** administer dose as soon as possible and resume monthly schedule.
- **> 6 weeks:** give oral aripiprazole for 14 days with the next administered injection.

How do I switch my patient to oral medication?

Restart aripiprazole at 5-10mg or other antipsychotic at low dose when the next injection is due. After 1-2 weeks increase the dose as needed.

Risperidone long acting injection

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[\[link11\]](#)

Risperidone LAI should be given fortnightly. The release profile consists of a small initial release of risperidone (< 1% of the dose), followed by a lag time of 3 weeks. The main release of risperidone starts from week 3 onwards, is maintained from 4 to 6 weeks, and subsides by week 7.

What should I do if my patient misses a dose?

Give the next dose as soon as possible and carry on fortnightly from that point. Oral supplementation may be needed in the interim for up to three weeks after the injection is given.

How do I switch my patient to oral medication?

Plasma levels start to drop below the steady state about 5 weeks after the last dose is given and fall to near baseline by 7-8 weeks. Oral risperidone or another antipsychotic may be started 5 weeks after the last injection with cautious titration upwards.

Consider paliperidone (PP1M) as an alternative.

Patients who have a GFR less than 50ml/min should not be switched to paliperidone.

When switching patients from risperidone long acting injection, initiate paliperidone (PP1M) therapy in place of the next scheduled injection. Paliperidone (PP1M) should then be continued at monthly intervals. The one-week initiation dosing regimen including the intramuscular injections (day 1 and 8, respectively) is not required. Patients previously stabilised on different doses of risperidone long acting injection can attain similar paliperidone steady-state exposure during maintenance treatment with paliperidone monthly doses according to the following:

Previous risperidone long acting injection dose	Paliperidone (PP1M) injection
25 mg every 2 weeks	50 mg monthly
37.5 mg every 2 weeks	75 mg monthly
50 mg every 2 weeks	100 mg monthly

Olanzapine long acting injection

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[\[link12\]](#)

[\[link17\]](#)

Olanzapine long acting injection can be given either every 2 weeks or every 4 weeks depending on clinical need.

It is a licensing requirement that olanzapine LAI should **be given in a healthcare setting to allow for monitoring for post-injection syndrome by qualified personnel for 3 hours following the injection.** During the COVID-19 this may not be possible and clinicians may need to weigh up risks and benefits of administration at home, with a shorter interval of monitoring (as the majority of reactions have been reported within the first hour after injection). If possible, ensure that the patient is not alone for the remaining time of the required 3 hours, and continue to be vigilant for signs and symptoms for the remainder of the day. Advise the patient not to drive or operate machinery.

What should I do if my patient misses a dose?

- **For a missed 2-weekly maintenance dose:** give up to 25% extra at the next two scheduled doses.
- **For a missed 4-weekly maintenance dose:** Give up to 25% extra with the next scheduled dose however consider the need for oral supplementation for a few days prior to giving this dose if appropriate.

How do I switch my patient to oral medication?

Olanzapine LAI provides a slow continuous release of olanzapine that continues for approximately six to eight months after the last injection. A very low dose of oral olanzapine or another antipsychotic may be initiated when the next injection is due, with careful monitoring especially in the first two months after discontinuation of Olanzapine LAI. Aim for gradual titration over 3-6 months to target clinical dose.

Zuclopenthixol Decanoate and Flupentixol Decanoate

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[\[link13\]](#)

Zuclopenthixol and Flupentixol depots can be given in intervals of one to four weeks.

In cases where the dosing interval needs to be extended it may be necessary to increase the dose administered. The maximum dose of zuclopenthixol that can be given at a single time point is 600mg.

The maximum dose of flupentixol that can be given at a single time point is 400mg.

What should I do if my patient misses a dose?

For those on weekly dosing: A dose can be given a day or two early or late without significant effects on plasma levels. If missing a week, give the next dose due on the scheduled date but add up to about 50–75% (within licensed limits), then revert to normal dose a week after that.

For those on fortnightly dosing: Give the missed dose a week late, then go to fortnightly from that date if possible (which will be a different week from the previous fortnightly routine).

