East London
NHS Foundation Trust

Prescribing Policy for Long-Acting Depots

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Services	Applicable to
Trustwide	√
Mental Health and LD	
Community Health Services	

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Version Control Summary

Version	Date	Author	Status	Comment
3.0	May 18	Natasha Patel	Final	Amalgamated all separate second generation long acting depot policies into this single document. **Summary** amended to include flow chart of what long acting depot to use. **Section 1** Introduction added **Section 2** Aim added **Section 4** added section about second generation antipsychotics **Appendix 1:** updated form and removed tick list and added free typing box **Appendix 5:** added GASS scale
3.1	Feb 2019	Chinedu Ogbuefi	Final	Information on stability of Risperdal Consta outside the recommended storage temperatures
4.0	March 2020	Lewis Pope, EPMA Lead Pharmacist; Tania Saheed, EPMA Pharmacist		**Section 4.4** – Prescribing depots in EPMA **Section 5.2 & 8.2** – EPMA dose frequency information for aripiprazole and paliperidone depots **Section 5.4, 6.3, 7.5, 8.5** – EPMA 'clinical drug information' additions
5.0	Feb 2021	Indreet Anand, Medicines Safety Officer Andrea Okoloekwe Interim deputy Chief Pharmacist Chinedu Ogbuefi, Lead Pharmacist Newham		Changes to the licensing of Aripiprazole long action injection (Abilify Maintena 400 mg) allows for a 'two injection start' dosing regimen upon initiation and for certain conditions of missed dosing. Policy updated to reflect above. Changes to: **Table 1b** **Section 5.2 & 5.5** Changes to **Table 1b** Changes to **section 5.1** to include lead/ clinical lead pharmacist Change to **section 5.2** to include amendment to route of administration Changes to **Section 8** paliperidone monthly LAI Addition of **section 9** Paliperidone palmitate 3 monthly LAI: licensing, dosing details Addition of section 10: Adverse Effects "Yellow Card" reporting Changes to Appendix 1&2: required sign off by Lead/Clinical Lead pharmacist

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Typical Antipsychotic Depots
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Patients who are intolerant to typical due to extrapyramidal side effects.

Consider for:

Atypical Antipsychotic Depots
Paliperidone LAI (monthly)
Risperidone Consta LAI
Aripiprazole Maintena

Unacceptable side effects at effective dose or lack of efficacy at therapeutic doses of above atypical

Consider for:

Atypical Antipsychotic Depots (Non-Formulary)
Olanzapine LAI
Paliperidone LAI (3 monthly)

Where possible, choice of antipsychotic should be made **jointly** by the patient and the clinician responsible for treatment based on an informed discussion of the relative benefits of the drugs and their side-effect profiles. If there are *no clinical reasons* the oily depot

injections should be first choice (most cost-effective). The efficacy for the treatment of schizophrenia is similar, but the side effects profile is different for each one.

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The Use Of Antipsychotic Long-Acting Injections In ELFT

1. Introduction

Long-acting or depot antipsychotic injections can be a useful form of administering antipsychotics in the treatment of schizophrenia, especially when adherence with oral medication is unreliable.

The introduction of atypical injections has produced an increased pressure on the drug budget, which may be justified if it can be shown to save hospital admissions, length of stay and show an improved quality of life compared with the alternatives available.

2. Aim

This policy is to provide information about the choice of typical and atypical antipsychotic long-acting injections available.

3. Choice of prescribing depot antipsychotics

3.1 The choice of long-acting injections medication is determined by the needs of the individual service user.

3.2 Long-acting injections should be a treatment option where a service user expresses a preference for such treatment after an acute episode because of its convenience, or as part of a treatment plan in which the avoidance of covert non-adherence (intentional or unintentional) with antipsychotic medication is a clinical priority[1].

3.3 Following full discussion between the responsible clinician and the service user, the decision to initiate long-acting antipsychotic injections must take into account the preferences and attitudes of the service user towards the mode of administration and organisational procedures (for example; home visits and location of clinics) related to the delivery of regular intramuscular injections[1]. Where more than one drug is appropriate, an antipsychotic of low acquisition cost should be selected.

3.4 As with oral antipsychotics, service users receiving long-acting injections must be maintained under regular clinical review, particularly in relation to the risks and benefits of the medication regimen.

4. Advice on prescribing Long Acting Injections.

4.1 Patients must be offered a patient information leaflet.

4.2 **Typical depots are long-acting preparations**. The service users should be exposed to the oral form of the medicine (or a test dose of the injection) prior to their first full dose of the injection to minimise the possibility of a long-lasting idiosyncratic reaction.

4.2.1 For typical long-acting antipsychotics, a test dose must be given. This is a test of the sensitivity or extrapyramidal side effects and any sensitivity of the base oil[2].

4.2.2 Begin with the lowest therapeutic dose. There is some information that low doses are at least as effective as higher doses. Low doses are likely to be better tolerated[2].

4.2.3 See table 1 for when the next dose should be administered.

4.2.4 Oral antipsychotics may also be prescribed initially. These should be gradually reduced and stopped once therapeutic maintenance dose has been established. If the total dosage exceeds BNF limits, the Trust High Dose Antipsychotic Therapy Policy must be implemented.

4.3 **Atypical long-acting antipsychotic injections AtLAI** have a relatively lower propensity for extrapyramidal side effects[2].

4.3.1 Atypical long-acting antipsychotic injections do not require test doses[2]. Patients to be prescribed risperidone injection or paliperidone monthly depot must be prescribed oral risperidone first to check for tolerability and response to treatment.
Patients prescribed aripiprazole or olanzapine depot must be prescribed the respective oral formulation first to check tolerability and response to treatment[4].

