journey to change

NHS
Tees, Esk and Wear Valleys
NHS Foundation Trust

Public – To be published on the Trust external website

Long-Acting Injectable (LAIs) Antipsychotics: Guidance for prescribing, administration and medicines management

Ref: PHARM-0081-v2.2

Status: Approved
Document type: Procedure

Contents

1 Introduction

Long-acting injectable (LAI) antipsychotics, or “depots”, are a useful and well-established form of administering antipsychotics in the management of schizophrenia and other indications. The introduction of long-acting formulations of second-generation (atypical) antipsychotics created an additional pressure on drug budgets, which may be justified if their use results in reduced hospital admissions, shortened length of stay and improved quality of life compared with the first generation (typical) agents.

This procedure is necessary to ensure that prescribing, administration and medicines management of these products is as safe and cost-effective as possible, minimising waste and risk of patient harm. It helps us deliver on our journey for change objectives as described below.

To co-create a great experience for our patients, carers, and families, so you will experience:

- **Outstanding** and compassionate care, all of the time.
- **Access** to the care that is right for you.
- **Support** to achieve your goals.
- **Choice** and control.

Medicines Optimisation is about ensuring that safe and effective choices are made with patients at the right time. This may mean not starting a medicine and may mean stopping a medicine, but all should be underpinned by shared decision making (NICE NG197).

To co-create a great experience for our colleagues, so you will be:

- **Proud**, because your work is meaningful.
- **Involved** in decisions that affect you.
- **Well led** and managed.
- That your workplace is **fit for purpose**.

Medicines Optimisation ensures that our medicines are stored and used in a safe and appropriate environment. This co-created guideline ensures that best practice is signposted to ensure they contribute to the most meaningful interventions.

To be a great partner, so we will:

- Have a **shared understanding** of the needs and the strengths of our communities
- Be **working innovatively** across organisational boundaries to improve services.
- Be **widely recognised** for what we have achieved together.

The effective communication and transfer of medicines across organisational boundaries is vital. Ensuring agreement to standards across the integrated care systems, or at a partnership or place level will reduce risk and maximise relationships to provide the best outcomes for our communities.

1.1 Advantages of depot injections

- Provide an option where compliance with oral treatment is consistently poor
- Increased bioavailability (less first-pass metabolism)
- Steady plasma levels compared to oral medication
- Reduction in relapse rate, severity of relapse and rehospitalisation
- Stable therapeutic effects
- Better downward titration to minimise side-effects
- Some evidence that long-acting injections cause less brain tissue loss and deterioration (CATIE study, Lieberman, 2005)

1.2 Disadvantages of depot injections

- Treatment cannot be stopped quickly if severe side-effects develop (dystonia, EPSE, NMS)
- Perception by the patient of "being controlled", losing control over their treatment, or possibly being punished.
- Pain at the site of injection, lasting possibly 10 days
- Tissue necrosis - over time hard plaques may form, which will reduce the ease of administration and the efficacy of the injection as well as causing discomfort.
- Loss of dignity with the gluteal route
- Need to be used with caution in combination with other medicines known to have a myelosuppressive potential, as these cannot rapidly be removed from the body in conditions where this may be required.

Over and above these factors, NICE CG178 recommends that consideration should be given to offering a depot / long-acting injectable antipsychotic to people with psychosis or schizophrenia who express a preference for such treatment after an acute episode.

Long-acting injections are NOT recommended for treatment-resistant schizophrenia as they have been found to be ineffective for many of those patients.

Choice and Medication offer a number of patient leaflets that may assist with shared decision making including a handy chart for comparison of drugs used in psychosis which allows for comparison of adverse effects, and a short and long version of a handy fact sheet comparing depot injections with oral antipsychotics.

1.3 Prescribing second-generation depots

Long-acting injections of second-generation antipsychotics (risperidone, paliperidone and aripiprazole) are more expensive than first-generation antipsychotic depots. However, this additional cost is justified if their use improves quality of life for patients from reduced side-effects, longer dose intervals and greater efficacy. They are suitable for any patient with an established response and tolerance to the same drug via oral administration, and where compliance with such treatment is consistently poor. Prospectively, paliperidone (Xeplion®, Trevicta®) should be used in preference to risperidone (Risperdal Consta®) because it offers advantages such as increased concordance (due to a longer dose interval), reduced nurse time and easier storage / preparation requirements.

2 Purpose

Following this procedure will help the Trust to:-

- Ensure that patients are offered depot preparations where appropriate, in line with national guidance.
- Ensure that prescribers have access to detailed prescribing information to support safe and effective prescribing of depot preparations.
- Ensure that those administering depot medications have all of the relevant information available to them to enable safe administration.
- Ensure that systems are in place to facilitate administration in a timely manner with appropriate documentation.
- Ensure that systems are in place to facilitate safe transfer of care of patients prescribed depot preparations, when necessary and appropriate

3 Who this procedure applies to

This procedure applies to all Trust staff involved in prescribing and administration of depot antipsychotic medication within in-patient and community settings.

4 Related documents

This procedure describes what you need to do to implement the prescribing and initiation, preparation and administration, storage and security and safe transfer of prescribing sections of the Medicines Overarching Framework in relation to depot antipsychotic medication.

This procedure also refers to:-

- ✓ Trust psychotropic drug monitoring guidance
- ✓ Shared care guidance (Aripiprazole, Paliperidone, Risperidone, First Generation Antipsychotics)
- ✓ Guidelines for the management of QTc prolongation with psychotropic medication
- ✓ Safe transfer of prescribing guidance
- ✓ Single application form
- ✓ Medicines ordering, storage, transfer, security and disposal
- ✓ Medicines retention of records
- ✓ Moving records and other sensitive information
- ✓ Hand Hygiene Procedure
- ✓ Standard (Universal) Precautions for infection prevention and control
- ✓ Safe Handling of Sharps
- ✓ Accidental inoculation
- ✓ Trust resuscitation policy (anaphylaxis)

The following are outside of the scope of this guidance:

- × **No longer available in the UK:** Fluphenazine and pipotiazine palmitate
- × **Not approved in TEWV:** Risperidone monthly injection (Okedi®), Paliperidone 6-monthly injection (Byannli®) and Aripiprazole 2-monthly injection (Abilify Maintena®)
- × **Restricted use only – see separate guidance:** Olanzapine Embonate monohydrate (Zypadhera®)
- × **NOT a depot – see separate guidance:** Zuclopenthixol Acetate (Clopixol Acuphase®)

5 Procedure for prescribing, communication, ordering, storage, administration & transportation

5.1 Prescribing

5.1.1 Prescribing Information

- Detailed monographs for all depot preparations currently approved for prescribing in TEWV are available in Appendix A covering licensed and approved indications; formulary and shared care status; treatment choice; initiation process; usual dose and administration frequency; pharmacokinetic and dose equivalence information; common adverse effects, cautions and contra-indications; switching strategies; monitoring and review requirements.
    - First Generation depots (FGAs):
        - FLUpentixol decanoate
        - Haloperidol decanoate
        - ZUCLOpenthixol decanoate
    - Second Generation depots (SGAs):
        - Aripiprazole (monthly)
        - Paliperidone (monthly and three-monthly)
        - Risperidone (two-weekly preparation only)
- Advice and information on adjusting the dose interval of first-generation antipsychotic depots is available in Appendix B

Switching between depots

- Advice is available on how to switch between depots in the individual monographs below, prescribers should keep in mind the following information:
    - Due to the pharmacokinetics of depots, the discontinued depot will continue to have therapeutic and adverse effects for some time after administration of the last dose (see pharmacokinetic information in individual monographs).
    - When selecting a dose of the new depot, the most recent dose of the discontinued depot should be used to calculate an approximate dose equivalence of the new depot; once the patient is established on the new depot the dose can be titrated according to clinical response.
    - Where required, i.e. when switching to a first generation depot, test doses of the new depot should be given prior to the formal switch
    - Advice within each of the individual drug monographs is based on switching once a patient has reached steady state on the initial depot; if steady state has not been reached, advice may differ, please seek pharmacy advice.

Stopping antipsychotic treatment completely

- If treatment with an antipsychotic depot is stopped without switching to another depot or to an oral antipsychotic, continue to monitor symptoms, mood and mental state for 2 years (may be undertaken in primary care)

5.1.2 Prescribing for community patients

- On initiation of a depot, a product-specific “Depot Antipsychotic Prescription & Administration Record” (hereafter referred to as “depot chart”) must be completed and must be kept in a designated file, accessible to all members of the team as appropriate.

- Blank depot charts can be ordered via Trust Pharmacy teams.
- When the drug, dose or frequency is changed the current prescription on the depot chart should be discontinued and a new prescription written (on a new chart if necessary).
- All relevant information regarding the current depot prescription must be communicated with relevant members of the team via an agreed route, e.g. MS Teams or email notification group.
- A "Medication Treatment Plan" case note entry on the electronic patient record must be completed to document the relevant prescribing information, using intervention activity code MED1. Staff should cut and paste the template below into the record to ensure such entries are standardised.

Depot Injection Prescribing Template
Drug:
Dose:
Frequency / dose interval:
Administration site(s):
Notes:

- In certain circumstances, it may be necessary to obtain a named patient supply of a depot – for example, a patient in a care home where the depot is administered by care home rather than TEWV staff. In this case, an FP10 must be written for supply by either a community pharmacy or Trust dispensary. If supplied by a Trust dispensary, a copy of the current depot chart must be provided with the FP10.

5.1.3 Prescribing for in-patients

- On admission, all pre-admission depot prescriptions must be identified and prescribed on the EPMA system, once details have been confirmed (see below).
- The relevant community team should be informed of the admission and advised to discontinue and file the current depot chart and await details of ongoing prescription to be provided at discharge.
- Prior to prescribing, the drug, dose, frequency, and date and site of last administration (e.g. left/right, deltoid/gluteal) must be reconciled via the electronic patient record (EPR) and/or verbal contact with the community team or GP. This is primarily the responsibility of the prescriber but if the information is not initially available, may be completed by pharmacy staff during the medicines reconciliation process.
- The date of next administration should be added to the ward's Visual Control Board (VCB) and/or any other tool used to manage depot due dates.
- At discharge, the current drug, dose and frequency of the depot must be communicated to the community team and/or GP via a notification on the electronic patient record, the discharge letter, or other agreed route, even if no changes have been made during admission. This is particularly important if the depot prescription has been changed during admission, to prevent accidental administration of the previous depot.

- On discharge, if prescribing is to remain with the Trust, arrangements should be made with the community team to ensure that a new depot chart is produced in time for the next dose, regardless of whether any changes to the prescription occurred during admission.

5.1.4 Deprescribing

- At least an annual review of patients prescribed LAIs/depots is recommended, this should include assessment for tolerability and safety.
- For patients with stable illness requiring continued antipsychotic treatment, dose reduction may be considered on the basis that patients often receive supratherapeutic doses. It is recommended that the dosage of continued treatment should be at least 50% of the standard daily dosage for the condition being managed (this may be lower than the maximum licensed dose of an individual drug) as reduction below this level is associated with a greater risk of relapse.
- Long-term follow up is recommended when antipsychotic dosage is decreased, particularly to very low doses. Such reduction is associated with a greater risk of treatment failure, hospitalisation and relapse, which may only become evident over the longer term.
- Discontinuation of medication should not be seen as the ultimate goal of the process, but sometimes is the result. An intermittent, targeted (symptom-triggered) treatment approach with antipsychotics is not as effective as continuous treatment but may be preferable to no treatment.
- There is no simple formula to decide whether or when to reduce the dose of continuing antipsychotic treatment, a risk/benefit assessment must be carried out for every patient, factors to consider include:
  - Is the patient symptom-free and if so for how long? (excluding any long-standing, non-distressing symptoms that have previously been non-responsive to medication)
  - How severe, tolerable or disabling are the side effects?
  - What is the previous pattern of illness? (consider the speed of onset, duration and severity of past relapses and any dangers or risks posed to self or others)
  - Has dose reduction been attempted before? If so, what was the outcome?
  - What are the patient's current social circumstances? Is it a period of relative stability, or should stressful life events be anticipated?
  - What is the potential social cost of relapse? (e.g. is the patient the main income earner for a family?)
  - Is the patient able to monitor their own symptoms and seek appropriate help if necessary?
- If after careful consideration the decision is taken to reduce the dose, where appropriate, the patient's family or carer (s) should be involved in this decision and a clear explanation of actions to take if/when symptoms return or worsen should be given. The following steps can then be taken:
  - Discontinue any co-prescribed oral antipsychotic medication first.
  - Where product license allows (e.g. flupentixol/zuclopenthixol), the interval between injections should be increased up to a maximum of four weeks before decreasing the dose.
  - The dose should be reduced by no more than a third at any one time (Special considerations apply to Risperdal Consta). Dose adjustments may be limited by product availability e.g. paliperidone is only available in fixed-dose pre-filled syringes at doses of 50mg, 75mg, 100mg & 150mg/month.

