Tees, Esk and Wear Valleys NHS
NHS Foundation Trust

Shared care guidelines

Drug	**PALIPERIDONE PALMITATE** long-acting injection (Xeplion® / Trevicta®)
Specialty	ALL SPECIALTIES (excluding Children & Young People's Services)
Indication	SCHIZOPHRENIA
Overview	Paliperidone is a metabolite of risperidone which binds strongly to serotonergic 5-HT_2 & dopaminergic D_2-receptors; also blocking $alpha_1$-adrenergic receptors & slightly less, H_1-histaminergic & $alpha_2$-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.

Specialist responsibilities

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.

Initial prescription - dosage and administration: *(see BNF, SPC and North of England Guidance for prescribing LAI for full details)*

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 deltoid 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.

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:

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

Following the initial dose, Trevicta® should be administered by intramuscular injection (deltoid or gluteal) **once every 3 calendar months** (± 2 weeks).

Monitoring – see appendix 1:

The baseline efficacy and tolerability of antipsychotic medication should be established by the use of objective and validated measures.

- **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 measures, 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.

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.

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 (faxed or 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:

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.

Secondary care contacts:	Contact details (address/telephone no):
Care coordinator (name):	
Consultant (name):	
Prescriber (name):	
Signature & date:	

Fax back acceptance of prescribing responsibility by GP (or 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: *(Please print name in BLOCK CAPITALS)*	
Signature/ Practice Stamp:	
Date:	

Please fax back to:
Fax number:
or return as soon as possible to:

Appendix 1 Monitoring requirements for antipsychotic long-acting injections (from *North of England Guidance for prescribing LAI)*

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	√	√
Urea and electrolytes, (including creatinine or estimated GFR)	Pateints with renal impairment may have reduced capacity to excrete drugs and dose reductions may be required. Hypolkaleamia is linked to QTc lengthening and other ECG abnormaliites	√		√
Lipids (Total cholesterol, HDL cholesterol, Total/ HDH-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.	√	√	√
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	√		√
Blood Glucose FBG/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 antipscyhotics and it is important to monitor this during peiods of initation and stabilisation. Longer term it is important to montior and manage factors that inluence a patients CV risk	√	Frequently during dose titration (determined by clinical situation) and also after 12 weeks	√
Prolactin	Antipsychotics can increase prolactin levels. This can inhibit sex hormones – oestrogen and testosterone and may ↑ risk of osteoporosis	√	√	√

Test/ Measurement	Why is it important?	Baseline	Annually
ECG (QTc Interval)	Many antipsychotics are associated with ECG changes and some are linked to prolongation of the QT interval. All new inpatients should have an ECG on admission. For long stay patients and those in the community. When clinically indicated ECGs should be performed at baseline and annually. Factors that may determine if ECG monitoring is clinically indicated include: • If there is a personal history of cardiovascular disease (e.g. - known ischaemic / structural heart disease QT prolongation), • If physical examination identifies cardiovascular risk factors • If patients on antipsychotics that require ECG monitoring e.g. - haloperidol or pimozide (check summary of product characteristics for more information) • If a patient is on high dose antipsychotic therapy (HDAT) • If patient is on other drugs known to cause ECG abnormalities (e.g. Tricycylic antidepressants, erythromycin, anti-arrhythmics – see BNF for further information) • If the patient has Factors which may predispose to arrhythmias including: ○ Electrolyte abnormalities – hypokalaemia, hypocalcaemia, hypomagnesaemia ○ Systemic disease – liver disease, renal disease, hypothyroidism		
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	√	√
Drug screening		If indicated by history or clinical picture	
Review of the side effects of drug treatment, efficacy and adherence	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 : • Extrapyramidal symptoms, akathisia, dystonia and tardive dyskinesia • Common side effects e.g. – sedation • Less common but serious adverse effects e.g. palpitations. An appropriate rating scale may be useful (e.g. GASS)	√	√
References	Maudsley Prescribing Guidelines 11th edition (2013) SPC of individual medicines, available at www.medicines.org.uk BNF 68, September 2014 Royal College of Psychiatrists Consensus Statement on high dose antipsychotic prescribing May 2006 Lester UK Adaptation Positive Cardiometabolic Health Resource June 2014 - www.rcpsych.ac.uk/quality/NAS/resources		

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.

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.