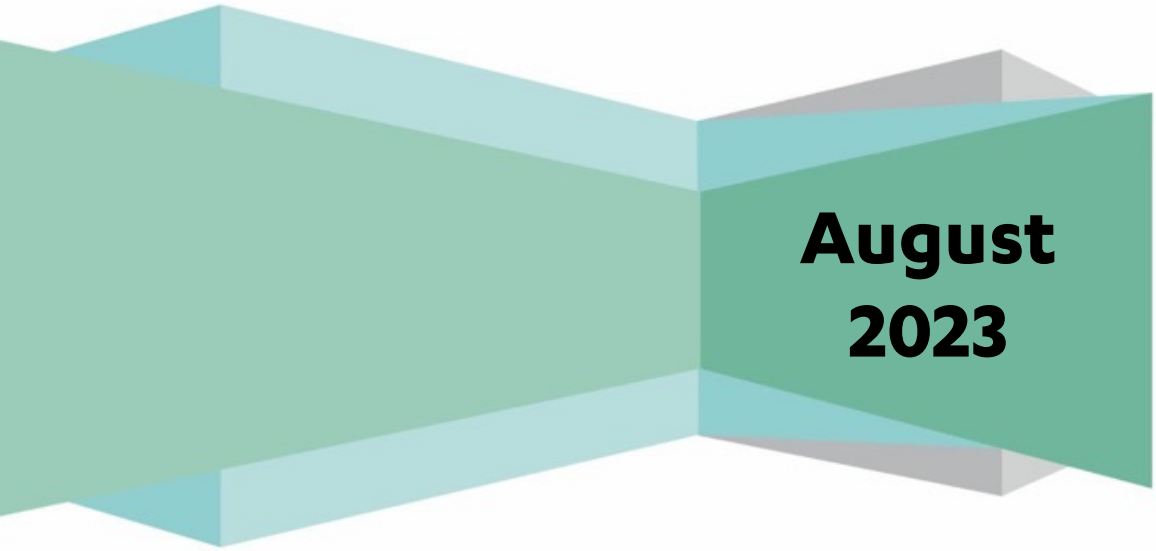
Guidance on the Administration to Adults of Oil-based Depot and other Long-acting Intramuscular Antipsychotic Injections

7th Edition



Janssen commissioned this guidance and also met its publication costs

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For further details on dosing and intramuscular administration of specific agents please refer to the relevant Summary of Product Characteristics (SmPC)

Guidance on the Administration to Adults of Oil-based Depot and other Long-Acting Intramuscular Antipsychotic Injections.

Appendix 1 of this document contains Six Standard Operating Procedures (SOPs) for the administration to adults of oil-based depot and other long-acting antipsychotic injections: These may be copied and used by an organisation or healthcare professional

SOP 1. General Preparation for Deep Intramuscular (IM) Injection

SOP 2. Z-track Administration Technique

SOP 3. Deltoid Administration Technique

SOP 4. Dorsogluteal Administration Technique

SOP 5. Ventrogluteal Administration Technique

SOP 6. Vastus Lateralis Administration Technique

This document may be downloaded from the following websites:

College of Mental Health Pharmacy www.cmhp.org.uk
'Reach 4 Resource' www.reach4resource.co.uk

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Target Audience	Clinicians working for NHS and Independent Mental Health Service Providers
Description	This document sets out evidence-based guidance on the administration to adults of oil-based depot and other long-acting intramuscular antipsychotic injections which may be adopted by healthcare professionals as a framework for best practice
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Disclaimer: Always refer to the most up to date information by consulting the latest published approved Summary of Product Characteristics [SmPC] for any individual product.

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1. Scope of this Guidance

1.1 Injection technique is traditionally based on practice which is underpinned by evidence from expert opinion and clinical experience. It is then disseminated by modelling the technique to subsequent generations of clinicians. This is a much lower level of evidence than that normally required to demonstrate the efficacy of an intervention or technique such as by a randomised controlled trial (RCT). The best quality evidence is obtained from primary research where rigorous methodological and ethical standards are applied to confirm or refute cause and effect. Within primary research the level of evidence varies from well-conducted and adequately powered RCTs to evidence from uncontrolled (naturalistic or observational) studies and/or published case reports or series. This guidance has been produced following an extensive and systematic review of the literature and provides references to the primary research where this is available. There is, however, a paucity of good-quality evidence for some of the issues considered and where this is the case this is reflected in the guidance.

1.2 This guidance provides a flexible framework within which clinicians working for mental health service providers in the UK may consider their own clinical policies; it supports how these may be adapted locally to further enhance the safe administration of oil-based depot and other long-acting intramuscular antipsychotic injections.

1.3 This guidance takes into account the requirement of the Care Quality Commission for clinicians to continue to provide evidence of safe practice in the care of their patients.[1]

1.4 This guidance provides a framework for clinical quality standards in harmony with the provision of information for NHS Resolution,[2] the Care Quality Commission[1] and the pledges made by the NHS Constitution.[3]

1.5 The framework is intended to enhance governance arrangements for upholding the professional code of practice of the Nursing and Midwifery Council (NMC),[4] the professional guidance on the administration of medicines in healthcare settings by the Royal Pharmaceutical Society (RPS) and Royal College of Nursing (RCN),[5] and the recommendations from the National Patient Safety Agency (NPSA, now NHS Improvement).[6]

1.6 This guidance is intended to support culture change for safer patient care by providing information on service improvement that can be harnessed and used collectively in a coordinated way by organisations. It can be used as a catalyst for nurse leaders to inspire, prepare and equip nurses with defined technical skills and competencies for the procedure.

2. Guiding Principles

This document is underpinned by the following principles:

2.1 The need for clinical competence in order to reduce the risks associated with human error and provide safe care through systematic and meticulous practice.

2.2 The requirement for a clinically driven national resource derived from the current evidence base to support local practitioners. This includes adherence to the principles of guidance from the NPSA (now NHS Improvement).[6]

2.3 The opportunity to offer the experienced practitioner a flexible framework within which they may make appropriate clinical judgments.

2.4 The need to manage the care of those with long-term conditions appropriately.

2.5 The requirement to provide information that is accessible to patients and carers as well as to clinicians.

2.6 The need to contribute to enhanced treatment choice, and the right of an individual to be offered a choice of antipsychotic and its formulation where alternatives exist.

2.7 The recognition of an individual's right to be offered a choice of injection site for the administration of a long-acting intramuscular antipsychotic injection where the licence permits.

2.8 The need to influence public perception and diminish notions of coercion and stigma associated with the use of such injections, particularly in the context of mental health legislation.

2.9 The necessity to preserve the dignity of and respect for the patient, by the promotion of good practice in the administration of oil-based depot and other long-acting intramuscular antipsychotic injections.

3. Introduction and Background

3.1 Oil-based depot and other long-acting intramuscular antipsychotic injections are key interventions for a significant number of people in the recovery phase of a severe and enduring mental illness such as schizophrenia.[7,8] In 2009 it was reported that between 29% and 30% of patients with schizophrenia in the UK were prescribed a long-acting injectable antipsychotic.[9]

3.2 Long-acting antipsychotic injections should be considered for people with psychosis or schizophrenia who would prefer such a formulation after an acute episode or where avoiding covert non-adherence (either intentional or unintentional) to oral antipsychotic medicines is a clinical priority within the treatment plan.[7,8]

3.3 First generation antipsychotics are more often associated with extrapyramidal side effects and a higher risk of tardive dyskinesia than second generation antipsychotics.[7,8] This risk of adverse effects and the associated stigma have previously influenced treatment choice in favour of an oral second generation rather than a long-acting first-generation formulation. The availability of long-acting intramuscular second-generation antipsychotic injections now means that choosing a long-acting intramuscular formulation does not automatically mean treatment with a first-generation antipsychotic.

3.4 Medicines optimisation is an individualised person-centred approach to the use of medicines that involves engaging with patients to get their medicines right for them. It ensures the best possible outcomes by minimising risk and maximising benefit using evidence-based decision making. It requires effective patient engagement and professional collaboration.[10] The treatment of schizophrenia may be optimised by[7,8]

- offering a choice of treatments
- prescribing an effective, optimum dose for an appropriate period of time before considering a dose change or switch
- providing adherence support regularly and frequently
- offering a long-acting injectable antipsychotic
- ensuring physical health is not compromised further

3.5 The safe administration of oil-based depot and other long-acting intramuscular antipsychotic injections is an integral part of the work of registered practitioners in mental health care. Errors can be minimised through the application of a framework such as this guidance that identifies the technical competency required for all aspects of the procedure.

4. Oil-based Depot Injections: Test Dose Calculation

4.1 Oil-based depot antipsychotic injections are all licensed to be given by deep intramuscular injection into the gluteal muscle at intervals of one to four weeks. Some (flupentixol and zuclopenthixol*) are also licensed to be given into the lateral thigh (vastus lateralis) (see Appendix 2). They all have a similar licensed indication, which is for the maintenance treatment of schizophrenia and other psychoses.[11,12]

4.2 For these oil-based depot antipsychotic injections, a small test dose of the injection must be given before the full treatment schedule is initiated. This is to confirm tolerability to both the active ingredient as well as the oily vehicle, since any adverse effect will be prolonged.[11,12]

4.3 Full details of test doses for the oil-based depot injections are given in each individual Summary of Product Characteristics (SmPC)[11] and in the British National Formulary (BNF).[12] Treatment may normally be initiated four to seven days after a successful test dose.[11,12]

4.4 A calculation may be necessary to work out the injection volume required for a test dose.

Example: The test dose of fluphenazine decanoate for an adult is 12.5 mg.[25] The smallest dose/volume available of fluphenazine decanoate is 0.5 ml ampoules containing 12.5 mg in 0.5 ml. The test dose for an adult is therefore 0.5 ml. If, however, only the 25 mg in 1 ml ampoule was available, the test dose would be 25 mg (1 ml) divided by 2 which equates to 0.5 ml of the 25 mg in 1 ml strength.

See Appendix 6: Dose Calculation Workbook

*See prescribing information for further details on both named products.

5. Other Long-Acting Intramuscular Antipsychotic Injections

5.1 Aripiprazole long acting injection[14] is licensed for the maintenance treatment of schizophrenia in adults stabilised with oral aripiprazole. It is presented as a polymer of aripiprazole monohydrate, a dry powder for reconstitution and suspension in the solvent supplied (water for injection). Separate vials containing the 300 mg and 400 mg doses are available. Pre-filled syringes are also available to save reconstitution.

Aripiprazole long-acting injection may be injected into either the gluteal or the deltoid muscle from where the active moiety is slowly released into the circulation. Maximum plasma concentration is achieved at a median T_{max} of 7 days after gluteal muscle injection and 4 days after deltoid muscle injection. Doses must not be divided; the suspension should be injected slowly as a single injection. The elimination half-life ($t_{½}$) is 29.9 days for a 300 mg dose and 46.5 days for a 400 mg dose when administered monthly as recommended. Steady state is attained by the fourth injection. It should be stored at room temperature. Tolerability to oral aripiprazole should be established prior to initiating the injection in any patient naïve to aripiprazole.

The recommended starting and maintenance dose is 400 mg administered once-monthly (no sooner than 26 days after the previous injection). Initial dose titration is not required but there is choice of start regime, both which ensure therapeutic plasma concentrations are maintained during initiation of therapy: In the "one injection start" regime one 400 mg injection of aripiprazole long-acting injection is administered alongside 10 mg to 20 mg oral aripiprazole which is then continued one a day for 14 consecutive days and then stopped. In the second "two injection start" regime two separate injections of 400mg aripiprazole long-acting injection are administered at separate injection sites (into different muscles), alongside administration of one 20mg dose of oral aripiprazole. Ongoing supplementation with oral aripiprazole is not required. If there are adverse reactions with the 400 mg dosage, a reduction to 300 mg once monthly should be considered.

5.2 Olanzapine long acting injection[15] consists of olanzapine pamoate monohydrate powder together with a solvent which when combined form a prolonged release suspension for deep intramuscular gluteal injection. Vials containing olanzapine pamoate monohydrate equivalent to 210 mg. 210 mg, 300 mg and 405 mg of olanzapine are available which, when reconstituted as directed, contain 150 mg olanzapine per ml. Whilst a test dose is not required, patients should have been successfully treated with oral olanzapine before receiving the long-acting injection in order to establish tolerability and response. The release characteristics of olanzapine long-acting injection are not dissimilar to those of the first-generation oil-based depots. There is an early initial release of active antipsychotic after administration. This is in contrast to risperidone long-acting injection (see Section 5.4).

After each injection, patients must be observed for post-injection syndrome (signs and symptoms consistent with olanzapine overdose) in a healthcare facility by appropriately qualified personnel for at least 3 hours (see the SmPC for full details).

5.3 Paliperidone palmitate 1 monthly long acting injection[16] is the palmitate ester of paliperidone formulated as nanoparticles suspended in an aqueous solution. These nanoparticles dissolve very slowly from the injection site before being hydrolysed to paliperidone and absorbed into the systemic circulation. This extended period of time for release allows for monthly dosing. Release of the active substance starts as early as day 1, gradually rises to reach maximum plasma concentrations at a median T_{max} of 13 days and lasts for at least 4 months.

Paliperidone palmitate 1 monthly is licensed for the maintenance treatment of schizophrenia in adult patients stabilised with oral paliperidone or risperidone. It may also be used in patients who are not currently on risperidone or paliperidone but who have responded to them in the past (as long as they are not acutely agitated and only have mild to moderate psychotic symptoms). This latter part of the licence allows the use of paliperidone palmitate in selected patients in the acute setting. A test dose is not required but response and tolerability to either oral risperidone or paliperidone must have been established prior to commencing treatment.

Paliperidone palmitate 1 monthly LAI is available in four dose strengths, 50 mg/ml, 75 mg/ml, 100 mg/ml and 150 mg/ml, all presented in pre-filled syringes. To attain therapeutic plasma levels as rapidly as possible, the first two doses (150 mg and 100 mg) must be administered into the deltoid muscle 7 days apart (± 4 days). Following this initial titration period, monthly dosing should commence using either the deltoid or dorsogluteal site. There are special requirements regarding needle selection from the pack for deltoid injection in patients who weigh ≥90 kg. (See Section 14.9)

5.4 Paliperidone palmitate 3-monthly long-acting injection.[17] It is indicated for the maintenance treatment of schizophrenia in adult patients who have been clinically stable on 1-monthly paliperidone palmitate long-acting injection, preferably for 4 months or more and who do not require dose adjustment. This allows selected patients to maintain an optimal plasma level of antipsychotic with fewer administrations. It is available in pre-filled syringes containing 175 mg, 263 mg, 350 mg or 525 mg prolonged-release suspension of paliperidone for injection.

This 3-monthly injection should be initiated in place of the next scheduled dose of 1-monthly paliperidone palmitate long-acting injection. The dose should be based on the previous 1-monthly paliperidone dose using a 3.5-fold higher dose. A dosing table is available in the SmPC.[17]

Following initiation, it should be administered by intramuscular injection once every 3 months (± 2 weeks). If needed, dose adjustment can be made every 3 months in increments within the range of 175 mg to 525 mg based on individual patient tolerability and/or efficacy. Due to the long-acting nature of this formulation, 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.

5.5 Paliperidone 6-monthly injection[18] is indicated for the maintenance treatment of schizophrenia in adult patients who have been clinically stable on 1-monthly paliperidone palmitate injection at doses of 100 mg or 150 mg or 3-monthly paliperidone palmitate long-acting injection at doses of 350 mg or 525 mg, and in those patients who do not require dose adjustment. Patients should preferably have been clinically stable for four months or more for those treated with the 1-monthly injection, and for at least one injection cycle for those receiving the 3-monthly injection

The 6-monthly injection is administered in place of the next scheduled dose of the 1-monthly injection (± 7 days) or the 3-monthly injection (±14 days). 700mg and 1000mg prolonged release suspension for injection are available and the SmPC includes tables to illustrate the correct dose when transitioning from the different doses and injection frequency types.

Following the initial dose, the injection is administered every 6-months and if necessary, up to 2 weeks before or up to 3 weeks after the 6-month timepoint. If needed dose adjustment can be made every 6-months between the dose levels of 700 mg and 100 mg based on individual patient tolerability and/or efficacy. Due to its long-acting nature the patient's response to an adjusted dose may not be apparent for several months. If the patient remains or becomes symptomatic, they should be managed according to clinical practice.

5.6 Risperidone long-acting injection (RLAI)[13] consists of risperidone encapsulated in microspheres of a biodegradable polymer which, after reconstitution are suspended in an aqueous vehicle. Vials are available containing 25 mg, 37.5 mg and 50 mg risperidone. It is licensed for the maintenance treatment of schizophrenia in patients currently stabilised with oral antipsychotics.

A test dose is not required. Instead, response and tolerability should normally be confirmed by a previous course of oral risperidone. In those patients who have already demonstrated a response to risperidone, the effective oral dose is used as a guide to the initial intramuscular dose.

Note: Therapeutic plasma levels of risperidone will not normally be achieved until 3-4 weeks after the first injection.[13] This means that it will not begin to exert a significant clinical effect before the third injection has been given. Patients should, if possible, continue to take oral risperidone (or in exceptional cases their previous oral antipsychotic) for at least 3 weeks after receiving the first dose of risperidone long-acting injection. This also means that at least 3 injections of a particular dose must be given before increasing that dose. This contrasts with traditional depots where peak plasma levels are achieved between 3 and 5 days following the first administration.

5.7 Risperidone ISM is a powder and solvent for prolonged-release suspension for intramuscular injection. The contents of two pre-filled syringes containing the active drug within a biodegradable polymer as a powder for reconstitution, and a water-soluble solvent are mixed vigorously together to form a suspension which is then administered intramuscularly into either the deltoid or gluteal muscle. After administration, the product's polymeric component precipitates in situ, forming an implant containing risperidone trapped in a polymeric matrix, which biodegrades to provide sustained release for up to one month.[19] Pre-filled syringes are available containing 75mg or 100 mg risperidone. It is indicated for the treatment of schizophrenia in adults for whom tolerability and effectiveness have been established with oral risperidone.

A test dose is not required, response and tolerability must be confirmed by a previous course of oral risperidone. Patients who are currently stabilised on an oral risperidone (mild to moderate symptoms) do not require titration when switching to Risperidone ISM. Patients who are currently stabilised on other oral antipsychotics (not risperidone) but with a history of a previous response to risperidone will require a period of treatment with oral risperidone before initiating treatment with Risperidone ISM. The titration period must be long enough to confirm tolerability and responsiveness to oral risperidone (at least 6 days). For patients who have never been treated with risperidone the tolerability and responsiveness to risperidone must be confirmed with a period of oral risperidone treatment before initiating treatment with Risperidone ISM. The duration of the titration period in risperidone naive patients is recommended to be at least 14 days. Once a response to oral risperidone has been established, the effective oral dose is used as a guide to the initial intramuscular dose which must be initiated approximately 24 hours after the last oral risperidone dose. A dosing table is available in the SmPC.[20]

When switching from patients who have been stabilised on risperidone bi-weekly injection Risperidone ISM should be initiated in place of the next scheduled injection of the risperidone bi-weekly formulation (at two weeks) and then continued every 28 days. The recommended dose to maintain a similar moiety steady-state exposure is available in the SmPC.[20]

Risperidone ISM can be administered into either the deltoid or gluteal muscle and the appropriate needle for the muscle chosen should be selected from the manufacturer's pack i.e., a 1" needle is provided for a deltoid injection, or a 2" needle for gluteal injection.

Following initiation, Risperidone ISM should be administered every 28 days by intramuscular injection and dose adjustments can be made every 28 days according to patient's clinical response and tolerability. 75 mg every 28 days is the generally recommended maintenance dose. Supplemental oral risperidone is not recommended. If the patient remains symptomatic, they should be managed according to clinical practice.

Care should be taken to avoid missed doses because during the first week of a missed dose the median trough concentration of Risperidone ISM decreases by approximately 50%.[20] Risperidone ISM can be administered up to 3 days before the scheduled next dose to avoid a missed dose if the patient is not going to be able to attend their scheduled appointment. If a dose is delayed the injection should be administered as soon as possible and the next injection scheduled according to this last injection date.

The prolonged release characteristics of Risperidone ISM must also be considered when switching to another antipsychotic. For example, when switching to oral risperidone it is recommended to start the oral risperidone 28 days after the last Risperidone ISM injection.

5.8 Long-acting intramuscular antipsychotic injections in phase 3 trials

This section includes products not licenced in the UK at time of preparing this document. Unlicenced medicines can be prescribed when clinical need cannot be met by licensed medicines. In these circumstances the prescriber must justify the use of the medicine and support their decision to prescribe with appropriate evidence and experience.[21] Information about the unlicensed status of the medicine being considered should be included in the information exchanged with the patient and their carers as part of the documented shared decision and consent process. Always refer to the SmPC once available.

Long-acting formulations of aripiprazole in phase 3 trials[22] include an extended-release pro-drug for intramuscular administration using NanoCrystal® technology, and a second formulation that uses a nano-crystalline milled dispersion of the same pro-drug to increase bioavailability when initiating treatment. **Aripiprazole lauroxil** is available in four strengths to be administered at monthly, 6-weekly, or two-monthly intervals into the deltoid or gluteal muscle (depending on the dose administered). Aripiprazole lauroxil requires supplementation with oral aripiprazole for the first 21 days of treatment. **Aristada Inito** is designed for initiation of an aripiprazole long-acting injection regime without the need for oral aripiprazole supplementation, it should not be used for repeat dosing.