- Decrements should, if possible, be made no more frequently than every three months, preferably every six months or more. The slower the rate of withdrawal, the longer the time to relapse.

• If the patient becomes symptomatic during the dose reduction process, this should not be seen as a failure but as an important step in determining the minimum effective dose required by that patient. Increasing the dose back to one that was previously effective may be appropriate. Due to the time lag to reach steady following dose adjustment of the LAI/depot, it may be appropriate to consider a short top up course of oral medication to cover this period e.g. similar to the cross-over recommended when initiating the LAI/depot (See individual drug monograph).

5.2 Communication

5.2.1 Community Team

- It is recommended that each community team sets up a 'Depot Notification Group' on MS Teams or Outlook to facilitate communication. However, if local processes are already in place that enable effective communication, then these can be maintained. The group should include staff involved in prescribing, ordering, storing, administering, and monitoring depot medication.
- Each community team will identify a suitable staff member who will be responsible for the upkeep of the notification group.
- Use of a visual control board is recommended as an aide memoir for depot administration due dates. This could be a physical VCB, an electronic VCB or a shared Outlook calendar.

5.2.2 In-patient Team

- Use of a visual control board is recommended as an aide memoir for depot administration due dates. This could be a physical VCB, an electronic VCB or a shared Outlook calendar.

5.3 Ordering

5.3.1 Community Team

- The depot injections covered by this procedure will be supplied as stock to community clinics, from Trust dispensaries, in full boxes where possible so that the original packaging can be maintained to increase safety and reduce the risk of errors in product selection.
- In cases where the Trust is responsible for prescribing and a named patient supply is needed via FP10 prescription for administration by external staff (e.g. patient in a care home), the community team must have robust procedures in place to ensure that supplies are maintained to enable consistent administration on the due date.
- Where responsibility for prescribing and supply has transferred to primary care, but administration is undertaken by the TEWV team (e.g. patients in care homes without qualified nursing staff) the community team must have robust procedures in place to ensure repeat prescriptions are requested in a timely manner and depot supplies and administration are maintained.
- The receipt of stock and named patient supplies by the community team does not need to be logged but stock must be stored appropriately as soon as possible as described below.

5.3.2 In-patient Team

- Depot injections which are on the ward stock list are topped up to a minimum level weekly by the Trust pharmacy team.
- Any depot injections not kept as ward stock will be ordered and dispensed on a named patient basis. This will routinely be done by pharmacy as part of their ward visits but can be done by wards using a named patient order form if necessary, e.g. at a weekend.

5.4 Storage

5.4.1 All Trust Teams

- All depot medication on Trust premises should be stored in accordance with both manufacturer and Trust medication storage requirements. These will include:
  - Suitable clinic space
  - Safe and secure medication storage including appropriately sized medication cabinets which meet legal storage requirements
  - Room temperature monitoring
  - Fridge temperature monitoring where applicable (N.B. the cold chain should be maintained for Risperdal Consta until such time that it is due to be administered).
- All paperwork must be securely stored for audit purposes. Patient identifiable information will need to be stored for the minimum period, depending on the record type.
- When a depot is stopped or the dose altered, any named patient (non-stock) supplies should be held in a quarantine area awaiting processing by the Trust pharmacy team.

5.4.2 Community Team only

- If depot injections are stored in the patients' home environment, the administering staff member should confirm with the patient that the medication has been stored according to manufacturer's requirements in terms of temperature, exposure to light, etc. N.B. this only applies when depot injections are prescribed and supplied by primary care but administered by TEWV staff. Depot injections supplied to the community team as stock must never be left or stored in a patient's home.

5.5 Administration

5.5.1 Community Team only

- It is **strongly recommended** that the first (including test dose) and second dose of a new depot treatment are administered in a clinical setting with access to emergency adrenaline for anaphylaxis (1 mg in 1 ml).
- If there are exceptional circumstances, following an adequate risk assessment, where one of the first two dose administrations needs to be in the patient's home, then the responsible nurse should ensure they have appropriate training for managing anaphylaxis (as defined in the Resuscitation Policy) and have immediate access to adrenaline 1 mg in 1ml (for which a supply may need to be ordered on prescription for the individual rather than taking emergency supplies away from the team base).
- **Preparing for administration outside of clinic setting e.g. patients' home:**
  - For depots which are not provided as single dose packs (i.e. FGAs), a single dose can be prepared into a suitable receptacle to take to a patient's home or place of

residence for administration – it is not necessary to take the original pack (full or part-used).

- **Prior to leaving the clinic:**
  - Ensure that the drug and strength of the ampoule(s)/pre-filled syringe selected from the cupboard is compatible with the drug and dose prescribed on the depot chart and that the selected medication has not passed its expiry date.
  - Best practice is that another member of staff independently checks the prepared ampoule(s)/PFS ("second check"), but self-checking is acceptable if staff/service pressures do not allow this.
  - Ensure that all consumables needed for administration e.g., needles, syringes (if not supplied with medication – see appendix C) are available and within their expiry date, and a sharps box is available.
  - The depot chart must be signed out of the depot chart file using the log sheet and signed back in on the staff member's return to the clinic base. If the staff member does not return to base on that day the chart must be kept secure in line with section 8 of the Moving records and other sensitive information procedure.
- **At the point of administration:**
  - Appropriateness of the administration of an antipsychotic depot should be assessed by a practitioner prior to administration based on an individual case by case assessment. If the patient presents under the influence of alcohol or illicit substances, consider whether the patient is able to consent to the depot and if there are any identified risks to giving the injection, e.g. ability of the patient to sit still during administration.
  - Consumption of alcohol is not in itself a contra-indication to administration of an antipsychotic depot. If a patient presents as heavily intoxicated, it should be noted if this is abnormal for that patient; consider if this is a sign of worsening mental health; offer support or signposting if appropriate. If in any doubt, or to check for interactions or effects of illicit substances, consult the prescribing clinician or pharmacy team.
  - If the patient regularly presents intoxicated, consider switching to a depot considered to be safer in combination with alcohol (e.g. paliperidone) or scheduling administration to an earlier time of day to minimise prior drinking
- **Following administration:**
  - Details of the next due date/appointment should be added to the team VCB/diary or other agreed tool to manage depot due dates.

5.5.2 All Settings

- All nurses are expected to follow good practice guidance for the task of administration of injections including the Hand Hygiene procedure and the Standard (Universal) Precautions for Infection Prevention and Control policy.
- When a depot is to be administered in a clinic environment, the following should be confirmed:
  - The clinic is a safe environment and is clean and tidy.
  - There are facilities available to maintain the patient's confidentiality.
  - There are hand washing facilities, sharps boxes and waste bins available in the immediate vicinity.

- Trust policies for safe handling of sharps, accidental inoculation, anaphylaxis (ensure familiar with Trust Resuscitation policy) and disposal of medication should be followed where appropriate/relevant throughout the administration process.
- All depots selected for administration from stock should ideally be checked by a second member of staff unless staff/service pressures do not allow this within reasonable time. In these circumstances, the nurse preparing the dose must be extra vigilant with their self-checking procedure. This check should include:
    - Correct patient
    - Correct drug
    - Correct strength (if >1 ampoule is needed, each ampoule should be the same strength and have the same batch number)
    - Correct volume (using >1 ampoule of the same strength if necessary)
    - Correct frequency – e.g. for two-weekly injections, check the last dose was administered 14 days previously (see Appendix D for acceptable tolerances).
    - Site of last injection to enable site rotation, e.g. alternating between L/R side, and ensure that the site for this injection is licensed for the medication being administered (see Appendix C) or that an agreement for unlicensed use has been discussed with the prescriber and patient and is clearly documented prior to administration.
    - Appropriate needle/syringe for administration is selected (recommendations based on site and sometimes BMI see Appendix C).
    - Expiry date of medication and any consumables.
    - Any drug specific reconstitution recommendations detailed within the package insert.
    - No known allergies to drug or any product excipients.
    - Any new or worsening side effects.
    - Obtain consent for administration.
- When appropriate, immediately prior to administration, it is recommended that the drug, dose, frequency and expiry date are also checked with the patient/carer.
- Ensure arrangements are in place for any post-injection monitoring where applicable (e.g. Olanzapine depot requires 3 hours post-injection observation – see separate guidelines).
- Under no circumstances should the administration of each dose be split between two or more injection sites
- Once the depot medication has been administered to the appropriate intramuscular site, this should be recorded in the administration record on the in-patient prescription and administration chart or community depot chart according to the Trust procedure and should include the signature of both the staff member administering the medication and the staff member providing the second check (where applicable).
- The next due date should be calculated based on prescribed frequency and added to the team VCB/calendar. For community patients, an appointment should be arranged based on staff and patient availability (e.g. planned holidays) utilising the administration tolerances if necessary.
- If an inpatient is going to be on leave when their next dose is due, the administration tolerances can be used to give the dose before the period of leave, or a soon as they return, whichever is more appropriate.

- For administration outside of a clinic setting, any sharps etc should be safely disposed of and removed from the administration location.
- An entry to record administration should be made on the electronic patient record (by cutting and pasting the following administration template):

Depot Administration Template

Consent Obtained:

Drug name/strength of product used:

Batch number:

(N.B. For Risperdal Consta the batch number to be recorded is the one on the outer box (the kit number). The batch number on the ampoule should not be used.)

Expiry Date:

Dose administered:

Site of Administration:

Reported side effects:

Date next dose due:

Notes:

For community administration:

Location of depot administration i.e. residence, clinic:

- Every effort should be made to administer doses of a depot injection on the due date. However, it is recognised this may not always be possible, e.g. due to patient non-attendance or absence from home when visited. When this happens as a single, isolated event, assess the risk from the patient not receiving their depot on the due date and utilise acceptable tolerances as described below; if it is a recurrent event, consider implementing a patient-specific reminder process, e.g. text or phone call on day before appointment/visit.
- There may also be occasions when it is planned to give a dose early or late, e.g. if the patient is going on holiday or unavoidable service/staffing pressures exist. In these circumstances, the tables in Appendix D provide a tolerance, around the due date, within which the dose can be given without a clinically significant impact on efficacy or need for supplementary action (e.g. temporary dose adjustment). Nursing staff may administer individual doses within these tolerances without prescriber approval but **must not** repeatedly utilise these tolerances (other than as described in the paragraph below) as this may affect long-term efficacy or tolerability. If a missed dose cannot be given within these tolerances, refer to the guidance in the attached drug monographs with regard to supplementary action, and discuss with the prescriber – additional prescriptions may be required, e.g. a "once only" dose on the inpatient prescription chart or community depot chart. **An incident must be reported if a dose is not given within tolerances due to staff or service error.**
- For second-generation antipsychotic "monthly" depots (i.e. aripiprazole and paliperidone) in community settings ONLY - routine use of agreed tolerances for administration is acceptable in order to manage this workload within a team's usual depot clinic. In this scenario, doses for a particular patient should be administered at a fixed depot clinic once per month, e.g. the second Tuesday of the month (if the normal clinic day is Tuesday). This approach uses the

tolerances and deviates from the ideal to a lesser extent than administration every 28 days (see example in table below) and ensures that the patient only receives 12 doses per year, while allowing management of workload within existing clinic arrangements. [N.B. if a patient requires a dose outside this pattern care should be taken to ensure the new administration date still falls within the agreed tolerance; if not, discuss with prescriber and seek advice on possible supplementary action]

Administration schedule →	**Monthly[1]** (e.g. on 10th)		**Fixed clinic[2]** (2nd Tuesday)		**Every 4 weeks[3]**	
Month ↓	Admin Date	Variance from ideal	Admin Date	Variance from ideal	Admin Date	Variance from ideal
July 2023	10th	-	11th	-	11th	-
August 2023	10th	0	8th	-3 days	8th	-3 days
September 2023	11th	+1 day	12th	+1 day	5th	-6 days

1. IDEAL - each dose administered on the same date every month e.g. 10th July, then 10th August etc, as intended by manufacturer. Where this is not possible, the licensed tolerances enable the dose to be moved within a window around each due date. In this example, 10th September is a Sunday so the dose could be delayed until Monday 11th. Patient receives 12 doses per year, as intended, using tolerances appropriately and minimally.
2. ACCEPTABLE - each dose administered at a fixed weekly depot clinic. Patient receives 12 doses per year, utilising tolerances repeatedly but appropriately to manage workload within existing clinic arrangements.
3. NOT RECOMMENDED - each dose administered every 28 days at the weekly clinic. Utilises tolerances repeatedly and excessively. Patient receives each dose earlier than ideal, and 13 doses per year, therefore is HDAT.

