

Shared care guidelines

Drug	PALIPERIDONE PALMITATE long-acting injection (Xeplion® / Trevicta®)										
Specialty	ALL SPECIALTIES (<u>excluding</u> Children & Young People's Services)										
Indication	SCHIZOPHRENIA										
Overview	<p>Paliperidone is a metabolite of risperidone which binds strongly to serotonergic 5-HT₂ & dopaminergic D₂-receptors; also blocking alpha₁-adrenergic receptors & slightly less, H₁-histaminergic & alpha₂-adrenergic receptors. Paliperidone palmitate is administered monthly (Xeplion®) or 3-monthly (Trevicta®). It should be initiated by a specialist with expertise in schizophrenia as part of a comprehensive treatment plan but prescribing, administration & monitoring responsibility can transfer to GPs under these shared care guidelines.</p>										
Specialist responsibilities	<p>Pre-treatment: (see SPC for Xeplion or Trevicta for full details of contra-indications & cautions) Assess suitability for treatment with paliperidone palmitate by reviewing the patient's medical history, completing a physical examination and completing the baseline monitoring as detailed in appendix 1; dose adjustment is necessary in renal impairment.</p> <p>Initial prescription - dosage and administration: (see BNF, SPC for full details)</p> <p>Xeplion® The recommended initiation is with a dose of 150 mg on day 1 and 100 mg one week later (day 8), both administered in the <u>deltoid</u> muscle in order to attain therapeutic concentrations rapidly. The third dose should be administered one calendar month after the second initiation dose; thereafter, maintenance doses should be administered calendar monthly (± 7 days) into either the deltoid or gluteal muscle. The recommended monthly maintenance dose is 75 mg; some patients may benefit from lower or higher doses within the recommended range of 25 mg to 150 mg based on individual patient tolerability and/or efficacy; patients who are overweight or obese may require doses in the upper range.</p> <p>Trevicta® Patients who are clinically stable, have received Xeplion® at the same dose for four months or more and don't require further dose adjustment, can be transferred to Trevicta®. Trevicta® should be initiated in place of the next scheduled dose of Xeplion® (± 7 days). The Trevicta® dose should be based on the previous Xeplion® dose using a 3.5-fold higher dose as follows:</p> <table border="1" style="width: 100%; text-align: center;"> <thead> <tr> <th>If the last dose of Xeplion is:</th> <th>Initiate Trevicta at the following dose:</th> </tr> </thead> <tbody> <tr> <td>50 mg</td> <td>175 mg</td> </tr> <tr> <td>75 mg</td> <td>263 mg</td> </tr> <tr> <td>100 mg</td> <td>350 mg</td> </tr> <tr> <td>150 mg</td> <td>525 mg</td> </tr> </tbody> </table> <p>Following the initial dose, Trevicta® should be administered by intramuscular injection (deltoid or gluteal) once every 3 calendar months (± 2 weeks).</p> <p>Monitoring – see appendix 1: The baseline efficacy and tolerability of antipsychotic medication should be established by the use of objective and validated measures.</p> <ul style="list-style-type: none"> • Side effects – use LUNSERS or GASS to assess tolerability at each review • Physical Health monitoring – for the first 12 months of treatment, then at each review (at least annually); see physical parameters in appendix 1 • Clinical response – use an appropriate measure, e.g. PANSS (positive and negative syndrome scale), CGI (clinical global impressions) and GAF (global assessment of functioning), to assess response prior to transfer and at each review. <p>Where tolerability or clinical response is not demonstrated, the LAI should not continue to be prescribed. The on-going clinical need and patient preference for a LAI should be reviewed at least annually.</p>	If the last dose of Xeplion is:	Initiate Trevicta at the following dose:	50 mg	175 mg	75 mg	263 mg	100 mg	350 mg	150 mg	525 mg
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Title	Shared care guidelines – Paliperidone LAI		
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Protocol Number	PHARM-0093-v2	Date of Review	01 October 2024

**Specialist responsibilities
(continued)**

Transfer of prescribing / communication

Prescribing, administration and monitoring responsibility may be transferred to the patient's GP after 3 months or once the treatment has been stabilised, whichever is the longer. The request must be made using the attached form with a covering clinic letter and a copy of this guideline (with contact details added) – the following details should be clearly communicated at transfer, and after each subsequent review:

- **Diagnosis**
- **Dose** of paliperidone and **formulation** (monthly or 3-monthly)
- **Date** and **site** of last administration, and **date when next dose is due**
- Completed and required **monitoring**
- **Discontinued medication** for same diagnosis
- **Date** of next specialist review

The transfer request should be sent one month in advance of the patient needing their next dose. Acceptance should not be assumed until the GP responds positively using the attached form (scanned & e-mailed to the specialist team)

GP responsibilities

Transfer of prescribing / communication:

Notify specialist immediately (within 2 weeks) if transfer of prescribing and monitoring responsibility is not accepted so that alternative arrangements can be put in place. Contact specialist if communication of prescribing, administration & monitoring requirements is not clear.

Maintenance (repeat) prescription:

Prescribe paliperidone LAI (by brand name) in accordance with specialist advice received on transfer and following reviews

Xeplion[®] recommended maintenance dose is 75 mg each calendar month; some patients may benefit from lower or higher doses within the recommended range of 25 to 150 mg based on individual patient tolerability and/or efficacy.

Trevicta[®] dose range is 175 mg to 525 mg every 3 calendar months, based on previous dose of Xeplion and according to individual patient tolerability and/or efficacy.

Administration:

Both preparations of paliperidone LAI can be administered into either the deltoid or gluteal muscle. See relevant [SPC](#) and appendix 2 for detailed information regarding administration and action to take in response to missed or delayed doses.

Monitoring – see appendix 1:

Efficacy and tolerability measures should be completed by the specialist team prior to transfer and at each review. Physical health monitoring should be completed by the specialist team for the first 12 months, then at each review (at least annually); any additional physical health monitoring by GP should be communicated to the specialist.

Referral:

Seek advice or refer back to the specialist should any of the following occur:

- Significant adverse reaction or intolerable side effects
- Lack of efficacy/ patient's condition deteriorates
- Development of co-morbidities
- Pregnancy
- Failure to attend for administration of paliperidone within permitted timeframe for the formulation prescribed.(+/- 7 days for Xeplion; +/- 14 days for Trevicta)

Adverse events

See [BNF](#) and [SPC](#) for full details of known adverse effects.

Short-term side effects include insomnia and headache. These effects should not persist. Paliperidone can raise the levels of plasma glucose, lipids and prolactin. Weight gain is common. Akathisia and extrapyramidal side effects may occur at higher doses. Paliperidone has a low effect on the cardiac QTc interval (average change <10 msecs). Report any suspected adverse events to MHRA via the [Yellow Card scheme](#)

Specialist contact details

(to be added by specialist prescriber when transferring prescribing)

Name:

Base:

Telephone no:

E-mail address:

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AMBER ▲	TRANSFERRING PRESCRIBING OF LONG ACTING / DEPOT INJECTIONS
GP details:	
Patient details (name/address/DOB/NHS number):	
Diagnosis:	
Medication details: The patient is stabilised on: (list dose, frequency and brand. Specify clinical indications if first line option not prescribed or non-standard formulation prescribed):	
Discontinued medication (list details of any drugs discontinued when this AMBER treatment initiated):	
Last Administration (details of date and site of administration and date next dose due):	
Monitoring results:	
Secondary care review frequency:	
Actions requested of GP: Please continue to issue prescriptions and administer monthly (Xeplion®) or three monthly (Trevicta®) until advised otherwise The treatment has been explained to the patient and they understand they should contact you for future prescriptions. You will be informed of any changes to treatment, if you are not required to issue prescriptions or if treatment is to be discontinued. Please contact the prescriber on the number below if there is any change in the patient's condition, if the patient fails to regularly collect prescriptions, if non-compliance with treatment is suspected or you require advice.	