6. Advantages and Disadvantages of Depot and other Long- Acting Intramuscular Antipsychotic Injections

6.1 Premature discontinuation of oral antipsychotics is common in patients with schizophrenia and is a frequent cause of relapse.[23-28] Long-acting oil-based depot intramuscular antipsychotic injections were originally developed to improve and support treatment adherence and reduce the relapse rate in this population.[26,28]

6.2 Advantages of depot and other long-acting antipsychotic injections from a healthcare professional's perspective include:

- Reduced necessity for tablets or capsules to be taken on a daily basis.
- Reduced uncertainty about the amount of medicine taken or not taken.
- No influence of first-pass metabolism thus improved bioavailability.
- More consistent delivery of antipsychotic with more stable plasma levels over time which can minimise side effects and reduce variations in symptom control.
- A wider window of opportunity to re-engage assertively with a patient if they refuse an injection as plasma levels take longer to decline after the last dose than with oral formulations.
- Earlier detection of non-adherence which can be followed up quickly, resulting in potentially reduced relapse rates, leading to better outcomes.
- Possibly reduced risk of admission with potential resultant cost savings.
- Potentially reduced need for repeat prescriptions since the dosing interval of such formulations can be up to 6-monthly depending on the product. This may also lead to cost savings.
- Longer intervals between administration can reduce the need for frequent clinical appointments which could be beneficial to patient employment, travel and holidays and enable more clinical time to be allocated to psychosocial interventions.
- Reduced risk of accidental or deliberate self-harm through overdose.
- The potential to enhance the therapeutic relationship and partnership working with the patient and their carers (if appropriate) by the regular frequent contact required.

6.3 Disadvantages of depot and other long-acting antipsychotic injections from a healthcare professional's perspective include:

- Pain, erythema, swelling at the site of injection as well as nodule formation, particularly with oil-based injections.
- Risk of damage to nerves, arteries or veins.
- If side effects occur, they will be prolonged until the plasma level falls.
- There may be an allergy to an oily vehicle; hence the necessity for a test dose of the oil-based depot formulations.
- The need to confirm efficacy of, and tolerability to, the oral formulations of the non-oil- based long-acting injections where required and practical.
- It can take several weeks for plasma levels to reach steady state.
- Injection technique competence, assessment and training are required.
- Potential logistical difficulties which may arise from the need to administer an injection to a patient who is in employment.
- The requirement to attend a traditional 'depot clinic' may be considered stigmatising by some but research has highlighted the opposite may be true, with patients valuing contact with other patients and staff as well as the medication management interventions available to them there.[28,29]
- Some people have a dislike or even a phobia of needles.
- Social embarrassment and the need for chaperoning and gender matching depending on patient preference and the choice of injection sites available within the product license.
- Staffing and medicine storage issues.
- The fact that depot injections have been viewed by some as stigmatising and coercive.

6.4 Healthcare professionals' perceptions of the advantages and disadvantages of these formulations may differ from those of patients. When considering the choice of treatment, patient opinion should be sought and taken into account.[28,29]

6.5 Advantages of depot and other long-acting injections from a patient perspective:

- You don't have to remember to take your medicines every day.
- You don't have to worry about family or others reminding you to take your medicine.
- You don't have to worry about accidentally forgetting to take your medicine.
- Injections may be a better way of ensuring that you get the medicine you need to keep you well than tablets or capsules.
- Tablets and capsules can serve as a daily reminder that 'You are ill'.
- Injections can be given every 1 to 6 weeks and allow you more freedom to get on with your life and put your illness behind you.
- Injection clinics can be a source of social interaction for some people – and there may also be educational material available there.
- If you forget to go for your injection, someone will remind you.
- You may have fewer side effects with an injection (because the levels in the blood don't go up and down so much).
- You don't have to remember to take your medicines with you if you go away for a short holiday.

6.6 Disadvantages of depot and other long-acting injections from a patient perspective:

- Some people don't like needles.
- You have to expose your buttocks, thigh, or shoulder – this may be embarrassing.
- You may have to wait around until the nurse finds a chaperone.
- The injection might be painful, and the injection site may be sore afterwards.
- Some people develop nodules or lumps at the site of the injection.
- Some people can get nerve damage if the injection is given badly or at the wrong site.
- If side effects occur, they may persist for several weeks after the injection is stopped.
- Some feel that an injection stigmatises them or that they are being forced to have treatment against their will.

6.7 Preventing relapse is essential not only because a relapse in schizophrenia is costly but also because relapse duration and treatment intensity have been associated with tissue loss in some brain regions together with changes in ventricular volume.[30]

High-quality evidence to support a positive effect of long-acting injectable antipsychotics on adherence and the prevention of relapse has been sparse. Only a small benefit over oral therapy has been demonstrated in randomised controlled trials.[31] One of the problems may be that clinical trial design investigating this area is inappropriate and creates a bias against the long-acting injectable formulation.[32] In a systematic review and meta-analysis of long- term studies however, long-acting injectable antipsychotics reduced relapse rates for outpatients with schizophrenia from an average of 33.2% to 21.5%. This represents a 10% absolute and a 30% relative risk reduction for relapse.[33]

A nationwide cohort study from Finland also concluded that the use of long acting formulations was associated with a significantly lower risk of re-hospitalisation than oral formulations of the same antipsychotic.[34] A meta-analysis of mirror image studies subsequently confirmed that long-acting antipsychotic injections reduce both the risk of hospital admission as well as the number of admissions compared to oral antipsychotics.[35] Such studies where patients act as their own controls compare periods of oral antipsychotic treatment with treatment with long- acting injectable formulations of the same antipsychotic in the same patient for similar periods. They are considered a better paradigm than randomised-controlled trials for such comparisons as they may better reflect the real-world impact of long-acting injectable formulations.[35]

7. Safer Care through Risk Management

7.1 Patient safety is always the highest priority.

7.2 There is a body of evidence that demonstrates the contribution of human factors as well as system failures to patient harm.[36] This guidance is designed to minimise the risk of human error through the encouragement of systematic, safe practice.

7.3 When an injection is to be given, it is best practice to have a second registered practitioner available to double check at every stage of the procedure.[6] However, this is not always possible in a community setting. In such circumstances, it would be deemed good practice for the patient or carer if appropriate to act as second checker with a record of this in the clinical notes.

7.4 If at any time a registered practitioner has any concerns during a double check, the procedure must be stopped and a review must take place in discussion with the second-check registered practitioner.[5,6]

7.5 All untoward events, including where a patient experiences an adverse event associated with a specific product, must be reported and recorded in accordance with the local risk- management and untoward-incident-reporting procedures. Local policy will determine how all such untoward events are reported including through the UK Medicines and Healthcare products Regulatory Agency (MHRA) Yellow Card Scheme.[37]

7.6 A registered practitioner who is undertaking the administration of a depot or other long-acting intramuscular antipsychotic injection must have:[4,5]

- knowledge and understanding of the legislation, regulation and guidance applicable to the procedure
- knowledge of the therapeutic use, normal dosage, side effects, precautions and contraindications of the injection being administered
- competence in the technical performance of the procedure to ensure nothing is overlooked during the preparation, administration and following the procedure
- an individual responsibility to keep knowledge and skills up to date and only work within the limits of their competence
- the ability to apply a human factor risk reduction methodology to their practice to minimise any harm to the patient before, during and after the procedure
- compassion and respect for the patient and they must pay attention to their dignity

7.7 During transit of certain injections, material may accumulate in the top or bottom of an ampoule. This can be dislodged by gently tapping it before opening or by holding the top of the ampoule and swinging the arm in a large arc.

Caution must be exercised when opening glass ampoules.

There are two main types of ampoule (see diagrams on the opposite page):

- Spot ampoules – always break away from the spot.
- Ring cut ampoules – can be broken in any direction.

The technique for opening each of these is shown below.

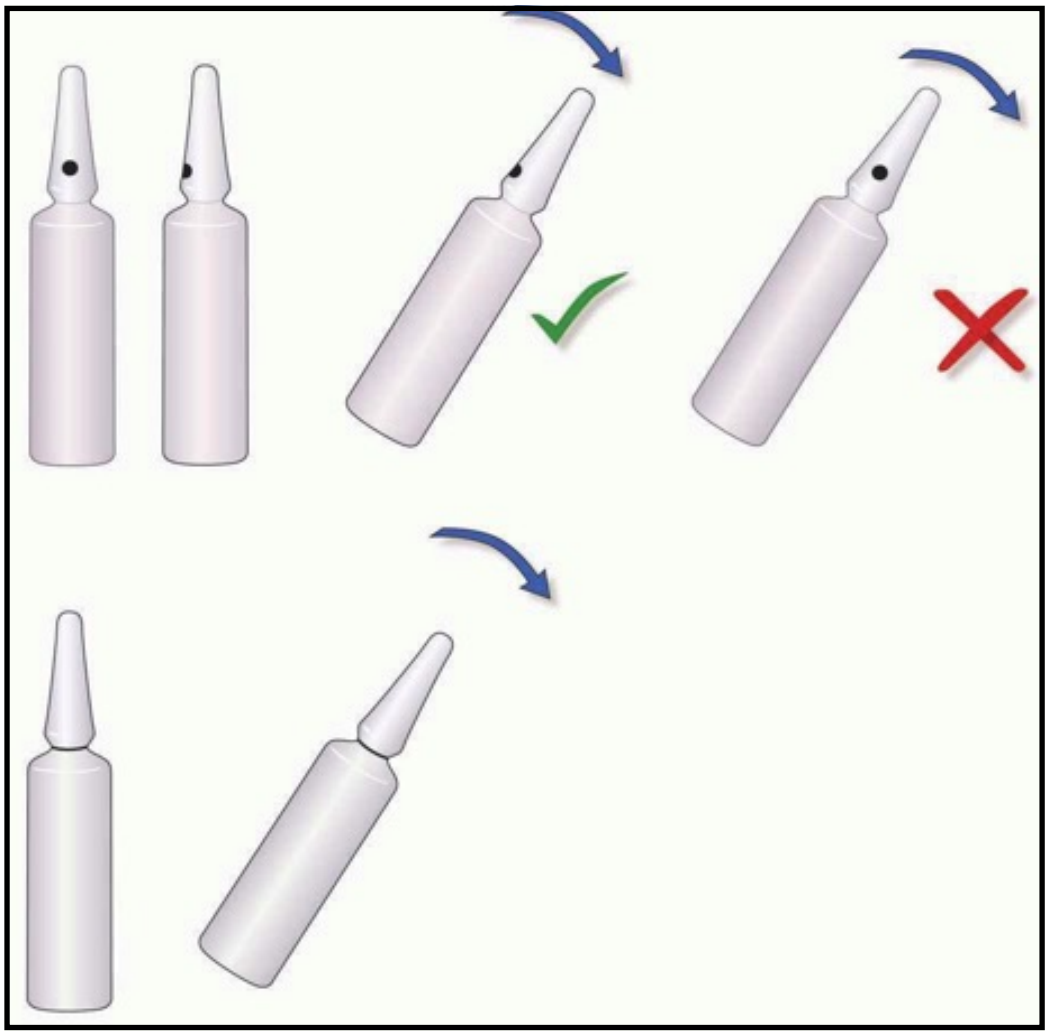

Figure 1

Ring cut ampoules are more likely to shatter than spot ampoules.

Historically, spot ampoule technology preceded ring-cut ampoule technology, but manufacturers are returning to it.

8. The Patient Experience

8.1 Registered practitioners have a responsibility to consider the potential stigma associated with the diagnosis and treatment of a mental illness. They should provide information to support the patient and their carers and encourage them, together with the general public, to engender a positive, balanced attitude. The environment in which it is planned to administer the medicine and exchange information can influence the perception of a good patient experience.[38,39]

8.2 An oil-based depot or other long-acting antipsychotic injection should be offered to anyone who expresses a preference for such a formulation even after an acute episode or when the need to avoid covert non-adherence (either intentional or unintentional) is a clinical priority.[7,8]

8.3 The choice and formulation of antipsychotic should be a joint decision between the patient and their clinician taking into consideration the risks and benefits of the treatment including the relative potential of individual antipsychotics to cause side effects such as extrapyramidal side effects (EPS) and metabolic side effects, including weight gain.[7,8]

8.4 When starting an oil-based depot or other long-acting intramuscular antipsychotic injection the preferences and attitude of the patient towards regular intramuscular injections and the intended environment for such administration, for example in the home or the location of clinics, must be considered and recorded.[7]

8.5 Where, according to the product licence, a choice of injection site exists, the patient should, if possible, be offered that choice. The risks and benefits of each potential administration site should be discussed compassionately with the patient with particular reference to dignity issues and the environment in which the administration will take place. The practitioner may like to discuss some or all of the following with the patient:

- They may not have to take off as much clothing which may be less embarrassing, more
- respectful and less anxiety-provoking especially if they have sexual delusions or where cultural and/or religious issues must be considered
- They may not have to worry so much about what to wear to have the injection
- They may find it easier to talk to the doctor or nurse if they don't have to expose themselves
- Where a choice of injection site exists, offering that choice may improve trust and thus the therapeutic relationship
- A choice of site allows for more extensive rotation, therefore more time for recovery of the
- site between injections and fewer long-term injection site complications
- Some injection sites may be perceived as less stigmatising than others
- There may be more potential for face-to-face contact with their nurse and the whole process may be less impersonal
- Such choice may help to improve adherence
- Many injections are given via sites other than the dorsogluteal site and by making the process more akin to a general medical process, the stigma associated with antipsychotic injections may be reduced

8.6 The availability of three long-acting intramuscular antipsychotic injections licensed to be given at the deltoid site (risperidone, paliperidone and aripiprazole) requires both confidence and competence on the part of the registered practitioner to describe this choice to the patient and if it is their first administration, confidence on the part of the patient in accepting treatment in this manner.

9. Patient Choice and Shared Decision Making

9.1 Choice is about the power to make decisions; it gives people more control over their lives. Decisions can be made entirely by another person or a team which can be appropriate if no decision places the individual or others at risk, or if the patient requests others to make the decision for them. Sometimes people prefer decisions to be made by those they perceive to be more knowledgeable than they are.

9.2 In contrast, a shared decision is where the healthcare professional (and/or team) and the individual patient pool their knowledge and understanding of what is needed to allow them to come to a joint decision. In this situation the decision follows an exchange of information where all viewpoints are expressed, listened to and respected, questions are answered, and additional information sought and provided where required.

9.3 The patient must be able to consider and weigh up the information provided in order to arrive at a decision as to whether or not to proceed with an oil-based depot or another long- acting antipsychotic injection and they must be able to retain the key points of any discussion with the registered practitioner and communicate this decision back to them.

9.4 There are many factors that the patient will wish to consider and all of these should be thoroughly explored in a person centred manner with the clinical team together with the legal responsibilities that registered practitioners have in England and Wales in accordance with the Mental Health Act 2007[40] and Mental Capacity Act 2005,[41] and in Scotland in accordance with the Mental Health (Care and Treatment) (Scotland) Act 2003,[42] as well as the Adults with Incapacity (Scotland) Act 2000[43] and in Northern Ireland in line with any relevant legislative and good practice guidance.

9.5 Patient choice may be facilitated by accessing the Choice and Medication website via your organisation's subscription at: https://www.choiceandmedication.org. As well as a series of frequently asked questions about mental illnesses and their treatment, there are 'handy charts' to enable the comparison of treatments, including oil-based depots and other long-acting intramuscular antipsychotic injections. This site is designed for use by patients, carers and professionals alike.

9.6 This process of coming to a shared decision is also called concordance, in contrast to adherence which is medicine-taking behaviour.[44] Pragmatic models and frameworks to support the shared decision-making process include the Elicit-Provide-Elicit model[45] and the recommendations made by NICE for patient decision aids used in consultations involving medicines, covered in NICE Guideline NG5.[10]

10. Switching Antipsychotics

10.1 Sometimes it is deemed appropriate to change or switch an antipsychotic in order to achieve a better outcome for an individual patient. This may be due to lack of efficacy, intolerable side effects, poor adherence, physical health issues or patient choice.

10.2 Such a switch may be between oral antipsychotics, long-acting injectable antipsychotics, or from an oral to a long-acting injectable antipsychotic formulation or vice versa.

10.3 Key objectives when switching antipsychotics include the need to minimise risk to mental stability as well as any possible adverse effects. All potential problems should be anticipated and detailed in a comprehensive management plan. Most importantly, the switch must be completed to avoid unnecessary polypharmacy/polyprescribing.

10.4 The pharmacokinetic and pharmacodynamic profiles of both antipsychotics involved must inform the switching strategy. This will enable successful titration and dosing by allowing the prediction and thus avoidance of possible problems such as adverse effects or withdrawal symptoms.

10.5 Differences in elimination half-lives ($t_{1/2}$) and peak plasma concentrations (C_{max}) lead to different plasma profiles. The elimination half-life of an antipsychotic normally determines its dosing regimen. It is the time taken for the plasma concentration to fall by half its original value. For oral formulations it takes approximately five half-lives to reach steady state. It takes the same time for an oral antipsychotic to disappear from the plasma when it is discontinued at steady state.

10.6 Such information together with knowledge of the respective receptor affinities allows the prediction of therapeutic effects plus withdrawal and rebound effects which can occur during discontinuation and switching especially if the new antipsychotic does not share the same receptor profile and affinity with the first.

10.7 A specific switching strategy based on such knowledge can enhance effectiveness and avoid undesirable effects. There are at least eight different possible strategies for switching oral antipsychotics.[44]

10.8 Due to the various techniques employed to produce a long-acting injectable formulation, the time to steady state cannot be calculated as five half-lives with long-acting antipsychotic injections in the same way as with oral formulations. Details of their pharmacokinetic parameters together with specific switching strategies taken from each individual SmPC[11] and the Maudsley Prescribing Guidelines[23] may be found on the following pages.

10.9 Whenever possible a specialist mental health pharmacist should be enlisted to assist in drawing up a management plan with an appropriate switching strategy.

10.10 Drawing up a management plan with an appropriate switching strategy.

Approximate Pharmacokinetic Data for Oil-based Depot and Other Long-acting Antipsychotic Injections[11,23]

Antipsychotic	Concurrent admin. of oral	Time to peak plasma conc. (C_{max})	Mean Elimination half-life ($t_{½}$)	Time to Steady State (SS)	Usual dosing interval
Oil-based Depot Antipsychotic Injections					
Flupentixol decanoate (Depixol)	1 week	7 days	8-17 days	2 months	2-4 weeks
Fluphenazine decanoate (Modecate)*	1 week	8-12 days	10 days	2 months	2 weeks
Haloperidol decanoate (Haldol)	4 weeks	3-9 days	21 days	2-4 months	4 weeks
Pipotiazine palmitate (Piportil)*	1 week	7-14 days	15 days	2 months	4 weeks
Zuclopenthixol decanoate (Clopixol)	3 weeks	4-7 days	19 days	3 months	1-4 weeks
Other Long-acting Antipsychotic Injections					
Aripiprazole (Abilify Maintena)	One inj. Start = 2 weeks, Two inj. start = single oral dose on initiation only.	7 days (gluteal inj.) 4 days (deltoid inj.)	30 days - 300mg dose 46 days - 400mg dose	4 months	4 weeks
Olanzapine pamoate (ZypAdhera)	N/A	2-3 days	30 days	3 months	2-4 weeks dep. on dose
Paliperidone palmitate - 1 monthly (Xeplion) (PP1M)	N/A	13 days (an average 28% higher C_{max} was observed with deltoid compared with gluteal injection.)	29 – 45 days	5 months	4 weeks
Paliperidone palmitate -3 monthly (Trevicta) (PP3M)	N/A	30-33 days (11-12% higher with deltoid compared with gluteal injection.)	84-95 days following deltoid injection and 118-139 days following gluteal injection.	N/A as pt. will already be at SS on initiation having been on PP1M For 4 months	12 weeks

Paliperidone palmitate – 6 monthly (Byannli) (PP6M)	N/A	33 days -700 mg dose 35 days - 1000 mg dose	148 days - 700 mg dose 159 days - 1000 mg dose	N/A as pt. will already be at SS on initiation having either been on PP1M for 4 months or PP3M for at least one injection cycle	24 weeks
Risperidone (Risperdal Consta)	2 weeks	4–5 weeks	4 days	2 months	2 weeks
Antipsychotic	Concurrent admin of oral	Time to peak plasma conc. (C_{max})	Mean elimination half-life ($t_{1/2}$)	Time to Steady State (SS)	Usual dosing interval
Risperidone ISM (Okedi)	N/A	Following IM injection, a small amount of the drug is released resulting in an initial peak in concentration after 24 to 48 hours. A second peak occurs between Days 18 and 25.[45]	23-26 days	1 month	28 days
*Modecate and Piportil have been discontinued in the UK by the manufacturers. However unlicensed products are available on a 'named patient basis' for patients for whom there is no alternative.					

Switching strategies[11,20,23]	
Switching TO an oil-based depot	
From an oral antipsychotic	• Continue the oral antipsychotic for 1 – 4 weeks from the first oil-based depot injection – depending on the "time to steady state" of the oil-based depot
From another oil-based depot	• Give the new oil-based depot instead of the next due injection of the first oil- based depot. • Do not give any more doses of the first oil-based depot
From another long-acting antipsychotic injection (LAI) **but not Risperidone LAI (Risperdal Costa), Paliperidone LAI three-monthly (PP3M), or Paliperidone LAI six-monthly (PP6M)**	• Give the oil-based depot instead of the next due injection of the LAI • Do not give any more doses of the LAI
From risperidone LAI	• Give the oil-based depot 2–4 weeks **after** the last injection of risperidone LAI **was due**. i.e., 4-6 weeks after the last injection of risperidone LAI was given. (The last injection of risperidone LAI provides therapeutic plasma levels for 4 - 6 weeks with a post dose peak at 5 weeks) • Do not give any more risperidone LAI
From Paliperidone LAI three-monthly (PP3M) and Paliperidone LAI six-monthly (PP6M)	• The prolonged release characteristics of PP3M or PP6M **must** be considered when planning the switch • Transition to the Paliperidone LAI one-monthly (PP1M) formulation is required first by starting PP1M when the next PP3M or PP6M injection is due (a dose conversion chart is available in the SmPC). • Alternatively, for patients on PP6M, transition to paliperidone prolonged-release tablets for oral administration 6-months after the final PP6M injection can be considered (a dose conversion chart is available in the SmPC). • Once the transition to PP1M or oral paliperidone prolonged release tablets is complete the strategy for a switch from PP1M or oral antipsychotics explained above can be implemented.