5.6 Transportation

5.6.1 Community Teams only

- All depot injections must be transported in a safe, lockable bag, kept out of sight wherever possible, e.g. in a locked car boot, as per the requirements documented in the Medicines Overarching Framework. Depots which are provided as a single dose pack (i.e. SGAs) must be transported in their original pack; single ampoules from a multidose pack (i.e. FGAs) must be transported in a suitable receptacle. Unused injections must be returned to the clinic as soon as practicable.
- The depot chart should be transported with the depot injection safely and returned to the depot file in the clinic at the end of the working day. If the staff member does not return to base on that day the chart must be kept secure in line with section 8 of the Moving records and other sensitive information procedure.
- Staff are expected to plan their depot administration visits accordingly when they will be transporting a refrigerated item, i.e. Risperdal Consta®, to ensure the medication is maintained at the appropriate temperature. Risperdal Consta® cannot be administered cold, straight from the fridge. It should be removed from the fridge and allowed to sit at room temperature for at least 30 minutes before reconstituting. This must be built into the time allocated for the home visit.

5.7 Transfers of patients between teams/settings

Tables covering the recommended actions and advice for transfers of newly initiated and existing depot patients within the Trust (e.g. in-patients to community team and vice versa) and outside of the Trust (e.g. patients moving to/from out of area, patient admitted to Acute Trust etc.) can be found in Appendix E.

5.8 Caseload standards

The following standards have been agreed for the assessment of compliance with these procedures at team level:

5.8.1 Inpatient teams

For all current patients:

1. All doses administered during the current inpatient stay have been recorded in EPMA and the EPR (over the last 4 weeks on long-stay wards, e.g. SIS)
2. A full assessment of side-effects, using a recognised rating scale, has been completed within two weeks of admission/initiation (within the last 12 months for long-stay wards, e.g. SIS)

For recently discharged patient (within last four weeks):

3. Evidence of communication in the EPR, to community team or GP, of drug, dose, frequency and date of next dose

Overall team:

4. Depot products (stock and non-stock) are stored in an appropriate cupboard, in date and clearly segregated / labelled to avoid selection errors (including Clopixol Acuphase if stored with depots)

5.8.2 Community teams

For all patients (or an appropriate sample):

1. Current depot treatment (provided by TEWV) has been communicated to the patient's GP (correctly appears on SCR/GNCR/YHCR)
2. Date of prescriber signature of original prescription or the most recent signed review on current chart is within the last 6 months
3. A full assessment of side-effects, using a recognised rating scale, has been completed within the last 12 months
4. All dose administrations in the last 12 months have been recorded in EPR

Overall team:

5. Depot products (stock and non-stock) are stored in an appropriate cupboard, in date and clearly segregated / labelled to avoid selection errors

6 Definitions

Term	Definition
ADR	Adverse Drug Reaction
BMI	Body Mass Index
C_{max}	Maximum Concentration reached
CMHT	Community Mental Health Team
CNS	Central Nervous System
CPN	Community Psychiatric Nurse
Depot / LAI	Long-acting injectable antipsychotic
ECG	Electrocardiogram
EDL	Electronic Discharge Letter
EPMA	Electronic Prescribing & Medicines Administration
EPR	Electronic Patient Record
EPSE	Extra-pyramidal Side Effects
FGA	First-Generation Antipsychotic
HDAT	High Dose Antipsychotic Treatment
SGA	Second-Generation Antipsychotic
SPC	Summary of Product Characteristics
VCB	Visual Control Board

7 How this procedure will be implemented

• This procedure will be published on the Trust's intranet and external website.
• Line managers will disseminate this procedure to all Trust employees through a line management briefing.
• Publication of the procedure will be communicated via the Care Group Medicines Management Groups, the Medicines Optimisation Newsletter and opportunistically at any other relevant meetings

7.1 Training needs analysis

Staff/Professional Group	Type of Training	Duration	Frequency of Training
Nursing staff	Administration of deep intramuscular injections (practical)	-	Once only in core training
Nursing staff	Injection Awareness test (e-learning)	-	Every 3 years
Nursing staff	Administration of specific products (online from manufacturers)	-	As required

8 How the implementation of this procedure will be monitored

Auditable Standard/Key Performance Indicators		Frequency/Method/Person Responsible	Where results and any Associate Action Plan will be reported to, implemented and monitored; (this will usually be via the relevant Governance Group).
1	Medication incident reports	Monthly; by medicines safety team	Medicines Management Group; Drug & Therapeutics Committee
2	Standards in section 5.8	Annually, assessment via Trust pharmacy team	Medicines Management Group; Drug & Therapeutics; Committee; Care Group QAIGs

9 References

Bazire, S. (2020). Psychotropic Drug Directory 2020/21. (Lloyd-Reinhold Publications)

Correll CU, Kim E, Sliwa JK, Hamm W, Gopal S, Mathews M, Venkatasubramanian R, Saklad SR. Pharmacokinetic Characteristics of Long-Acting Injectable Antipsychotics for Schizophrenia: An Overview. CNS Drugs. 2021 Jan;35(1):39-59. doi: 10.1007/s40263-020-00779-5. Epub 2021 Jan 28. PMID: 33507525; PMCID: PMC7873121.

Feetam, C & White, J (2020). Guidance on the Administration to Adults of Oil-based Depot and other Long-Acting Intramuscular Antipsychotic Injections. 6th Edition.

Lieberman JA et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. NEJM 2005; 353: 1209-23

Meyer, J.M. (2013). Understanding depot antipsychotics: an illustrated guide to kinetics . CNS Spectrums, 18, pp. 55-68 doi:10.1017/S1092852913000783

Soliman E, Ranjan S, Xu T, Gee C, Harker A, Barrera A, Geddes J. A narrative review of the success of intramuscular gluteal injections and its impact in psychiatry. Biodes Manuf. 2018;1(3):161-170. doi: 10.1007/s42242-018-0018-x. Epub 2018 Jul 27. PMID: 30546922; PMCID: PMC6267269.

Taylor, DM., Barnes, TRE., and Young, AH. (2021). The Maudsley Prescribing Guidelines in Psychiatry. 14th edition. (Wiley Blackwell).

10 Document control (external)

To be recorded on the policy register by Policy Coordinator

Date of approval	22 September 2022
Next review date	30 April 2026
This document replaces	PHARM-0081-v2.1
This document was approved by	Drug and Therapeutics Committee
This document was approved	23 May 2024
This document was ratified by	n/a
This document was ratified	n/a
An equality analysis was completed on this policy on	19 December 2022
Document type	Public
FOI Clause (Private documents only)	n/a

Change record

Version	Date	Amendment details	Status
2	22 Sept 2022	New document – replacing previous documents: PHARM-0081-v1.6 Depot Injections - Community services procedure PHARM-0089-v1 Depot & Long Acting Injections – Inpatient Services Guidance on the Use of Antipsychotic Long-acting Injections in North of England (TEWV version), July 2017	Superseded
2.1	23 Nov 2023	• Section 5.1.1 – advice added about switching between depots and stopping treatment (also added to product monographs in appendix A) • Section 5.1.2 – advice added about patient-specific supplies • Section 5.5.1 – advice added about risks of administration in association with alcohol use • Section 5.5.2 – advice added about using ampoules of same strength and batch size; advice added about utilising acceptable tolerances for “monthly” depots in team clinics • Appendix A: flupentixol decanoate monograph – warning of increased suicidality in early weeks of treatment added	Superseded
2.2	23 May 2024	• Section 4 – aripiprazole 2-monthly injection added to products which are non-formulary and out of scope • Section 5.1.4 added - advice on deprescribing • Section 5.8 added – caseload standards • Section 8 – reference to standards in section 5.8 added	Approved
2.2	11 June 2025	• Review date extended to 30 April 2026	published

Appendix A – Antipsychotic Depot injection Monographs

First generation antipsychotic depot injections

FLUpentixol Decanoate (Depixol®, Psytixol®)		
Presentation:		20 mg in 1 ml ampoule 40 mg in 2 ml ampoule 50 mg in 0.5 ml ampoule (concentrate) 100 mg in 1 ml ampoule (concentrate) 200 mg in 1 ml ampoule (low volume)
Licensed Indication:		Treatment of schizophrenia and other psychoses in those stabilised on oral therapy.
Formulary status:		**Amber Shared Care**
Comments:		May have an activating effect (aggression/mood elevation) and an increased incidence of extrapyramidal side-effects (EPSEs) compared to zuclopenthixol and second-generation antipsychotics.
Cautions:		Use with caution in patients with physical health co-morbidities May increase risk of suicide/suicidal thoughts/self-harm in early weeks of treatment and following dose changes – alert patient (and carers) to report any clinical worsening See product information (select brand/strength) for details.
Contra-indications:		• Hypersensitivity to the active substance or to any of the excipients. (Base oil: Depixol® – thin vegetable oil from coconut; Psytixol® – triglycerides, medium chain) • Circulatory collapse, depressed level of consciousness due to any cause (e.g., intoxication with alcohol, barbiturates, or opiates), coma. • Not recommended for initiation in excitable or agitated patients. • Avoid in pregnancy and breast feeding
Initiation process:		Test dose recommended: 20mg, then wait one week before starting maintenance dose.
Usual dose & frequency of administration:	**Maintenance:**	50 mg 4-weekly to 300 mg 2-weekly
	Maximum dose:	400 mg/week *(in terms of dopamine blockade, this is a much higher dose equivalence than other depots)*

	Max single dose:	400 mg
	Over 65s:	Reduce initial dose by 25-50%
Dose equivalence:		Oral 2 – 3 mg/day = depot 10-20 mg/week
Pharmacokinetic information:	**Duration of action:**	3-4 weeks
	Peak:	7-10 days
	Time to steady state:	10-12 weeks
	Elimination half-life:	8 days (single dose); 17 days (multiple dose)
	Initiation phase:	2nd- 4th dose
	Maintenance:	5th dose onwards
Switching strategies: *N.B when selecting a dose of the new depot, the most recent dose of the current depot should be used to calculate an approximate dose equivalence; once the patient is established on the new depot the dose can be titrated according to clinical response.*		
Switching <u>to</u> Flupentixol depot:	**From oral:**	Continue oral flupentixol for ONE week after the first flupentixol depot injection.
	From another depot *(not risperidone – see below)*:	Give flupentixol on the due date of the next dose of the original depot, instead of the original depot; do not give any more doses of the original depot.
	From risperidone 2-weekly depot:	Give flupentixol depot 2–4 weeks after the last injection of risperidone 2-weekly depot was due. i.e. 4-6 weeks after the last injection of risperidone was given; do not give any more risperidone. (The last injection of risperidone 2-weekly depot provides therapeutic plasma levels for 4 - 6 weeks with a post dose peak at 5 weeks).
Switching <u>from</u> Flupentixol depot to oral:	**From weekly injection:**	Stop depot; start half the oral equivalent dose on the day when the next weekly injection was due; after one week of half-dose, increase to full equivalent dose daily.
	From two weekly injection:	Stop depot; start half the oral equivalent dose on the day when the next two weekly injection was due; after one week of half-dose, increase to full equivalent dose daily.

