Ref: IMOCSCG004
South East London Shared Care Prescribing Guideline for paliperidone long-acting injection for the treatment of schizophrenia in adults
Original approval date: April 2015 **Last updated and approved:** October 2023 **Review date:** October 2025 (or sooner if evidence or practice changes)

SHARED CARE PRESCRIBING GUIDELINE

Paliperidone long-acting injections (Xeplion™ for 1-monthly injection, Trevicta™ for 3-monthly injection and Byannli™ for 6-monthly injection) for the treatment of schizophrenia in adults

NOTES to the GP

The information in the shared care guideline has been developed in consultation with South East London ICB and it has been agreed that paliperidone long-acting injection is suitable for shared care.

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing paliperidone long-acting injection for the treatment of schizophrenia in adults.

The questions below will help you confirm this:

- Is the patient's condition predictable or stable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.

If the answer is NO to any of these questions you should contact the requesting consultant or your local ICB Medicines optimisation Team. There may be implications for the patient where the invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **It is important that patients are consulted about treatment and are in agreement with it**.

Prescribing should follow requirements in the South East London Interface Prescribing Policy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

Once you have read the shared care guideline and considered the information above, please complete the GP decision form on the next page and email back to the requesting clinician if you are in agreement to participate in shared care.

If you are not in agreement, please include reasons for this.

GP DECISION FORM

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of paliperidone long-acting injection for the treatment of schizophrenia in adults can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

AGREEMENT TO PARTICIPATE IN SHARED CARE

Paliperidone long-acting injection for the treatment of schizophrenia in adults

Xeplion™
Trevicta™
Byannli™
Please delete as appropriate

Consultant/Specialist Name:	**Patient name:**
Consultant/Specialist signature:	**Patient Hospital Number:** **Patient NHS Number:**
Date completed:	**Patient/carer Agreement:**
Hospital/specialist requesting shared care:	Patient / carer agrees to shared care ☐ Patient /carer does not agree to shared care ☐
GP Name:	
This is to confirm that I agree to participate in shared care for paliperidone long-acting injection for the treatment of schizophrenia for this patient as outlined in this shared care document	
GP Signature:	
Date signed:	

ACTION

1. HOSPITAL / COMMUNITY CONSULTANT **Tick to confirm**

- Explain shared care to patient/ carer and obtain agreement Date agreement obtained:_____ ☐
- Indicate requesting hospital /clinic ☐
- Complete and sign agreement ☐
- Email full shared care guideline (including signed agreement to GP) ☐
- Place original in patient's notes ☐

2. GP PRACTICE

- If **in agreement** to participate in shared care, sign and email (via secure NHS.net) this sheet back **within 2 weeks** of receipt **of request from specialist** to either:

Email address (via secure nhs.net):…… [TRUST to ADD email address]

- If **you do not agree** to participate in shared care, contact consultant and local Primary Care ICB Medicines optimisation Team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the local Primary Care ICB Medicines optimisation team should be informed.
- Once decision reached file a copy in the Patient's medical notes.

Paliperidone long-acting injection for the treatment of schizophrenia in adults

1. CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the community consultant and the GP are in agreement that the patient's condition is stable or predictable.
- The community mental health team (CMHT) will continue to administer the long-acting injection until the GP agrees to shared care

2. AREAS OF RESPONSIBILITY

Consultant / Specialist team responsibilities

- To initiate paliperidone long-acting injection and assess its effects (clinical benefit and side effects)
- To inform the patient of potential side effects of the medication.
- To supply treatment and administer injections for the first 12 months.
- To inform patients that further injections will be administered at their GP practice.
- To inform GP that that the patient has been on paliperidone long-acting injection for a minimum of 12 months.
- To inform the GP of the results of baseline and subsequent tests including plasma glucose, plasma lipids and ECG and weight. This will not be necessary if the GP is already monitoring physical health.
- To inform the GP of how often the patient will be reviewed by psychiatric team.
- To review patient at the request of GP should any problems arise (side-effects / lack of efficacy).
- To inform the GP within 2 weeks of any changes to treatment.
- To report any suspected adverse effects to the MHRA: https://yellowcard.mhra.gov.uk/
- To complete the shared care guideline form and send to the GP.

General Practitioner/practice responsibilities

- To consider shared care proposal within 2 weeks of receipt. If you agree to request to continue prescribing as detailed in shared care guideline confirmation to the requesting consultant is required **within 2 weeks** of receipt of this guideline by completing and returning the agreement on pages 2 and 3.
- If you do not agree to shared care discuss with requesting consultant or local primary care medicines optimisation team within 2 weeks of receipt of shared care request.