Switching strategies [11,20,23]	
Switching TO Aripiprazole LAI	
From oral antipsychotics	**<u>One injection start regime:</u>** • Plateau cross taper the oral antipsychotic to oral aripiprazole over 2 weeks • Start the aripiprazole LAI with one injection • Continue oral aripiprazole for two more weeks then stop **<u>Two injections start regime:</u>** • Plateau cross taper the oral antipsychotic to oral aripiprazole over 2 weeks • Start the aripiprazole LAI with two injections in separate sites (muscles*), along with one 20mg dose of aripiprazole, *For known CYP2D6 poor metabolisers DO NOT inject into both gluteal muscles, use either both deltoid muscles or one deltoid and one gluteal muscle.
From oil-based depot or another LAI antipsychotic **except risperidone LAI (Risperdal Costa), Paliperidone LAI three-monthly (PP3M) or Paliperidone LAI six-monthly (PP6M)**	• Start oral aripiprazole on the day the last depot or LAI antipsychotic dose was due • Start the aripiprazole LAI after two weeks and follow the one injection or two injections start regime as for a switch from oral antipsychotics (explained above). • If the one injection start regime is used stop the oral aripiprazole two weeks later
From risperidone LAI TO Aripiprazole LAI	• Start oral aripiprazole 2-4 weeks **after** the last injection of risperidone LAI **was due**. i.e.,4-6 weeks after the last injection of risperidone LAI **was given**. Do not give any more risperidone LAI (The last injection of risperidone LAI provides therapeutic plasma levels for 4 -6 weeks with a post dose peak at 5 weeks) • Start the LAI aripiprazole two weeks later and follow the one injection or two injections start regime as for a switch from oral antipsychotics (explained above). • If the one injection start regime is used stop the oral aripiprazole two weeks later
From Paliperidone LAI three-monthly (PP3M) and Paliperidone LAI six-monthly (PP6M) - The prolonged release characteristics of PP3M or PP6M **must** be considered	• Start PP1M when the next PP3M or PP6M injection is due (a dose conversion chart is available in the SmPC). • Alternatively, for patients on PP6M, transition to paliperidone prolonged-release tablets for oral administration 6-months after the final PP6M injection can be considered (a dose conversion chart is available in the SmPC). • Once the transition to PP1M or oral paliperidone prolonged release tablets is complete the strategy for a switch from PP1M or oral antipsychotics to Aripiprazole LAI explained above can be implemented.

Switching strategies[11,20,23]	
Switching TO Olanzapine LAI	
Following a successful trial of oral olanzapine	• A direct switch to olanzapine LAI is possible
From another oral antipsychotic	• A direct switch is possible but prior oral antipsychotics are probably best reduced slowly after starting olanzapine oral or LAI
From an oil-based depot or another LAI antipsychotic except risperidone LAI (Consta), Paliperidone LAI 3-monthly (PP3M) or Paliperidone LAI 6-monthly (PP6M)	• Oral olanzapine or olanzapine LAI can be started on the day the previous oil-based depot or LAI was due. • Do not give another dose of the first oil-based depot or LAI
From risperidone LAI (Consta)	• Begin the olanzapine LAI 2-4 weeks after the last injection of risperidone risperidone LAI (Consta) was due. i.e., 4-6 weeks after the last injection of risperidone LAI (Consta) was given. (The last injection of risperidone LAI (Consta) provides therapeutic plasma levels for 4 -6 weeks with a post dose peak at 5 weeks) • Do not give any more risperidone LAI (Consta)
From Paliperidone LAI three-monthly (PP3M) and Paliperidone LAI six-monthly (PP6M) - The prolonged release characteristics of PP3M or PP6M must be considered	• The first step is to start PP1M when the next PP3M or PP6M injection is due (a dose conversion chart is available in the SmPC). • Alternatively, for patients on PP6M, transition to paliperidone prolonged-release tablets for oral administration 6-months after the final PP6M injection can be considered as an alternative to the transition to PP1M (a dose conversion chart is available in the SmPC). • Once the transition to PP1M or oral paliperidone prolonged release tablets is complete the strategy for a switch from PP1M or oral antipsychotics to Olanzapine LAI explained above can then be implemented.
Switching TO Paliperidone LAI One monthly (PP1M)	
From oral paliperidone or oral risperidone	• Give the two initiation doses of 150 mg on treatment day 1 and 100 mg one week later on day 8, both into the deltoid muscle as per the SmPC16 • The third dose should be administered one month after the second initiation dose • No oral supplementation is necessary during initiation of paliperidone LAI (PP1M
From other oral antipsychotics	• Give the two initiation doses followed by the maintenance dose as above • Reduce the oral antipsychotic over 1-2 weeks following the first injection of PP1M

Switching strategies[11,20,23]	
From an oil-based depot or another LAI antipsychotic except risperidone LAI (Consta) TO Paliperidone LAI One monthly (PP1M)	• Start the PP1M at the maintenance dose when the next injection of an oil-based depot or other LAI antipsychotic was due instead of the oil-based depot or LAI • No initiation doses are required • Do not give another dose of the oil-based depot or LAI
From risperidone LAI (Consta)	• No initiation doses of PP1M are necessary • Begin an equivalent dose of PP1M 2-4 weeks after the last injection of risperidone LAI (Consta)I was due. i.e., 4-6 weeks after the last injection of risperidone LAI (Consta) was given. (The last injection of risperidone LAI (Consta) provides therapeutic levels for 4-6 weeks with a post dose peak at 5 weeks) • Do not give any more risperidone LAI (Consta).
Switching TO Paliperidone LAI three monthly (PP3M) *	
From paliperidone LAI one monthly (PP1M) (only those stable on PP1M, preferably for the past 4 months or more, and not requiring a dose increase may be switched to PP3M)	• Patients must have been adequately treated with PP1M (preferably for four months or more), be stable and not require any dose adjustment • PP3M should be initiated in place of the next scheduled dose of PP1M (± 7 days). • The PP3M dose should be based on the previous PP1M dose using a 3.5-fold higher dose • A dose conversion chart is available in the SmPC of PP3M17 • If needed, dose adjustments can be made every 3 months in increments within the range of 175 mg eq. to 525 mg eq. based on individual patient tolerability/efficacy • Due to the long-acting nature of PP3M, 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
Switching TO Paliperidone LAI sixth monthly (PP6M) *	
From paliperidone LAI one monthly (PP1M) (only those stable on PP1M, preferably for the past 4 months or more, and not requiring a dose increase may be switched to PP3M)	• Patients must have been adequately treated with PP1M (preferably for four months or more), be stable and not require any dose adjustment • It is recommended that the last two doses of PP1M before switching to PP6M should have been at the same dose. • PP6M should be initiated in place of the next scheduled dose of PP1M (± 7 days). • The PP6M dose should be based on the previous PP1M dose using the dose conversion chart available in the SmPC of PP6M

Switching strategies[11,20,23]	
Switching TO Paliperidone LAI sixth monthly (PP6M) * From paliperidone LAI one monthly (continued):	• If needed, dose adjustments can be made every 6 months **between the dose levels of 700 mg and 1000 mg** based on individual patient tolerability and/or efficacy • Due to the long-acting nature of PP6M, 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.
Switching TO risperidone LAI (Consta)	
From oral risperidone	• **Either**: Switch to oral risperidone and titrate to an effective dose. • If tolerated and effective prescribe an equivalent dose of risperidone LAI (Consta) 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 LAI (Consta) and then slowly discontinue the oral antipsychotic after 3 -4 weeks. • Be prepared to continue the oral antipsychotic for longer if necessary
From an oil-based depot or other LAI except **Paliperidone LAI Three monthly (PP3M) or Paliperidone LAI Six monthly (PP6M)**	Give risperidone LAI (Consta) **one week before** the last injection of oil-based depot or other LAI is given
From Paliperidone LAI Three monthly (PP3M) and Paliperidone LAI Six monthly (PP6M) - The prolonged release characteristics of PP3M or PP6M **must** be considered from other oral antipsychotics	• Start PP1M when the next PP3M or PP6M injection is due (a dose conversion chart is available in the SmPC). • Alternatively, for patients on PP6M, transition to paliperidone prolonged-release tablets for oral administration 6-months after the final PP6M injection can be considered (a dose conversion chart is available in the SmPC). • Once the transition to PP1M or oral paliperidone prolonged release tablets is complete the strategy for a switch from other LAI or oral antipsychotics to risperidone LAI (Consta) explained above can be implemented.
Switching To Risperidone ISM (Okedi)	
From oral risperidone	• Once response and tolerability to oral risperidone is established the appropriate dose of Risperidone ISM (Okedi) injection can be administered with no need for titration or cross-tapering. • Do not give a further dose of the oral risperidone.
From another oral antipsychotic (not risperidone)	• For patients with a history of a previous response and tolerability to risperidone treatment with oral risperidone must continue for at least 6 days before commencing Risperidone ISM. • The duration of the titration period in risperidone naive patients is recommended to be at least 14 days.

From Risperidone LAI (Risperdal Consta)	• Patients stabilised on antipsychotics deferent from risperidone should be titrated with oral risperidone before treatment with Risperidone ISM. The duration of the titration period should be at least 6 days • The manufacturers of Okedi only offer guidance on switching to Okedi from bi-weekly risperidone injection.
From another long-acting antipsychotic injection (LAI) **but not Risperidone LAI (Risperdal Costa), Paliperidone LAI three-monthly (PP3M), or Paliperidone LAI six-monthly, (PP6M)**	• Response and tolerability to oral risperidone must be established first requiring a switch to oral risperidone as described in the relevant section of the table above, followed by an adequate period of time as detailed above for risperidone responders, or risperidone naive patients. • When switching from Risperidone LAI (Risperdal Consta) implement the regime described above
From Paliperidone LAI Three monthly (PP3M) and Paliperidone LAI Six monthly (PP6M) - The prolonged release characteristics of PP3M or PP6M **must** be considered from other oral antipsychotics	• Start PP1M when the next PP3M or PP6M injection is due (a dose conversion chart is available in the SmPC). • Alternatively, for patients on PP6M, transition to paliperidone prolonged-release tablets for oral administration 6-months after the final PP6M injection can be considered (a dose conversion chart is available in the SmPC). • Once the transition to PP1M or oral paliperidone prolonged release tablets is complete the strategy for a switch from other LAI or oral antipsychotics to Risperidone ISM (Okedi) explained above can be implemented.

*To ensure a homogenous suspension before administration PP3M requires vigorous and fast shaking with the tip up and a loose wrist for at least 15 seconds and PP6M requires two 15 second shakes with a 15 second rest between them. Both should be administered within 5 minutes of shaking.

11. Consent to Treatment: England and Wales

11.1 Assessment of capacity to consent is a critical part of preparation for the procedure and must be consistent with guidance from the Care Quality Commission,[47] the Mental Health Act 2007[42] the Mental Capacity Act 2005[41] and the recommendations in NICE Guideline NG108 on decision making and mental capacity.[48] Practitioners need to be especially familiar with Part 4 of the Mental Health Act 2007 relating to consent to treatment and Part 4a relating to the treatment of community patients not recalled to hospital.

11.2 A patient must be assumed to have capacity unless it is established that they lack capacity.[48] If there is any doubt about the capacity of the patient, then a documented assessment must be undertaken, and the injection must not be given until this is clarified.

11.3 Obtaining consent from a patient is a complex process and must take into consideration the patient's ability to understand information about oil-based depot and other long-acting intramuscular antipsychotic injections, their routes of administration as well as the risks and benefits of such treatments.

11.4 The process of consent must not involve coercion of the patient to agree to treatment and on this basis, it is essential to promote practice that is in accordance with the Mental Health Act 2007[40] and the Mental Capacity Act 2005.[41]

11.5 For any patient detained under any of the Mental Health Act sections 4, 5(2), 5(4), 35, 135,136, 37(4) or 45A, consent to treatment provisions, as defined in part 4, do not apply and they are in the same legal position as patients who are not subject to the Mental Health Act 2007. This means that they can refuse treatment. Part 4 similarly does not apply to patients who are conditionally discharged under Sections 42(2), 73 and 74 of the Mental Health Act 2007 and have not been recalled to hospital.[40]

11.6 Consent to treatment provision under Part 4 applies to patients who are detained under Section 2, 3, 36, 37 (except 37(4)), 38, 44, 45A, 47, and 48. Patients who are on a Supervised Community Treatment Order (CTO) cannot be compelled to accept treatment they absolutely refuse unless they are recalled to hospital and their section 3 reinstated. This means that the registered practitioner has to make sure that they are legally entitled to administer medication and that the appropriate Mental Health Act documentation is completed accurately and, in the case of medication received for at least 3 months, form T3 is available with the prescription/ administration card.[40]

11.7 Section 62 of the Mental Health Act 2007[40] allows for the emergency treatment of a detained patient whatever section they are on, providing it is necessary to save life or prevent serious harm. The treatment should be non-hazardous and not have irreversible effects.[40] Rapid tranquillisation with the use of short-acting intramuscular antipsychotics may feature here but the initiation of oil-based depot or other long-acting intramuscular antipsychotics cannot be justified under Section 62 provisions.

11. Consent to Treatment: Scotland

11.1 /S Assessment of capacity to consent is a critical part of preparation for the procedure and must be consistent with the Mental Health (Care and Treatment) (Scotland) Act 2003[42] and its Code of Practice,[49] Consent to Treatment Guidelines of the Mental Welfare Commission for Scotland,[50] and the Adults With Incapacity (Scotland) Act 2000[43] along with its Code of Practice.[51] Practitioners need to be especially familiar with Part 16 of the Mental Health (Care & Treatment) (Scotland) Act 2003[42] relating to safeguards on medical treatments.

11.2 /S The law of Scotland generally presumes that adults are capable of making decisions for themselves. That presumption can be overturned in relation to particular matters or decisions on evidence of impaired capacity. If in doubt, a documented assessment must take place first.

11.3 /S Obtaining consent from a patient is a complex process and must take into consideration the patient's ability to understand information about oil-based depot and other long-acting intramuscular antipsychotic injections, their routes of administration, as well as the risks and benefits of such treatment.

11.4 /S The process of consent must not involve coercion of the patient to agree to treatment and on this basis, it is essential to promote practice that is in accordance with the Mental Health (Care and Treatment) (Scotland) Act 2003[40] and the Adults with Incapacity (Scotland) Act 2000.[43]

11.5 /S Under Part 16 of the Mental Health (Care and Treatment) (Scotland) Act 2003,[43] treatment can be given for the first 2 months from the first date of treatment as part of a Compulsory Treatment Order or an Interim Compulsory Treatment Order. After 2 months specific safeguards are activated. Under Section 238 of Part 16 of the 2003 Act, where a patient is capable of consenting and consents, then the patient's Responsible Medical Officer is required to certify that the necessary conditions are met using a T2 form. Under Section 241 of Part 16 of the Mental Health (Care and Treatment) (Scotland) Act 2003,[43] where the patient is incapable of consenting or does not consent, then a Designated Medical Practitioner can authorise treatment using a T3 form only if the necessary conditions are met.

11.6 /S Under Section 112 of the Mental Health (Care & Treatment) (Scotland) Act 2003,[43] a patient on a Compulsory Treatment Order or an Interim Compulsory Treatment Order which imposes an attendance requirement with a view to receiving treatment who fails to comply with the attendance requirement can be compelled to attend any hospital or the required place of attendance and detained there for no more than 6 hours.[43] However, treatment cannot be forced outside of a hospital setting. Under Section 113 of the Mental Health (Care and Treatment) (Scotland) Act 2003[43] if a patient is subject to a Compulsory Treatment Order or an Interim Compulsory Treatment Order which does not authorise detention in hospital and the patient fails to comply with any measure specified in the treatment order and it is a matter of urgency then the patient may be taken into hospital for a period of up to 72 hours.

11.7 /S In Scotland a patient cannot be treated under Part 16 of the Mental Health (Care & Treatment) (Scotland) Act 2003[43] under a Section 36 Emergency Detention Certificate without their consent unless the need for treatment is urgent, as per Section 243 of the Mental Health (Care & Treatment) (Scotland) Act 2003.[43] Rapid tranquillisation with the use of a short-acting intramuscular antipsychotic may feature here but the initiation of an oil-based depot or other long-acting intramuscular antipsychotic could not be justified.

11. Consent to Treatment: Northern Ireland

11.1 /NI Assessment of capacity to consent is a critical part of preparation for the procedure and must be consistent with the Mental Health (Northern Ireland) Order 1986, the Mental Capacity Act, 2016 and their codes of practice, alongside professional[52,53] practice guidelines from the General Medical Council,[54] the Royal Pharmaceutical Society (RPS) and Royal College of Nursing (RCN),[5] the Northern Ireland Social Care Council[55] and the Regulation and Quality Improvement Authority.[56]

11.2 /NI The law of Northern Ireland presumes that adults are capable of making decisions for themselves and Part 1 (Section 4) of the Mental Capacity Act (Northern Ireland) 2016[53] defines someone who is unable to make a decision for themselves as a person who:

a) is unable to understand the information relevant to the decision.
b) is not able to retain that information for the time to make the decision.
c) is not able to appreciate the relevance of that information and to use and weigh that information as part of making the decision, or.
d) is not able to communicate their decision (whether by talking, using sign language or by any other means).

The registered practitioner caring for the patient must therefore presume the patient has the capacity to consent to treatment; however, if there is any doubt about the capacity of the patient, then a documented assessment must be undertaken, and the treatment not given until this is clarified.

11.3 /NI New deprivation of liberty regulations[57] within the Mental Capacity (Northern Ireland) Act (2016)[53] commenced on 2 December 2019 including the formal assessment of capacity and statutory forms for use by professionals. This phase of implementation in December 2019 excluded persons who are liable to be detained for treatment under the Mental Health (Norther Ireland) Order 1986[52] to ensure legal certainty and clarity until all parts of the Act commence.

11.4 /NI Obtaining consent from a patient is a complex process and must take into consideration the patient's ability to understand information about oil-based depot and other long-acting intramuscular antipsychotic injections, their routes of administration as well as the risks and benefits of such treatments.

11.5 /NI The process of consent must not involve coercion of the patient to agree to treatment and on this basis, it is essential to promote practice that is in accordance with the law, alongside professional practice standards and guidelines. The Royal College of Nursing, for example, publishes practical guidance to consent in Northern Ireland for registered nurses and nursing support staff.

11.6 /NI Patients admitted for assessment under the Mental Health (Northern Ireland) Order 1986[52] can refuse treatment during the assessment period (i.e., if they are on forms 5, 7, 8 or 9) but not once they are detained for treatment. Once detained, a course of medicines for mental disorder can be given for up to 3 months without consent or need for an independent medical opinion. The patient must be made aware of their right to appeal detention under the Mental Health Order.

11.7 In accordance with section 58(2) and 58(3) of the Mental Capacity (Northern Ireland) Act, 2016 information must be provided to the patient about any decision that relates to deprivation of their liberty in a format that is suitable to them and must be provided orally, as well as in writing.[53]

11.8 /NI After 3 months have elapsed from the start of medical treatment then either forms 22 or 23 need to be completed for treatment to proceed. This requires that a doctor (as stipulated in Part IV of the Order) certifies that either the patient is capable of giving valid consent and does so or that the patient either lacks capacity to consent or has not given consent, but the treatment should proceed for the therapeutic needs of the patient.

11.9 /NI Article 68 of the Mental Health (NI) Order 1986[52] allows for the urgent treatment of a detained patient providing it is necessary to save life or prevent a serious deterioration in the condition of the patient or serious suffering by the patient. Rapid tranquillisation with the use of a short-acting intramuscular antipsychotic or benzodiazepine may feature here but the initiation of long-acting intramuscular antipsychotic formulations is unlikely to be justified under this provision.

11.10 /NI All patients can withdraw consent at any time. If this occurs, a review of the patient's mental state, their capacity to give valid consent and a discussion with the multidisciplinary team is appropriate

12. Patient Preparation

12.1 There are some key principles in the preparation of the patient which are crucial to gaining patient and carer confidence. These include the demonstration of compassion, a personalised approach and a desire to work in partnership with the patient and their carer(s) where appropriate.

12.2 The administration of any medicine is an opportunity for assessment and information exchange with the patient and their carers (where appropriate). Preparation should include an assessment to see if the physical and/or mental health of the patient has changed since the previous contact. Any beneficial effects or side effects experienced since the last injection should be considered and questions asked of the patient and their carer (if appropriate) to elicit any concerns or information needs.

12.3 Preparation at the point of administration will include the registered practitioner exercising accountability for checking the following: checking the prescription to confirm that the dose is due and that it hasn't already been given; that the intended route, dose and formulation all correlate accurately with the prescription; that there are no contraindications; that any dose calculation is accurate; that the patient's capacity to consent is confirmed and that the preparation of the injection for administration is correct and that it is in date.[5,6] It is good practice for a second-registered practitioner to double check these too.[6] In the absence of a second professional it is good practice to get the patient or carer to check the expiry date of the injection and that the dose is correct according to the prescription, etc. and record this in the notes.

12.4 Finally, the registered practitioner must confirm both verbally and via the available documentation that the patient does not have any allergy/sensitivity or religious/cultural beliefs which preclude the administration of the injection. This includes allergy/sensitivity to, or concerns regarding, the vehicle (e.g., sesame oil) or any excipient such as benzyl alcohol.

12.5 Since the last administration of the injection, any change in capacity must be considered and again if there is any doubt about this, an assessment must be undertaken.

13. Imminent Clinical Preparation for the Procedure

13.1 The patient should be made aware of the imminent procedure and their capacity and consent should be assessed and confirmed respectively and recorded in their clinical notes.