Alternately: give 75% of the previous dose a week after the due dose was missed, then 75% again a week later, then go back to the original dose every 2 weeks. Or: add (up to) 50% to the next due fortnightly dose (i.e. 28 days after the last dose was given).

The dose chosen will need to consider licensed limits.

For those on three-weekly dosing: Restart at the next dose (i.e. 6/52 after last dose given) at the usual dose plus 33-50% then revert to the usual dose.

For those on four-weekly dosing

- One week late – Give the missed dose a week late then carry on as before.
- 2 weeks late – Can give the normal dose two weeks late then two weeks after that give 50% of the normal dose then revert to normal four weekly dosing.
- 3 weeks late – Start again with the usual dose.

How do I switch my patient to oral medication?

For those on weekly dosing:

Start half the oral equivalent dose on the day when the next weekly injection is due. After a week of half dose, increase to full dose equivalent dose.

For those on fortnightly dosing:

Start half the oral equivalent dose on the day when the next injection is due. After one week increase to full equivalent daily oral dose.

For those on three or four weekly dosing:

Start an equivalent oral dose on the day when the next injection is due.

Haloperidol long acting injection

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[\[link14\]](#)

Haloperidol decanoate is usually given in four weekly intervals although the dosing interval may be adjusted according to clinical need. The maximum single dose that should be given is 300mg.

What should I do if my patient misses a dose?

For those on weekly dosing: A dose can be given a day or two early or late without significant effects on plasma levels. If missing a week, give the next dose due on the scheduled date but add up to about 50–75% (within licensed limits), then revert to normal dose a week after that.

For those on fortnightly dosing:

- Up to 6 days late – give the full dose then resume as normal.
- One week late – give 50% full dose then resume normal dosing the following week.

For those on three weekly dosing: At the next scheduled dose (i.e. 6/52 after the last dose given) restart the usual dose plus 50% then revert to the previous dosage schedule.

For those on four weekly dosing: Restart at the usual dose plus up to 50% then revert to four weekly intervals.

How do I switch my patient to oral medication?**For those on weekly dosing:**

Start 25% oral equivalent dose when next injection is due for one week, then 33% oral equivalent for one week, then 66% oral equivalent for one week, then 100% oral equivalent.

For those on fortnightly dosing:

On the date the next depot is due, start 25% of the target dose for one week, then 50% target dose for two weeks, then the full dose.

For those on three or four weekly dosing:

Start with half the target oral dose for a week when the next depot is due. Then increase to full target oral dose.

Fluphenazine decanoate

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[\[link15\]](#)

Fluphenazine decanoate can be given in intervals of up to four weeks. The maximum single dose that can be given is 100mg.

Note: The branded version of fluphenazine decanoate was discontinued worldwide in 2018. Generic stocks may be available in some parts of the world. There are no generic products available in the UK.

What to do if my patient misses a dose:

For those on weekly dosing:

A dose can be given a day or two early or late without significant effects on plasma levels. If missing a week, give the next dose due on the scheduled date but add up to about 50–75% (within licensed limits), then revert to normal dose a week after that.

For those on fortnightly dosing:

- Up to 6 days late – give the full dose then resume previous dosing schedule as normal.
- One week late – give 50% full dose then resume previous dosing schedule the following week.

For those on three weekly dosing:

At the next scheduled dose (i.e. 6/52 after the last dose given) restart the usual dose plus 50% then revert to the previous dosage schedule.

For those on four weekly dosing:

Restart at the usual dose plus up to 50% then continue at four weekly dosing.

How do I switch my patient to oral medication?

According to the manufacturer's literature, it is not possible to predict an oral equivalent dose of fluphenazine as there is wide individual response to the depot. Oral fluphenazine is not available in the UK.

Fluphenazine decanoate half-life is up to 100 days after multiple dosing although levels may fall below therapeutic dose after four weeks. Therefore, when switching to oral antipsychotic, cautiously introduce oral medication when injection is next due and amend dose according to clinical need and adverse effects.

[Link9]: Psychotropic Drug Directory 2018 (S. Bazire). Lloyd-Reinhold Publications.