Please refer to the SPC (Summary of Product Characteristics) for full details on all Atypical long-acting antipsychotic injections: http://emc.medicines.org.uk/

4.3.2 See table 1 for when the next dose should be administered.

Table 1a[4-12]: Typical long-acting antipsychotics

Injection	Test dose	Dose range	Duration of action (weeks)	Peak (days)	Interval
Flupenthixol deaconate in thin vegetable oil (derived from coconuts)	20mg (consider 5- 10mg in elderly patients)	50 every four weeks - 400mg/week	3-4	7-10	Weekly to four weekly
Haloperidol decanoate in sesame oil	50mg every four weeks (12.5 – 25mg every four weeks in elderly patients)	50-300mg every four weeks	6	3-9	Four weekly
Zuclopenthixol decanoate in thin vegetable oil (derived from coconuts)	100mg (consider 25-50mg in elderly patients)	200-600mg every one to four weeks. Maximum: 600mg every week.	2-4	4-9	Weekly to four
Note: Do not confuse with Zuclopenthixol acetate injection THIS IS ACUPHASE – NOT A DEPOT INJECTION. DO NOT USE AS A DEPOT.					

Table 1b[4-12]: Atypical long-acting antipsychotics					
Injection	**Test dose**	**Dose range**	**Duration of action (weeks)**	**Peak (days)**	**Interval**
Aripiprazole (powder and solvent for prolonged release suspension)	None. Response & tolerability to oral aripiprazole must be checked prior to initiating the depot.	**TWO INITIATION OPTIONS:** (see SPC for full details) •One injection start: *400mg/month, continue oral aripiprazole 10-20mg for 14 days after injection. •Two injection start: two separate injections of *400 mg at separate injection sites and a 20 mg dose of oral Aripiprazole.		5-7	After initiation: - maintenance dose of 400 mg once monthly as a single injection, minimum of 26 days between injections. If ADR occurs, consider reduction to a 300mg dose.
	*300mg dose for CYP2D6 poor metabolisers; see SPC for dose adjustments due to interactions with CYP2D6 and/or CYP3A4 inhibitors and/or CYP3A4 inducers: https://www.medicines.org.uk/emc/product/7965/smpc				
Olanzapine (powder and solvent for prolonged release suspension)	None. Tolerability to oral olanzapine must be checked prior to initiating the depot.	150mg every two weeks to 405mg every month	6	4	Two to four weekly
Paliperidone monthly LA (prolonged release suspension)	None. Response and tolerability to oral risperidone must be checked prior to initiating the depot.	25-150mg/month	25-49 days	3-10	Monthly (not every **28 days or every 4 weeks** this results in one less depot per year)

Paliperidone 3 monthly LA (prolonged release suspension)	None. Response and tolerability to at least monthly paliperidone LA for 4 months or more prior to approval	175,263,350,525 mg/3 monthly	84-95 days if deltoid inj 118-139 days if gluteal inj		3 monthly
Risperidone (powder and solvent for prolonged release suspension)	None. Response and tolerability to oral risperidone must be checked prior to initiating the depot.	25-50mg/2weeks. Initial lag period means oral/IM supplementation is required.	5-6 weeks, will not start until 3-4 weeks after administration.	28-42	Two weekly

4.4 Prescribing depots in EPMA

4.4.1 Depot injections will have default frequencies set as per the BNF.
4.4.2 The depot start date will automatically set to the current or following day depending on the time the prescription is written. The first administration date can be changed in the 'order entry' tab at the point of prescribing.

4.4.3 When making an amendment to the depot prescription (change of dose, frequency or strength of formulation), it is important to consider the date of when the last dose was administered and set the 'first administration' date accordingly.

5. Aripiprazole long acting injection (ALAI) (Abilify Maintena)

Aripiprazole long acting injection (ALAI) is an atypical antipsychotic licensed for maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole.

ELFT Medicines Committee have approved its use as an AMBER drug with restrictions, this policy will ensure that this medicine is used safely and is targeted towards the most appropriate patients within ELFT.

5.1 Indications for ALAI within ELFT

Use of ALAI may be considered suitable in the following circumstances:

- Good response to oral aripiprazole but non- compliant oral treatment

- Patients who have had an unsuccessful trial of a typical antipsychotic depot due to poor tolerability (EPSE's or hyperprolactinaemia)

- Patients transferred from outside the Trust currently prescribed ALAI.

- Patients with increased cardio metabolic risk where ALAI considered best option

The consultant prescriber must complete an "Aripiprazole Injection Initiation Form" (appendix 1). This must be approved and signed by the Clinical / Associate Clinical Director and lead pharmacist/clinical lead pharmacist.

5.2 Additional information to consider when initiating ALAI

Ideally patients should have shown initial response to oral aripiprazole

ALAI is **not indicated** for treatment resistant schizophrenia, unlicensed indications or patients intolerant to oral aripiprazole.

If a trial of ALAI is not clinically advantageous, the consultant will stop ALAI and prescribe alternative treatment.

ALAI is intended to be **administered once monthly** as a single injection in the gluteal muscle (no sooner than 26 days after the previous injection). In EPMA, there is currently no option to prescribe once per calendar month - the frequency will default to 'once every 30 days'.

Loading dose required. The first injection can be administered following one of two regimes; 'one injection start' or 'two injection start', please refer to the SPC (Summary of Product Characteristic) for full details.