- To provide ongoing prescriptions for paliperidone long-acting injection. To adjust the dose as advised by the specialist.
- To administer the injections.
- To agree monitoring requirements with specialist.
- To report and seek advice regarding any concerns, for example: side-effects, co-morbidities, pregnancy, or lack of efficacy to the specialist team.
- To observe the patient for side effects of medication, including injection site reactions, such as pain, induration, pruritus and nodules.
- To inform the appropriate local mental health team if the patient does not attend the appointment for the injection or refuses to have the injection.
- Agree between the specialist team and GP who will contact the patient if he/she misses their appointment.
- To refer back to specialist if the patient's condition deteriorates / GP has concerns about the treatment.
- To stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- To report any suspected adverse effects to the MHRA via the Yellow Card scheme: https://yellowcard.mhra.gov.uk/

Patient's / Carer's responsibilities

- To contact the specialist or GP if he or she does not have a clear understanding of any aspect of the treatment.
- To inform prescribing specialist, GP and other healthcare professionals of any other medication being taken, including over the counter products, alternative therapies or recreational drugs.
- To inform community pharmacists that they are prescribed paliperidone long-acting injection before purchasing medication over-the-counter.
- To attend all specialist and GP appointments.
- To take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others.
- To inform GP or hospital specialist of any concerns about treatment.
- To read the patient information leaflet included with the medication.
- To report any adverse effects or warning symptoms to GP or specialist.
- Inform GP and specialist if intending to become pregnant.
- To report to GP if pregnant or breastfeeding.
- To inform GP and community mental health team of any changes in addresses or telephone contact numbers.

3. CLINICAL INFORMATION

NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for paliperidone long-acting injection when prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk)

Licensed indication(s)

Xeplion™ (1-monthly injection)
Maintenance treatment of schizophrenia in adult patients stabilised with paliperidone or risperidone.
Trevicta™ (3-monthly injection)
Maintenance treatment of schizophrenia in adult patients who are clinically stable on 1-monthly paliperidone palmitate long-acting injection.
Byannli™ (6-monthly injection)

Maintenance treatment of schizophrenia in adult patients who are clinically stable on 1-monthly or 3-monthly paliperidone palmitate long-acting injection.

Place in Therapy

Paliperidone long-acting injection is approved for use in South East London in line with SEL IMOC Recommendation 024 and its licensed indication as above in adult patients with schizophrenia. Patients will be transferred to the GP under shared care after 12 months of treatment under the specialist team. Xepilon™ and Trevicta™ can be administered in either the deltoid or gluteal muscle and thus may be considered for those who do not wish to have the injection in the gluteal muscle.
Byannli™ can only be administered in the gluteal muscle.

Note: Paliperidone is the major active metabolite of risperidone, i.e. 9-hydroxyrisperidone.

Dose & route of administration

Adults

Xeplion™ (1-monthly injection)
Initial loading doses to be administered intramuscularly in the **deltoid** muscle as shown below:

Day 1 - 150mg
Day 8 - 100mg
Note: Lower loading doses may be necessary in some patients. Loading doses will be administered by the CMHT unless otherwise agreed

***Maintenance doses* are shown below**:
Each month thereafter 50mg-150mg intramuscularly in either deltoid or gluteal muscle.
.
For advice on dosing in the elderly or those with renal impairment contact medicines information.

Trevicta™ (3-monthly injection)
Patients who are clinically stable on Xeplion™ may be switched to Trevicta™ 3-monthly injection 175 mg - 525 mg, depending on their Xeplion™ dose. Trevicta™ will usually be initiated by the specialist service
For advice on dosing in the elderly or those with renal impairment contact medicines information.

Byannli™ (6-monthly injection) – must be administered in the gluteal muscle only
Patients who are clinically stable on Xeplion™ or Trevicta™ may be switched to Byannli™ 6-monthly injection 700mg or 1000mg, depending on their Xeplion™ or Trevicta™ dose. Byannli™ will usually be initiated by the specialist service.

For advice on dosing in the elderly or those with renal impairment contact medicines information 020 3228 2317.

Duration of treatment

Indefinite. Long-term

Criteria for stopping treatment

- Significant adverse reaction
- Intolerable side effects
- Lack of efficacy
- At request of patient/family. Patient must discuss any decision to stop or change medication with the specialist team.