13.2 The patient should then be assisted, if necessary, into the chosen position for administration of the injection according to the appropriate chosen site.
See Appendix 1: Standard Operating Procedures 3-6 (SOPs 3–6).

13.3 If there is variance from the recommended position, this must be recorded in the clinical notes or record together with the rationale for this clinical decision. This is generally a more common issue when the procedure takes place in the patient's home rather than in a clinical environment. For example, where a choice of dorsogluteal or possibly ventrogluteal injection is made the patient may have a preference to stand to receive their injection rather than lie down. However, standard procedures and principles must still be adhered to. For example, the patient must be asked to take the weight off their foot on the side where the injection is to be administered to reduce tension and steps must be taken to ensure that the patient cannot fall and injure themselves or the registered practitioner.

13.4 Preparation for the administration of an injection begins with hand hygiene. Effective hand cleansing is the single most effective action in preventing the spread of infection and NHS England and NHS Improvement describe a hand-cleansing technique which should be adhered to.[58]

13.5 Skin cleansing around the injection site should be undertaken according to local trust policy, however, this is a widely debated topic with some evidence supporting the fact that in socially clean patients such skin cleansing is unnecessary.[59] If the skin is cleansed with an alcohol swab, a period of 60 seconds (or the recommended product-related specific time) must elapse before the injection is administered to ensure that the alcohol has dried on the skin and to avoid a stinging sensation for the patient. Cotton wool balls stored wet in a multi- use container must not be used.

13.6 It is important to evaluate the injection site pre- and post-injection observing for any swelling, pain, inflammation, infection, or tissue damage. If any of these is present it must be recorded in the patient's health record and the decision to proceed reviewed. These are all clinical indicators that further physical assessment is urgently needed prior to any subsequent injection and an alternative site may need to be considered before proceeding with the injection.

13.7 Any special instructions for post-injection monitoring in the product licence/summary of product characteristics (SmPC) MUST be planned for and followed. For example, after administration of olanzapine long-acting injection the patient must be monitored for at least 3 hours for signs and symptoms consistent with olanzapine overdose.[15]

14. Choice of Syringe and Needle

14.1 The expiry dates of all equipment must be checked before use. Syringes and needles must be used systematically, safely and securely and all risk associated with their use minimised.[1] Where an antipsychotic for injection is provided in a pack together with a syringe and needle for administration, the technology will have been subjected to a rigorous evaluation process in order for the company to gain a marketing authorisation (product licence) for their product. The syringe and needle provided **MUST ALWAYS** be used. It is important to read the manufacturer's instructions regarding syringe and needle selection as packs and presentations may vary. Always refer to the SmPC for guidance on the use of needles. Where the practitioner has to select an appropriate syringe and needle it is necessary to consider the following:

14.2 Syringes come in three main types of fittings: Luer lock, Luer slip tip and eccentric/ concentric Luer slip tip. The Luer lock type is generally used for intramuscular injections. The needle must be attached in a push-and-twist manner ensuring the chamfer of the needle is in the same line of sight as the graduation on the syringe. Simply sliding the needle hub onto the syringe will not ensure a secure fitting.

14.3 The smallest possible size of syringe should be selected to accommodate the volume of the product to be given.[60]

14.4 The gauge of the needle refers to the outer diameter of the needle, not the length of the needle nor its internal bore (lumen). Various needle lengths are available for any given gauge and some needles are manufactured with larger internal bores than standard to accommodate the particular needs of a specific product. Smaller gauge numbers indicate larger outer diameters. Needles in common medical use range from 7 gauge (the largest) to 33 (the smallest) on the Stubs scale. Inner diameter depends on both gauge and wall thickness. Thin-wall needles have identical outer diameters but larger inner diameters for a given gauge. 21-gauge needles (green hub) are most commonly used for intramuscular injections. The narrowest needle which complies with the product licence should be used. Where needles are supplied with the product by the manufacturer, they are part of the approved licence for the product, **ONLY** those needles should be employed.

14.5 Needle length is indicated on the needle pack in inches and/or millimetres. A variety of lengths is available and an assessment of the length of needle required to reach the muscle should be made by an assessment of the individual patient, taking into account any subcutaneous fat. Historically approximately 2–3 mm of the needle length was left outside the skin to allow the needle to be removed should it break. Although several nursing authors and textbooks continue to recommend this practice, they all tend to cite the opinion of one author.[61] Today's single-use hypodermic needles are subject to robust quality control on manufacture and as a result are unlikely to break. Therefore, this ritualistic practice needs to be balanced against the need to maximise the length of needle available to reach the muscle.

14.6 Research suggests that the thickness of subcutaneous tissue varies based on gender, weight and Body Mass Index (BMI), which should ideally be used to guide site and needle length for gluteal intramuscular injections. A few studies and one systematic review of skin to muscle depth at the dorsogluteal injection site have measured this distance and compared it to needle length, although with varied results and methodological limitations.[62-64] The dorsogluteal site focussed systematic review authors recommended use of needles longer than 38mm (1.5 inches) in women with a BMI of 25 or more, and in men (who have less subcutaneous fat at this site) with a BMI of 35 or more.[64] Authors of the single study that used ultrasound to measure subcutaneous tissue depth at both dorsogluteal and ventrogluteal sites recommend that both gluteal injection sites should be avoided in obese (BMI ≥30) individuals of any gender, unless a 51mm (2 inch) needle can be used.[64] However, these recommendations must be balanced with the knowledge that needles supplied with products as part of their licence will have been subject to rigorous phase 3 trials that included obese participants and should be used. If an HCP is concerned about the ability of the needle to reach the gluteus muscle in an individual patient, refer to the SmPC of the product to see if it allows use of an alternative injection site.

14.7 There are various reports and studies in the literature which propose a correlation between injection into fat and the development of granulomas.[65] However, it is important to note that the impact of injecting long-acting antipsychotics into fat has not yet been studied so potential effects on effectiveness or subsequent adverse effects are unknown.

14.8 Only the needles recommended and supplied by the manufacturer may be used for the injection of aripiprazole long-acting injection. For gluteal administration the recommended needle is a 38 mm (1.5 inch), 22-gauge hypodermic safety needle; for obese patients with a BMI >28 kg/m2, a 50 mm (2 inch), 21-gauge hypodermic safety needle should be used. For deltoid administration the recommended needle is a 25 mm (1 inch), 23-gauge hypodermic safety needle; for obese patients, a 38 mm (1.5 inch), 22-gauge hypodermic safety needle should be used.

14.9 Only the Needle-Pro® safety needles supplied in the pack may be used for administering olanzapine long-acting injection. For obese patients, the 50 mm needle is recommended. If the 50 mm needle is to be used for the injection, then the 38 mm safety needle should be used to withdraw the required volume of suspension. If the 38 mm needle is to be used for the injection, then the 50 mm safety needle should be used to withdraw the required volume slowly. Some excess suspension will remain in the vial. This is normal 'overage'. The needle safety device should be engaged, and the needle removed from the syringe. The remaining safety needle should then be attached to the syringe prior to injection.[15]

14.10 Only the Needle-Pro® safety needles supplied in the dose pack should be used for administering paliperidone palmitate long-acting injection. The needles must not be substituted between packs, or other commercially supplied needles due to their specific design which includes a thinner wall (and larger needle bore) than that provided for commercially supplied needles at the same gauge. Specific needles are supplied for the one monthly (PP1M), three monthly (PP3M) or sixth monthly (PP6M) formulations.[16,17,18] Where there is a choice of needle available within the dose pack the selection of needle will depend on the injection site to be used, and/or the patient's weight:

The recommended needle size for initial and maintenance administration of PP1M into the deltoid muscle is determined by the patient's weight:

≥ 90 kg, the 1½ inch, 22-gauge (grey hub) needle (38.1 mm x 0.72 mm) should be selected from the pack and used

< 90 kg, the 1-inch, 23-gauge (blue hub) needle (25.4 mm x 0.64 mm) should be selected from the pack and used.

The recommended needle size for administration of PP1M into the gluteal muscle is not determined by weight and the 1½-inch, 22-gauge (grey hub) needle (38.1 mm x 0.72 mm) should be selected from the pack and used.

The selection of the needle from the pack for administration of PP3M into the deltoid muscle is also determined by the patient's weight.

≥ 90 kg, the thin wall 1½ inch, 22-gauge (yellow hub) needle (0.72 mm x 38.1 mm) should be selected and used

< 90 kg, the thin wall 1 inch, 22-gauge (pink hub) needle (0.72 mm x 25.4 mm) should be selected and used.

The recommended needle size for administration of PP3M into the gluteal muscle is not determined by weight and the thin wall 1½ inch, 22-gauge (yellow hub) needle (0.72 mm x 38.1 mm) should be selected from the pack and used.

The recommended needle size for initial and maintenance administration of PP6M into the gluteal muscle is a thin wall 1½ inch, 20-gauge (yellow hub) needle (0.9 mm × 38 mm), regardless of body weight. After injection, the Needle-Pro® device should be engaged and both the used needle and unused needle discarded appropriately.[16]

If a substitute needle is ever required (e.g., due to potential contamination during preparation) these are available from the manufacturer and can be supplied through the local pharmacy service.

14.11 Only the Needle-Pro® safety needles supplied in the pack by the manufacturer may be used for administering risperidone long-acting injection (Consta). The packs contain two needles[15] and both are fitted with a Needle-Pro® safety device. The critical feature in each case is the needle bore. The 20g (yellow hub) needle has a thin wall and the 21g (green hub) needle has an ultra- thin wall. (These walls are thinner than standard 20g and 21g needles.) These thin walls result in a larger bore or lumen than standard needles. This is essential to allow the risperidone suspension to flow freely through the needle. The 2-inch 20g needle (yellow hub) must be used for the intra-gluteal injection and the 1-inch, thinner 21g needle (green hub) must be used for intra-deltoid injection.[17]

14.12 Only the sterile needles with safety shield supplied in the pack by the manufacturer may be used for administering risperidone ISM (Okedi). The packs contain two needles. The yellow 2- inch (0.90 x 51mm [20G]) with safety shield **must** be used for administration into a glutel muscle and the green 1-inch (0.80 x 25mm [21G]) with safety shield **must** be used for deltoid administration.[20]

14.13 Organisations implementing safer sharps procedures to meet European Union legislative requirements may wish to introduce a variety of needle protection mechanisms including retractable and safety needles (needles with a safety guard). When asked to use these the practitioner must make sure they have been trained in their use and that the particular device has been risk assessed for use with long-acting antipsychotic injections. For example, the correct gauge and range of needle lengths required must be available for the diluent and to meet the needs of individual patients and only needles supplied in product packs are to be used with these products. Healthcare professionals have a pivotal role to play in assessing risk and evaluating any proposed new safety devices introduced in their clinical area.[66]

14.14 It is common practice to change the needle used for drawing up to a different needle for administration. This is unnecessary unless there has been a risk of blunting the needle (e.g., by perforating a rubber bung or by scratching it on the inside of an ampoule). Blunt drawing-up needles with an internal filter are now available to prevent the accidental drawing up of contaminants from glass ampoules. However, the viscosity (thickness) of the oil and size of the molecules in some oil-based depot injections may make drawing up through a filter needle difficult and could result in some of the product being discarded with the draw-up needle when it is changed to the needle for administration. They are therefore NOT recommended for such injections.

15. Prevention and Control of Infection and Prevention of Inoculation Injury

15.1 The Health and Social Care Act 2008 Code of Practice sets out clear guidance to ensure that patients receive safe care in a clean environment and that the risk of healthcare-acquired infection is kept as low as possible.[67] Regulations implementing European Union [EU] law came into force across the UK on 11 May 2013[68] and apply across the NHS and independent healthcare sector. The 'Sharps Directive' – European Council Directive 2010/32/EU introduced new requirements for employees to report sharps injuries and employers to promote the safe use and disposal of sharps, provide information and training for employees, respond effectively if an injury occurs and review their procedures regularly.[69]

15.2 The standard safety procedures adopted in the United Kingdom for the prevention of inoculation incidents to healthcare practitioners are known as 'Standard' or 'Universal Precautions', where all blood and body fluids regardless of source are considered to contain infectious agents and are treated as such. Guidelines to this effect were published by the Department of Health in 1998 and are included in recent infection control guidance published and updated in response to the SARS Covid-19 pandemic. [58,70]

15.3 Hand hygiene before and after each patient contact and after contact with blood or other body fluids is the single most effective action that can be employed to prevent the spread of infection.

15.4 Personal Protective Equipment should be worn as appropriate and as directed by the UK Government. Certain medical and patient care activities that can result in the release of airborne particles (aerosols). The administration of an intramuscular injections is not considered an aerosol generating procedure.[58] The currently recommended PPE is disposable gloves, an apron and eye protection due to the risk of splashing of blood or other body fluids during the procedure.[58]

15.5 Any cuts or abrasions must be covered with waterproof dressings.

15.6 Immediately safely dispose of sharps into an appropriate, puncture-proof, labelled sharps bin that is not overfilled.

15.7 Never re-sheath needles or detach the needle from the syringe barrel prior to disposal.

15.8 The use of retractable needles and syringes significantly reduces the risk of exposure to blood-borne viruses (BBVs), but these may not be suitable for long-acting antipsychotic injections if the appropriate length and/or gauge of needle are not available from manufacturers.[69]

15.9 Any needle stick (inoculation) injury must be followed immediately by the application of first aid to bleed and wash the puncture. Local risk management procedures for reporting the incident must be followed and medical support sought through occupational health services.

15.10 Disposable gloves should be worn as part of standard precautions. These do not prevent needle stick (inoculation) injury but penetration through the wall of the glove by the needle will remove some of the blood before the needle next penetrates skin.

15.11 The report of a 9-year study conducted by Public Health England across 159 centres on significant occupational exposure to blood-borne viruses amongst healthcare workers, showed that needle stick injuries were the most commonly reported type of significant exposure, with 65% of such injuries caused by hollow-bore needles. 42% occurred amongst nurses and healthcare assistants and 41% amongst doctors. Despite not typically providing direct clinical care to individuals, 1.5% of the exposures occurred in ancillary staff, which highlights the need to provide safe working conditions for all staff working in healthcare settings.[71]

15.12 Should any accidental spillage or splash of medicine onto the skin or into the eye occur, the registered practitioner must follow their local risk management and untoward incident reporting procedures.

16. Choice of Injection Site

16.1 Most oil-based depot antipsychotic injections must be administered only into the gluteal muscle by deep intramuscular (IM) injection. The exceptions to this are flupentixol and zuclopenthixol depots which are also licensed to be administered via the lateral thigh. [73-75]

16.2 The Summary of Product Characteristics (SmPC)[11] for each antipsychotic injection contains full details of the sites for which each is licensed. These are all available online from the electronic Medicines Compendium: http://www.medicines.org.uk/emc/

16.3 The product licence for aripiprazole long-acting injection allows administration into either the gluteal or the deltoid muscles.[14]

16.4 The product licence for olanzapine long-acting injection allows administration only into the gluteal muscles.[15]

16.5 The product licence for one monthly paliperidone long-acting injection states that the first two initiation doses on Day 1 and Day 8 must be administered into the deltoid muscle in order to attain therapeutic concentrations rapidly, thereafter the monthly maintenance doses may be administered in either the deltoid or gluteal muscles.[16] The product licence for the three monthly paliperidone palmitate injection allows administration into either the deltoid or gluteal muscles and the product license for sixth monthly paliperidone palmitate only allows administration into the gluteal muscle. [17,18]

16.6 The product licence for risperidone long-acting injection (Consta) allows administration into either the gluteal or the deltoid muscles.[13]

16.7 The product licence for risperidone ISM (Okedi) allows administration into either the gluteal or the deltoid muscles.[20]

16.8 Where alternative sites of administration are possible, a joint decision on the preferred site is likely to influence adherence to future treatment and enhance the patient's perception of safety and dignity.

16.9 Any local procedure relating to privacy and dignity must be adhered to. This may include arrangements for working alone as a registered practitioner as well as chaperoning arrangements.

16.10 Whichever site is selected for administration of the injection, the registered practitioner must alternate between the left and right side of the body on each occasion the injection is administered. The site used on each occasion must be recorded in the patient's clinical record. Alternating injection sites can increase the time between injections in each site and allows more time for each site to heal, reducing the potential for damage to the injection site.

17. Deep Intramuscular Administration

17.1 Short-acting intramuscular injections provide fairly rapid uptake of the medicine into the circulatory system via the muscle fibres of skeletal muscle. They are normally aqueous.

17.2 An oil-based depot antipsychotic injection consists of the antipsychotic esterified to a decanoate or palmitate which is then dissolved in an oily vehicle. The volume to be injected is deposited deep into the muscle, usually the gluteal and forms a depot from where it leaches over time into the bloodstream according to its oil: water partition coefficient. This, together with the time taken for circulating enzymes to hydrolyse the ester back to its active base, is responsible for the prolonged action of these formulations.

17.3 Long-acting antipsychotic injections which are not oil-based (e.g., aripiprazole, olanzapine, paliperidone, risperidone) must also be administered by deep intramuscular injection.

17.4 When a deep intramuscular injection is administered the needle is passed through the epidermis and dermis of the skin and then through the subcutaneous fat layer, depositing the medicine into the skeletal muscle below.

17.5 Z-tracking is the recommended technique for all deep IM injections as it creates a broken injection pathway (the z-track) containing the medicine in the intended target muscle and preventing it from moving back up the track to leak out at the skin surface.[76] This has the advantage of achieving the correct plasma concentration whilst minimising the risk of pain or lesions at the injection site (see Appendix 1, SOP 2).

17.6 There are five main sites that can be used for deep intramuscular injection: the deltoid, the dorsogluteal, the ventrogluteal, the vastus lateralis, and the rectus femoris.[76] The product licences of individual antipsychotic injections indicate which sites are permitted. Currently none of the depot or other long-acting antipsychotic injections is licensed for administration at the rectus femoris site. A greater risk of muscle and nerve damage at the rectus femoris site has recently been demonstrated so use of this site is not recommended.[77]

17.7 Published guidance on the range and maximum volume of solution that the muscle fibres can comfortably and effectively accommodate at each intramuscular site appears largely based on opinion and usual practice (rather than primary research) and the amount of muscle mass at an injection site is likely to vary between individuals. Maximum volumes per site are included in some SmPCs for oil-based depot injections, but not all. In addition to this some licensed products intended for deep intramuscular injection far exceed the maximum volume usually cited in the nursing literature for the gluteal muscle (e.g., Pabrinex). There are specific advantages and disadvantages of different sites. These are detailed in the table on the following pages.

Injection Sites	Typical range and maximum volume cited in the nursing literature e.g. [78]	Muscle Used
Deltoid Injections into the mid deltoid muscle produce a quick uptake of the medicine. The maximum which can be safely injected is unknown and based on opinion. Common practice is to use this site for small-volume injections such as vaccinations.[79]	0.5-2ml	Deltoid
Dorsogluteal The dorsogluteal site, colloquially called the 'upper outer quadrant' of the buttocks, targets the gluteus maximus muscle and is commonly used for high-volume injections. When this site is used, there is a risk that the medicine will not reach the target muscle, but instead will be injected into subcutaneous fat [62,64]. As a result, delayed uptake of the medicine may occur and tissue irritation or the development of granulomas can result.[64] The clinical significance of delayed uptake is currently unknown. 38 mm needles should generally be used but may not reach the gluteal muscle in overweight women (BMI ≥25) or obese (BMI ≥30) patients of any gender. If a patient is obese, a 51mm needle or alternative injection site should be considered if available within the product licence (and dose pack). [62,64] Additionally, the system of visually bisecting the buttocks to landmark the site is flawed and can result in damage to the sciatic nerve or gluteal artery, both of which lie a few centimetres distal to the dorsogluteal injection site.[62] There may also be modesty issues associated with the use of this site.	1 to 4 ml Exceptions include Pabrinex Intramuscular High Potency Injection which requires a 7 ml injection high into the gluteal muscle, 5cm below the iliac crest[82]	Gluteus maximus
Vastus lateralis (lateral thigh) This site sits on the lateral (vastus lateralis) aspect of the thigh, part of a group of large, well-defined muscles in non-atrophied patients, the quadriceps femoris. Injections into this muscle produce a slower uptake of the medicine compared to the deltoid, but faster than gluteal muscles.[76] The site is easy to access. Femoral nerve injury due to inaccurate landmarking of the vastus lateralis site is rare but has been reported for analgesic injections post thigh surgery.[81]	1 to 5 ml [63]	Vastus lateralis
Ventrogluteal There are few disadvantages to using this site. It is relatively free of major nerves and blood vessels, the muscles are large and well defined, and the landmarks for administration are easy to locate. [83,84] Although it was once believed an additional advantage of this site was consistency of fat depth, original studies were in cadavers and more recent ultrasound research into obese men and women have found significant differences in fat depth here.[62,64] There may be modesty issues associated with the use of this site. UK HCPs generally lack competence and confidence in using this site.	2.5 to 5 ml [78] Exceptions include Pabrinex Intramuscular High Potency Injection which requires a 7 ml injection high into the gluteal muscle, 5cm below the iliac crest [82]	Gluteus medius and minimus

Maximum Volume for Oil-based Depot Administration into a Single Site		
Generic Name	**Brand/Trade Name**	**Max Volume**
Flupentixol decanoate 20 mg in 1 ml	Depixol Injection	3 ml[72]
Flupentixol decanoate 100 mg in 1 ml	Depixol Concentrate	2 ml[72]
Flupentixol decanoate 200 mg in 1 ml	Depixol Low Volume Injection	2 ml[73]
Fluphenazine decanoate 100 mg in 1 ml (Modecate is no longer marketed in the UK but an imported (unlicensed) product containing 100 mg in 1 ml of fluphenazine decanoate may be obtained on a 'named patient basis' for those patients for whom there is no alternative)	Modecate Injection	Not specified in the SmPC
Fluphenazine decanoate 100 mg in 1 ml (Modecate is no longer marketed in the UK but an imported (unlicensed) product containing 25 mg in 1 ml of fluphenazine decanoate may be obtained on a 'named patient basis' for those patients for whom there is no alternative)	Modecate Concentrate Injection	Not specified in the SmPC
Haloperidol decanoate 50 mg in 1 ml	Haldol Decanoate 50 mg in 1 ml	3 ml[85]
Haloperidol decanoate 100 mg in 1 ml	Haldol Decanoate 100 mg in 1 ml	3 ml[85]
Pipotiazine palmitate 50 mg in 1 ml (Piportil is no longer marketed in the UK but an imported (unlicensed) product containing 25 mg in 1 ml of pipotiazine palmitate may be obtained on a 'named patient basis' for those patients for whom there is no alternative)	Piportil Depot 5% w/v	Not specified in the SmPC[86]
Zuclopenthixol decanoate 200 mg in 1 ml	Clopixol Injection	2 ml[74]
Zuclopenthixol decanoate 500 mg in 1 ml	Clopixol Concentrate Injection	2 ml[74]

NB. Zuclopenthixol acetate 50 mg in 1 ml (Clopixol Acuphase) is not intended for long term use. It is indicated for the short-term management of acute psychosis, mania, or exacerbations of chronic psychosis.[75]
Please consult each product's SmPC for detailed prescribing information.