ALAI is only intended for IM use ONLY. The suspension should be injected slowly as a single injection (doses must not be divided) into either deltoid or the gluteal muscle. Sites of injections should be rotated. Please refer to SPC for full details: http://emc.medicines.org.uk/

5.3 Re-admitted Patients

Those patients that have been re-admitted as a result of relapse, either due to non-compliance or lack of efficacy with ALAI, should be reviewed and should not automatically be restarted on this drug. Consideration should be given to changing to a typical antipsychotic depot.

If clinical judgement deems ALAI to be the drug of choice, then the consultant prescriber must complete the "Aripiprazole Long-Acting Injection Continuation Form" (appendix 2). This must be approved by the Clinical / Associate Clinical Director and lead pharmacist/clinical lead pharmacist.

5.4 Dosing, Cautions and Contraindications

For full dosing information, cautions and contraindications staff should refer to BNF Complete, product SPC and/or 'clinical drug information' in EPMA

Dosage adjustments are required for known CYP2D6 poor metabolisers and in patients taking concomitant strong CYP3A4 inhibitors or strong CYP2D6 inhibitors for more than 14 days.

For information on switching please contact the pharmacy team

5.5 Missed doses of Aripiprazole long acting injection (ALAI) (Abilify Maintena)

Refer to the SPC (Summary of Product Characteristics) for full details

Missed doses of ALAI	
If 2nd or 3rd 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 or two separate injections given at one time, along with a single dose of 20 mg oral aripiprazole. Monthly injection schedule should then resume.
If 4th 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 or two separate injections given at one time, along with a single dose of 20 mg oral aripiprazole. Monthly injection schedule should then resume.

5.6 Storage

ALAI should be stored in a locked medicines cupboard at room temperature. Refrigerated storage is not required. Packs must not be exposed to temperatures in excess of 25^0C. After reconstitution, ALAI should be administered immediately. If not used immediately, it is considered suitable for use for a maximum of 4 hours, if stored below 25°C(Ref SPC).

5.7 Training

Nurses should familiarise themselves with the Summary of Product Characteristics before administering, including injection sites and needle size. http://emc.medicines.org.uk/

5.8 Product information

ALAI is available in a single 400mg vial that after reconstitution is 200mg/ml

For full Summary of Product Characteristics

5.9 Ordering

Aripiprazole should be ordered via your local directorate pharmacy team

6. Olanzapine Long Acting Injection (Zypadhera®)

Olanzapine long acting injection (LAI) is an atypical antipsychotic licenced for the maintenance treatment of adult patients with schizophrenia sufficiently stabilised during acute treatment with oral olanzapine.

Olanzapine LAI should not be used to treat patients with schizophrenia who are in an acutely agitated or severely psychotic state such that immediate symptom control is warranted.

6.1 Prescribing Olanzapine Long Acting Injection (OLAI) at ELFT

OLAI is **non-formulary** which means that its use within the Trust has not been approved and it will not be prescribed within associated CCGs.

Patients who have had an unsuccessful trial of a typical antipsychotic depot due to poor response or tolerability should be trialled on an alternative atypical antipsychotic before considering olanzapine LAI.

If OLAI is to be initiated within ELFT, the consultant must complete a “Request to use a non-formulary medicine” initiation form which must then be approved by the Chief Pharmacist or Medical Director. The form can be found here.

Patients transferred from another Trust may continue to be prescribed OLAI. A “Request to use a non-formulary medicine” continuation form must be completed. This is different to the above initiation form and can be found here.

6.2 Patient information

Patients must be advised of the risk of post injection syndrome and the need to be observed in a clinical or hospital setting for up to 3 hours after each injection. OLAI should not be initiated if the patient is unlikely to be compliant with this monitoring.

After administering the injection the nurse / doctor must check that the patient has a Zypadhera® patient information card. This card contains a record of the injection and important safety information for the patient on post-injection adverse events. All patients should be issued with a card if they are not already carrying one.

6.3 Dosing, cautions and contraindications

Patients should be treated initially with oral olanzapine before administering OLAI, to establish tolerability and response.

Recommended dose scheme:

Target oral olanzapine dose	Recommended starting dose of olanzapine LAI	Maintenance dose after 2 months
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

Supplementation with oral olanzapine is not recommended. If oral olanzapine supplementation is clinically indicated, then the combined total dose from both formulations should not exceed the corresponding maximum oral dose of 20mg/day.

Further information on dosing, cautions and contraindications can be obtained from the BNF, SPC and/or 'clinical drug information' in EPMA. Information on prescribing olanzapine LAI in special populations can also be found in these resources.

Please contact the pharmacy team for further advice, if required.

6.4 Administration

OLAI should only be administered by deep intramuscular gluteal injection by an appropriately trained healthcare professional.

OLAI must be administered in a healthcare facility where post-injection observation and access to appropriate medical care in the case of overdose can be assured.

After each injection, patients should be observed by an appropriately qualified member of staff for at least 3 hours for signs and symptoms of post-injection syndrome (see section 6.7).

Appendix 4 contains the monitoring form which should be completed every time OLAI is administered.

Prior to leaving the healthcare facility (if applicable), it should be confirmed that the patient is alert, oriented, and absent of any signs and symptoms of overdose. If an overdose is suspected, close medical supervision and monitoring should continue until examination indicates that signs and symptoms have resolved. If a doctor is unavailable, an ambulance must be called.

6.5 Post injection syndrome

Signs and symptoms are consistent with those of olanzapine overdose. They include sedation and/or delirium (confusion, disorientation, agitation, anxiety and other cognitive impairment), extrapyramidal symptoms, dysarthria, ataxia, aggression, dizziness, weakness, hypertension and convulsion.