Title	Shared care guidelines – Paliperidone LAI		
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Secondary care contacts:	Contact details (address/telephone no):
Care coordinator (name):	
Consultant (name):	
Prescriber (name):	
Signature & date:	

Acceptance of prescribing responsibility by GP (scan & e-mail)

Patient's name:	NHS Number:
Address:	
Medication:	
I confirm receipt of prescribing transfer information for the above patient and accept prescribing responsibility	
GP's name: <i>(Please print name in BLOCK CAPITALS)</i>	
Signature/ Practice Stamp:	
Date:	

Please scan and email back to:
Email address:
or return as soon as possible to:

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Appendix 1 Monitoring requirements for antipsychotic long-acting injections (from [PHARM-0082 Psychotropic Medication Monitoring Guide](#))

Test/ Measurement	Why is it important?	Baseline	3 months after initiation	Annually
Weight (Waist measurement and BMI where possible)	Antipsychotic drugs can cause weight gain and this can contribute to an ↑ risk of cardiovascular and metabolic problems	✓ Then weekly for the first 6 weeks	✓	✓
Lipids (Total cholesterol, HDL cholesterol, Total/HDL-cholesterol ratio, Triglycerides - fasting sample if possible)	Some antipsychotics can cause small adverse changes in lipid profiles. Triglyceride levels can rise during periods of weight gain.	✓	✓	✓
Blood Glucose - HbA_{1c}	Antipsychotics can increase the risk of developing diabetes.	✓	✓	✓
Blood Pressure (sitting / lying and standing) and pulse	Hypotension is a side effect of many antipsychotics and it is important to monitor this during periods of initiation and stabilisation. Longer term it is important to monitor and manage factors that influence a patient's CV risk	✓	Frequently during dose titration (determined by clinical situation) and also after 12 weeks	✓
Prolactin (see PHARM-0032 Hyperprolactinaemia)	Antipsychotics can increase prolactin levels. This can inhibit sex hormones – oestrogen and testosterone and may ↑ risk of osteoporosis	✓		
ECG (QTc Interval)	<p>Many antipsychotics are associated with ECG changes and some are linked to prolongation of the QT interval.</p> <p>All new inpatients should have an ECG on admission.</p> <p>For long stay patients and those in the community - ECGs should be performed at baseline and annually when clinically indicated. Factors that may determine if ECG is clinically indicated include:</p> <ul style="list-style-type: none"> personal history of cardiovascular disease (e.g. known ischaemic / structural heart disease QT prolongation), physical examination identifies cardiovascular risk factors antipsychotic that requires ECG monitoring i.e. haloperidol or pimozide (check summary of product characteristics for more information) high dose antipsychotic therapy (HDAT) concurrent drugs known to cause ECG abnormalities (e.g. tricyclic antidepressants, erythromycin, anti-arrhythmics – see BNF for further information) <ul style="list-style-type: none"> factors which may predispose to arrhythmias including electrolyte abnormalities (hypokalaemia, hypocalcaemia, hypomagnesaemia) and systemic disease (liver disease, renal disease, hypothyroidism) 	✓ (if clinically indicated)		✓ (if clinically indicated)
Review of the side effects of drug treatment, efficacy and adherence	<p>Before treatment the side effects the patient is least willing to tolerate should be assessed. On review the treatment efficacy, patient adherence and side effects experienced should be assessed, including :</p> <ul style="list-style-type: none"> Extrapyramidal symptoms, akathisia, dystonia and tardive dyskinesia Sexual side-effects Less common but serious adverse effects e.g. palpitations. <p>An appropriate rating scale may be useful (e.g. GASS, LUNSERS)</p>	✓	✓	✓

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Other tests to consider (not required for the drug itself)				
Test/ Measurement	Why is it important?	Baseline	3 months after initiation	Annually
Urea and electrolytes (including creatinine or estimated GFR)	Patients with renal impairment may have reduced capacity to excrete drugs and dose reductions may be required. Hypokalaemia is linked to QTc prolongation and other ECG abnormalities	✓		✓
Liver function (Bilirubin, Alk Phos, ALT, Albumin, Total protein, Gamma-GT)	Patients with hepatic impairment may have reduced capacity to metabolise drugs and dose reductions may be required. Drug induced liver damage can be due to direct dose related hepatotoxicity or hypersensitivity reactions. Risk factors for drug induced hepatotoxicity include - ↑age, female gender, alcohol, prescribed enzyme inducing drugs, obesity	✓		✓
Full Blood Count (Hb, WBC, Platelets)	BNF advises caution when using antipsychotics in patients with blood dyscrasias Antipsychotics can cause blood dyscrasias including agranulocytosis and leucopenia	✓		✓
Pregnancy test		If there is any uncertainty about the possibility of pregnancy, a urine pregnancy test should be carried out		
Smoking status	Linked to CV risk. Changes in smoking status may impact on drug metabolism, notably olanzapine and clozapine	✓	At each dose administration and each review	
Drug screening		If indicated by history or clinical picture		