	From three weekly injection:	Start a full equivalent oral dose 3 weeks after last depot given (i.e. on the day the next depot was due).
	From four weekly injection:	Start a full equivalent oral dose 4 weeks after last depot given (i.e. on the day the next depot was due).
Adjusting the interval between injections: see separate guidance		
Very common/common adverse effects:		Increased appetite, increased weight, insomnia, depression, nervousness, agitation, libido decreased, somnolence, akathisia, hyperkinesia, hypokinesia, tremor, dystonia, dizziness, headache, disturbance in attention, visual accommodation disorder, vision abnormal, tachycardia, palpitations, dyspnoea, dry mouth, salivary hypersecretion, constipation, vomiting, dyspepsia, diarrhoea, hyperhidrosis, pruritus, myalgia, micturition disorder, urinary retention, asthenia, fatigue.
QT prolongation impact: (Trust guidance)		Low effect <10 msec at therapeutic doses or in overdose
Monitoring & review requirements:		See Trust psychotropic drug monitoring guidance / shared care guidance
Administration window to maintain therapeutic levels:	**Weekly:**	+/- 2 days
	Two to four weekly:	-2 days / +7 days
Management of missed doses (outside of above windows):	**Weekly / two weekly:**	Give up to 50% extra (max. 400 mg in total) at next scheduled dose, then continue with normal dose & frequency
	Three weekly:	Up to 35 days since last dose – give the normal dose; then the next dose should be reduced by 50% and given on the date it would have been due with a 3-weekly schedule (i.e. 42 days after the previous dose); then continue with usual dose every 3 weeks. If >35 days since last dose – give usual dose +33-50%; then continue with usual dose every 3 weeks If >42 days since last dose - start again with normal dose every 3 weeks

	Four weekly:	Up to 42 days since last dose - give normal dose, then 2 weeks later give 50% of normal dose, then continue with normal dose every 4 weeks If >42 days since last dose, start again with normal dose every 4 weeks.
Further information:		Flupentixol Decanoate SPC (select brand/strength)

Haloperidol Decanoate (Haldol® Decanoate)		
Presentation:		50 mg per 1 ml ampoule 100 mg per 1 ml ampoule
Licensed Indication:		Maintenance treatment of schizophrenia and schizoaffective disorder in adult patients currently stabilised with oral haloperidol
Formulary status:		**Amber Shared Care**
Comments:		Consider augmentation with oral medication and/or management of side-effects with anticholinergics. **Baseline ECG essential**.
Cautions:		Use with caution in patients with physical health co-morbidities – see product information for details.
Contra-indications:		• Hypersensitivity to the active substance or to any of the excipients (benzyl alcohol, sesame oil). • Comatose state, central nervous system (CNS) depression, Parkinson's disease, dementia with Lewy bodies, progressive supranuclear palsy • Known QTc interval prolongation or congenital long QT syndrome, recent acute myocardial infarction, uncompensated heart failure, history of ventricular arrhythmia or torsades de pointes, uncorrected hypokalaemia, concomitant treatment with medicinal products that prolong the QT interval • Avoid in pregnancy
Initiation process:		Test dose recommended: 25 mg. After a test dose, wait 4-10 days before titrating to maintenance dose.
Usual dose & frequency of administration:	**Maintenance:**	50-200 mg every four weeks; maximal effect at 50 mg every 4 weeks, no evidence that doses above 100 mg every four weeks have any additional effects.
	Maximum dose:	300 mg but recommended to make an individual risk-benefit analysis for doses >200 mg
	Max single dose:	300 mg
	Over 65's:	Low initiation dose of 12.5-25 mg; 25-75 mg every four weeks most effective dose range; doses >75 mg every four weeks should only be considered in patients who have tolerated higher doses and after reassessment of the patient's individual benefit-risk profile.

<table>
<tr><td colspan="2">Dose equivalence:</td><td>Manufacturer recommends a depot dose 10-15 x the oral daily dose, i.e. depot dose will be 25 to150 mg for most patients.

Reference sources advise the following equivalence:
• Psychotropic Drug Directory (Bazire):
Oral 2.5 (1-5) mg/day = depot 10-15 (5-25) mg/week
• Maudsley Guidelines:
Oral 2 (1.5-5) mg/day =depot 15 (5-25) mg/week
• Meyer (see references):
Oral bioavailability = 65% (60-70%); e.g. 10 mg/day oral results in 182 mg/28 days of total drug exposure. Therefore, depot dose approx. 20 x oral daily dose provides equivalence
<table>
<tr><td>Oral dose</td><td>Manufacturer</td><td>PDD (Bazire)</td><td>Maudsley</td><td>Meyer</td></tr>
<tr><td>10 mg/day</td><td>25-37.5 mg /week</td><td>40-60 mg/week</td><td>75 mg/week</td><td>50 mg/week</td></tr>
</table></td></tr>
<tr><td rowspan="6">Pharmacokinetic information:</td><td>Duration of action:</td><td>6 weeks</td></tr>
<tr><td>Peak:</td><td>3-9 days</td></tr>
<tr><td>Time to steady state:</td><td>10-12 weeks (dosed every 4 weeks)</td></tr>
<tr><td>Elimination half-life:</td><td>18-21 days</td></tr>
<tr><td>Initiation phase:</td><td>2nd- 4th dose</td></tr>
<tr><td>Maintenance:</td><td>5th dose onwards</td></tr>
<tr><td colspan="3">Switching strategies:
N.B when selecting a dose of the new depot, the most recent dose of the current depot should be used to calculate an approximate dose equivalence; once the patient is established on the new depot the dose can be titrated according to clinical response.</td></tr>
<tr><td rowspan="3">Switching <u>to</u> Haloperidol depot:</td><td>From oral:</td><td>Continue oral haloperidol for FOUR weeks from the first depot injection. N.B. the combined total dose of haloperidol from both formulations must not exceed the equivalent to the maximum oral dose of 20 mg/day.</td></tr>
<tr><td>From another depot (not risperidone – see below) :</td><td>Give haloperidol depot on the due date of the next dose of the original depot, instead of the original depot. Do not give any more doses of the original depot.</td></tr>
<tr><td>From risperidone 2-weekly depot:</td><td>Give haloperidol depot 2–4 weeks after the last injection of risperidone 2-weekly depot was due. i.e., 4-6 weeks after the last injection of risperidone was given; do not give any more risperidone. (The last injection of risperidone 2-weekly depot provides therapeutic plasma levels for 4-6 weeks with a post dose peak at 5 weeks).</td></tr>
</table>

Switching <u>from</u> Haloperidol depot to oral:	**From weekly injection:**	Start 25% target oral dose equivalent on the date the next depot is due for one week, then 33% for one week, then 66% for one week, then 100% oral target dose.
	From two weekly injection:	Start 25% target oral dose equivalent on the date the next depot is due for one week, then 50% for two weeks, then 100% oral target dose.
	From three weekly injection:	Start 50% target oral dose equivalent on the date the next depot is due for one week, then increase to 100% oral target dose.
	From four weekly injection:	Start 50% target oral dose equivalent on the date the next depot is due for one week, then increase to 100% oral target dose.
Adjusting the interval between injections: see separate guidance		
Very common/common adverse effects:		Most commonly reported adverse reactions are extrapyramidal disorder (14%), tremor (8%), parkinsonism (7%), muscle rigidity (6%) and somnolence (5%).
QT prolongation impact: Trust guidance		Moderate effect – 10-20 msec at therapeutic doses. Contra-indicated with other QT-prolonging drugs.
Monitoring & review requirements:		See Trust psychotropic drug monitoring guidance / shared care guidance
Administration window to maintain therapeutic levels:	**Weekly:**	+/- 2 days
	Two to four weekly:	-2 days / + 6 days (two weekly) -2 days / + 7 days (three weekly) -2 days / + 14 days (four weekly)
Management of missed doses (outside of pre-defined administration tolerances stated above):	**Weekly:**	Consider giving up to 50% extra (max.300 mg in total) at next scheduled dose, then revert to normal dose weekly If >14 days since last dose, give double the normal dose (max. 300 mg in total), then revert to normal dose weekly
	Two weekly:	Consider giving up to 50% extra (max.300 mg in total) then revert to normal dose every two weeks If >28 days since last dose, give up to 75% extra (max.300 mg in total), then revert to normal dose every two weeks
	Three weekly:	If two weeks late, give 75% of usual dose then resume as before (i.e. give usual one week after the 75% dose has been given) If three weeks late, restart at usual dose plus 50%, then revert to usual dose every three weeks

	Four weekly:	If >42 days since last dose, give 60-75% of normal dose, then 1 week later give the full normal dose, then revert to normal dose every 4 weeks
Further information:		Haloperidol Decanoate SPC

ZUCLOpenthixol Decanoate (Clopixol®)		
Presentation:		200 mg per 1 ml ampoule 500 mg per 1 ml ampoule (Clopixol® Conc)
Licensed Indication:		Maintenance treatment of schizophrenia and paranoid psychoses.
Formulary status:		**Amber Shared Care**
Comments:		More sedating than flupentixol, therefore preferable in aggressive/agitated patients.
Cautions:		Use with caution in patients with physical health co-morbidities – see product information (select brand/strength) for details.
Contra-indications:		• Hypersensitivity to the active substance or to any of the excipients (Thin vegetable oil from coconuts) • Circulatory collapse, depressed level of consciousness due to any cause (e.g., intoxication with alcohol, barbiturates, or opiates), coma. • Avoid in pregnancy
Initiation process:		Test dose recommended: 100 mg, an interval of at least one week should be allowed before the second injection is given at a dose consistent with the patient's condition.
Usual dose & frequency of administration:	**Maintenance:**	200 mg every 3 weeks to 600 mg every week
	Maximum dose:	600 mg/week
	Max single dose:	600 mg
	Over 65's:	Initial dosage may need to be reduced to a quarter or half the normal starting dose in frail/older patients.
Dose equivalence:		Oral 25 mg daily (range 25-60 mg) = depot 100 mg per week (range 40-100 mg)
Pharmacokinetic information:	**Duration of action:**	2-4 weeks
	Peak:	4-9 days
	Time to steady state:	10-12 weeks
	Elimination half-life:	17-21 days

	Initiation phase:	2nd- 4th dose
	Maintenance:	5th dose onwards
Switching strategies: *N.B when selecting a dose of the new depot, the most recent dose of the current depot should be used to calculate an approximate dose equivalence; once the patient is established on the new depot the dose can be titrated according to clinical response.*		
Switching to Zuclopenthixol depot:	**From oral:**	Continue oral zuclopenthixol for THREE weeks after the first zuclopenthixol depot injection.
	From another depot *(not risperidone - see below):*	Give zuclopenthixol depot on the due date of the next dose of the original depot, instead of the original depot. Do not give any more doses of the original depot.
	From risperidone 2-weekly depot:	Give zuclopenthixol depot 2–4 weeks after the last injection of risperidone 2-weekly depot was due. i.e., 4-6 weeks after the last injection of risperidone was given; do not give any more risperidone. (The last injection of risperidone 2-weekly depot provides therapeutic plasma levels for 4 -6 weeks with a post dose peak at 5 weeks).
Switching from Zuclopenthixol depot to oral:	**From weekly injection:**	Stop depot, start half the equivalent oral dose on the day when the next depot injection is due. After a week of half-dose, increase to full equivalent daily dose.
	From two weekly injection:	Stop depot, start half the equivalent oral dose on the day when the next depot injection is due. After a week of half-dose, increase to full equivalent oral dose daily.
	From three weekly injection:	Start an equivalent oral dose 3 weeks after the last depot (i.e. on the day the next depot was due)
	From four weekly injection:	Start the full equivalent oral dose 4 weeks after the depot (i.e. on the day next depot was due)
Adjusting the interval between injections: See separate guidance		
Very common/common adverse effects:		Agitation; amenorrhoea; arrhythmias; constipation; dizziness; drowsiness; dry mouth; erectile dysfunction; fatigue; galactorrhoea; gynaecomastia; hyperglycaemia; hyperprolactinaemia; hypotension (dose-related); insomnia; leucopenia; movement disorders; muscle rigidity; neutropenia; parkinsonism; postural hypotension

