

## (COVID-19) Pharmacy and medication update

### Depot or long-acting injections (LAI) antipsychotic medication

It is likely that during the outbreak of COVID -19 capacity to administer depots may be reduced. For our patients missing medication is likely to result in deterioration in mental state with increased risk to themselves and others. This can be extremely damaging and is also likely to affect their ability to comply with precautions around reducing Covid-19 transmission and spread.

Consideration should be given to options which may reduce the amount of depot or LAI administrations that are required. This could be done by increasing the interval between depots.

Considering that depot and LAIs administration is a high transmission risk situation, please see the advice below:

- Increase 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. Please bear in mind the maximum licensed dose for a single injection. For example if a patient is on zuclopenthixol decanoate 400mg weekly, equivalent dose of 800mg every 2 weeks is above the licensed maximum dose for a single injection.
- For patients on risperidone LAI, consider paliperidone LAI as an alternative. Please note that patients who have a GFR less than 50ml/min should not be switched to paliperidone.
- For paliperidone monthly patients consider switching to paliperidone 3-monthly long-acting depot, where possible as per recommendations. A non-formulary form would need to be completed.
- Consider that all patients and staff are at risk of being carriers or have Covid-19 and close contact situations such as depot administration should be done only using personal protective equipment. Explain what you are doing and why and do this before meeting the patient so as not to alarm them.
- For patients with suspected or confirmed Covid-19, the depot should be given at home by someone wearing protective clothing using barrier nursing techniques. In some cases a clinical decision may be made to delay a depot or LAI if a patient is acutely physically unwell.
- Please see tables below for information about depot medications. This will help you make your prescribing decisions about dose frequency and what to do about missed doses.
- Where patients' depots or LAIs are switched or dosing intervals changed, they should be reviewed at least one week after 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.

Table 1 Official guidance on depot dose and interval

<i>Depot or LAI</i>	<i>UK Trade Name</i>	<i>Licensed injection site</i>	<i>Test dose (mg)</i>	<i>Dose range (mg/week)</i>	<i>Dosing interval (weeks)</i>
Aripiprazole	(Abilify Maintena)	Deltoid or gluteal	Not required**	300-400mg monthly	Monthly
Flupentixol Decanoate	(Depixol)	Buttock or thigh	20	50mg every 4 weeks to 400mg a week	2-4
Haloperidol Decanoate	(Haldol)	Gluteal region	25*	50-300mg every 4 weeks	4
Olanzapine pamoate	(ZypAdhera)	Gluteal	Not required**	150mg every 4 weeks to 300mg every 2 weeks	2-4
Paliperidone palmitate (monthly)	(Xeplion)	Deltoid or gluteal	Not required**	50-150mg monthly	Monthly
Paliperidone palmitate (3-monthly)	(Trevicta)	Deltoid or gluteal	Not required***	175-525mg every 3 months	3 months
Risperidone microspheres	(Risperidal Consta)	Deltoid or gluteal	Not required**	25-50mg every 2 weeks	2
Zuclopendixol Decanoate	(Clopixol)	Buttock or thigh	100	200mg every 3 weeks to 600mg a week	2-4

\*No test dose specified by manufacturer

\*\*Prior use of oral drug required to assess tolerability and effectiveness

\*\*\*Prior use of monthly paliperidone required

### Switching from risperidone LAI to paliperidone LAI

When switching patients from risperidone long acting injection, initiate paliperidone therapy in place of the next scheduled injection. Paliperidone 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:

<b>Doses of risperidone long acting injection and paliperidone needed to attain similar paliperidone exposure at steady-state</b>	
<b>Previous risperidone long acting injection dose</b>	<b>Paliperidone injection</b>
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

Table 2 Official guidance on missed doses of long acting injections (depots)

**Aripiprazole LAI (Abilify Maintena®)<sup>1</sup>**

If 2 <sup>nd</sup> or 3 <sup>rd</sup> dose is missed and time since last injection is:	Action
> 4 weeks and < 5 weeks	The injection should be administered as soon as possible and then resume monthly injection schedule.
> 5 weeks	Concomitant oral aripiprazole should be restarted for 14 days with next administered injection and then resume monthly injection schedule.
If 4 <sup>th</sup> or subsequent doses are missed (i.e., after attainment of steady state) and time since last injection is:	Action
> 4 weeks and < 6 weeks	The injection should be administered as soon as possible and then resume monthly injection schedule.
> 6 weeks	Concomitant oral aripiprazole should be restarted for 14 days with next administered injection and then resume monthly injection schedule.