18. Record Keeping

18.1 Good record keeping is essential for safe patient outcomes.

18.2 The clinical record should reflect the registered practitioner's full, chronological account of assessment, planning and care and provide information relevant to the procedure at the time of the administration of the injection.

18.3 No action or omission by the registered practitioner must compromise patient safety; records must demonstrate this duty of care. The Nursing and Midwifery Council (NMC) Code and Professional Standards of Practice and Behaviour for Nurses, Midwives and Nursing Associates, and the professional guidance on the administration of medicines in healthcare settings by the Royal Pharmaceutical Society (RPS) and Royal College of Nursing (RCN) clearly outline expectations relating to record keeping and should be adhered to.[4,5]

18.4 A registered practitioner administering an injection is required to following best practice in relation to record keeping as described below:

- Record an accurate reflection of all discussions about informed choice and decisions made.

- Ensure the assessment of the patient's capacity to consent is assessed and that all legal requirements of the Mental Health Act are met. Both must be recorded.

- Record the clinical intervention and specific references to any patient or carer concerns chronologically.

- As a minimum, the patient's clinical record must contain details of the date and time of the injection, the name of the medicine and dosage administered, the site of administration together with the registered practitioner's signature and where applicable a signature from a second registered practitioner. These will normally be recorded on the prescription and administration record. If a student administers the injection under supervision then their signature must be countersigned by the supervising registered practitioner.

- Any other comments that the patient or registered practitioner wish to be noted should also be recorded.

- Any deviation from normal practice must be clearly recorded with the rationale for the clinical decision to do so.

- Any untoward incident must be recorded in accordance with the local approved risk- management reporting system.[2,10]

19. Monitoring and Evaluation of Treatment

19.1 All patients must have their long-acting antipsychotic injection treatment reviewed by the clinical team on a regular basis according to local guidelines. Such reviews should consider effectiveness, including any changes in symptoms and behaviour, side effects, adherence and physical health.[7,8]

19.2 Such clinical reviews must be undertaken at least every 6 months in discussion with the patient, carer (where appropriate) and care team and will usually take place as part of the Care Programme Approach review.

19.3 Prior to administration of the next scheduled injection, a discussion with the patient and an assessment of the previous injection site must be undertaken to ascertain if there are signs of swelling, pain, inflammation, infection or tissue damage. These are all clinical indicators that further physical assessment is urgently needed prior to any subsequent injection administration.

19.4 Monitoring and evaluation must be undertaken in discussion with the patient and their carer (if appropriate) and should reflect a shared understanding of relapse plans and any concerns about treatment.

19.5 The physical health of people with schizophrenia should be monitored at least once a year with particular attention to cardiovascular disease risk assessment.[7,8] All organisations should have guidelines in place for this which should also include specific monitoring requirements for injectable long-acting antipsychotic treatment. Appendix 4 outlines these.

20. Clinical Outcome Indicators and Audit

20.1 Clinical Audit is a part of the risk management process that supports using information positively to maintain good practice and to improve practice through learning from practice outcomes. The Nursing and Midwifery Council (NMC) requires nurses and registered nursing associates to work with colleagues to evaluate the quality of their work and that of the team and preserve the safety of those receiving care.[4]

20.2 All untoward incidents that arise as a result of the care pathway within this document must be individually and collectively reviewed to provide sufficient knowledge to inform remedial action where necessary.[10]

20.3 The NPSA (now NHS Improvement) advised healthcare organisations to undertake an audit of medicines practice relating to injections every year and develop an action plan to improve local practice as a result of this when necessary. A template to undertake this is available from: https://healthcareea.vctms.co.uk/assets/content/9652/4759/content/injectable.pdf. This audit should cover all aspects of practice and patient safety data for injectable medicines.[6]

20.4 Organisations can use data from the Care Quality Commission's national and local annual patient survey programme to identify any issues arising from patients' experiences of medication management.

21. Training

21.1 There is a requirement that all registered practitioners involved in prescribing, preparing, administering and monitoring oil-based depot and other long-acting intramuscular antipsychotic injections receive training in order to be able to meet the expected level of competency and standards outlined to prevent harm to patients. This is made explicit by the NPSA (now NHS Improvement) guidance.[6]

21.2 It is a requirement that all service provider organisations demonstrate evidence of how risks are managed in relation to training requirements for their staff if there could be a negative impact on service delivery, business continuity and/or patient or staff safety.[2]

21.3 Training will be underpinned by the principles of patient experience, patient safety and efficient and effective delivery of care. Training should emphasise a person-centred approach, compassionate attitudes and a recognition that a positive patient experience will contribute to patient adherence to and satisfaction with their agreed treatment plan.

22. Glossary of Terms

Term	Definition
Clopixol Acuphase	This is the short-acting formulation of zuclopenthixol injection intended for acute management of psychosis or mania. It should not be confused with the standard longer acting zuclopenthixol depot injection as Acuphase releases the active zuclopenthixol much more quickly and more intensely and incorrect substitution could lead to severe adverse effects.
Deltoid site	The location for administration of injection into the deltoid muscle.
Depot	In mental health, this is the term used for oil-based, long-acting intra-muscular (IM) antipsychotic injections designed to be given by deep IM injection. They consist of the antipsychotic esterified to a decanoate or palmitate dissolved in an oily vehicle. The volume to be injected is deposited deep into the gluteal muscle and forms a depot from where it leaches over time according to its oil: water partition coefficient into the bloodstream. This, together with the time taken for circulating enzymes to hydrolyse the ester back to its active base, is responsible for the prolonged length of action of these formulations.
Dorsogluteal site	The location for administration of injection into the gluteus maximus muscle. Often referred to as the 'upper outer quadrant of the buttock'.
Excipient	An inert substance necessarily incorporated into the formulation. Al-though these are selected to be inactive, the patient could be allergic to them or object to them on religious or cultural grounds. Details of all excipients are available in the relevant SmPC.
First-pass metabolism	This occurs following the absorption from the gut of a medicine that has been taken orally. A significant proportion of that medicine is metabolised by the liver, usually to an inactive by-product, on its 'first pass' through that organ. This reduces its bioavailability.
Injection	Administering a medicine into a patient's body using a syringe and a needle.
Inoculation incident	Any incident where there is exposure to blood-borne viruses, this includes a blood splash or needle stick injury.
Long-acting injection (LAI)	In mental health, this is the term preferred for non-oil-based, long-acting intramuscular antipsychotic formulations such as aripiprazole (Abilify Maintena), olanzapine (ZypAdhera), paliperidone palmitate 1 monthly (Xeplion), paliperidone palmitate 3 monthly (Trevicta) and risperidone (Risperdal Consta) long-acting injections. The same careful injection technique is required to administer these products, but their release characteristics are very different to each other as well as to oil-based formulations.
Overage	The additional volume added to an ampoule in order to enable the full volume required to be extracted. The overage is invariably higher for oily injections as they are much more viscous (thicker) than aqueous injections. Such overages vary between countries and the British overage for oily injections is, for example, smaller than the Danish overage. This is why zuclopenthixol (Clopixol) and flupentixol (Depixol) injections always seem generously filled.

Rectus femoris	The rectus femoris muscle of the anterior/lateral thigh (not recommended for intramuscular injections).
Test dose	An initial low dose of an oil-based depot antipsychotic injection which must be given to assess for tolerability to both the active ingredient and its vehicle or any other excipient.
Vastus lateralis	The lateral quadriceps muscle.
Vehicle	An inert liquid in which a medicine is dissolved or suspended. Although these are selected to be inactive, the patient could be allergic to them or object to them on religious or cultural grounds. (e.g., sesame oil, benzyl alcohol). Details of all vehicles are available in the relevant SmPCs.
Ventrogluteal site	The location for administration of injection into the gluteus medius and gluteus minimus. Colloquially referred to as the 'hip site'.
Z-tracking	This is the recommended technique for all deep IM injections. it displaces superficial layers of skin and tissue creating a broken injection pathway (the z-track) containing the medicine in the intended target muscle and preventing it from moving back up the track to leak out at the skin surface.[81] This has the advantage of achieving the correct plasma concentration whilst minimising the risk of pain or lesions at the injection site.

23. Additional Reading

Hardy S, White J, Gray R. *The Health Improvement Profile: A manual to promote physical wellbeing in people with severe mental illness*. 2nd Ed. Keswick: M&K Publishing; 2018.

NHS England. *The Independent Mental Health Taskforce - The Five Year Forward View for Mental Health*. 2016. Available from: https://www.england.nhs.uk/wp-content/uploads/2016/02/Mental- Health-Taskforce-FYFV-final.pdf. Accessed June 2020.

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Waddell L, Taylor M. Attitudes of patients and mental health staff to antipsychotic long-acting injections: systematic review. *British Journal of Psychiatry*. 2009;195(S52):S43-50.

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24. Appendices

Appendix 1: Standard Operating Procedures (SOPs 1–6)
This appendix contains six Standard Operating Procedures (SOPs) for the administration of oil-based depot and other long-acting antipsychotic injections.
(These may be copied and used by any organisation or healthcare professional):

SOP 1. General Preparation for Deep Intramuscular (IM) Injection

SOP 2. Z-track Administration Technique

SOP 3. Administration Technique for the Deltoid Site

SOP 4. Administration Technique for the Dorsogluteal Site

SOP 5. Administration Technique for the Ventrogluteal Site

SOP 6. Administration Technique for the Vastus Lateralis site

Appendix 2: Oil-based Depot and Other Long-Acting Intramuscular Antipsychotic Injections

Appendix 3: Dose, Dosing Interval and Approximate Chlorpromazine Equivalents of Oil- based Depot Antipsychotic Intramuscular Injections

Appendix 4: Outline of Monitoring Requirements during Treatment with Long-acting Injectable Antipsychotics

Appendix 5: Guidance on Missed Doses of Long-acting Injectable Antipsychotics

Appendix 6: Antipsychotics Dose Calculation Workbook

Appendix 7: Questions to ask your Healthcare Professional
(These may be copied and given to a patient or carer)

Appendix 8: Human Factor Error Risk Reduction Checklist Template

Appendix 9: An Audit Tool for Oil-based Depot and Other Long-Acting Intramuscular Antipsychotic Injections (This may be copied and used by an organisation or healthcare professional)

SOP 1	Standard Operating Procedure 1 General Preparation for Deep Intramuscular (IM) Injection	Guidance Document Reference
Applicable to:	Registered practitioners required to administer oil-based depots and other long-acting intramuscular antipsychotic injections in the course of their practice.	
Process 1	Wash your hands according to accepted hand cleansing technique and put on disposable gloves and all other recommended Personal Protective Equipment.	15.2 15.3 15.4
Process 2	Check to see if the patient's physical or mental health has changed since the previous contact, including the health of the injection sites.	12.2 13.6 19.3
Process 3	Ask about perceived benefit and any side effects experienced since the last injection – if this is not the first.	12.2
Process 4	Check to ensure: • The prescription is legal and valid. • The dose is due. • The dose has not already been given. • There are no contraindications or allergies. • The injection is 'in date'	12.3 12.4 13.6
Process 5	Confirm that the patient has the capacity to consent and gives their consent to the procedure.	12.3 12.5 13.1
Process 6	Prepare the injection making any necessary dose calculation and using the correct equipment.	13.3 14.1 14.10
Process 7	Get a second registered practitioner, if available, to double check all items in processes 4, 5 & 7.	12.3
Process 8	If a second registered practitioner is not available, ask the patient to check that the correct injection and dose is to be administered and that the injection is in date.	12.3
Process 9	Choose the site of administration according to the licensed indication for the injection and in collaboration with the patient, proceed according to SOP 3, SOP 4, SOP 5 or SOP 6, whichever is appropriate.	16.1–16.10
Date of preparation:	**Authorised by:**	**Date of next review:**
June 2022		

SOP 2	Standard Operating Procedure 2 Z-track Administration Technique (See figure opposite)	Guidance Document Reference
Applicable to:	Registered practitioners required to administer oil-based depots and other long-acting intramuscular antipsychotic injections in the course of their practice. This technique should be used for all intramuscular injections.	17.4
Process 1	Pull the skin in the target area taut and to one side with either the thumb or side of the non-dominant hand and maintain this firm traction of the skin throughout the procedure.[81]	
Process 2	Insert the needle with a darting motion at 90 degrees to the skin surface to an adequate depth to allow the needle to penetrate the muscle.[81] Keep the graduation markings on the syringe barrel visible at all times	17.5 14.5
Process 3	**For dorsogluteal injections only** – for all other sites where there are no major blood vessels below the injection site, this is unnecessary[74] so go to Process 4. Steady the barrel of the syringe with the remaining fingers of the non- dominant hand and pull back on the plunger with the dominant hand to aspirate. Should blood appear in the syringe all the equipment must be discarded and the whole procedure started again.[74] If no blood appears, it is safe to continue.	
Process 4	Depress the plunger slowly (1 ml per 10 seconds) to allow the muscle fibres to expand to accommodate the drug.[81]	
Process 5	Wait a further 10 seconds before removing the needle and once it has been removed, only then release the traction on the skin.[59]	
Process 6	If necessary, the injection site may be wiped with a dry gauze swab.	
Process 7	A plaster may be applied if this is the patient's choice and if they have no known allergy to latex, iodine or Elastoplast®.	
Date of preparation:	**Authorised by:**	**Date of next review:**
June 2022		

Z-track Administration Technique

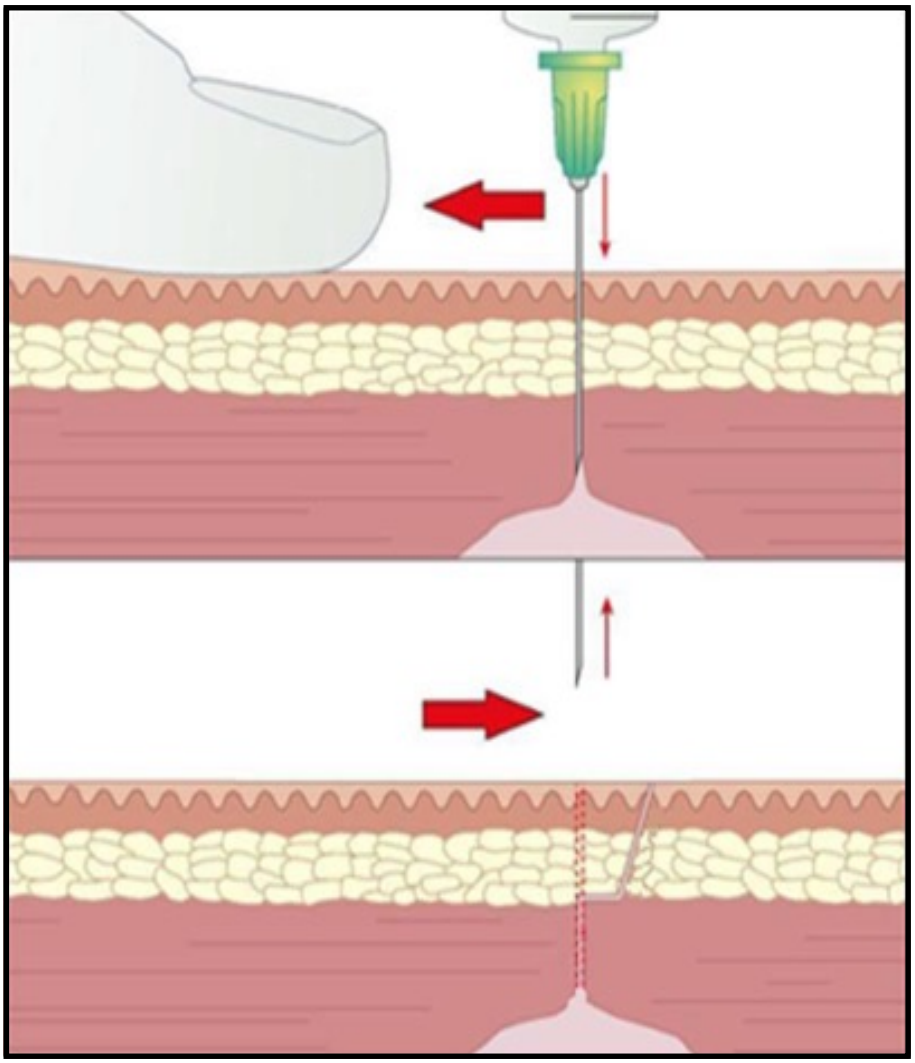

Figure 2: Z-track Technique

SOP 3	Standard Operating Procedure 3 Administration Technique for the Deltoid Site (See figures opposite)	Guidance Document Reference
Applicable to:	Registered practitioners required to administer a long-acting intramuscular antipsychotic injection at the deltoid site in the course of their practice.	17.4
Process 1	Ask the patient to sit down and loosen their clothes so their arm and shoulder are exposed. Ask them to position their arm across their body to relax the muscles (Fig 3a).	
Process 2	Follow processes 1–9 in SOP 1.	17.5 14.5
Process 3	Palpate the upper arm and find the landmarks of the acromion process and the axilla. The target injection site can be located by visualising an inverted triangle which extends from the base of the acromion process and extends down to a point level with the axilla. Now form a rectangle within the original triangle by placing two fingers below the acromion process to form the top edge of the rectangle and with the bottom edge level with the axilla. The side edges should be parallel to the arm. The injection site is in the middle of this visualised rectangle (Figs 3d & 3e).[83]	
Process 4	Clean the skin if necessary with soap and water or according to local policy	13.5
Process 5	Administer the injection using a Z-track technique (SOP 2) (Fig 2).	17.5
Process 6	Dispose of all equipment immediately with safe disposal of sharps into an appropriate, puncture proof, correctly labelled sharps bin. Do not re-sheath needle.	15.6 15.7
Process 7	Document on the prescription/administration chart and in the clinical record the date, time and dose of medication administered, injection site and side of the body plus any deviation from standard practice with a rationale for the clinical decision to do so.	18.4
Process 8	Exchange information about monitoring arrangements, how to manage common side effects and what to do if the patient experiences any change to their mental or physical health status before the next clinical contact.	19.4
Process 9	Remove personal protective equipment including gloves and wash your hands according to accepted hand-cleansing technique.	15.3- 15.10
Date of preparation:	**Authorised by:**	**Date of next review:**
September 2022		