		(dose-related); QT interval prolongation; rash; seizure; tremor; urinary retention; vomiting; weight increased.
QT prolongation impact: Trust guidance		No known effect
Monitoring & review requirements:		See Trust psychotropic drug monitoring guidance / shared care guidance
Administration window to maintain therapeutic levels:	**Weekly:**	+/- 2 days
	Two to four weekly:	-2 days / +7days
Management of missed doses (outside of pre-defined administration tolerances stated above):	**Weekly / two weekly:**	Consider giving up to 50% extra (max. 600 mg in total) at next scheduled dose, then revert to normal dose & frequency
	Three weekly:	Up to 35 days since last dose – give the normal dose 2 weeks late; then the next dose should be reduced by 50% and given on the date it would have been due with a 3-weekly schedule (i.e. 42 days after the previous dose); then continue with usual dose every 3 weeks. If >35 days since last dose – give usual dose +33-50% when next due (i.e. 6 weeks after last dose); then continue with usual dose every 3 weeks If >42 days since last dose, start again with normal dose every 3 weeks
	Four weekly:	Up to 42 days since last dose - give normal dose, then 2 weeks later give 50% of normal dose, then continue with normal dose every 4 weeks If >42 days since last dose, start again with normal dose every 4 weeks.
Further information:		Zuclopenthixol Decanoate SPC

Second Generation Antipsychotic Depot injections

Aripiprazole (Otsuka)	
Presentation:	400 mg pre-filled syringe 400 mg vial
Licensed Indication:	Maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole.
Formulary status:	**Amber Shared Care**
Comments:	• Adjust dose in patients who are taking concomitant strong CYP2D6 inhibitors, strong CYP3A4 inhibitors, and/or CYP3A4 inducers for more than 14 days. (See manufacturer's SPC for more information). • If prior response and tolerability to aripiprazole are known, pre-injection oral aripiprazole may not be required. However, for the one injection start regimen, attainment of effective aripiprazole plasma levels is dependent upon four weeks of oral supplementation. For the two injection start regimen, the pharmacokinetic modelling study was based on plasma levels from oral aripiprazole being at steady state on the day of initiation. • The recommended dose interval for aripiprazole depot is "monthly" (same calendar date each month) and should be followed. A 28-day dose interval is not recommended and any dose interval shorter than 28 days is considered as HDAT and is therefore not suitable for shared care.
Cautions:	Use with caution in patients with physical health co-morbidities – see product information (select formulation/strength) for details.
Contra-indications:	• Known hypersensitivity to aripiprazole or excipients (carmellose sodium, mannitol, sodium dihydrogen phosphate monohydrate, sodium hydroxide, water for injections) • Avoid in pregnancy and breast feeding, the long-acting properties of aripiprazole depot should be considered in patients of childbearing potential.
Initiation process: (Adjust initiation dose in patients taking concomitant strong CYP2D6 inhibitors, strong CYP3A4 inhibitors, and/or CYP3A4 inducers for more than 14 days - See manufacturers information).	**One injection start:** On the day of initiation, administer one injection of 400 mg into the gluteal or deltoid muscle and continue oral treatment with 10-20 mg/day for 14 consecutive days to maintain therapeutic concentrations during initiation of therapy. **Two injection start** (only recommended in working age adults)**:** On the day of initiation, administer two separate injections of 400 mg at separate injection sites (i.e. two different sites/two different muscles, e.g. one deltoid/one gluteal or two different deltoid), along with one x 20 mg dose of oral aripiprazole. (If oral treatment cannot be

		given at all, e.g. patient refused, this method should be used for initiation).
Usual dose & frequency of administration:	**Maintenance:**	300-400 mg once per calendar month If adverse effects with 400 mg dose, reduction to 300 mg/month should be considered.
	Maximum dose:	400 mg per month
	Max single dose:	400 mg
	Over 65's:	Safety & efficacy has not been established but off-label use in this group is pre-approved using the one injection start only
Dose equivalence:		400 mg monthly depot = 20 mg daily oral (guided by previous oral use)
Pharmacokinetic information:	**Duration of action:**	6–8 weeks
	Peak:	4–7 days (continuous treatment - 4 days deltoid; 7 days gluteal)
	Time to steady state:	4-5 months
	Elimination half-life:	30 days (300 mg monthly); 47 days (400 mg monthly)
	Initiation phase:	Dose 1 to 3
	Maintenance:	Dose 4 onwards
Switching strategies:		
Switching to Aripiprazole depot:	**From oral:**	If switching from a different oral antipsychotic, cross taper from that antipsychotic to oral aripiprazole over 2 weeks (e.g. start 5mg/day aripiprazole increasing stepwise to e.g. 15mg/day, reducing the previous antipsychotic by 25% twice a week). **One injection start:** Start the aripiprazole depot, continue oral aripiprazole for two more weeks then stop. **Two injection start:** Start the aripiprazole depot as above, stop oral aripiprazole.
	From another depot (not risperidone depot – see below):	Start oral aripiprazole for two weeks, starting on the day the last depot dose is due. **One injection start:** Start the aripiprazole depot after two weeks of oral treatment, stop the oral aripiprazole two weeks later. **Two injection start:** Start the aripiprazole depot as above after two weeks of oral treatment, stop oral aripiprazole.

	From risperidone 2-weekly depot:	Start oral aripiprazole 2-4 weeks after the last injection of risperidone 2-weekly depot was due, i.e. 4-6 weeks after the last injection of risperidone was given. Do not give any more risperidone (The last injection of risperidone provides therapeutic plasma levels for 4 -6 weeks with a post dose peak at 5 weeks). **One injection start:** Start the aripiprazole depot two weeks later, stop the oral aripiprazole two weeks after that. **Two injection start:** Start the aripiprazole depot as above after two weeks of oral treatment, stop oral aripiprazole.
Switching from monthly Aripiprazole depot to oral:		Restart oral aripiprazole at 5-10mg/day when the next injection would have been due, increase dose after 1-2 weeks as needed.
Very common/common adverse effects:		Weight increased, diabetes mellitus, weight decreased, agitation, anxiety, restlessness, insomnia, extrapyramidal disorder, akathisia, tremor, dyskinesia, sedation, somnolence, dizziness, headache, dry mouth, musculoskeletal stiffness, erectile dysfunction, injection site pain, injection site induration, fatigue, blood creatine phosphokinase increased.
QT prolongation impact: Trust guidance		Low effect <10 msec at therapeutic doses or only in overdose.
Monitoring & review requirements:		See Trust psychotropic drug monitoring guidance / shared care guidance
Administration window to maintain therapeutic levels (monthly dose):		**Dose two & three:** 26 - 35 days since previous dose. **Dose four onwards:** 26 – 42 days since previous dose.
Management of missed doses (outside of pre-defined administration tolerances stated above):	**Second or third dose:**	**> 4 weeks and < 5 weeks since last injection:** The injection should be administered as soon as possible and then the monthly injection schedule should be resumed. **> 5 weeks since last injection:** 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.
	Fourth dose onwards:	**> 4 weeks and < 6 weeks since last injection:** The injection should be administered as soon as possible and then the monthly injection schedule should be resumed. (If given up to two weeks late, restart monthly injection on the previous planned monthly date, i.e. 2-4 weeks after the late dose, leaving 4 weeks before the next dose can lead to some subtherapeutic levels for several months). **> 6 weeks since last injection:** 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 it is 6-8 weeks since last injection, oral aripiprazole may be needed for up to 4 weeks while resuming monthly injection on the previous dates).
Further information:		Aripiprazole Otsuka SPC

Paliperidone palmitate (Xeplion®, Trevicta®)		
Presentation:		Xeplion® (monthly injection) – 50 mg in 0.5 ml, 75 mg in 0.75 ml, 100 mg in 1 ml & 150 mg in 1.5 ml pre-filled syringe Trevicta® (3-monthly injection) - 175 mg in 0.875 ml, 263 mg in 1.315 ml, 350 mg in 1.75 ml & 525 mg in 2.625 ml pre-filled syringe
Licensed Indication:		Maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone.
Formulary status:		**Amber Shared Care**
Comments:		It is recommended that patients try at least 3 days oral risperidone for tolerability. In selected adult patients with schizophrenia and **previous responsiveness** to oral paliperidone or risperidone, Xeplion® may be used without prior stabilisation with oral treatment if psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed.
Cautions & Contra-indications include:		Use with caution in patients with physical health co-morbidities – see product information (select brand/strength) for details. Avoid in pregnancy and breast feeding. Consideration should be given to the long-acting nature of these products, paliperidone has been detected in plasma up to 18 months after a single dose of Trevicta®. Maternal exposure before and during pregnancy may lead to adverse reactions in the newborn child.
Initiation process:		Patients should be initiated on the MONTHLY injection (Xeplion®), 150 mg on treatment day 1 and 100 mg one week later (day 8), both administered in the deltoid muscle to attain therapeutic concentrations rapidly. (Improvement in psychotic symptoms has been seen as early as day 4). The third dose should be administered one month after the second initiation dose.
Usual dose & frequency of administration:	**Maintenance:**	The recommended MONTHLY maintenance dose is 75 mg; some patients may benefit from lower or higher doses within the recommended range of 25 to 150 mg based on individual patient tolerability and/or efficacy. Patients who are overweight or obese may require doses in the upper range. Monthly maintenance doses can be administered in either the deltoid or gluteal muscle.