**Paliperidone 1-monthly LAI (Xeplion®)<sup>2</sup>**

2 <sup>nd</sup> initiation dose (100mg) and time since last injection is:	Action
< 4 weeks	100mg should be injected into the deltoid muscle as soon as possible. <b>A third paliperidone injection of 75 mg (deltoid or gluteal) should be administered 5 weeks after the first injection (regardless of the timing of the second injection).</b> The normal monthly cycle of injections in either the deltoid or gluteal muscle of 50 mg to 150 mg based on individual patient tolerability and/or efficacy should be followed thereafter.
> 4 weeks and < 7 weeks	Day 1 – 100mg deltoid injection asap Day 8 – 100mg deltoid injection Day 36 - Resume the normal monthly cycle of injections (deltoid or gluteal) based on individual patient tolerability and/or efficacy.
> 7 weeks	Day 1 – 150mg deltoid injection asap Day 8 – 100mg deltoid injection Day 36 – Resume the normal monthly cycle of injections (deltoid or gluteal) based on individual patient tolerability and/or efficacy.
Monthly maintenance dose and time since last injection is:	Action
< 6 weeks	Administer depot as soon as possible
> 6 weeks and < 6months	<b>50mg – 100mg:</b> Day 1 – Deltoid injection at same dose patient was previously stabilised on asap Day 8 – another Deltoid injection (same dose) Day 36 – Resume the normal monthly cycle of injections (deltoid or gluteal) based on individual patient tolerability and/or efficacy. <b>150mg:</b> Day 1 – 100mg deltoid injection asap Day 8 – 100mg deltoid injection Day 36 - Resume the normal monthly cycle of injections (deltoid or gluteal) based on individual patient tolerability and/or efficacy.
> 6 months	Day 1 – 150mg deltoid injection asap Day 8 – 100mg deltoid injection Day 36 – Resume the normal monthly cycle of injections (deltoid or gluteal) based on individual patient tolerability and/or efficacy.

**Paliperidone 3-monthly LAI (Trevicta®)<sup>3</sup>**  
**Missed doses**

If scheduled dose is missed and the time since last injection is	Action
> 3½ months up to 4 months	The injection should be administered as soon as possible and then resume the 3-monthly injection schedule.
4 months to 9 months	<b>Use the recommended re-initiation regimen shown in the table below.</b>
> 9 months	Re-initiate treatment with 1-monthly paliperidone palmitate injectable as described in the prescribing information for that product. TREVICTA can then be resumed after the patient has been adequately treated with 1-monthly paliperidone palmitate injectable preferably for four months or more.

**Recommended re-initiation regimen after missing 4 months to 9 months of TREVICTA**

If the last dose of TREVICTA was	Administer 1-monthly paliperidone palmitate injectable, two doses one week apart (into deltoid muscle)		Then administer TREVICTA (into deltoid or gluteal muscle)
	Day 1	Day 8	1 month after day 8
175 mg	50 mg	50 mg	175 mg
263 mg	75 mg	75 mg	263 mg
350 mg	100 mg	100 mg	350 mg
525 mg	100 mg	100 mg	525 mg

**Risperidone LAI (Risperidone Consta®)<sup>4</sup>**

Time since last injection	What happens to risperidone plasma levels?	Plan
2-6 weeks	Therapeutic risperidone plasma levels remain	Administer depot asap
>6 weeks but < 7 weeks	Risperidone plasma level starts to decrease and may become subtherapeutic after a further 1-3 weeks	Administer depot as usual but monitor mental state closely and, if necessary, give oral risperidone
>8-9 weeks	All risperidone will have been eliminated from the body	Administer depot asap and give oral risperidone for at least 3 weeks until plasma level becomes therapeutic again

**Olanzapine LAI (Zypadhera®)<sup>5</sup>**

The absorption half-life for OLAI is 30 days. Therefore, each injection releases measurable olanzapine for 5–6 months.

Target oral olanzapine dose	Recommended starting dose of ZYPADHERA	Maintenance dose after 2 months of ZYPADHERA treatment
10 mg/day	210 mg/2 weeks or 405 mg/4 weeks	150 mg/2 weeks or 300 mg/4 weeks
15 mg/day	300 mg/2 weeks	210 mg/2 weeks or 405 mg/4 weeks
20 mg/day	300 mg/2 weeks	300 mg/2 weeks

The manufacturer of Zypadhera® does not provide advice on missed doses.

For further information please refer to:

- Trust Depot antipsychotic medication: guidelines for prescribing and administering
- Maudsley Prescribing Guidelines

## References

1. Medicines.org.uk. (2016). Abilify Maintena 300mg & 400mg powder and solvent for prolonged-release suspension for injection and suspension for injection in pre filled syringe - Summary of Product Characteristics (SPC) - (eMC). [online] Available at: <http://www.medicines.org.uk/emc/medicine/31386> [Accessed 09/12/2016].
2. Medicines.org.uk. (2016). Xeplion 25 mg, 50 mg, 75 mg, 100 mg, and 150 mg prolonged-release suspension for injection - Summary of Product Characteristics (SPC) - (eMC). [online] Available at: <http://www.medicines.org.uk/emc/medicine/31329> [Accessed 09/12/2016].
3. Medicines.org.uk. (2016). TREVICTA 175mg, 263mg, 350mg, 525mg prolonged release suspension for injection - Summary of Product Characteristics (SPC) - (eMC). [online] Available at: <http://www.medicines.org.uk/emc/medicine/32050> [Accessed 09/12/2016].
4. Medicines.org.uk. (2016). RISPERDAL CONSTA 37.5 mg powder and solvent for prolonged-release suspension for intramuscular injection - Summary of Product Characteristics (SPC) - (eMC). [online] Available at: <http://www.medicines.org.uk/emc/medicine/30449> [Accessed 09/12/2016].
5. Medicines.org.uk. (2016). ZYPADHERA 210 mg, 300 mg, and 405 mg, powder and solvent for prolonged release suspension for injection - Summary of Product Characteristics (SPC) - (eMC). [online] Available at: <http://www.medicines.org.uk/emc/medicine/21361> [Accessed 09/12/2016].
6. Heres S, Kraemer S, Bergstrom RF, and Detke HC (2014). Pharmacokinetics of olanzapine long-acting injection: the clinical perspective. *International Clinical Psychopharmacology* 2014, 29:299–312