Monitoring Requirements including frequency

Consultant (unless GP already monitoring physical health)

Baseline plasma glucose (fasting, or random plus HbA1c), lipids, prolactin, weight/BMI, BP, pulse, ECG, FBC, U&Es and CPK

GP:

Annual plasma glucose (fasting, or random plus HbA1c), lipids, prolactin, weight/BMI, ECG, BP, pulse, FBC, U&Es

Note: Paliperidone is known to cause weight gain, dyslipidemia and glucose dysregulation. Paliperidone has a low effect on the cardiac QTc interval. However, patients with schizophrenia have a higher risk of sudden cardiac death than the general population. Thus the recommendation for annual ECG.

Follow up arrangements

- The patient should be seen by the CMHT at least once a year.
- Where there are local ICB commissioned mental health primary care services in place and there is agreement, the annual review may be carried out by the primary care service.
- In addition, the patient may be referred for a review by the CMHT if there are concerns about the patient's mental state or the long-acting injection treatment.
- The patient should be referred to A&E for out of hours specialist psychiatric care.

Practical issues including other relevant advice/information

Reminder: this list is not exhaustive - for full details of adverse effects and all potential drug interactions refer to latest Summary of Product Characteristics (SPC) available via www.medicines.org.uk.

- The maintenance dose may be reduced if poorly tolerated. However, contact community psychiatrist or medicines information for advice before making dose adjustments.
- The maintenance dose of Xeplion™ should be administered once every calendar month (i.e. not every 28 days). If necessary, the dose may be administered up to 7 days before or after the maintenance dose is due.
- The maintenance dose of Trevicta™ should be administered once every 3 months. If necessary, the dose of Trevicta™ may be given up to 2 weeks before or after the dose is due.
- The maintenance dose of Byannli™ should be administered once every 6 months. If necessary, the dose of Byannli™ may be given up to 2 weeks before or 3 weeks after the dose is due.

Missed doses (see SPC for further details)

- Xeplion™ should be administered at the usual maintenance dose if the last injection was administered *within* the previous 6 weeks.
- Additional injections are required if more than 6 weeks have elapsed since the last injection. If more than 6 weeks have elapsed since the last injection the GP should contact medicines information or the consultant for advice on additional doses.
- Trevicta™ should be administered at the usual maintenance dose if the last injection was administered *within* the previous 4 months. If more than 4 months have elapsed since the last injection the GP should contact medicines information or the consultant for advice on additional doses. For further details see SPC.
- Byannli™ should be administered at the usual maintenance dose if the last injection was administered *within* the previous 6 months and 3 weeks. If a dose of Byannli™ is delayed, the next dose should be administered 6 months after the **originally scheduled dose**. If more than 6 months and 3 weeks have elapsed since the last injection the GP should contact medicines information or the consultant for advice on additional doses. For further details see SPC.

Interactions

- Paliperidone is not extensively metabolised. However, plasma levels of paliperidone may be affected by carbamazepine. In practice, dose adjustments would not be expected. Smoking does not affect plasma levels of paliperidone.

Side 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 at clinical doses). For advice on management of adverse effects contact medicines information or the CMHT.

Administration *(see SPC for further details)*

Xeplion™

- The dose is available in pre-filled syringes of 50mg, 75mg, 100mg and 150mg. Reconstitution is not necessary. The injection must be administered using the needles provided in the pack. Needles from the Trevicta™ pack or other commercially available needles must not be used when administering Xeplion™.
- The injection is intended for intramuscular use only and 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.
- For deltoid muscle administration the 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.
- For 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™

- The dose is available in pre-filed syringes of 175mg, 263mg, 350mg and 525mg. Reconstitution is not necessary. The injection must be administered using the needles provided in the pack. Needles from the Xeplion™™ pack or other commercially available needles must not be used when administering Trevicta™.
- The injection is intended for intramuscular use only and 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.
- 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.
- For deltoid muscle administration the recommended needle size is determined by the patient's weight. For those ≥ 90 kg, the thin wall 1½ inch, 22 gauge (0.72 mm x 38.1 mm) needle should be used. For those < 90 kg, the thin wall 1 inch, 22 gauge (0.72 mm x 25.4 mm) needle should be used. It should be administered into the centre of the deltoid muscle. Deltoid injections should be alternated between the two deltoid muscles.
- For gluteal administration the recommended needle size is the 1½ inch, 22 gauge (0.72 mm x 38.1 mm) needle regardless of body weight. It should be administered into the upper-outer quadrant of the gluteal muscle. Gluteal injections should be alternated between the two gluteal muscles.

Byannli™

- Byannli™ is for gluteal intramuscular use only. It must not be administered by any other route. Each injection must be administered only by a healthcare professional giving the full dose in a single injection. It should be injected slowly, deep into the upper-outer quadrant of the gluteal

muscle. A switch between the two gluteal muscles should be considered for future injections in the event of injection site discomfort.