		Adjustment of the maintenance dose may be made monthly. When making dose adjustments, the prolonged release characteristics of Xeplion® should be considered, as the full effect of maintenance doses may not be evident for several months. The recommended dose interval for Xeplion® is "monthly", this should be followed. A 28-day dose interval is not recommended and any dose interval shorter than 28 days is considered as HDAT and is therefore not suitable for shared care. Patients who are clinically stable after at least four identical doses of the monthly injection may be transferred to the THREE-MONTHLY preparation (Trevicta®) – see below for dose conversion. Maintenance doses of Trevicta® may be administered in deltoid or gluteal muscle. Adjustment of the 3-monthly dose may be made at the same interval as administration at increments within the available dose range. Due to the long-acting nature of this preparation, the patient's response to an adjusted dose may not be apparent for several months. If the patient remains symptomatic, they should be managed according to clinical practice. [N.B. the SIX-MONTHLY preparation, Byannli® is not approved for use in the Trust; approval for use in exceptional, named-patient cases must be requested using the single application form. If approved, shared care would not apply]
	Maximum dose:	Xeplion®: 150 mg per month Trevicta®: 525 mg every 3 months
	Max single dose:	Xeplion®: 150 mg Trevicta®: 525 mg
	Over 65's:	Check renal function – if normal, dose as per adults <65, efficacy and safety not established in over 65's but pre-approved for off-label use.
Dose equivalence:		Depot paliperidone 100 mg/month or 350 mg/3 months = oral **risperidone** 4 mg/day or risperidone depot 50 mg/2 weeks
Pharmacokinetic information:	**Duration of action:**	Xeplion®: Up to 4 months Trevicta®: Up to 18 months

	Peak:	Xeplion®: 13 days Trevicta®: 30-33 days (median, C_{max} 11-12 % higher with deltoid compared with gluteal injection.)
	Time to steady state:	Xeplion®: 5 months (loading doses increase therapeutic levels rapidly but time to steady state is unaffected) Trevicta®: should be at steady state when transferred from Xeplion
	Elimination half-life:	Xeplion®: 25-49 days Trevicta®: 84-95 days (Deltoid), 118-139 days (Gluteal)
	Initiation phase:	Xeplion®: Dose 1 and 2 Trevicta®: not applicable
	Maintenance:	Xeplion®: Dose 3 onwards Trevicta®: all doses
Switching strategies:		
Switching <u>to</u> Paliperidone MONTHLY depot (Xeplion®):	**From oral risperidone / paliperidone:**	Follow initiation process above, no oral supplementation is necessary during initiation of MONTHLY paliperidone depot. ("Bridging" people with oral risperidone for 7 or more days after the first dose of MONTHLY paliperidone depot significantly reduces hospital days, compared with stopping risperidone as soon as paliperidone depot started).
	From another oral antipsychotic:	Follow initiation process above, reduce the oral antipsychotic over 1-2 weeks (four-week dose reduction recommended for olanzapine, quetiapine & clozapine to minimise any rebound) following the first injection of MONTHLY paliperidone depot.
	From another depot (not risperidone – see below):	Start MONTHLY paliperidone depot at the maintenance dose on the due date of the next injection of the original depot, instead of the original depot . No initiation doses are required, do not give another dose of the previous depot.
	From risperidone 2-weekly depot:	No initiation doses of paliperidone depot are necessary. Begin an equivalent dose of MONTHLY paliperidone depot 2-4 weeks after the last injection of risperidone 2-weekly depot was due. i.e., 4-6 weeks after the last injection of risperidone was given. (The last injection of risperidone 2-weekly depot provides therapeutic levels for 4-6 weeks with a post dose peak at 5 weeks). Do not give any more risperidone.

<table>
<tr><td rowspan="6"></td><td>From THREE-MONTHLY paliperidone depot (Trevicta®):</td><td colspan="2">Doses of monthly paliperidone depot (Xeplion) for patients switching from THREE monthly depot (Trevicta):</td></tr>
<tr><td></td><td>If the last dose of paliperidone THREE monthly depot (Trevicta) is:</td><td>Initiate monthly paliperidone depot (Xeplion) 3 months later at the following dose</td></tr>
<tr><td></td><td>175 mg</td><td>50 mg</td></tr>
<tr><td></td><td>263 mg</td><td>75 mg</td></tr>
<tr><td></td><td>350 mg</td><td>100 mg</td></tr>
<tr><td></td><td>525 mg</td><td>150 mg</td></tr>
<tr><td rowspan="3">From SIX-MONTHLY paliperidone depot (Byannli®):</td><td colspan="2">Doses of MONTHLY paliperidone depot for patients switching from SIX monthly paliperidone depot:</td></tr>
<tr><td>If the last dose of paliperidone SIX MONTHLY depot is</td><td>Initiate MONTHLY paliperidone depot 6 months later at the following dose</td></tr>
<tr><td>700 mg</td><td>100 mg</td></tr>
<tr><td></td><td>1000 mg</td><td>150 mg</td></tr>
<tr><td rowspan="8">Switching <u>from</u> Paliperidone MONTHLY depot (Xeplion®):</td><td>To oral (RISPERIDONE):</td><td colspan="2">Stop paliperidone depot; start oral on the date next dose of depot was due and gradually titrate up dose e.g., 25% target oral dose for three weeks, 50% target oral dose for three weeks, 75% target oral dose for three weeks, then 100% target oral dose</td></tr>
<tr><td rowspan="7">To paliperidone THREE-monthly depot (Trevicta®):</td><td colspan="2">The THREE-MONTHLY depot should be initiated in place of the next scheduled dose of the monthly depot (± 7 days). The dose should be based on the previous monthly dose using a 3.5-fold conversion factor as shown in the following table:</td></tr>
<tr><td colspan="2">Paliperidone THREE-monthly depot doses for patients adequately treated with monthly paliperidone palmitate injectable</td></tr>
<tr><td>If the last dose of monthly paliperidone depot is</td><td>Initiate Paliperidone THREE monthly depot at the following dose</td></tr>
<tr><td>50 mg</td><td>175 mg</td></tr>
<tr><td>75 mg</td><td>263 mg</td></tr>
</table>

<table>
<tr><td></td><td></td><td>
<table>
<tr><td>100 mg</td><td>350 mg</td></tr>
<tr><td>150 mg</td><td>525 mg</td></tr>
</table>
There is no equivalent dose of the THREE-monthly for the 25 mg dose of monthly paliperidone
</td></tr>
<tr><td>Switching from paliperidone THREE-monthly depot (Trevicta®):</td><td>To oral:</td><td>If THREE-monthly paliperidone depot is discontinued, its prolonged release characteristics must be considered. (For example, when switching to paliperidone oral, the manufacturer recommends starting daily dosing of oral medication three months after the last injection, and a gradual dose increase, after 7 weeks, then 13 weeks, dependent on depot dose and individual patient response).</td></tr>
<tr><td rowspan="2">Switching from paliperidone SIX-monthly depot (Byannli®):</td><td>To oral:</td><td>If SIX-monthly paliperidone depot is discontinued, its prolonged release characteristics must be considered. (For example, when switching to paliperidone oral, the manufacturer recommends starting daily dosing of oral medication six months after the last injection, and a gradual dose increase, at 3 months intervals, dependent on depot dose and individual patient response).</td></tr>
<tr><td>To paliperidone THREE-monthly depot (Trevicta®):</td><td>
<table>
<tr><th colspan="2">Doses of THREE-monthly paliperidone depot for patients switching from SIX-monthly depot:</th></tr>
<tr><th>If the last dose of paliperidone SIX-MONTHLY depot is</th><th>Initiate THREE-monthly paliperidone depot 6 months later at the following dose</th></tr>
<tr><td>700 mg</td><td>350 mg</td></tr>
<tr><td>1000 mg</td><td>525 mg</td></tr>
</table>
</td></tr>
<tr><td colspan="2">Very common/common adverse effects:</td><td>Weight gain, depression, fatigue, EPSE, slowed reaction times, sexual dysfunction hyperprolactinaemia, reduction in bone density, incontinence.</td></tr>
<tr><td colspan="2">QT prolongation impact:
Trust guidance</td><td>Low effect <10 msec at therapeutic doses or only in overdose.</td></tr>
<tr><td colspan="2">Monitoring & review requirements:</td><td>See Trust psychotropic drug monitoring guidance / shared care guidance</td></tr>
<tr><td>Administration window to maintain</td><td>Monthly (Xeplion®):</td><td>Dose 2: 3-11 days after dose 1
Dose 3 onwards: ONE month +/- 7 days</td></tr>
</table>

therapeutic levels:		N.B. patients receiving fewer than 12 injections/year as a result of multiple delayed doses have an increased risk of relapse.
	THREE monthly (Trevicta®):	THREE months +/- 14 days
Management of missed doses (outside of pre-defined administration tolerances stated above):	**Paliperidone MONTHLY depot (Xeplion®):**	**Missed dose 2:** **<4 weeks from first injection:** administer second injection of 100 mg in the deltoid muscle as soon as possible. A third dose of 75 mg in either the deltoid or gluteal muscles should be administered 5 weeks after the first injection (regardless of the timing of the second injection), then follow normal monthly cycle in either deltoid or gluteal muscle, dose based on tolerability/efficacy. **4-7 weeks from first injection:** Resume dosing with a deltoid injection of 100 mg as soon as possible then another deltoid injection of 100 mg one week (+/- 4 days) later, then follow normal monthly cycle, dose based on tolerability/efficacy. **> 7 weeks from first injection:** Restart using standard initiation doses and dosing schedule as described in initiation section. **Missed dose 3 onwards:** **1 month to 6 weeks since last injection:** If less than 6 weeks have elapsed since the last injection, then the previously stabilised dose should be administered as soon as possible, followed by injections at monthly intervals (i.e., move the next due date to a month after most recent injection). **Missed monthly maintenance dose (> 6 weeks to 6 months) & usual maintenance dose 25-100 mg/month:** administer a deltoid injection as soon as possible at the same dose the patient was previously stabilised on then another deltoid injection (same dose) one week later (day 8), then follow normal monthly cycle in either deltoid or gluteal muscle, dose based on tolerability/efficacy. **Missed monthly maintenance dose (> 6 weeks to 6 months) & usual maintenance dose 150 mg/month:** administer a deltoid injection as soon as possible at the 100 mg dose then another deltoid injection one week later (day 8) at the 100 mg dose, then follow normal

<table>
<tr><td></td><td></td><td>monthly cycle in either deltoid or gluteal muscle, dose based on tolerability/efficacy.
Missed monthly maintenance dose > 6 months: Restart using standard initiation doses and dosing schedule as described in initiation section.</td></tr>
<tr><td></td><td>Paliperidone THREE-MONTHLY depot (Trevicta®):</td><td>> 3½ months up to 4 months after last injection: The injection should be administered as soon as possible and then resume the 3-monthly injection schedule.
4 months to 9 months after last injection – see table:
<table>
<tr><th rowspan="2">Last dose of Paliperidone THREE-monthly was</th><th colspan="2">Administer monthly paliperidone depot, two doses one week apart (into deltoid muscle)</th><th>Then administer Paliperidone THREE- monthly depot (into deltoid or gluteal muscle)</th></tr>
<tr><th>Day 1</th><th>Day 8</th><th>1 month after day 8</th></tr>
<tr><td>175 mg</td><td>50 mg</td><td>50 mg</td><td>175 mg</td></tr>
<tr><td>263 mg</td><td>75 mg</td><td>75 mg</td><td>263 mg</td></tr>
<tr><td>350 mg</td><td>100 mg</td><td>100 mg</td><td>350 mg</td></tr>
<tr><td>525 mg</td><td>100 mg</td><td>100 mg</td><td>525 mg</td></tr>
</table>
> 9 months since last injection: Restart and stabilise on paliperidone MONTHLY depot, after a minimum of FOUR months, can switch back to THREE-monthly paliperidone depot.</td></tr>
</table>

Risperidone (Risperdal Consta®)		
Presentation:		25 mg, 37.5 mg and 50 mg vials
Licensed Indication:		Maintenance treatment of schizophrenia in patients currently stabilised with oral antipsychotics.
Formulary status:		**Amber Shared Care**
Comments:		**For continuation of established patients only**. New patients should be initiated on paliperidone in preference to risperidone; do not initiate in new patients unless all other depot options have been exhausted or are contra-indicated, single application form required for initiation (exceptional cases only). Testing tolerability with oral risperidone (e.g. 2 mg/day titrated up if necessary) for at least 3 days is desirable. Injection requires refrigeration and reconstitution. Initial 3-week lag period, oral or IM medication will need to be continued.
Cautions:		Use with caution in patients with physical health co-morbidities – see product information (select strength) for details.
Contra-indications:		Hypersensitivity to the active substance or to any of the excipients - [poly-(d, l-lactide-co-glycolide), polysorbate 20, carmellose sodium, disodium hydrogen phosphate dihydrate, citric acid anhydrous, sodium chloride, sodium hydroxide, water for injection. Avoid in pregnancy.
Initiation process:		For most patients the recommended dose is 25 mg intramuscular every two weeks. For those patients on a fixed dose of oral risperidone for two weeks or more, see below for recommended dose equivalence.
Usual dose & frequency of administration:	**Maintenance:**	25-50 mg every TWO weeks
	Maximum dose:	50 mg
	Max single dose:	50 mg
	Over 65's:	Dose as per adults under 65 years
Dose equivalence:		Manufacturer suggests 25 mg / 2 weeks depot = 4 mg daily oral, 37.5-50 mg depot – be guided by previous oral use.
	Duration of action:	4–6 weeks