Administration Technique for the Deltoid Site

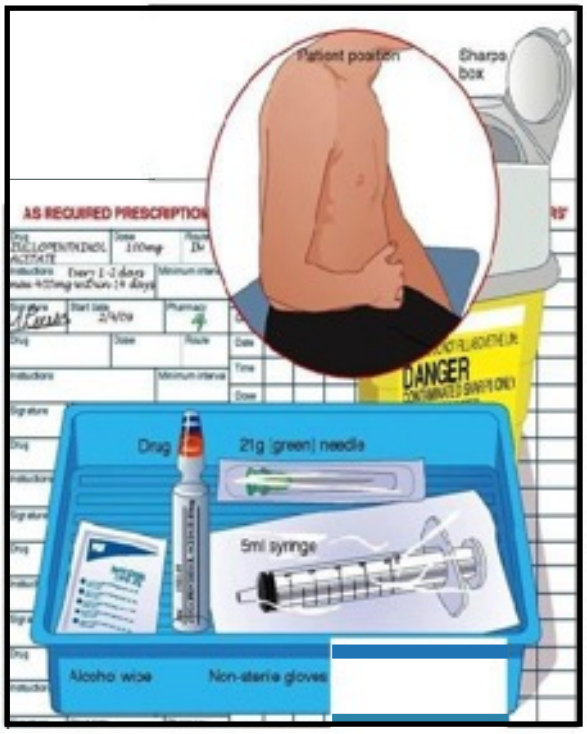

Figure 3a

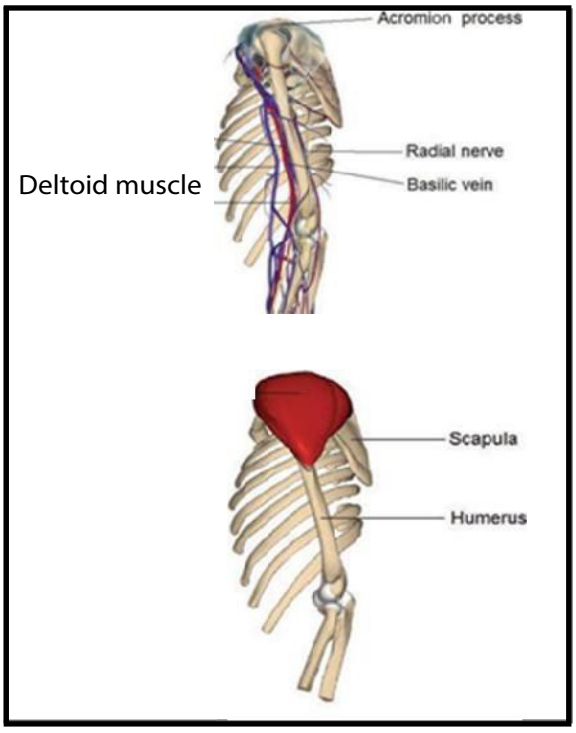

Figure 3b & 3c

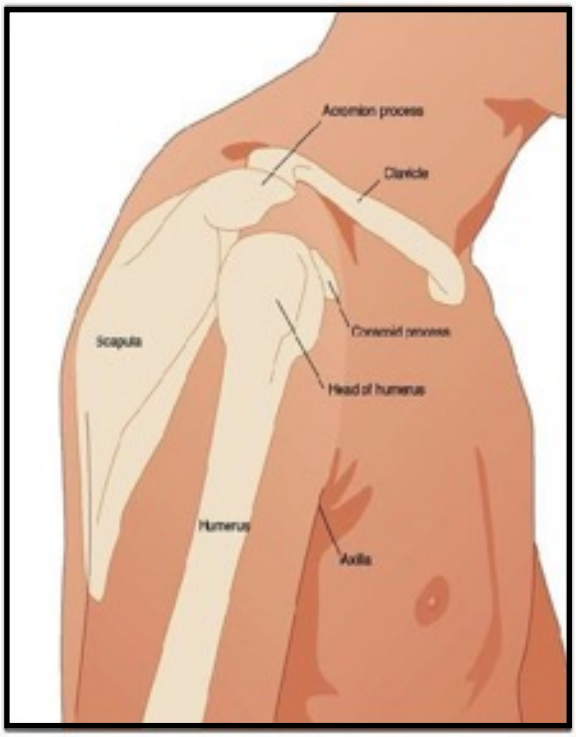

Figure 3d

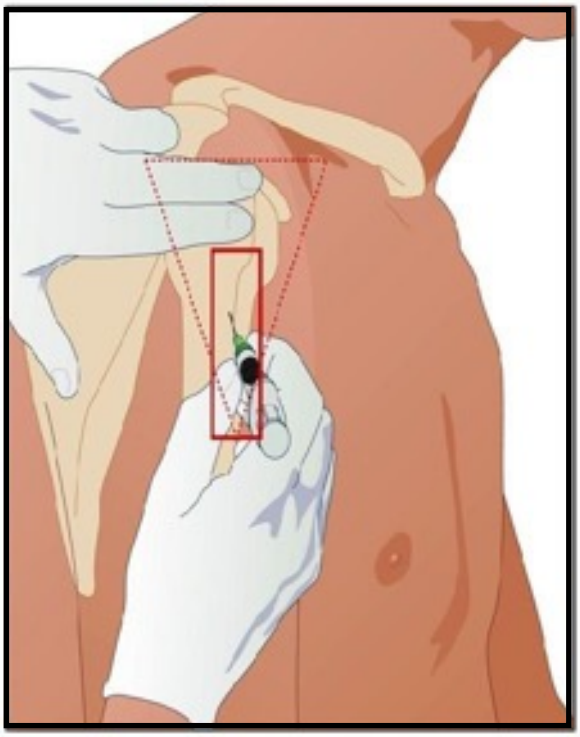

Figure 3e

SOP 4	Standard Operating Procedure 4 Administration Technique for the Dorsogluteal Site (See figures opposite)	Guidance Document Reference
Applicable to:	Registered practitioners required to administer a long-acting intramuscular antipsychotic injection at the dorsogluteal site in the course of their practice.	
Process 1	Follow processes 1–9 in SOP 1.	
Process 2	Ask the patient to lie down and loosen their clothes so one buttock is exposed. Ask them to either lie on their front or side with the femur internally rotated to minimise pain on administration (Fig 4a).	13.2 13.3
Process 3	If a syringe and/or needle is provided in the product pack by the manufacturer this MUST be used. If not select an appropriate needle length to reach the gluteus muscle. Consider the Body Mass Index (BMI) and gender of the patient. In obese patients with a BMI of 30 or more, a 51mm needle or alternative injection site may be required.	14.1-14.10
Process 4	Draw an imaginary cross onto one buttock and identify the upper outer quadrant. Divide this first quadrant into quarters. The injection site is located within the upper outer quadrant of the upper outer quadrant, approximately 5 cm to 7.5 cm below the iliac crest (Fig 4e).[83]	
Process 5	Clean the skin only if necessary, with soap and water or according to local policy.	13.5
Process 6	Administer the injection using a Z-track technique (SOP 2) (Figs 2 & 4f).	17.5
Process 7	Dispose of equipment immediately with safe disposal of sharps into an appropriate, puncture-proof, correctly labelled sharps bin. Do not re-sheath needle.	15.6 15.7
Process 8	Document on the prescription/administration chart and in the clinical notes record the date, time and dose of medication administered, injection site and side of the body plus any deviation from standard practice with rationale for the clinical decision to do so.	18.4
Process 9	Exchange information about monitoring arrangements, how to manage common side effects and what to do if the patient experiences any change to their mental or physical health status before the next clinical contact.	19.4
Process 10	Remove personal protective equipment including gloves and wash your hands according to accepted hand-cleansing technique.	15.3- 15.10
Date of preparation:	**Authorised by:**	**Date of next review:**
September 2022		

Administration Technique for the Dorsogluteal Site

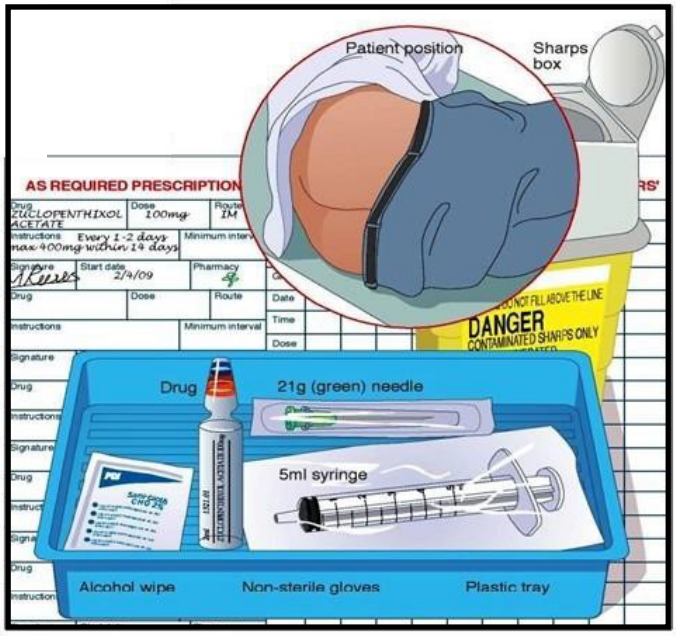

Figure 4a

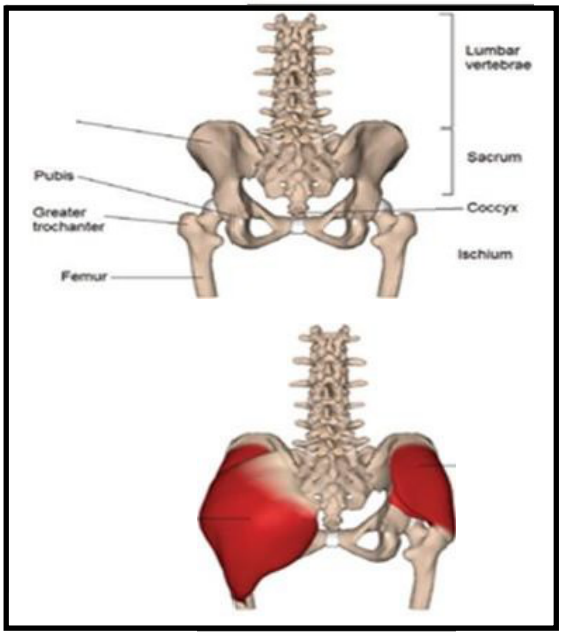

Figure 4b& 4c

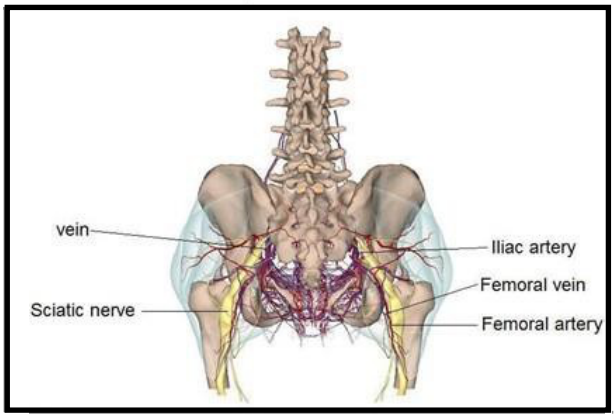

Figure 4d

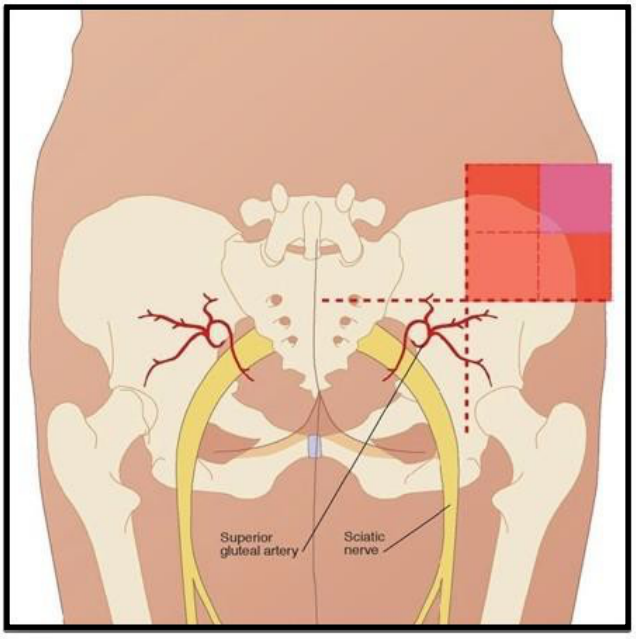

Figure 4e

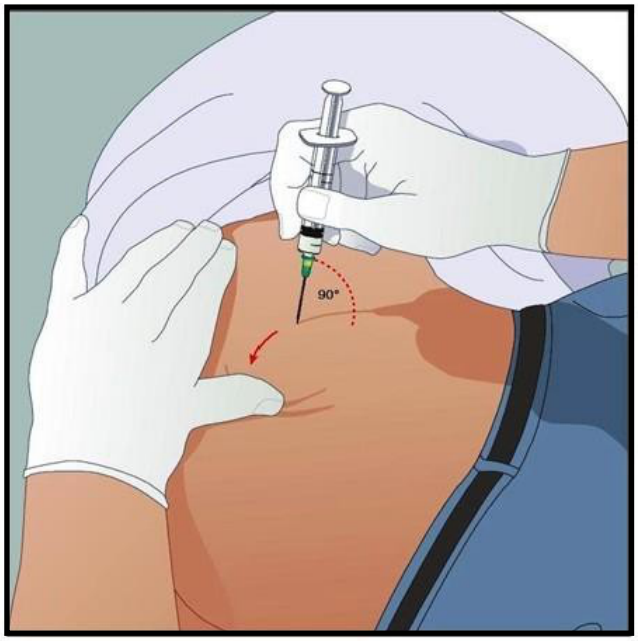

Figure 4f

SOP 5	Standard Operating Procedure 5 Administration Technique for the Ventrogluteal Site (See figures opposite)	Guidance Document Reference
Applicable to:	Registered practitioners required to administer a long-acting intramuscular antipsychotic injection at the ventrogluteal site in the course of their practice.	
Process 1	Follow processes 1–9 in SOP 1.	
Process 2	Ask the patient to lie down on their side and expose their hip (Fig 5a).	13.2 13.3
Process 3	Palpate the greater trochanter (Fig 5d). Place the heel of the opposite hand to the patient's leg on the greater trochanter (i.e., your left hand on their right leg or vice versa). Locate and place index finger on the anterior superior ileac spine and travel along it until your index finger is in line with the vertical axis of the body. Your thumb should be pointing towards the front of the leg. Spread the middle finger to form a 'V'. The injection site is in the middle of this 'V', level with the first knuckles of your fingers (i.e., proximal interphalangeal joints) (Fig 5d).[84]	
Process 4	Visualise the site and remove your hand to prevent needle stick injury.	
Process 5	Clean the skin only if necessary with soap and water or according to local policy.	13.5
Process 6	Administer the injection using a Z-track technique (SOP 2) (Fig 2).	17.5
Process 7	Dispose of equipment immediately with safe disposal of sharps into an appropriate, puncture-proof, correctly labelled sharps bin. Do not re-sheath needle.	15.6 15.7
Process 8	Dispose of equipment immediately with safe disposal of sharps into appropriate, puncture-proof, correctly labelled sharps bin. Do not re-sheath needle.	18.4
Process 9	Document on the prescription/administration chart and in the clinical record the date, time and dose of medication administered, injection site and side of the body plus any deviation from standard practice with a rationale for the clinical decision to do so.	19.4
Process 10	Exchange information about monitoring arrangements, how to manage common side effects and what to do if the patient experiences any change to their mental or physical health status before the next clinical contact.	15.3- 15.10
Date of preparation:	**Authorised by:**	**Date of next review:**
September 2022		

Administration Technique for the Ventrogluteal Site

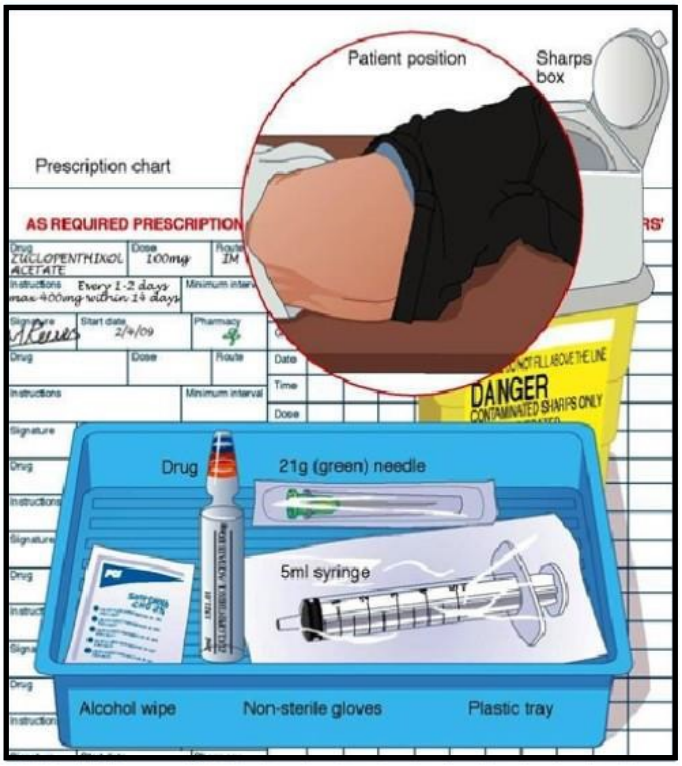

Figure 5a

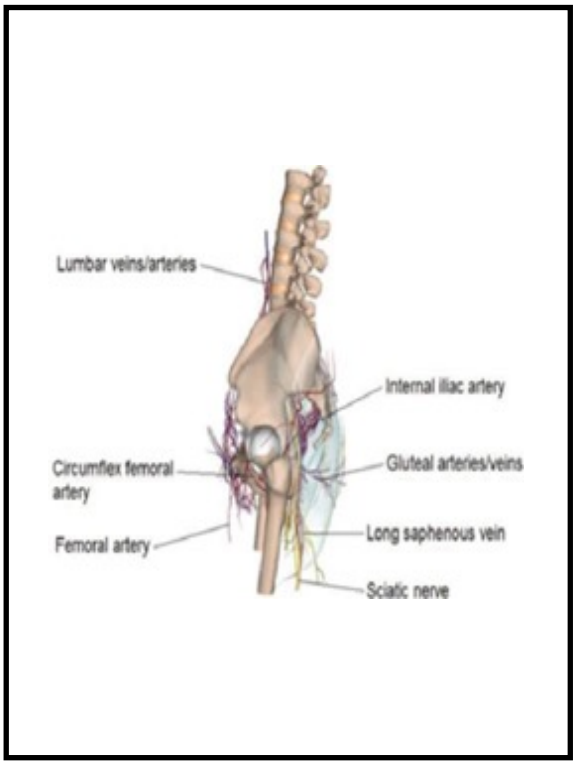

Figure 5b

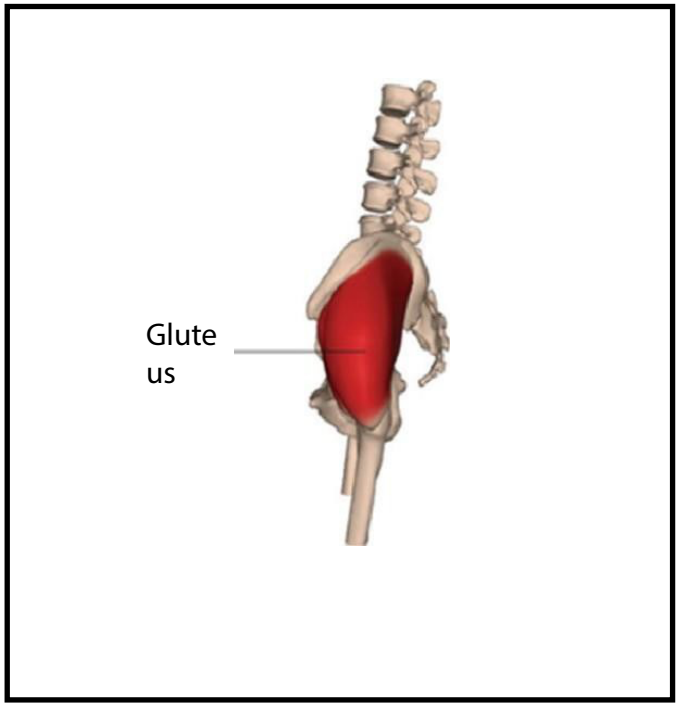

Figure 5c

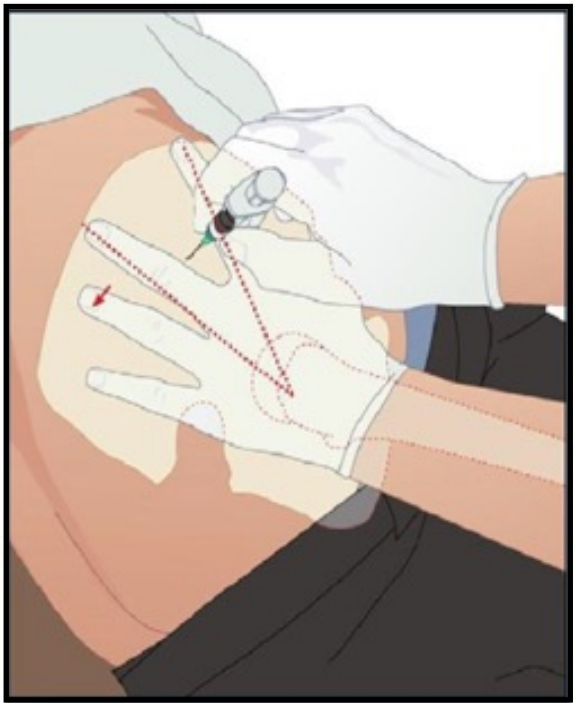

Figure 5d

SOP 6	Standard Operating Procedure 6 Administration Technique for the Vastus Lateralis site (See figures opposite)	Guidance Document Reference
Applicable to:	Registered practitioners required to administer a long-acting intramuscular antipsychotic injection at the vastus lateralis site in the course of their practice.	
Process 1	Follow processes 1–9 in SOP 1.	
Process 2	Ask the patient to either sit or lie down and expose their upper legs (Fig 6a).	13.2 13.3
Process 3	**The vastus lateralis** site targets the lateral side of the quadriceps femoris group of muscles and is situated in the anterior lateral aspect of the thigh. It is located by placing the little finger of one hand on the lateral femoral condyle of the knee and the little finger of the other hand on the greater trochanter. Now try to touch both thumbs together. Both hands are then spanning the distance and the injection site is at the midpoint (Fig 6e).[83]	
Process 4	Visualise the site and remove your hand to prevent needle stick injury.	
Process 5	Clean the skin only if necessary with soap and water or according to local policy.	13.5
Process 6	Administer the injection using a Z-track technique (SOP 2) (Fig 2).	17.5
Process 7	Dispose of equipment immediately with safe disposal of sharps into appropriate, puncture-proof, correctly labelled sharps bin. Do not re-sheath needle.	15.6 15.7
Process 8	Document on the prescription/administration chart and in the clinical record the date, time and dose of medication administered, injection site and side of the body plus any deviation from standard practice with a rationale for the clinical decision to do so.	18.4
Process 9	Exchange information about monitoring arrangements, how to manage common side effects and what to do if the patient experiences any change to their mental or physical health status before the next clinical contact.	19.4
Process 10	Remove personal protective equipment including gloves and wash your hands according to accepted hand-cleansing technique.	15.3- 15.10
Date of preparation:	**Authorised by:**	**Date of next review:**
September 2022		