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Appendix 2 – Administration Information

Administration

Xeplion® (See [SPC](#) for further details)

- Available in pre-filled syringes of 50mg, 75mg, 100mg and 150mg.
- Do not store above 30°C
- The injection should be administered slowly as a single injection into either the gluteal or the deltoid muscle. The injection sites should be rotated between the two gluteal or deltoid muscles. Care should be taken to avoid inadvertent injection into a blood vessel.

Deltoid muscle administration, recommended needle size is determined by the patient's weight:

- For those ≥ 90 kg, the 1½ inch, 22 gauge needle (38.1 mm x 0.72 mm) is recommended.
- For those < 90 kg, the 1-inch, 23 gauge needle (25.4 mm x 0.64 mm) is recommended.
- Deltoid injections should be alternated between the two deltoid muscles.

Gluteal muscle administration, the recommended needle size is:

- The 1½-inch, 22 gauge needle (38.1 mm x 0.72 mm).
- Administration should be made into the upper-outer quadrant of the gluteal area.
- Gluteal injections should be alternated between the two gluteal muscles.

Trevicta® (See [SPC](#) for further details)

- Available in pre-filled syringes of 175mg, 263mg, 350mg and 525mg.
- The injection should be administered slowly as a single injection into either the gluteal or the deltoid muscle. The injection sites should be rotated between the two gluteal or deltoid muscles. Care should be taken to avoid inadvertent injection into a blood vessel.
- A switch from gluteal to deltoid (and vice versa) should be considered for future injection in the event of injection site discomfort.
- Trevicta® must be administered using **only** the thin wall needles provided in the Trevicta® pack, other needles must not be used.
- The contents of the pre-filled syringe should be inspected visually for foreign matter and discolouration prior to administration.
- To avoid incomplete administration, it is important to shake the syringe vigorously with the tip up and a loose wrist for at least 15 seconds to ensure a homogeneous suspension. Trevicta® should be administered within 5 minutes after shaking. If more than 5 minutes pass before injection, shake vigorously again for at least 15 seconds to re-suspend the medicinal product.
- 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 of Trevicta®.

Deltoid muscle administration, recommended needle size is determined by the patient's weight:

- For those ≥ 90 kg, the thin wall 1½ inch, 22 gauge needle (38.1 mm x 0.72 mm) is recommended.
- For those < 90 kg, the thin wall 1-inch, 23 gauge needle (25.4 mm x 0.64 mm) is recommended.
- Deltoid injections should be administered into the centre of the deltoid muscle and alternated between the two deltoid muscles.

Gluteal muscle administration, the recommended needle size, regardless of body weight is:

- The thin wall 1½-inch, 22 gauge needle (38.1 mm x 0.72 mm).
- Administration should be made into the upper-outer quadrant of the gluteal area.
- Gluteal injections should be alternated between the two gluteal muscles.

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Missed doses

Xeplion® (See [SPC](#) for further details)

- Initiation doses will be administered by the specialist service, as per [SPC](#).
- After initiation, the recommended injection cycle is once per calendar month, it is not necessary to give every 28 days
- To avoid a missed monthly dose, patients may be given the injection up to 7 days before or after the monthly time point.
- If a monthly maintenance dose is missed, if less than 6 weeks have elapsed since last injection, the previously stabilised dose should be administered as soon as possible, followed by injections at monthly intervals.
- If more than 6 weeks have elapsed since last injection, seek specialist advice.

Trevicta® (See [SPC](#) for further details)

- The recommended injection cycle is once every 3 months
- To avoid a missed 3 monthly dose, patients may be given the injection up to two weeks before or after the 3-month time point.
- If the scheduled 3 monthly maintenance dose is missed, if less than 4 months have elapsed since the last injection, the previously stabilised dose should be administered as soon as possible, followed by injections at 3 monthly intervals.
- If 4 months or more have elapsed since last injection, seek specialist advice.

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