Pharmacokinetic information:	**Peak:**	5–6 weeks
	Time to steady state:	6–8 weeks
	Elimination half-life:	4 days
	Initiation phase:	2nd to 4th dose
	Maintenance:	5th dose onwards
Switching strategies:		
Switching to Risperidone 2-weekly depot:	**From oral risperidone:**	Give the equivalent dose of risperidone depot, continue with the oral risperidone for at least 3 weeks then taper down over 1-2 weeks. Be prepared to continue oral risperidone for longer if necessary.
	From another oral antipsychotic:	**Either:** Switch to oral risperidone and titrate to an effective dose, if tolerated and effective prescribe an equivalent dose of risperidone depot and continue with the oral risperidone for at least 3 weeks then taper down over 1-2 weeks, be prepared to continue oral risperidone for longer if necessary **Or:** Give an appropriate dose of risperidone depot and then slowly discontinue the oral antipsychotic after 3 - 4 weeks. Be prepared to continue the oral antipsychotic for longer if necessary
	From another depot:	Give risperidone 2-weekly depot one week before the last injection of previous depot is given.
Switching from Risperidone 2-weekly depot to oral:	**To oral:**	Plasma levels start to drop below the steady state about five weeks after the last dose of depot is given and fall to near baseline after 7-8 weeks. This must be considered when adding an oral antipsychotic to avoid the risk of additive ADRs and NMS.
Very common/common adverse effects:		The most frequently reported adverse drug reactions (ADRs) (incidence ≥ 1/10) are: insomnia, anxiety, headache, upper respiratory tract infection, parkinsonism, and depression. ADRs that appeared to be dose-related included parkinsonism and akathisia.
QT prolongation impact: Trust guidance		Low effect <10 msec at therapeutic dose or only in overdose

Monitoring & review requirements:		See Trust psychotropic drug monitoring guidance / shared care guidance
Administration window of TWO weekly dose to maintain therapeutic levels:		2 weeks +/- 2 days
Management of missed doses (outside of pre-defined administration tolerances stated above):	**Two weekly:**	**Do not give a double or higher dose because that could lead to toxic levels 3-5 weeks later.** The delayed release profile from risperidone depot means that a dose can be given as soon as possible after the missed dose and carried on every two weeks from that point. Oral supplementation may be needed. **Or:** give the missed two weekly dose one week late and carry on fortnightly from then or if you need to go back to the original two weekly scheduled days, give 50% of the two-weekly dose on the next scheduled date (e.g., a week after the dose given a week late), then the usual dose schedule from that point on. Manage the low plasma levels 3-5 weeks later with oral supplementation. **If two doses missed:** give the missed dose as soon as possible and carry on from that point every two weeks, oral supplementation might be needed. **If three doses missed:** give a dose as soon as possible and carry on from that point every two weeks, oral supplementation may be needed for 3 – 4 weeks.
Further information:		Risperdal Consta SPC (select strength)

Appendix B – Adjustment of dose frequency: First generation antipsychotic depots (FLUpentixol, Haloperidol, ZUCLOpenthixol)

Increasing dose interval of First-generation depot:	**From WEEKLY to every TWO weeks:**	Add 25% to the final WEEKLY dose, miss a week then give double the previous weekly dose every TWO weeks
	From every TWO weeks to every THREE weeks:	Add up to 20-25% to the last TWO weekly injection, then move to injections every THREE weeks at 1.5 times the previous dose.
	From every THREE weeks to every FOUR weeks:	Leave FOUR weeks since the last dose, then start with the previous dose plus 33% every FOUR weeks.
Reducing dose interval of First-generation depot:	**From every FOUR weeks to every THREE weeks:**	THREE weeks after the last dose was given, start THREE weekly injection at 75% of previous dose
	From every FOUR weeks to every TWO weeks:	TWO weeks after the last dose was given, start TWO weekly injection at 50% previous dose
	From every THREE weeks to every TWO weeks:	TWO weeks after the last dose was given, start TWO weekly injection at around 66% previous dose.
	From every TWO weeks to weekly:	Give the last TWO weekly dose as usual, miss a week, then start weekly at 50% of the previous fortnightly dose. Plasma levels may take 4-6 weeks to stabilise, no other dose adjustment seems necessary.

Appendix C - Licensed administration sites, volumes, dose intervals, needle & storage requirements

Drug	Usual dose interval	Maximum single dose	Max.volume per single injection site	Needle/ syringe supplied in pack	Licensed administration sites	Needle requirements	Storage requirements
Aripiprazole	Monthly[1]	400 mg	Fixed dose	Yes	Gluteal	38 mm (1.5 inch), 22-gauge safety needle. BMI >28: 51 mm (2 inch), 21-gauge safety needle.	Room Temperature
					Deltoid	25 mm (1 inch), 23-gauge safety needle. BMI> 28: 38 mm (1.5 inch), 22-gauge safety needle.	
Flupentixol decanoate	2-4 weeks	400 mg	2 ml	No	Gluteal	Usually 21-gauge, needle length dependent on BMI/sex, see below*	Room Temperature
					Lateral thigh	Usually 21-gauge, 25 mm (1 inch) – 38 mm (1.5 inch) needle, dependent on BMI	
Haloperidol decanoate	4 weeks	300 mg	3 ml	No	Gluteal	Usually 21-gauge, needle length dependent on BMI/sex*	Room Temperature
Paliperidone palmitate (monthly – Xeplion®)	Monthly[1]	150 mg	Pre-filled syringe	Yes	Gluteal	38mm (1.5 inch), 22-gauge needle	Room Temperature
					Deltoid	Weight < 90 kg: 25mm (1 inch), 23-gauge needle Weight ≥ 90 kg: 38mm (1.5 inch), 22-gauge needle	
Paliperidone palmitate (3 monthly – Trevicta®)	3 months[1]	525 mg	Pre-filled syringe[2]	Yes	Gluteal	38mm (1.5 inch), 22-gauge needle	Room Temperature
					Deltoid	Weight < 90 kg: 25mm (1 inch), 23-gauge needle Weight ≥ 90 kg: 38mm (1.5 inch), 22-gauge needle	
Risperidone (Risperdal Consta®)	2 weeks	50 mg	Fixed dose	Yes	Gluteal	51 mm (2 inch) 20-gauge safety needle	Store in a refrigerator (2-8°C).
					Deltoid	25 mm (1 inch) 21-gauge safety needle	
Zuclopenthixol decanoate	1-4 weeks	600 mg	2 ml	No	Gluteal	Usually 21-gauge, needle length dependent on BMI/sex*	Room Temperature
					Lateral thigh	Usually 21-gauge, 25mm (1 inch) - 38mm (1.5 inch) needle, dependent on BMI	

1. Where a dose interval is specified in "months" it should be administered on the same **date** each time e.g. 28th January, then 28th February for monthly, 28th April for 3-monthly, etc; where the due date falls outside normal service hours, it should be scheduled as close to the due date as possible, within the allowed administration tolerances. (Appendix D)
2. Paliperidone 3 monthly LAI requires vigorous shaking with the tip up and a loose wrist for at least 15 seconds to ensure a homogeneous suspension prior to administration and should be administered within 5 minutes of shaking. If more than 5 minutes pass before injection, shake vigorously again for at least 15 seconds to re-suspend the medicinal product.

***Recommended needle length for gluteal injections, only where needle not supplied in manufacturers pack – (use hypodermic safety needle):**

		Ventrogluteal	Dorsogluteal
BMI < 25	Men	32mm (1.25 inch)	38mm (1.5 inch)
	Women		
BMI ≥ 25 but < 30	Men		
	Women	38mm (1.5 inch)	
BMI ≥ 30	Men	51mm (2 inch)	
	Women		

All needles and syringes used should be checked to ensure they are within their stated expiry date prior to use; the smallest possible size of syringe should be selected to accommodate the volume of product to be administered.

Please note: If an injection is not licensed for administration to the site requested by the patient, please discuss with the prescriber/pharmacy prior to administration. The rate of absorption differs at different sites, so an alternative unlicensed site may not be suitable, or a dose/administration frequency adjustment may be necessary. Patient consent must be obtained and clearly documented for any unlicensed use. The maximum volume that can be administered to each injection site is detailed below:

Site	Muscle used	Maximum Volume	Comments
Deltoid	Deltoid	Unknown (0.5-2ml in practice)	Fastest uptake
Dorsogluteal	Gluteus maximus	1-3ml	Potential for delayed uptake due to subcutaneous fat
Lateral Thigh	Vastus lateralis	1-3ml	Slower uptake than deltoid, faster than gluteal
Ventrogluteal	Gluteus medius & minimus	1-3ml	Maybe the best site for cachectic adults

Appendix D - Managing delayed or missed doses

Every effort should be made to administer doses of a depot injection on the due date. However, it is recognised this may not always be possible, e.g. due to patient non-attendance or absence from home. There may also be occasions when it is planned to give a dose early or late, e.g. if the patient is going on holiday or unavoidable service/staffing pressures exist.

In these circumstances, the tables below provide a tolerance, around the due date, within which the dose can be given without a clinically significant impact on efficacy or need for supplementary action (e.g. temporary dose adjustment). Nursing staff may administer individual doses within these tolerances without prescriber approval but must not repeatedly utilise these tolerances as this may affect long-term efficacy or tolerability.

If a missed dose cannot be given within these tolerances, refer to the guidance in the attached drug monographs with regard to supplementary action, and discuss with the prescriber – additional prescriptions may be required, e.g. a "once only" dose on the inpatient prescription chart or community depot chart. **An incident must be reported if a dose is not given within tolerances due to staff or service error.**

<table>
<tr><th rowspan="2">Drugs administered at WEEKLY dose intervals:</th><th colspan="3">Tolerances (based on usual dose interval)</th></tr>
<tr><th>Weekly</th><th>TWO Weekly</th><th>FOUR Weekly</th></tr>
<tr><td>Flupentixol Decanoate</td><td rowspan="3">+/- 2 days</td><td colspan="2">- 2 / +7 days</td></tr>
<tr><td>Haloperidol Decanoate</td><td>-2 / +6 days</td><td>-2 / +14 days</td></tr>
<tr><td>Zuclopenthixol Decanoate</td><td colspan="2">- 2 / +7 days</td></tr>
<tr><td>Risperidone
(Risperdal Consta®)</td><td></td><td>+/- 2 days</td><td></td></tr>
</table>

Drugs administered at MONTHLY dose intervals:	Tolerances (based on usual dose interval)	
	MONTHLY	THREE Monthly
Aripiprazole	26-42 days after last dose (Dose 4 onwards)[1]	
Paliperidone (MONTHLY)	+/- 7 days (Dose 3 onwards)[2]	
Paliperidone (THREE monthly)		+/- 14 days

1. Aripiprazole – 26-35 days after previous dose for doses two and three; 26-42 days after previous dose for dose four onwards.
2. Paliperidone monthly – second initiation dose can be given between 3-11 days after first dose; from third dose onwards, the dose can be given 7 days before or after due date, but the aim should be to administer as close to the due date as possible.