Administration Technique for the Vastus Lateralis Site

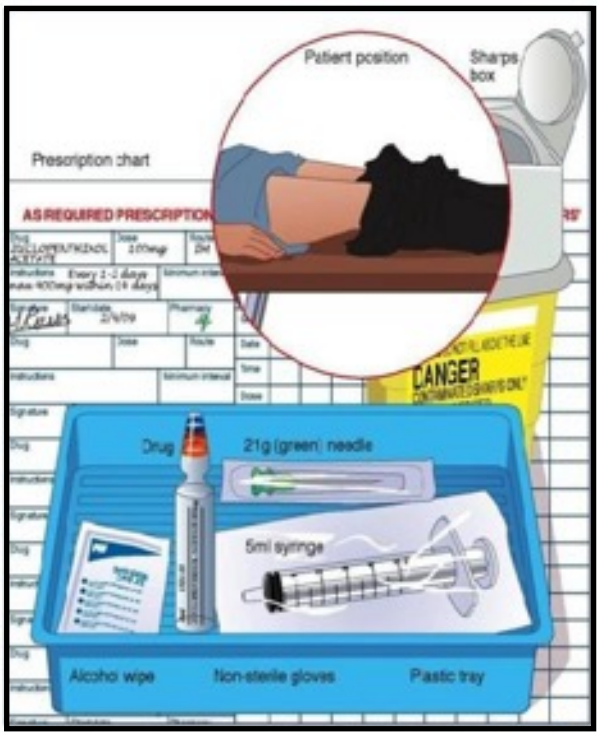

Figure 6a

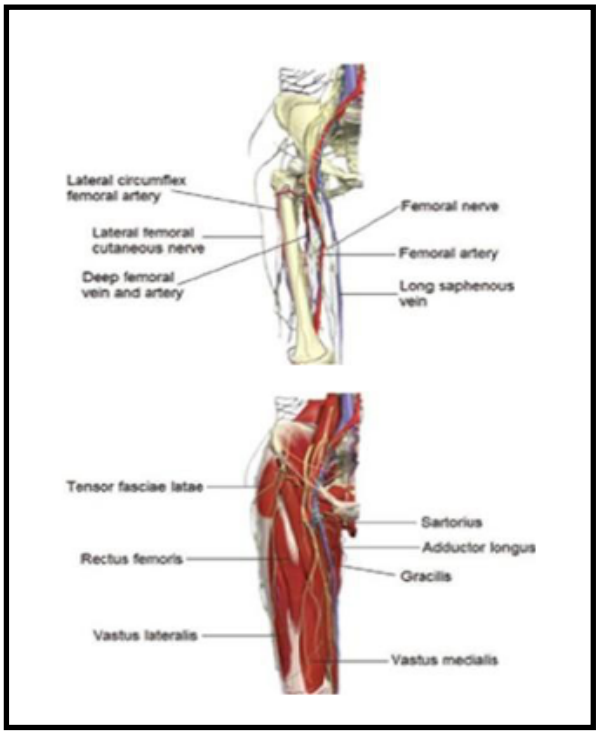

Figure 6b& 6c

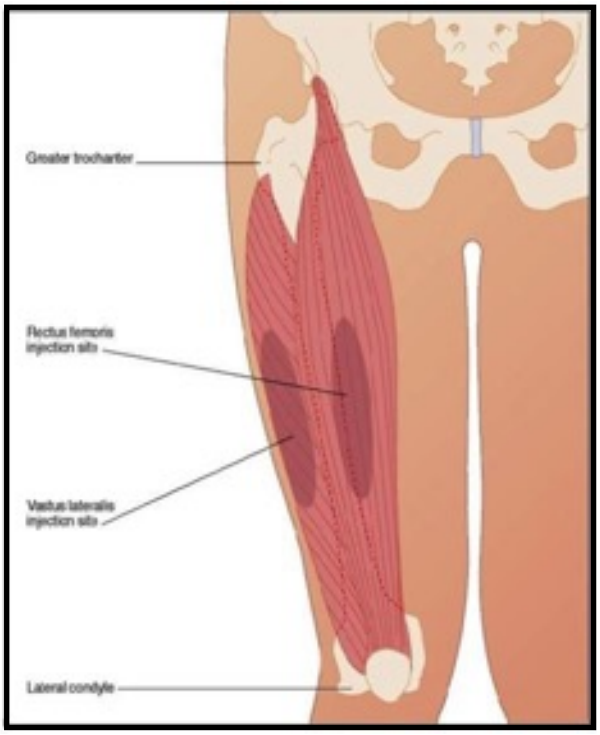

Figure 6d

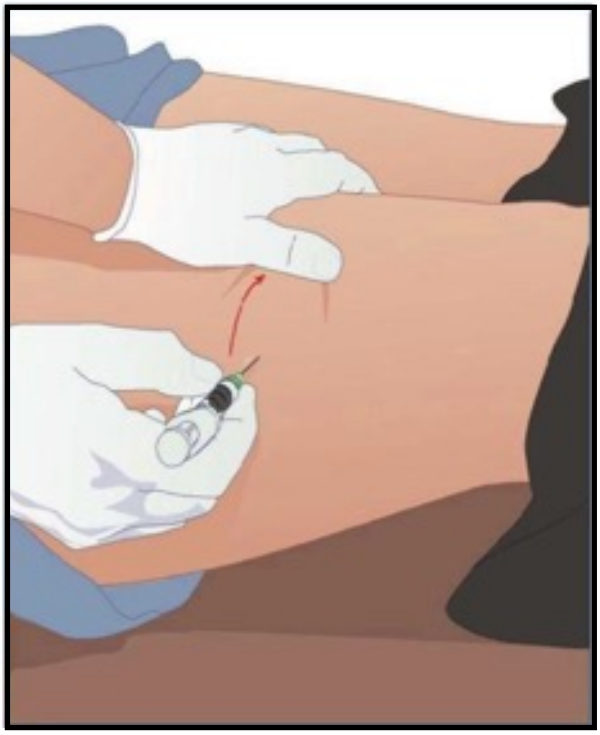

Figure 6e

Appendix 2: Oil-Based Depot and Other Long-Acting Intramuscular Antipsychotic Injections[11,20,23]

Oil-Based Depot Intramuscular Antipsychotic Injections

General note: The viscosity of all oil-based injections is reduced at warmer temperatures, i.e., they will become less sticky and easier to draw up and administer when close to body temperature. The viscosity (thickness) of sesame oil is higher (thicker) than thin vegetable oil.

Antipsychotic Generic Name and Formulation	UK Brand name	Standard dose range for adult maintenance	Practice points
Flupentixol decanoate[65,66] In thin vegetable oil (derived from coconuts)	Depixol Injection: 20 mg in 1 ml Depixol Concentrate Injection: 100 mg in 1 ml Depixol Low Volume Injection: 200 mg in 1 ml	50 mg every 4 weeks to 300 mg every 2 weeks BNF Max: 400 mg weekly	**Route:** Deep intramuscular injection into the upper outer buttock (dorsogluteal) or lateral thigh (vastus lateralis) • The maximum volume into a single site should not exceed 2 ml • A test dose of 20 mg is indicated
Fluphenazine decanoate in sesame oil Modecate is no longer marketed in the UK but an imported (unlicensed) products containing 25 mg in 1 ml and 100 mg in 1 ml of fluphenazine decanoate are available on a 'named patient basis' for those patients for whom there is no alternative	Modecate Injection: 25 mg in 1 ml Modecate Conc. Injection: 100 mg in 1 ml	12.5 mg (6.25 mg for patients over 60) to 100 mg every 2–5 weeks	**Route:** Deep intramuscular injection into the gluteal region A test dose of 12.5 mg (6.25 mg in the elderly) is indicated
Haloperidol decanoate[85] in sesame oil	Haldol decanoate: 50 mg in 1 ml Haldol decanoate: 100 mg in 1 ml	50 mg every 4 weeks to 300 mg every 4 weeks If 2-weekly administration is preferred, these doses should be halved	**Route:** Deep intramuscular injection into the gluteal region using an appropriate needle, preferably 2–2.5 inches long, of at least 21 gauge A test dose of 25 mg (12.5 mg in the elderly) is indicated
Pipotiazine palmitate[86] in sesame oil Piportil is no longer marketed in the UK but an imported (unlicensed) product containing 25 mg in 1 ml of pipotiazine palmitate is available on a 'named patient basis' for those patients for whom there is no alternative	Piportil Depot 5% w/v (50 mg in 1 ml)	50 mg (5–10 mg in elderly) to 100 mg every 4 weeks BNF max. 200 mg every 4 weeks	**Route:** Deep intramuscular injection into the gluteal region A test dose of 25 mg (5–10 mg in elderly) is indicated
Zuclopenthixol decanoate[74,75] In thin vegetable oil (derived from coconuts)	Clopixol Injection (200 mg in 1 ml) Clopixol Conc. Injection (500 mg in 1 ml)	200 mg to 500 mg every 1–4 weeks BNF Max: 600 mg every week	**Route:** Deep intramuscular injection into the upper outer buttock (dorsogluteal) or lateral thigh (vastus lateralis) • The maximum volume into a single site should not exceed 2 ml • A test dose of 100 mg (25–50 mg in the elderly) is indicated

Other Long-Acting Intramuscular Antipsychotic Injections			
Antipsychotic Generic Name and Formulation	**UK Brand name**	**Standard dose range for adult maintenance treatment**	**Practice points**
Aripiprazole[14] Powder and solvent for prolonged-release suspension for deep intramuscular injection	Abilify Maintena 400 mg & pre-filled syringes are also available to save reconstitution	**Initiation** There are two different start regimes: The **one injection start regime** requires treatment with 10 mg to 20 mg oral aripiprazole to be continued for 14 consecutive days to maintain therapeutic aripiprazole concentrations during initiation of therapy The **two-injection start regime** (into different muscles*), along with one 20mg dose of aripiprazole does not require ongoing oral supplementation. **Thereafter** 400 mg monthly	**Route:** Deep intramuscular injection into either the gluteal or the deltoid muscle • Patients should normally be initially successfully treated with oral aripiprazole before receiving the long- acting injection in order to establish tolerability and response • Initial dose titration is not required • It should be administered once monthly as a single injection (no sooner than 26 days after the previous injection). Detailed instructions regarding missed doses are provided in the SmPC • There are two different start regimes: The one injection start regime requires treatment with 10 mg to 20 mg oral aripiprazole to be continued for 14 consecutive days to maintain therapeutic aripiprazole concentrations during initiation of therapy, the two-injection start regime (into different muscles*), along with one 20mg dose of aripiprazole does not require ongoing oral supplementation. • *For known CYP2D6 poor metabolisers DO NOT inject into both gluteal muscles, use either both deltoid muscles or one deltoid and one gluteal muscle. • If there are adverse reactions with the 400 mg dosage, a reduction to 300 mg once monthly should be considered.

Other Long-Acting Intramuscular Antipsychotic Injections			
Antipsychotic Generic Name and Formulation	**UK Brand name**	**Standard dose range for adult maintenance treatment**	**Practice points**
Olanzapine pamoate monohydrate[15] Powder and solvent for prolonged release suspension for deep intramuscular injection	ZypAdhera 210 mg ZypAdhera 300 mg ZypAdhera 405 mg Powder and solvent for prolonged release suspension for deep intramuscular injection. When reconstituted with the supplied solvent all vials provide a final concentration of 150 mg olanzapine per 1 ml. Hence for a 150 mg dose 1 ml of a reconstituted vial is administered. For economic reasons to reduce wastage this should always be the 210 mg preparation	150 mg – 300 mg olanzapine every 2 weeks Doses may be adjusted to allow a 4- weekly frequency noting that 405 mg 4- weekly substitutes for 210 mg 2-weekly regimen	**Route:** Deep intramuscular gluteal injection • Only needles supplied in the dose pack should be used • Online training provided by the manufacturer is available to practitioners unfamiliar with this product • Fractions of a dose may not be administered • Patients should be initially successfully treated with oral olanzapine before receiving the long-acting injection in order to establish tolerability and response. • A dosing table in the SmPC provides the information for equivalent long-acting IM dose to oral regimen in place • Fractions of a dose may not be administered • The initiation of long-acting IM olanzapine should be made without recourse to cross-tapering of oral medication. Although this may feel counter-intuitive, non-oil-based long-acting antipsychotics must be seen as products with discrete pharmacokinetic properties • After each injection, patients must be observed for post-injection syndrome (signs and symptoms consistent with olanzapine overdose) in a healthcare facility by appropriately qualified personnel for at least 3 hours

Other Long-Acting Intramuscular Antipsychotic Injections			
Antipsychotic Generic Name and Formulation	**UK Brand name**	**Standard dose range for adult maintenance treatment**	**Practice points**
Paliperidone palmitate[16] (PP1M) Prolonged-release suspension for injection	Xeplion 50 mg Xeplion 75 mg Xeplion 100 mg Xeplion 150 mg Supplied in pre-filled syringes	**Initiation:** **Day 1:** 150 mg into the deltoid muscle **Day 8:** 100 mg into the deltoid muscle **One month later:** 75 mg – 150 mg according to clinical need into either the deltoid or gluteal muscles. **Thereafter:** once a calendar month (not 28 days)	**Route:** By deep IM injection. The Day 1 and Day 8 initiation doses must each be administered into the deltoid muscle in order to attain therapeutic plasma concentrations rapidly. Following the second dose, monthly maintenance doses can be administered in either the deltoid or gluteal muscle • A switch from gluteal to deltoid (and vice versa) should be considered in the event of injection site pain if the discomfort is not acceptable. It is also recommended to alternate between left and right sides. Fractions of a dose should not be administered • Only needles supplied in the dose pack should be used • Fractions of a dose may not be administered.
Paliperidone palmitate[17] (PP3M) Prolonged-release suspension for injection	Trevicta 175 mg Trevicta 263 mg Trevicta 350 mg Trevicta 525 mg Prolonged-release suspension of paliperidone for injection in pre- filled syringes	Dosing is based on the last dose of one monthly paliperidone injection using a 3.5-fold higher dose A dosing table is available in the SmPC[17]	**Route**: Deep intramuscular injection into either the gluteal or the deltoid muscle. Only needles supplied by the manufacturer should be used • Detailed instructions regarding missed doses are provided in the SmPC • If needed, dose adjustment can be made every 3 months in increments within the range of 175 mg to 525 mg based on individual patient tolerability and/or efficacy • Due to the long-acting nature of this formulation the patient's response to an adjusted dose may not be apparent, if the patient remains symptomatic, they should be managed according to clinical practice • To avoid incomplete administration, the pre-filled syringe must be shaken vigorously for at least 15 seconds within 5 minutes prior to administration to ensure a homogeneous suspension. In the event of an incompletely injected dose, the dose remaining in the syringe should not be re-injected and another dose should not be given since it is difficult to estimate the proportion of the dose actually administered. The patient should be closely monitored and managed as clinically appropriate until the next scheduled 3-monthly injection • Details regarding what should be done when doses are missed may be found in the SmPC • Fractions of a dose may not be administered.

Other Long-Acting Intramuscular Antipsychotic Injections			
Antipsychotic Generic Name and Formulation	**UK Brand name**	**Standard dose range for adult maintenance treatment**	**Practice points**
Paliperidone palmitate[18] (PP6M) Prolonged-release suspension for injection every 6 months	Byannli 700 mg Byannli 1000 mg Prolonged-release suspension of paliperidone for injection in pre-filled syringes	Dosing depends on the transition from the PP1M or PP3M dose that has achieved clinical stability in the individual patient A dosing table is available in the SmPC	**Route:** Deep intramuscular injection into the gluteal muscle. Only needles supplied by the manufacturer should be used. • Detailed instructions regarding missed doses are provided in the SmPC • If needed, dose adjustment can be made by transitioning between the 700 mg and 1000 mg dose based on individual patient tolerability and/or efficacy • Due to the long-acting nature of this formulation the patient's response to an adjusted dose may not be apparent, if the patient remains symptomatic, they should be managed according to clinical practice • To avoid incomplete administration, the pre-filled syringe must be shaken vigorously for at least 15 seconds, followed by a 5 second rest and a further 15 second vigorous shake within 5 minutes prior to administration to ensure a homogeneous suspension. In the event of an incompletely injected dose, the dose remaining in the syringe should not be re-injected and another dose should not be given since it is difficult to estimate the proportion of the dose actually administered. The patient should be closely monitored and managed as clinically appropriate until the next scheduled 6- monthly injection • Details regarding what should be done when doses are missed may be found in the SmPC • Fractions of a dose may not be administered.

Other Long-Acting Intramuscular Antipsychotic Injections			
Antipsychotic Generic Name and Formulation	**UK Brand name**	**Standard dose range for adult maintenance treatment**	**Practice points**
Risperidone[13] Powder and solvent for prolonged-release suspension for intramuscular injection	Risperdal Consta 25 mg Risperdal Consta 37.5 mg Risperdal Consta 50 mg Powder and solvent for prolonged- release suspension for deep intramuscular injection Also available in pre-filled syringes to save reconstitution	25 mg to 50 mg every 2 weeks BNF Max. Dose: 50 mg every 2 weeks	**Route:** Deep intramuscular gluteal or deltoid injection using either the supplied 20g 50 mm safety needle (gluteal) or the 21g 25 mm safety needle (deltoid) also supplied. Injections should alternate between buttocks or right and left arms • Only needles supplied in the dose pack should be used • Refrigerated storage and maintenance of the cold chain is essential until administration • A test dose is not indicated but tolerability and efficacy of oral risperidone must be confirmed before treatment is initiated • Fractions of a dose may not be administered • The maximum volume that may be administered in to one site is less restrictive but for overall comfort not more than single diluent volume should be injected in to any one site. When administering doses above 50 mg (unlicensed) it is considered acceptable practice by the authors to use the reconstituted higher-strength injection as a diluent for the second vial • After a single intramuscular injection, the release profile consists of a small initial release of risperidone (<1% of the dose), followed by a lag time of 3 weeks. The main release of risperidone starts from week 3 onwards, is maintained from 4 to 6 weeks, and subsides by week 7. Oral antipsychotic supplementation should therefore be given during the first 3 weeks of treatment • The combination of the release profile and the dosage regimen (intramuscular injection every 2 weeks) results in sustained therapeutic plasma concentrations. • Therapeutic plasma concentrations remain until 4 to 6 weeks after the last injection.

Risperidone ISM[20,87] powder and solvent for prolonged release suspension for injection	Okedi 75 mg, Okedi 100 mg Powder and solvent for prolonged release suspension for injection	Initiation is after tolerability and response has been established to oral risperidone. 75 mg or 100 mg every 28 days BNF Max.Dose: 100 mg every 28 days	**Route:** Deep intramuscular gluteal or deltoid injection using the supplied sterile 20g 51mm safety needle (gluteal) or21g 25mm safety needle (deltoid). Injections should alternate between the two dorsogluteal, or two ventrogluteal sites or right and left arms (deltoid sites). • Only needles supplied in the dose pack should be used • Does not require refrigeration but should be stored below 30° C in the original packaging to protect from moisture • A test dose is not indicated but tolerability and efficacy of oral risperidone must be confirmed before treatment is initiated • Fractions of a dose may not be administered • The maximum volume that may be administered into one site is less restrictive but for overall comfort not more than single diluent volume should be injected in to any one site. • The combination of the release profile and the dosage regimen (intramuscular injection every 28 days) results in sustained therapeutic plasma concentrations • Therapeutic plasma concentrations start to decline by up to 50% in the week after the next 28-day dose if this dose is missed

Appendix 3: Dose, Dosing Interval[12] and Approximate Chlorpromazine Equivalents[88] of Oil-based Depot Antipsychotic

Antipsychotic Generic Name	Trade Name	Dose (mg)	Normal Dosing Interval	Approximate Dose Equivalent to Chlorpromazine 100 mg a day[88]	Range of Values from the Literature[88]
Flupentixol decanoate	Depixol	40 mg	2-weekly	10 mg per week	10–20 mg per week
Fluphenazine de-canoate	Modecate	25 mg	2-weekly	5 mg per week	1–12.5 mg per week
Haloperidol de-canoate	Haldol	100 mg	4-weekly	15 mg per week (500 mg of chlorpromazine a day is equivalent to 100 mg of haloperidol decanoate monthly) (25 mg of fluphenazine decanoate 2-weekly or 40 mg of flupentixol decanoate 2-weekly is equivalent to 100 mg of haloperidol decanoate monthly)	5–25 mg per week
Pipotiazine palmitate (No longer marketed in the UK but imported on a 'Named Patient Basis' for those patients for whom there is no alternative)	Piportil	50 mg	4-weekly	10 mg per week	10–12.5 mg per week
Zuclopenthixol decanoate	Clopixol	200 mg	2-weekly	100 mg per week	40–100 mg per week

Appendix 4: Outline of Monitoring requirements during treatment with long-acting injectable antipsychotics[7,8,12,23,89-93]

Test, Measurement or Assessment	Reason	Frequency		
		At Baseline	At 3 months	Annually
Weight to include waist circumference or hip to waist ratio and Body Mass Index (BMI) calculation where possible	• Some antipsychotics have the potential to cause weight gain • This can contribute to increased cardiovascular (CV) risk and metabolic problems	✓ Then weekly for the first 6 weeks	✓	✓
Urea & electrolytes including creatinine or estimated Glomerular Filtration Rate (GFR)	• Renal impairment can reduce the capacity to excrete certain medicines and a dose reduction may be necessary • Hypokalaemia (low potassium) can contribute to QTc lengthening and other ECG abnormalities	✓		✓
Lipids (Total cholesterol, HDL, cholesterol, Total/HDH–cholesterol ratio. Triglycerides) -a fasting sample if possible	• Some antipsychotics can cause small adverse changes in lipid profiles which can contribute to CV risk and metabolic problems • Triglyceride levels can rise during weight gain	✓		✓
Liver Function (Bilirubin, alkaline phosphatase, ALT, albumin, total protein, gamma-GT)	• Hepatic impairment can reduce the ability to metabolise certain medicines and a dose reduction may be necessary • Drug-induced liver damage can be due to direct dose-related hepatotoxicity or hypersensitivity. • Risk factors for hepatotoxicity include age, female gender alcohol, obesity, enzyme- inducing medicines	✓		✓
Full blood count	• Some antipsychotics can cause blood dyscrasias such as agranulocytosis and leukopenia	✓		✓
Blood Glucose: – fasting if possible or preferably glycated haemoglobin (HbA1c)	• Some antipsychotics can increase the risk of developing diabetes	✓		✓

Prolactin	• Some antipsychotics can increase prolactin levels leading t o gynaecomastia, • galactorrhoea, amenorrhoea and sexual dysfunction and a possible increased risk of osteoporosis	✓	✓	✓
Blood pressure (Sitting/lying and standing and pulse)	• Some antipsychotics can cause hypotension particularly during initiation • Factors that can influence/ indicate CV risk should be monitored regularly	✓	Also during dose increase	✓
Alcohol intake	• High alcohol intake is associated with multiple physical and mental health risks	✓		✓
Smoking status	• Smoking is associated with CV risk	✓		✓
Review of effectiveness, side effects, adherence	• Before initiation of treatment, it should be ascertained which **side effects** the patient is least willing to tolerate. • On review any side effects experienced should be assessed including extrapyramidal side effects (EPSE): akathisia, dystonia and tardive dyskinesia (TD) plus sedation- common, palpitations – less common • The Glasgow Antipsychotic Side-effect Scale (GASS) may be of use[94] • **Effectiveness** of treatment should be regularly reviewed • Whilst non-adherence is more easily identified with a long-acting injection some oral formulations may be co-prescribed and **adherence** with these should be confirmed where possible	✓	**And as indicated** ✓ ✓ ✓	✓ ✓ ✓ ✓

Electrocardiograph (ECG)	• Certain antipsychotics have been associated with ECG changes, some of which may be linked to QT prolongation • All inpatients should have an ECG on admission • Long stay patients and those living in the community should have an ECG at baseline and annually when there are clinical indications such as - a personal history of CV Disease e.g., known ischaemic/structural heart disease, QT prolongation etc. - CV risk factors identified in a physical examination -the SmPC of the antipsychotic prescribed requires ECG monitoring e.g., Haloperidol decanoate[86] - 'high dose antipsychotic therapy' (HDAT) is prescribed[89] - if other medicines known to cause ECG abnormalities are co-prescribed e.g., tricyclic antidepressants, anticholinergics, erythromycin, anti-arrhythmics etc. • If other factors have been identified which may predispose an individual to arrhythmias such as - electrolyte abnormalities such as hypokalaemia, hypocalcaemia, hypomagnesaemia - organic disease such as liver disease, renal disease, hypothyroidism			
General physical health enquiry	• Monitoring provides an opportunity for intervention regarding sexual health, contraception, pregnancy, oral and eye health, nutritional status, diet and physical activity, use of illicit substances/ non-prescribed medicines and vaccination status.	✓		✓

Appendix 5: Guidance on Missed Doses of Long-acting Injectable Antipsychotics[95]

It is always good practice to consult relevant product SmPC while dealing with missed doses.