In most cases, initial signs and symptoms appeared within 1 hour following injection and in all cases full recovery was reported to have occurred within 24 - 72 hours after injection.

For the remainder of the day after injection, patients should be advised to be vigilant for signs and symptoms of overdose secondary to post-injection adverse reactions, be able to obtain assistance if needed, and should not drive or operate machinery.

6.6 Monitoring Post Initiation

All patients initiated on OLAI would require three monthly reviews (see appendix 2 for monitoring tool).

6.7 Storage

OLAI must be stored in a locked medicines cabinet. Do not refrigerate or freeze.

After reconstitution in the vial, OLAI should be used immediately. If the product is not used right away, it will remain stable for up to 24 hours at room temperature. Any olanzapine LAI that has been reconstituted for longer than 24 hours must be discarded.

6.8 Ordering

Olanzapine should be ordered via your local directorate pharmacy team.

7. Risperidone Long-Acting Injection (Risperdal Consta)

Risperidone long-acting injection (RLAI) was introduced as the first atypical long-acting intramuscular injection. It is licensed for the maintenance treatment of adult patients with schizophrenia, whose condition has been stabilised with, or there has been a previous response to, oral risperidone.

Following approval by the Trust's Medicines Committee for use of Risperidone Consta as an AMBER drug with restrictions, this policy will ensure that this medicine is used safely and is targeted towards the most appropriate patients within ELFT.

7.1 Indications for Risperidone Long-Acting Injection (RLAI) within ELFT

Use of Risperidone Consta may be considered suitable in the following circumstances:

- Patients who have had an unsuccessful trial of a typical antipsychotic depot due to poor tolerability (EPSE's).
- Patients transferred from outside the Trust currently prescribed risperidone consta.

The consultant prescriber must complete a "Risperidone Injection Initiation or continuation Form" (appendix 1). This must be approved and signed by the Clinical / Associate Clinical Director. The approved form must be presented to pharmacy with the prescription before the drug can be issued.

7.2 Prescribing of Risperidone Long-Acting Injection

There is a very large, and growing, cost associated with risperidone long-acting injection compared to other typical depot antipsychotic medication, but there is also a changing emphasis and understanding regarding the benefit/side effect profile of typical and atypical antipsychotic medication that is reflected in the most recent NICE guidelines. Consequently when a depot is indicated, the routine first-line use of risperidone should no longer be assumed.

7.3 New patients

For new patients requiring a depot injection, where all things are equal a typical depot injection should be considered.

Should RLAI be the first-line choice, the consultant prescriber must complete a "Risperidone Injection Initiation Form" (appendix 1). This must be approved by the Clinical / Associate Clinical Director. The approved form must be presented to pharmacy with the prescription.

Clinical reasons for prescribing risperidone depot may include a previous history of extrapyramidal or prolactin-related side-effects with typical antipsychotics. If this is the case then doses of more than 25mg / 2 weeks risperidone should only cautiously be prescribed.

7.4 Re-admitted Patients

Those patients that have been re-admitted as a result of relapse, either due to non-compliance or lack of efficacy with risperidone injection, should be reviewed and should not automatically be restarted on risperidone injection. Consideration should be given to changing to a typical antipsychotic depot.

If clinical judgement deems risperidone injection to be the drug of choice, then the consultant prescriber must complete the "Risperidone Long-Acting Injection Continuation Form" (Appendix 2). The approved form must be presented to pharmacy with the prescription.

7.5 Dosing, Cautions and Contraindications

For full dosing information, cautions and contraindications staff should refer to BNF Complete, product SPC and/or 'clinical drug information' in EPMA.

7.5 Storage

RLAI must be stored and transported between temperatures of 2-8^{0}C. Storage at 8-25^{0}C reduces the shelf life to 7 days. Packs must not be exposed to temperatures in excess of 25^{0}C. After reconstitution, RLAI should be administered immediately. If not used immediately, it is considered suitable for use for a maximum of 6 hours, if stored below 25^{0}C.

Teams must have a medicine fridge and be comply with the Trust Refrigerator Monitoring Procedure.

7.6 Stability

- If refrigeration is unavailable, Risperdal Consta (RLAI) can be stored at temperatures not exceeding 25°C for no more than 7 days prior to administration.
- Deviations from the storage recommendations in the Summary of Product Characteristics (SmPC) cannot be recommended and, as such would be considered outside of the license and the responsibility of the clinician
- The stability data below was generated under tightly controlled conditions. Deviations from these recommendations are not advised. For further assistance or questions, contact your pharmacy team.

Temperature Range	Duration	Use within
>8°C to 25°C	7 days	36 months
-20°C to 2°C	30 days	36 months
>25°C	Marketed product should not be administered to patients if product is exposed to temperatures >25°C	Do not use
Freeze/Thaw-Shipping Simulation Studies (-25°C to 25°C)	Up to 7 Cycles over 14 days	36 months

I. Controlled Room Temperature

Excursions >8°C and ≤ 25°C for no more than 7 days are justified based on acceptable data from CRT stability studies. If the Risperdal Consta dose pack has been removed from the refrigerator and has not been reconstituted, the dose pack may be returned to the refrigerator. The temperature during the excursion must not exceed 25°C and should not exceed 7 days. The shelf life will not be affected if stored according to these specifications.

The SmPC recommends the dose pack is removed from the refrigerator and allow to sit at room temperature for at least 30 minutes before reconstituting; this allotted time must be included within the 7 days.