Appendix E - Transfers of patients between teams/settings

<table>
<tr><th rowspan="2">Transfer From:</th><th rowspan="2">Transfer To:</th><th colspan="2">Recommended Action/Advice:</th></tr>
<tr><th>Newly Initiated depot:</th><th>Existing depot:</th></tr>
<tr><td rowspan="2">In-patients</td><td rowspan="2">Community Team</td><td>Ascertain who will be initially responsible for prescribing and administering the depot in the community.
Contact the CPN / community team verbally, advise them of the upcoming transfer/discharge and invite them to the discharge planning meeting. This contact should also be documented on the electronic patient record (EPR), including the name of the community staff member spoken to, so the community team can access it easily.</td><td>Contact the CPN / community team verbally, advise of the upcoming transfer/discharge, invite them to attend the discharge planning meeting and notify them of any depot prescription changes. This contact should also be documented on electronic patient record (EPR), including the name of the community staff member spoken to, so the community team can access it easily.</td></tr>
<tr><td colspan="2">On discharge:
• Details of the depot must be documented within the electronic discharge letter (EDL) and must include drug name, dose, frequency and date & site of last administration. This must be added in the “comments” section of the medication grid on EDL.
• Date & place of the next injection should be arranged & <u>communicated to the patient</u>.
• Prior to discharge, the in-patient team must ensure arrangements to enable completion of a NEW community depot chart in time for the next dose (including obtaining depot supply) and ensure any previous depot charts are cancelled. This may be achieved by (check local arrangements):
o Sending prescription details from EPMA in an email to the generic CMHT (or CMHT pharmacy team) mailbox – marked as HIGH PRIORITY
o In-patient team writing the new depot prescription and sending to CMHT base
o Task allocation at discharge meeting where CMHT are present</td></tr>
</table>

Transfer From:	Transfer To:	Recommended Action/Advice:	
		Newly Initiated depot:	**Existing depot:**
In-patients	**Primary care**	Not applicable – newly initiated depots should be transferred to the relevant community team in the first instance who will then transfer to primary care under shared care arrangements (see below).	Only appropriate if transfer to primary care had already occurred prior to admission and there has been no change to the depot prescription during the admission. Confirmation of ongoing treatment to be communicated in discharge letter. If date of next dose is shortly after discharge, consider giving dose early (before discharge) if therapeutic window allows, or arranging administration via community team to allow discharge communication to be received by GP practice. If transfer had not occurred pre-admission, or the depot prescription has changed during admission, transfer to community team in the first instance (who will then transfer to primary care when appropriate).
Community Team	**In-patients**		If responsibility for prescribing sits with the GP, contact the relevant surgery to suspend prescription issues while the patient is in hospital. Contact the relevant in-patient unit to ensure that staff are aware of the current depot injection, dosage, and frequency which the patient should be receiving, including next due date.
Community Team A	**Community Team B**		The depot chart should be transferred from the current community team to the new community team and can continue to be used until the prescription expires (after 6 months) or is changed. A corresponding entry should be made on the electronic patient record when this has been

Transfer From:	Transfer To:	Recommended Action/Advice:	
		Newly Initiated depot:	**Existing depot:**
			completed. The current community team retains responsibility until the transfer of care has taken place.
Community Team	**Other mental health service NHS Trust**		A referral should be made, marking if urgent, clearly identifying depot medication, prescribed dosage, last date administered and next due date. The existing team retains responsibility until the transfer of care acknowledged and received.
Community Team	**Primary Care**	Not applicable – transfer should not take place until at least 3 months after initiation– see shared care agreements	Can be transferred to primary care after 3 months or once treatment is stabilised, whichever is longer. Complete drug-specific shared care request. Transfer request should be sent at least one month in advance of patient needing their first dose from GP; GP asked to respond to this request within 2 weeks. If refused, continue administration by community team. If accepted, document transfer on EPR and cancel depot chart.
Community Team	**Acute Trust**		On admission to the acute trust, the current community depot chart should be discontinued; a new chart should be written when the patient is discharged back into the community setting. The community team should ensure they maintain regular contact with the acute care team and that clear arrangements are made regarding the prescribing, supply and administration of depot injections. Contact the relevant GP surgery, if applicable, to suspend prescriptions while the patient is in hospital.

<table>
<tr><th rowspan="2">Transfer From:</th><th rowspan="2">Transfer To:</th><th colspan="2">Recommended Action/Advice:</th></tr>
<tr><th>Newly Initiated depot:</th><th>Existing depot:</th></tr>
<tr><td rowspan="2">In-patients</td><td rowspan="2">Acute Trust</td><td colspan="2">The inpatient team should ensure they maintain regular contact with the acute trust team and ensure that clear arrangements are made regarding the prescribing, supply and administration of depots:</td></tr>
<tr><td>If the patient will be returning to TEWV as an inpatient:
Maintain regular contact with the ward on which the patient is residing and prompt them when the depot is due to be administered.
When the patient returns to TEWV: a reconciliation of medication should be undertaken to ensure that the details of any depot doses administered whilst under the care of the acute trust are documented within the EPR and the date the next dose is due is transferred into the relevant places e.g. VCB etc.
If the patient is likely to be discharged directly to the community from the acute trust:
Ascertain which team will take over the depot management and advise them of the potential discharge. This should also be documented on EPR, including the name of the community staff member spoken to, so the community team can access it easily. The community team should ensure that they have all of the information they require to safely prescribe</td><td>If the patient will be returning to TEWV as an inpatient:
Maintain regular contact with the ward on which the patient is residing and prompt them when the depot is due to be administered. Contact the designated community team and advise them of the transfer. Give contact details of the hospital and ward that the patient has transferred to. Document the conversation on EPR including the name of the staff member spoken to.
When the patient returns to TEWV: a reconciliation of medication should be undertaken to ensure that the details of any depot doses administered whilst under the care of the acute trust are documented within the EPR and the date the next dose is due is transferred into the relevant places e.g. VCB etc.
If the patient is likely to be discharged directly to the community from the acute trust:
Ascertain which team will take over the depot management and advise them of the potential discharge. This should also be documented on EPR, including the name of the community staff member spoken to, so the community team can access it easily. The community team should ensure that they have all of the information they require to safely prescribe and re-start administration of the depot in the community e.g. date and site of last administered dose.</td></tr>
</table>

<table>
<tr><td rowspan="3">Transfer From:</td><td rowspan="3">Transfer To:</td><td colspan="2">Recommended Action/Advice:</td></tr>
<tr><td>Newly Initiated depot:</td><td>Existing depot:</td></tr>
<tr><td>and re-start administration of the depot in the community. e.g. date and site of last administered dose.</td><td></td></tr>
<tr><td colspan="3">On discharge from TEWV:
• Details of the depot must be documented within the electronic discharge letter (EDL) and must include drug name, dose, frequency and date & site of last administration. This must be added in the “comments” section of the medication grid on EDL.
• Date and place of the next injection should be arranged & communicated to the patient prior to discharge.
• Prior to discharge, the in-patient team must ensure arrangements to enable completion of a NEW community depot chart in time for the next dose (including obtaining depot supply) and ensure any previous depot charts are cancelled.
This may be achieved by (check local arrangements):
○ In-patient team writing the new depot prescription and sending to CMHT base
○ Task allocation at discharge meeting where CMHT are present
○ E-mail to generic CMHT (or CMHT pharmacy team) mailbox (with high priority)
○ Scanning front page of drug chart (depot section) to CMHT</td></tr>
<tr><td>Acute Trust</td><td>Community Team</td><td></td><td>The community team should maintain regular contact with the acute trust team and ensure that clear arrangements are made regarding the prescribing, supply and administration of depots for the duration of the admission when a patient has been admitted directly from the community. This should also be documented on EPR, including the name of the acute trust staff spoken to and details of the arrangements made regarding continuation of depot medication.</td></tr>
</table>

Transfer From:	Transfer To:	Recommended Action/Advice:	
		Newly Initiated depot:	**Existing depot:**
			When informed that the patient is being discharged, the community team should ensure that they have all of the information they require to safely prescribe and re-start administration of the depot in the community e.g. date and site of last administered dose.

Equality Analysis Screening Form

Please note: The Equality Analysis Policy and Equality Analysis Guidance can be found on the policy pages of the intranet

Section 1	Scope
Name of service area/directorate/department	Pharmacy
Title	Long-Acting Injectable Antipsychotics: Guidance for prescribing, administration and medicines management
Type	Guidance
Geographical area covered	Trustwide
Aims and objectives	• Ensure that patients are offered depot preparations where appropriate, in line with national guidance. • Ensure that prescribers have access to detailed prescribing information to support safe and effective prescribing of depot preparations. • Ensure that those administering depot medications have all of the relevant information available to them to enable safe administration. • Ensure that systems are in place to facilitate administration in a timely manner with appropriate documentation. • Ensure that systems are in place to facilitate safe transfer of care of patients prescribed depot preparations, when necessary and appropriate
Start date of Equality Analysis Screening	21 July 2022
End date of Equality Analysis Screening	19 Dec 2022

Section 2	Impacts
Who does the Policy, Service, Function, Strategy, Code of practice, Guidance, Project or Business plan benefit?	Prescribers, nursing staff, pharmacy staff and patients

Will the Policy, Service, Function, Strategy, Code of practice, Guidance, Project or Business plan impact negatively on any of the protected characteristic groups?	• **Race** (including Gypsy and Traveller) **NO** • **Disability** (includes physical, learning, mental health, sensory and medical disabilities) **NO** • **Sex** (Men, women and gender neutral etc.) **NO** • **Gender reassignment** (Transgender and gender identity) **NO** • **Sexual Orientation** (Lesbian, Gay, Bisexual, Heterosexual, Pansexual and Asexual etc.) **NO** • **Age** (includes, young people, older people – people of all ages) **NO** • **Religion or Belief** (includes faith groups, atheism and philosophical beliefs) **NO** • **Pregnancy and Maternity** (includes pregnancy, women who are breastfeeding and women on maternity leave) **NO** • **Marriage and Civil Partnership** (includes opposite and same sex couples who are married or civil partners) **NO** • **Armed Forces** (includes serving armed forces personnel, reservists, veterans and their families) **NO**
Describe any negative impacts	
Describe any positive impacts	This guidance makes these treatments accessible to all patients within boundaries of licensing restrictions and accepted “off-license” clinical practice

Section 3	**Research and involvement**
What sources of information have you considered? (e.g. legislation, codes of practice, best practice, nice guidelines, CQC reports or feedback etc.)	Yes – see references section
Have you engaged or consulted with service users, carers, staff and other stakeholders including people from the protected groups?	Yes

If you answered Yes above, describe the engagement and involvement that has taken place	Service user and carer representatives at Drug & Therapeutics Committee when this guidance was considered and approved
If you answered No above, describe future plans that you may have to engage and involve people from different groups	

Section 4	**Training needs**
As part of this equality analysis have any training needs/service needs been identified?	Yes
Describe any training needs for Trust staff	IM injection training as part of core student nurse training In-house e-learning on injection awareness (3-yearly)
Describe any training needs for patients	No
Describe any training needs for contractors or other outside agencies	No

Check the information you have provided and ensure additional evidence can be provided if asked

Approval checklist

To be completed by lead and attached to any document which guides practice when submitted to the appropriate committee/group for consideration and approval.

	Title of document being reviewed:	Yes/No/ Not applicable	Comments
1.	**Title**		
	Is the title clear and unambiguous?	Y	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Y	
2.	**Rationale**		
	Are reasons for development of the document stated?	Y	
3.	**Development Process**		
	Are people involved in the development identified?	Y	
	Has relevant expertise has been sought/used?	Y	
	Is there evidence of consultation with stakeholders and users?	Y	
	Have any related documents or documents that are impacted by this change been identified and updated?	Y	
4.	**Content**		
	Is the objective of the document clear?	Y	
	Is the target population clear and unambiguous?	Y	
	Are the intended outcomes described?	Y	
	Are the statements clear and unambiguous?	Y	
5.	**Evidence Base**		
	Is the type of evidence to support the document identified explicitly?	Y	
	Are key references cited?	Y	
	Are supporting documents referenced?	Y	
6.	**Training**		
	Have training needs been considered?	Y	
	Are training needs included in the document?	Y	

	Title of document being reviewed:	Yes/No/ Not applicable	Comments
7.	**Implementation and monitoring**		
	Does the document identify how it will be implemented and monitored?	Y	
8.	**Equality analysis**		
	Has an equality analysis been completed for the document?	Y	
	Have Equality and Diversity reviewed and approved the equality analysis?	N	
9.	**Approval**		
	Does the document identify which committee/group will approve it?	Y	
10.	**Publication**		
	Has the document been reviewed for harm?	Y	
	Does the document identify whether it is private or public?	Y	public
	If private, does the document identify which clause of the Freedom of Information Act 2000 applies?	N/A	