Aripiprazole LAI (Abilify Maintena)[14]

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

Paliperidone 1-monthly LAI (Xeplion) PP1M[16]

2nd initiation dose (100mg) and time since last injection is:	**Action**
> 4 weeks	100mg should be injected into the deltoid muscle as soon as possible. **A third paliperidone injection of 75 mg (deltoid or gluteal) should be administered 5 weeks after the first injection (regardless of the timing of the second injection).** The normal monthly cycle of injections in either the deltoid or gluteal muscle of 50mg to 150mg based on patient tolerability and/or efficacy should be followed thereafter.
> 4 weeks and < 7 weeks	Day 1 - 100mg deltoid injection asap Day 8 - 100mg deltoid injection Day 36 - resume the normal monthly cycle of injections (deltoid or gluteal) based on patient tolerability and/or efficacy.
> 7 weeks	Day 1 - 50mg deltoid injection asap Day 8 - 100mg deltoid injection Day 36 - Resume the normal monthly cycle of injections (deltoid or gluteal) based on patient tolerability and/or efficacy.

Monthly maintenance dose and time since last injection is:	**Action**
> 6 weeks	Administer depot as soon as possible
> 6 weeks and < 6 months	**50mg – 100mg:** Day 1 - deltoid injection at same dose patient was previously stabilised on asap Day 8 - another deltoid injection (same dose) Day 36 - resume the normal monthly cycle of injections (deltoid or gluteal) based on individual patient tolerability and /or efficacy. **150mg:** Day 1 - 100mg deltoid injection asap Day 8 - 100mg deltoid injection Day 36 - resume the normal monthly cycle of injections (deltoid or gluteal) based on individual patient tolerability and/or efficacy.
> 6 months	Day 1 - 150mg deltoid injection asap Day 8 - 100mg deltoid injection Day 36 - resume the normal monthly cycle of injections (deltoid or gluteal) based on individual patient tolerability and / or efficacy.

Paliperidone 1-monthly LAI (Trevicta) PP1M[17]

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

Recommended re-initiation regimen after missing 4 months to 9 months of paliperidone 3- monthly LAI (Trevicta) PP3M[17]

If the last dose of Trevicta was:	Administer 1-monthly paliperidone palmitate injectable, two doses one week apart (into deltoid muscle)		Then administer Trevicta (into deltoid or gluteal muscle)
	Day 1	Day 2	1 month after day 8
175 mg	50 mg	50 mg	175 mg
263 mg	75 mg	75 mg	263 mg
350 mg	100 mg	100 mg	350 mg
525 mg	100 mg	100 mg	525 mg

Paliperidone palmitate 6-monthly LAI (Byannli) PP6M[18]

To avoid a missed dose of PP6M, patients may be given the injection up to 2 weeks before or up to 3 weeks after the scheduled 6-month time point

If scheduled dose is missed and the time since last injection is:	Action
Up to 6 months and 3 weeks	The injection should be administered as soon as possible and then resume the 6-monthly injection schedule.
> 6 months and 3 weeks up to < 8 months	**The injection should not be administered.** Use the recommended re-initiation regimen with 1-monthly paliperidone palmitate (PP1M) as shown in the table below
≥ 8 months to ≤ 11 month	**The injection should not be administered.** Use the recommended re-initiation regimen with 1-monthly paliperidone palmitate (PP1M) as shown in the table below
> 11 months	**The injection should not be administered.** Re-initiate treatment with 1-monthly paliperidone palmitate injectable as described in the prescribing information for that product. PP6M can then be resumed after the patient has been adequately treated with 1-monthly paliperidone palmitate injectable, preferably for four months or more

Recommended re-initiation regimen after missing > 6 months and 3 weeks up to < 8 months of Paliperidone palmitate 6-monthly LAI (Byannli) PP6M

If the last dose of Byannli was:	Administer 1-monthly paliperidone palmitate injectable (into deltoid muscle)	Then administer Byannli (into gluteal muscle)
	Day 1	1 month after day 1
700 mg	100 mg	700 mg
1000 mg	150 mg	1000 mg

Recommended re-initiation regimen after missing ≥ 8 months to ≤ 11 months of Byannli

If the last dose of Byannli was:	Administer 1-monthly paliperidone palmitate injectable (into deltoid muscle)		Then administer Byannli (into gluteal muscle)
	Day 1	Day 8	1 month after Day 8
700 mg	100 mg	100 mg	700 mg
1000 mg	100 mg	100 mg	1000 mg

Risperidone LAI (Risperdal Consta)[13]

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

Risperidone ISM (Okedi) [20]

Time since last planned injection	What happens to risperidone ISM plasma levels	Plan
One week	Therapeutic plasma levels start to decline by 50%	Administer next injection asap

Olanzapine LAI (ZypAdhera)[15]

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

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

The manufacturer of ZypAdhera does not provide advice on missed doses.

Guidance supplied and reproduced with permission from Professor David Taylor, South London & Maudsley NHS Foundation Trust.[95]

Appendix 6: Dose Calculation Workbook

Test Dose Calculations for Oil-Based Depot Intramuscular Antipsychotic Injections

For oil-based depot intramuscular antipsychotic injections it is good practice to give a test dose before treatment is initiated to assess for tolerability to both the active ingredient as well as to the oily vehicle. Occasionally patients with nut allergy may react to the oil. If a full dose is given from the outset then patients may experience more severe, protracted discomfort.

How much? A worked example:

The amount recommended for a test dose is stated by the manufacturer in the Summary of Product Characteristics (SmPC)[11] and in the British National Formulary (BNF).[12] A calculation may therefore be required to work out the injection volume required for such a test dose.

For example:

The test dose of flupentixol decanoate for an adult is 10 mg

Flupentixol decanoate is available in ampoules containing 20 mg in 1 ml 10 mg is therefore contained in 1/20 x 10 = ½ ml = 0.5 ml

Thus, to give a 10 mg test dose of flupentixol decanoate, 0.5 ml of the solution containing 20 mg in 1 ml is required

Try this example yourself:

The test dose of zuclopenthixol decanoate is 50 mg

Zuclopenthixol decanoate is available in 1 ml ampoules containing 200 mg in 1 ml and you want to give 50 mg. What volume should you draw up? Work out your answer in the box below.

Answer:

To give a 50 mg test dose of zuclopenthixol decanoate, 0.25 ml of a solution containing 200 mg in 1 ml is required. If you have the correct answer could you show a colleague how you worked it out?

The ***line statement method*** is a good way to reassure both yourself and a second person of how the correct answer was reached:

Start with the product in front of you: 200 mg in 1 ml

÷ 2 = 100 mg in 0.5 ml

÷ 2 = **50 mg in 0.25 ml**

With this method you will see that whatever you do to the left-hand side in terms of a mathematical application you do to the right-hand side. This principle never changes however hard the figures may look.

Try this next example:

What volume of zuclopenthixol decanoate is required to administer a 350 mg dose using the 200 mg in 1 ml ampoule? Work out your answer in the box below.

Answer:

To give a 350 mg dose of zuclopenthixol decanoate, 1.75 ml of a solution containing 200 mg in 1 ml is required.

The ***line statement method*** is a good way to reassure both yourself and a second person of how the correct answer was reached:

Line 1: You start with: 200 mg in 1 ml

Line 2: ÷ 2 = 100 mg in 0.5 ml

Line 3: ÷ 2 = 50 mg in 0.25 ml

You need 350 mg: 350 ÷ 50 = 7

Multiply line 3 by 7 because 7 x 50 mg = 350 mg

350 mg = 7 x 0.25 = 1.75 ml

350 mg is contained in 1.75 ml of the solution containing 200 mg in 1 ml

For those who prefer a different way and/or like algebra we can identify a generic equation for this process:

Imagine you have an ampoule containing **X** mg of antipsychotic in 1 ml
You are required to administer a dose of **Y** mg, and you need to know the volume to draw up the volume required = **Y** x the volume **X** mg is contained in **X**

Putting the figures from the previous example into this equation:

$$\text{The volume required} = \frac{350 \times 1}{200} = 1.75 \text{ ml}$$

Based on a real scenario from clinical practice look at the following depot prescription and identify the dose volume required and consider how you would respond to the following prescription.

Rx Depixol 37.5 mg 2-weekly

What volume is required to administer this dose? Work out your answer in the box below:

Flupentixol decanoate (Depixol) comes in two strengths: 20 mg in 1 ml and 100 mg in 1 ml.

Calculation

Response & Reflection

Answer:

Looking at	20 mg	in	1 ml	
÷ 2	10 mg		0.5 ml	line 2
÷ 2	5 mg	in	0.25 ml	line 3
÷ 2	2.5 mg	in	0.125 ml	line 4
Multiply line 2 by 3	30 mg	in	1.5 ml	line 5
Add line 3	5 mg	in	0.25 ml	line 6
Add line 4	2.5 mg	in	0.125 ml	line 7
Add lines 5,6 & 7	**37.5 mg**	**in**	**1.875 ml**	

37.5 mg of flupentixol decanoate (Depixol) is contained in 1.875 ml of a solution containing 20 mg in 1 ml (or 0.375 ml of the solution containing 100 mg in 1 ml).

However, neither of these is an accurately measurable volume and the prescription should be referred back to the prescriber for review. Although depot dosing is not an exact science, approximating impossible volumes is not good medicines management.

Please note that long-acting injections of olanzapine, paliperidone and risperidone are all supplied as dose packs and the entire contents of the ampoule should be injected according to the prescribed dose. No dose calculations are necessary with these products.

Appendix 7: Questions to ask your Healthcare Professional

(This page may be printed/copied and given to a patient or carer)

The professionals working in partnership with you must give you enough information when planning your care for you to be able to make informed choices about your treatment. They should anticipate your needs and try to design your care with these in mind.

Before your appointments it may help if you write down some of the questions you might want to ask as you think of them. You may wish to include your carers or relatives in talking through what would be helpful to you.
Some of the things you may wish to consider asking could include:

- What is a depot injection?
- What is a long-acting antipsychotic injection and do these differ from depots?
- How are these different to my tablets?
- How does a depot injection work?
- How does a long-acting injection work?
- What side effects will I have and will they be worse than taking tablets?
- How will I change over from tablets to injections?
- How often will I need an injection?
- Will I need to have it for the rest of my life?
- Can I have the injection at home or will it be given somewhere else?
- Will I need to get undressed?
- Can I give myself this injection?
- What benefit will I have as a result of swapping from tablets to an injection?
- Are there any risks I need to know about?
- Are there any risks at the time of the injection being given to me and will it hurt?
- How will having an injection affect my life and make me feel?
- Will it make me tired?
- Will I be able to drive my car and operate machinery at work?
- Do I have to tell my employer about this treatment?
- Will the injection affect my sleep?
- Will it affect my sex life?
- If I don't want to accept an injection, what will this mean for my care?
- If I do accept treatment by injection, can I change my mind if I don't like it at any time?
- Can you give me an injection against my wishes?

Appendix 8: Human Factor Error Risk Reduction Checklist Template

Human Factor Error Risk Reduction Checklist for the Administration of a Long-Acting Intramuscular Injection	Rationale for the Double Check	Registered Nurse Check Name, Date & Signature	Second Professional Double Check Name, Date & Signature
Assessment of capacity to consent	Legal requirement		
Read the patient's clinical record	Need up-to-date clinical knowledge of patient		
Check there are no changes to the patient's health that require review	Reduces the risk of adverse patient outcome		
Check the patient understands all the information relevant to treatment and has the capacity to confirm their decision to proceed	Compliance with the legal requirements of the Mental Health Capacity Act 2005		
The capacity of the patient is confirmed and recorded	Their capacity may change between injections and needs to be confirmed		
The prescription is accurate and conforms with the local Medicines Code	Prescription inaccuracy will place both patient and practitioner at risk		
Ask the patient when their last injection was given	Cross check that the current injection has not already been given and that the prescription and or clinical notes were not signed in error		
The product licence for the injection is for the site planned	Not all injections are for use in all muscle groups or injection sites		
Hand hygiene observed before and after patient contact. Use disposable gloves, apron and eye protection where appropriate	Prevention of infection		
Medical devices assembled in accordance with non-touch technique	Prevention of infection		
Read the label, check the injection is in date and cross check the label against the prescription	Confirm the right medicine, right dose, right frequency, right patient, right formulation, right route, right time		
Check any calculation of dose volume	Reduces the risk of the wrong dose being administered		
Check the patient's allergy status	Reduces the risk of anaphylaxis		
Check the previous injection site	Adverse reaction outcome assessment		
Check the patient is in the appropriate position for administration of the injection for the site selected	To support accuracy of location of muscle group and prevent discomfort		

Appendix 8 continued: Human Factor Error Risk Reduction Checklist Template			
Human Factor Error Risk Reduction Checklist for the Administration of a Long-Acting Intramuscular Injection	**Rationale for the Double Check**	**Registered Nurse Check Name, Date & Signature**	**Second Professional Double Check Name, Date & Signature**
Landmark and locate the injection site	Prevents damage to nerve structures and blood vessels		
Clean the injection site if required. If using an alcohol-based swab, allow to dry for 60 seconds	Reduces discomfort		
Use Z-track technique and keep the graduation markings on the syringe barrel visible	Prevents discomfort and back flow of medication. If the needle and syringe become disconnected, it will be impossible to establish how much medication has been administered		
Insert needle and check for aspirate before proceeding (only necessary for the dorsogluteal site)	Prevents administration into the bloodstream		
Injection should be given at a rate of 1 ml in 10 seconds	To allow the muscle fibres to expand to absorb the solution. Reduces the risk of syringe barrel 'locking' and incomplete administration of the dose		
Retract or remove the needle from the patient 10 seconds after administration of the injection	To allow the medication to diffuse at the point of entry		
Dispose of all sharps immediately following withdrawal from patient	Minimises the risk of blood-borne virus transmission and contamination		
Dispose of all equipment safely and appropriately	Reduces the risk of contamination and inoculation injury		
Observe the patient for deviations from expected outcomes during the procedure	Allows rapid action by assessing for any untoward event and formulating a plan of care through intervening with speed. Compliance with risk management processes and reporting of untoward events		
The administration record must be signed and all necessary clinical recording made	Accurate recording of the procedure and any deviations from the norm is essential		
Advise the patient when to get in touch and who to contact if they have concerns about their wellbeing following the administration and ensure a patient information leaflet is given for reference	The patient has all the necessary information to make continued healthcare decisions		

Appendix 9: An Audit Tool for Oil-based Depot and Other Long-Acting Intramuscular Antipsychotic Injections

	Criteria: Aspect of Clinical Care	Adherence rate: Standard	Examples of Assurance evidence	Exceptions	Assessment of non-adherence: Standard achieved	Action required	Lead responsibility & timescale for completion
Organisational							
1	The registered practitioner has access to evidence based, up-to-date procedural guidance/ good practice documents that describe safe practice for prescribing, preparing, administering and monitoring injectable medicines	100%	Intranet clinical policies and procedures Clinical policies and procedures folder Good practice data base National Patient Safety Agency information Policy and procedure approval date from local sign-off committee Distribution list for clinical area	None identified			
2	All registered practitioners who are expected to administer an injectable medicine have received training within the clinical team	100%	Training data base	None identified			

	Criteria: Aspect of Clinical Care	Adherence rate: Standard	Examples of Assurance evidence	Exceptions	Assessment of non-adherence: Standard achieved	Action required	Lead responsibility & timescale for completion
Prescription and administration documents							
3	Patient's full name is correctly entered onto every sheet of the prescription/ administration document	100%	Prescription/administration document is cross-referenced with patient NHS identification records document	None identified			
4	Allergy section is fully completed	100%	Prescription/administration document	None identified			
5	The prescription is legible	100%	Prescription/administration document	None identified			
6	Each prescription is dated accurately	100%	Prescription/administration document	None identified			
7	Each prescription has the prescriber's signature	100%	Prescription/administration document Pharmacy signatory records for registered practitioners	None identified			
8	Dosage and frequency instructions are recorded	100%	Prescription/administration document	None identified			
9	The antipsychotic is administered as prescribed with respect to - The time - Frequency - Date	100%	Prescription/administration document	Where clinical review indicates change and is recorded in the notes with prescription adjustment by the prescriber			

	Criteria: Aspect of Clinical Care	Adherence rate: Standard	Examples of Assurance evidence	Exceptions	Assessment of non-adherence: Standard achieved	Action required	Lead responsibility & timescale for completion
Medical/nursing notes							
10	A physical healthcare assessment has been undertaken in the last year	100%	Medical/nursing notes	None identified			
11	It has been documented that joint decision making between the prescriber and patient regarding the antipsychotic has taken place	100%	Medical/nursing notes	None identified			
12	Documented evidence of information on this treatment having been given to the patient	100%	Medical/nursing notes	None identified			
13	If the patient lacks capacity the decision is discussed with the carer or advocate	100%	Medical/nursing notes	None identified			
14	Adherence has been discussed and recorded at the point of prescription	100%	Medical/nursing notes Pharmacy records	None identified			
15	The patient has been asked whether they would prefer a long-acting injection to an oral formulation by the prescriber	100%	Medical/nursing notes Pharmacy records	None identified			
16	Side effects have been assessed and recorded in the notes within the last six months	100%	Medical/nursing notes Pharmacy records	None identified			

	Criteria: Aspect of Clinical Care	Adherence rate: Standard	Examples of Assurance evidence	Exceptions	Assessment of non-adherence: Standard achieved	Action required	Lead responsibility & timescale for completion
Medical/nursing notes (continued)							
17	The antipsychotic is prescribed within the standard dosage range and frequency interval in accordance with recommendations in the BNF and SmPC	100%	Prescription/ administration document	None identified			
18	If the antipsychotic is pre- scribed outside recommended BNF/SmPC limits there is a clearly recorded clinical rationale for this decision	100%	Medical/nursing notes Prescription/ administration document	None identified			
19	Therapeutic response to treatment is recorded at clinical reviews at least 3 monthly	100%	Medical/nursing notes Pharmacy records	None identified			
20	The patient has undergone a clinical review within the last 3 months	100%	Medical/nursing notes	None identified			

	Criteria: Aspect of Clinical Care	Adherence rate: Standard	Examples of Assurance evidence	Exceptions	Assessment of non-adherence: Standard achieved	Action required	Lead responsibility & timescale for completion
Medical/nursing notes (continued)							
26	An evaluation of the injection site has been made: a) Pre-injection b) Post-injection Reference has been made to: c) Observation for swelling d) Pain e) Inflammation f) Infection g) Tissue viability damage h) Patient concerns	100%	Medical/nursing notes	None identified			
27	At the time of each injection the following is recorded: Name of antipsychotic Date of administration Time of administration Dose administered Injection site Side in which it was given (L) or (R)? (cross-reference with prescription/ administration document)	100%	Medical/nursing notes Prescription/ administration document	None identified			
28	The injection site is rotated after each administration	100%	Medical/nursing notes Prescription/ administration document	None identified			
29	Side effects of the previous injection have been assessed and documented in the notes	100%	Medical/nursing notes	None identified			

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