II. Frozen

Stability data exists for product (microspheres and diluent) that has inadvertently been frozen ≤ 30 days at ≥-20°C to 2°C. There were no changes in quality attributes. Frozen product should be returned to refrigerated temperatures (2° - 8°C).

III. Freeze/Thaw Conditions

Freeze/Thaw-Simulated Shipping Studies support up to 7 freeze/thaw cycles (-25°C to 25°C) over 14 days. This data shall be used to justify excursions during shipments for up to 7 days and is also used to justify storage at ambient temperatures for up to 7 days just prior to patient administration.

7.7 Ordering

Risperidone should be ordered via Polarspeed. Please see Trust SOP - Management of Risperidone Long Acting Injection for Community Clinics for further information

8. Paliperidone (monthly) Long Acting Injection (PLAI)- Xeplion®

Paliperidone long acting injection (PLAI) is an atypical antipsychotic licensed for the maintenance treatment of adult patients with schizophrenia, whose condition has been stabilised with, or there has been a previous response to, oral risperidone or paliperidone. *(Note: oral paliperidone is non–formulary within ELFT due to limited clinical benefit data and a greater cost acquisition compared to oral risperidone.) Paliperidone available as monthly or 3 monthly injections*

Following approval by the Trust's Medicines Committee for use of PLAI -**Xeplion®** as an AMBER drug with restrictions, this policy will ensure that this medicine is used safely and is targeted towards the most appropriate patients within ELFT.

8.1 Indications for PLAI Xeplion® within ELFT

Use of PLAI **Xepilion®**

may be considered suitable in the following circumstances:

- Patients who have had an unsuccessful trial of a typical antipsychotic depot due to poor tolerability (EPSE's) and who are also unsuitable candidates for Risperidone Long Acting Injection due to the fortnightly frequency of administration.

- Patients transferred from outside the Trust currently prescribed PLAI **Xeplion®**.

The consultant prescriber must complete a "Paliperidone Injection Initiation Form" (appendix 1). This must be approved and signed by the Clinical / Associate Clinical Director and Lead/Clinical Lead Pharmacist.

8.2 Additional information to consider when initiating PLAI Xeplion®

Patients currently stable and compliant on an antipsychotic depot **should not** be automatically switched to **Xeplion®** unless there is an indication to do so.

It is **not indicated** for treatment resistant schizophrenia, unlicensed indications or patients intolerant to oral risperidone.

Ideally, patients starting PLAI **Xeplion®** should have previously demonstrated a response to risperidone.

If a trial of **Xeplion®** is not clinically advantageous, the consultant will discontinue and prescribe alternative treatment.

PLAI **Xeplion®** is intended for once monthly injection **(i.e. once per calendar month rather than 4- weekly)**, by intramuscular route into the deltoid or gluteal

muscle. In EPMA, there is currently no option to prescribe once per calendar month - the frequency will default to 'once every 30 days'.

Teams may wish to consider fixing the administration to a specific day of the month e.g. the first Tuesday to facilitate monthly administration. Whilst this will mean that there is a five week interval between injections on some occasions, this will not affect efficacy but will result in the intended 12 injections per year.

PLAI **Xeplion®** has a higher acquisition cost than RLAI; if the recommended monthly injection regime is not followed, this will have a significant cost impact for the Trust.

8.3 Re-admitted Patients

Those patients that have been re-admitted as a result of relapse, either due to non-compliance or lack of efficacy with PLAI **Xeplion®** , should be reviewed and should not automatically be restarted on this drug. Consideration should be given to changing to a typical antipsychotic depot.

If clinical judgement deems PLAI to be the drug of choice, then the consultant prescriber must complete the "Paliperidone Long-Acting Injection Continuation Form" (appendix 2). The completed form should be presented to the Clinical / Associate Clinical Director and the Lead/Clinical Lead Pharmacist for approval.

8.4 Dosing, Cautions and Contraindications

For full dosing information, cautions and contraindications staff should refer to BNF Complete and/or 'clinical drug information' on EPMA.

8.5 Initiating paliperidone long acting injection

Switching from a typical depot antipsychotic

- No loading dose required
- Administer PLAI **Xeplion®** at the time next scheduled depot is due
- ***Note: there are no dose equivalents between paliperidone and typical depots – choice of dose should be based on individual patient assessment.***

It is suggested that the dose does not exceed 75mg initially and that the patient is monitored in terms of response and side effect profile.

Switching from Risperidone Consta

- No loading dose required
- Administer equivalent dose of PLAI **Xeplion®** at the next scheduled depot dose

Dose		
Risperidone Oral (mg/day)	Risperidone Consta (mg/2 weeks)	**Paliperidone palmitate Injection(Xeplion®) (mg/4 weeks)**
2	25	50

3	37.5	75
4	50	100
6	-	150

8.6 Storage

PLAI **Xeplion®** should be stored in a locked medicines cupboard at room temperature. Refrigerated storage is not required. Packs must not be exposed to temperatures in excess of 30^0C.

8.7 Training

Nurses should familiarise themselves with the Summary of Product Characteristics before administering, including injection sites and needle size.

Training and advice is available from specialist nurses at Janssen Cilag on request.

8.8 Product information

PLAI Xeplion is available in the following strengths 50mg, 75mg, 100mg, 150mg

For full Summary of Product Characteristics of Paliperidone, see http://emc.medicines.org.uk/

8.9 Ordering

Paliperidone monthly injection should be ordered via Polarspeed for service users in the community. Please see Trust SOP - Management of Risperidone Long Acting Injection for Community Clinics for further information.