- The needle for administration of Byannli™™ is a thin wall 1½ inch, 20 gauge (0.9 mm × 38 mm) needle, regardless of body weight. Byannli™ must be administered using only the thin wall needle that is provided in the Byannli™ pack. Needles from the 3-monthly or 1-monthly paliperidone palmitate injectable pack or other commercially available needles must not be used when administering Byannli™.
- The contents of the pre-filled syringe should be inspected visually for foreign matter and discolouration prior to administration. This highly concentrated product requires specific steps to ensure complete resuspension.
- It is important to shake the syringe with the syringe tip cap pointing up using a very fast up and down motion with a loose wrist for at least 15 seconds. Rest briefly, then shake again in the same way, using a very fast up and down motion with a loose wrist for a further 15 seconds to resuspend the medicinal product. Byannli™ should be administered immediately. If more than five minutes passes before the injection is administered, shake the syringe again, as above to resuspend the medicinal product (see *Information intended for healthcare professionals*).
- 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 of Byannli™.

Pregnancy and breast-feeding

- There are limited data on the safety of paliperidone in pregnancy and breastfeeding. GPs should contact the Medicines Information service if pregnancy is suspected or planned.

Information provided to the patient

Patients should be asked to contact their GP if:

- They have concerns about their medication
- They are considering stopping medication.
- Are considering becoming pregnant
- Suspect they are pregnant
- Wish to breastfeed
- Have been prescribed medication by another specialist service, so that drug interactions can be checked.

4. COMMUNICATION AND SUPPORT:
Please also refer to patient's clinic letters for specific clinic contact details if required.

South London and Maudsley (SLAM): switchboard 020 3228 6000	
Medication – Prescribing advice, interactions, availability of medicines Medicines Information	Tel: 020 3228 2317 Email: Pharmacy_Staff_Medicines_Information@slam.nhs.uk
Oxleas NHS Trust switchboard : 01322 625700	
Medication – Prescribing advice, interactions, availability of medicines Medicines information	Tel: 01322 625002 Email: oxl-tr.medicinesinfo@nhs.net

Evidence Base for treatment and key references

1. Attard A, Olofinjana O, Cornelius V, Curtis V, Taylor D. Paliperidone palmitate long-acting injection - prospective year-long follow-up of use in clinical practice. ***Acta Psychiatrica Scandinavica 2014***; 130 (1): 46-51.
2. Taylor D and Olofinjana O. Long-acting paliperidone palmitate – interim results of an observational study of its effect on hospitalization. ***International Clinical Psychopharmacology 2014***; 29 (4): 229–234
3. McEvoy JP, Byerly M, Hamer RM, Dominik R, Swartz MS, Rosenheck RA, Ray N, Lamberti JS, Buckley PF, Wilkins TM, Stroup TS. Effectiveness of paliperidone palmitate vs haloperidol decanoate for maintenance treatment of schizophrenia: a randomized clinical trial. ***JAMA 2014***; 311 (19): 1978-1987
4. Alphs L, Benson C, Cheshire-Kinney K, Lindenmayer JP, Mao L, Rodriguez SC and Starr HL. Real-World outcomes of paliperidone palmitate compared to daily oral antipsychotic therapy in schizophrenia: a randomized, open-label, review board-blinded 15-month study. ***J Clin Psychiatry 2015***; 76 (5):554-561
5. Taylor D et al. The Maudsley Prescribing Guidelines in Psychiatry. ***14th Edition 2021***
6. Janssen-Cilag Ltd. Xeplion™ 50 mg, 75 mg, 100 mg and 150 mg prolonged release suspension for injection. SPC (Last updated Sep 2021). https://www.medicines.org.uk/emc/search?q=Xeplion™
7. Janssen-Cilag Ltd. Trevicta™ 175mg, 263mg, 350mg and 525mg prolonged release suspension for injection. SPC (Last updated Sept 2021) https://www.medicines.org.uk/emc/product/7230/smpc#POSOLOGY
8. 8. Janssen-Cilag Ltd. Byannli™ 700mg and 1000mg prolonged release suspension for injection. SPC (Last updated Jan 2022) https://www.medicines.org.uk/emc/product/13307/smpc
9. 9. Najarian et al, A Randomized, Double-Blind, Multicenter, Noninferiority Study Comparing Paliperidone Palmitate 6-Month Versus the 3-Month Long-Acting Injectable in Patients With Schizophrenia. *International Journal of Neuropsychopharmacology* (2021)1–14 **https://doi.org/10.1093/ijnp/pyab071**