9.0 Paliperidone (3 monthly) Long Acting Injection PLAI Trevicta®

Indications for PLAI Trevicta® within ELFT

Following review at the Trust's Medicines Committee for use of PLAI -**Trevicta**® it has been categorised as a RED drug with restrictions (will not be prescribed within associated CCGs), this policy will ensure that this medicine is used safely and is targeted towards the most appropriate patients within ELFT.

NON-FORMULARY: PLAI Trevicta is Non-formulary; its use within the Trust has not been approved and it will not be prescribed within associated CCGs. Requesting consultant should a non-formulary for approval by the Clinical Director/Associate Clinical Director and Lead Pharmacist/Clinical Lead Pharmacist – please search 'non formulary on the intranet to download this form for completion.

- "Request to use a non-formulary medicine" initiation form which must then be approved by the Chief Pharmacist or Medical Director. The form can be found here.

- Patients transferred from another Trust may continue to be prescribed. A "Request to use a non-formulary medicine" continuation form must be completed. This is different to the above initiation form and can be found here.

9.1 Use of PLAI **Trevicta®**

may be considered suitable in the following circumstances:

- Patients transferred from outside the Trust currently prescribed PLAI **Trevicta®**.
- Patients who are adequately treated with 1-monthly paliperidone palmitate injectable (preferably for four months or more) and do not require dose adjustment may be switched to 3-monthly paliperidone palmitate injection.

The consultant prescriber must complete a "Paliperidone Injection Initiation Form" (appendix 1). This must be approved and signed by the Clinical / Associate Clinical Director and the Lead/Clinical Lead Pharmacist. .

9.2 Additional information to consider when initiating PLAI Trevicta®

The following criteria to be met before initiating PLAI Trevicta®:

- Patient is currently receiving paliperidone 1-monthly
- Has received at least 4 paliperidone 1-monthly injections and NO further dose adjustment are required i.e. reached a stable dose
- Patient is clinically stable on the one monthly Paliperidone injection with well controlled symptoms and a dose change is unlikely to be necessary
- Paliperidone 1-monthly is well tolerated

Also note:
TREVICTA should not be used to manage acutely agitated or severely psychotic states when immediate symptom control is warranted.

Patients currently stable and compliant on an antipsychotic depot **should not** be automatically switched to **Trevicta®**

It is **not indicated** for treatment resistant schizophrenia, unlicensed indications or patients intolerant to PLAI Xepillion®.

Patients starting PLAI **Trevicta®** should have previously demonstrated a response to PLAI Xepillion®.

If a trial of **Trevicta®** is not clinically advantageous, the consultant will discontinue and prescribe alternative treatment.

PLAI **Trevicta®** is intended for three monthly injection **(i.e. once every 3 calendar months)**, by intramuscular route into the deltoid or gluteal muscle. The full dose

should be administered in a single injection. It should be injected slowly, deep into the deltoid or gluteal muscle – please refer to the full Summary of Product Characteristics (http://emc.medicines.org.uk/). Rotate injection sites. In EPMA, there is currently no option to prescribe 3 monthly frequency – Please use the patient note function on EPMA, patient record and any other reminder tools such as diaries to document next dose due date

Teams may wish to consider fixing the administration to a specific day of the month e.g. the first Tuesday every 3 months to facilitate administration. Whilst this will mean that there might be greater than 12 weeks interval between injections on some occasions, this will not affect efficacy but will result in the intended 4 injections per year.

PLAI **Trevicta®** has a higher acquisition cost than Xepillion® (3 x cost) therefore care to order not more than 4 injections /year as this will have a significant cost impact for the Trust.

9.3 Re-admitted Patients

Those patients that have been re-admitted as a result of relapse, either due to non-compliance or lack of efficacy with PLAI **Trevicta®** , should be reviewed and should not automatically be restarted on this drug. Consideration should be given to changing to a typical antipsychotic depot.

If clinical judgement deems PLAI to be the drug of choice, then the consultant prescriber must complete the "Paliperidone Long-Acting Injection Continuation Form" (appendix 2). The completed form should be presented to the Clinical / Associate Clinical Director and the Lead/Clinical Lead Pharmacist for approval.

9.4 Dosing, Cautions and Contraindications, Special Warnings and precautions for use

For full dosing information, cautions and contraindications staff should refer to BNF Complete and/or Trevicta®, see http://emc.medicines.org.uk/

TREVICTA should not be used to manage acutely agitated or severely psychotic states when immediate symptom control is warranted.

9.5.1 Initiating paliperidone long acting injection Trevicta®

Switching from a typical depot antipsychotic
Patients should not be switched directly from other antipsychotics as 3-monthly paliperidone palmitate injectable should only be initiated after the patient is stabilised on the 1-monthly paliperidone palmitate injectable (after 4 or more injections).

Switching from PLAI Xepillion® to Trevicta®
TREVICTA should be initiated in place of the next scheduled dose of 1-monthly paliperidone palmitate injectable (± 7 days). The TREVICTA dose should be based on the previous 1-monthly paliperidone palmitate injectable dose using a 3.5-fold higher dose shown in the following table:

TREVICTA doses for patients adequately treated with 1-monthly paliperidone palmitate injectable Xepillion	
If the last dose of 1-monthly paliperidone palmitate Xepillion injectable is	**Initiate TREVICTA at the following dose**
50 mg	175 mg
75 mg	263 mg
100 mg	350 mg
150 mg	525 mg

Adapted from Trevicta SPC (https://www.medicines.org.uk/emc/product/7230/smpc)

9.5.2 **Switching from Trevicta**

Switching from TREVICTA to other antipsychotic medicinal products

If TREVICTA is discontinued, its prolonged release characteristics must be considered.

Switching from TREVICTA to 1-monthly paliperidone palmitate injectable Xepillion®

For switching from TREVICTA to 1-monthly paliperidone palmitate injectable, 1-monthly paliperidone palmitate injectable should be administered at the time the next TREVICTA dose was to be administered using a 3.5-fold lower dose shown in the following table.

The initiation dosing is not required. The 1-monthly paliperidone palmitate injectable should then continue to be dosed at monthly intervals as previously described

Doses of 1-monthly paliperidone palmitate injectable for patients switching from TREVICTA	
If the last dose of TREVICTA is	**Initiate 1-monthly paliperidone palmitate injectable 3 months later at the following dose**
175 mg	50 mg
263 mg	75 mg
350 mg	100 mg
525 mg	150 mg

Adapted from Trevicta SPC (https://www.medicines.org.uk/emc/product/7230/smpc)

9.5.3 Missed doses

TREVICTA should be injected once every 3 months. To avoid a missed dose of TREVICTA patients may be given the injection up to 2 weeks before or after the 3-month time point.

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	Use the recommended re-initiation regimen shown in the table below.
> 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.

Adapted from Trevicta SPC **(**(https://www.medicines.org.uk/emc/product/7230/smpc)

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[a] 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

Adapted from Trevicta SPC (https://www.medicines.org.uk/emc/product/7230/smpc)

9.6 Storage

PLAI **Trivecta®** should be stored in a locked medicines cupboard at room temperature. Refrigerated storage is not required. Packs must not be exposed to temperatures in excess of 30^0C.

9.7 Training

Nurses should familiarise themselves with the Summary of Product Characteristics before administering, including injection sites and needle size. (click here https://www.medicines.org.uk/)

Training and advice is available from specialist nurses at Janssen Cilag on request.

9.8 Product information

PLAI Trivecta is available in the following strengths 175mg, 263mg,350mg and 525mg

For full Summary of Product Characteristics of Paliperidone, see http://emc.medicines.org.uk/

9.9 Ordering

Paliperidone 3 monthly injection should be ordered via Polarspeed for service users in the community. Please see Trust SOP - Management of Risperidone Long Acting Injection for Community Clinics for further information.

10.0 Adverse Effects

Report any suspected adverse reactions via:

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard

or search for MHRA Yellow Card in the Google Play or Apple App Store.

11.0 Related future actions

The initiation/continuation forms will be audited regularly by the pharmacy team.

References

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection, summary of product characteristics, last updated on the eMC: November 2020. https://www.medicines.org.uk/emc/product/7965/smpc

ZYPADHERA 210 mg, 300 mg, and 405 mg, powder and solvent for prolonged release suspension for injection. Summary of product characteristics. Last updated on eMC December 2020Accessed via https://www.medicines.org.uk/emc/product/6429/smpc Sussex Partnership NHS Foundation Trust, Olanzapine long-acting (Zypadhera) – Guidelines for Prescribing and Administration.

Guidance on the use of newer (atypical) antipsychotic drugs for the treatment of schizophrenia. NICE technology appraisal guidance 43 (2002).

Schizophrenia: core interventions in the treatment and management of schizophrenia in primary and secondary care. NICE clinical guideline 1 (2002).

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Risperdal Consta. Summary of Product Characteristics. Janssen- Cilag Ltd. Updated December 2018 https://www.medicines.org.uk/emc/product/1690

Psychosis and schizophrenia in adults: prevention and management. NICE Clinical Guideline (CG178) 2014

Xeplion. Summary of Product Characteristics. Janssen- Cilag Ltd. October 2018 https://www.medicines.org.uk/emc/product/7652/smpc

Paliperidone Long Acting Injection (Xeplion ®) Guidelines for Prescribing and Administration. Sussex Partnership NHS Foundation Trust. March 2013

Guidelines for initiation and use of risperidone long-acting injection and paliperidone long acting injection.Northamptonshire Healthcare NHS Foundation Trust. November 2011
Risperidone Long Acting Injection (RLAI): Storage and Stability. Janseen – Cilag Ltd. August 2018

Trivecta Summary of Product Characteristics (SPC) Janssen-Cilag Updated October 2019 https://www.medicines.org.uk/emc/product/7230/smpc

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Appendix 1

Aripiprazole/Paliperidone/Risperidone Long Acting Injection

Initiation Form

1. **Patients details:**

Name: DOB: RIO no.: Consultant: Ward:

2. Current drug treatment

Drug	Dose	Route	Date started

3. Long Acting Injection being requested for initiation (circle one):

Aripiprazole//Paliperidone/Risperidone

4. Reason for prescribing atypical long-acting injection

_____
_____
_____
_____
_____
_____

5. Current patient status

In patient	
Out-patient – supported accommodation	
Out-patient – self carer	
Other, please describe	

Consultant Prescriber's signature: _____

Print Name:_____ Date_____

Clinical/ Associate Clinical Director's Signature: _____ Date _____
Lead Pharmacist/Clinical Lead Pharmacist signature: _____ Date_____

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Appendix 2

Aripiprazole/Paliperidone/Risperidone Long Acting Injection

Re-initiation / Continuation form

1. Patients details:

Name: DOB: Hospital no.: Consultant: Ward:

2. Current drug treatment

Drug	Dose	Route	Date started

3. Reason for continuing (circle one and give reason):
Aripiprazole /Paliperidone/Risperidone
_____
_____
_____
_____

4. Current patient status

In patient	
Out-patient – supported accommodation	
Out-patient – self carer	
Other, please describe	

6. Please state any adverse effects experienced:
(state "none" if none experienced)

Consultant Prescriber's signature: _____

Print Name:_____ Date:_____Clinical/ Associate Clinical Director's Signature: _____ Date _____

Lead Pharmacist/Clinical Lead Pharmacist Signature: : _____ Date_____

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Appendix 3

Atypical Long-Acting Injection (LAI) Post-Initiation Follow Up (3 Monthly)

1. Patient Details

NAME	
GENDER	
DOB	
RIO NUMBER	
CONSULTANT	
WARD/CMHT	

2. Current Drug Treatment

DRUG	**DOSE**	**ROUTE**	**DATE STARTED**

3. Number of hospital admissions post initiation of atypical LAI:

4. CGI change

- Very much improved ☐
- Much improved ☐
- Minimally improved ☐
- No change ☐
- Minimally worse ☐
- Much worse ☐
- Very much worse ☐

5. Side effect tolerability (use GASS Rating scale, *see Appendix 3A*):

6. Comments for consultants:

_____
_____
_____
_____
_____
_____
_____
_____
_____

Please return completed form to Local Clinical Director

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Appendix 4

Observation form for post injection syndrome – to be carried out for at least THREE HOURS after administration of olanzapine LAI

Patient name: _____ NHS number _____

Date of birth _____ Ward _____

Post injection syndrome

- Usually occurs within 3 hours of administering olanzapine LAI.
- Needs urgent medical attention. An ambulance must be called if a doctor is unavailable.
- Signs and symptoms include **sedation and/or delirium (confusion, disorientation, agitation, anxiety and other cognitive impairment), extrapyramidal symptoms, dysarthria, ataxia, aggression, dizziness, weakness, hypertension and convulsion.**
- The 3-hour observation period should be extended as clinically appropriate for patients who exhibit any signs or symptoms consistent with olanzapine overdose.

Time	Allocated staff member	Observations – are there any signs and symptoms of post injection syndrome?
15 mins post injection ___:___	Name: Sig:	
30 mins post injection ___:___	Name: Sig:	
45 mins post injection ___:___	Name: Sig:	
1hr post injection ___:___	Name: Sig:	
1hr 15 mins post injection ___:___	Name: Sig:	
1hr 30 mins post injection ___:___	Name: Sig:	
1hr 45 mins post injection ___:___	Name: Sig:	
2hr 00 mins post injection ___:___	Name: Sig:	
2hr 15 mins post injection ___:___	Name: Sig:	
2hr 30 mins post injection ___:___	Name: Sig:	
2hr 45 mins post injection ___:___	Name: Sig:	
Prior to leaving healthcare facility (if applicable) ___:___	Name: Sig:	

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Appendix 5: GLASGOW ANTIPSYCHOTIC SIDE EFFECT RATING SCALE (GASS)

NAME: _____ AGE: _____ SEX: M / F Please list current medication and total daily doses below:_____

_____

This questionnaire is about how you have been recently. It is being used to determine if you are suffering from excessive side effects from your antipsychotic medication. Please place a tick in the column which best indicates the degree to which you have experienced the following side effects. Tick the **end** box if you found that the side effect distressed you.

*Over the **past week:***	*Never*	*Once*	*A few times*	*Everyday*	*Tick this box if distressing*
I felt sleepy during the day					
I felt drugged or like a zombie					
I felt dizzy when I stood up and/or have fainted					
I have felt my heart beating irregularly or unusually fast					
My muscles have been tense or jerky					
My hands or arms have been shaky					
My legs have felt restless and/or I couldn't sit still					
I have been drooling					
My movements or walking have been slower than usual					
10. I have had, or people have noticed uncontrollable movements of my face or body					
11. My vision has been blurry					
12. My mouth has been dry					
13. I have had difficulty passing urine					
14. I have felt like I am going to be sick or have vomited					
15. I have wet the bed					
16. I have been very thirsty and/or passing urine frequently					
17. The areas around my nipples have been sore and swollen					
18. I have noticed fluid coming from my nipples					
19. I have had problems enjoying sex					
20. I have been constipated					
21.Men only: I have had problems getting an erection					
22. Women only: I have noticed a change to my periods					

Tick yes or no for the following questions about the last three months	No	yes	Tick this box if distressing.
23.**Men and Woman:** I have been gaining weight			

STAFF INFORMATION

1. Allow the patient to fill in the questionnaire themselves. Questions 1-20 relate to the previous week and questions 21-22 to the last three months

2. Scoring

   For questions 1-20 award 1 point for the answer 'once', 2 points for the answer 'a few times' and 3 points for the answer 'everyday'.
   Please note zero points are awarded for an answer of 'never'.
   For questions 21 and 22 award 3 points for a 'yes' answer and 0 points for a 'no'.
   Total for all questions=

3. For male and female patients a total score of :

   0-21= absent/mild side effects
   22-42= moderate side effects
   43 and over= severe side effects

4. Side effects covered by questions

   1-2 sedation and CNS side effects
   3-4 cardiovascular side effects
   5-10 extra-pyramidal side effects
   11-13 anticholinergic side effects
   14 gastro intestinal side effects
   15 genitourinary side effects
   16 screening for diabetes mellitus
   17-21 prolactinaemic side effects
   22 weight gain

The column relating to the distress experienced with a particular side effect is not scored, but is intended to inform the clinician of the service user's views and condition.