Frimley Health and Care

NHS Frimley

For use in Surrey Heath & North East Hants & Farnham

AMBER shared care protocol:

Paliperidone long-acting injection for patients within adult services, where a Locally Commissioned Service is in place

Review date :03/05/2027.

This amber shared care protocol is for paliperidone long-acting injections – 1 month, 3 month or 6 months. This protocol replaces the current shared care which is only applicable for 1 month or 3 months long-acting injections of paliperidone.

Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision-making approach; discuss the benefits and risks of the treatment with the patient and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate and optimise treatment as outlined in section 5.
- Transfer to primary care is normally after the patient has been treated for 6 months if prescribed the 1 or 3 months long acting paliperidone depot or after 1 year if prescribed the 6 months long acting paliperidone depot:

Treatment	Minimum length of time before stepping up to extended interval	How long the patient should receive treatment from SABP (Surrey and Borders Partnership) before transferring to primary care

Paliperidone 1 month long-acting depot	3m before step up to 3m 1yr before step up to 6m	Monthly injections supplied by SABPT for the first 6 months
Paliperidone 3 month long-acting depot	1yr before step up to 6m	3-monthly injections supplied by SABPT to complete treatment for a minimum total of 6 months (Note, the first four months' treatment may be provided by use of the 1-monthly injections)
Paliperidone 6 month long-acting depot	N.B step up to 6m *will be considered after one year of treatment at a stable dose using the 1- and 3-monthly formulations, either alone or in combination, at an equivalent dose, with no dose adjustment over the year prior to switching*	First 6-monthly injection supplied by SABPT

- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Once treatment is optimised, complete the shared care documentation, and send to patient's GP (general practitioners) practice detailing the diagnosis, current and ongoing dose, baseline, and most recent test results, confirm the monitoring schedule and when the next monitoring is required. Include contact information (section 13).
- Conduct the required monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Give advice to primary care on continuing treatment if a woman becomes or wishes to become pregnant or breastfeed.
- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- If accepted, prescribe ongoing treatment as detailed in the specialists' request and as per section 5 taking into any account potential drug interactions in section 7.

- Adjust the dose of paliperidone long-acting injection prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in section 9.
- Assess for possible interactions with paliperidone when starting new medicines (see section 7), taking into account the extended action of the injection, with release of paliperidone occurring up to 4 months after the administration of the 1-monthly injection, 18 months after the 3-monthly injection, and plasma levels still detectable up to 4 years after the last injection of the 6-monthly injection.
- Manage any adverse effects as detailed in section 10 and discuss with specialist team when required.
- Discuss other adverse effects with the specialist team as clinically appropriate (see section 10).
- Contact the specialist team for advice if the patient becomes or plans to become pregnant.
- Stop treatment as advised by the specialist.

Patient and/or carer responsibilities

- Receive paliperidone long-acting injections as prescribed and do not stop taking it without speaking to their primary care prescriber or specialist.
- Tell anyone who prescribes them a medicine that they are taking paliperidone, or that they have received it in the last 4 months (if 1-monthly), 18 months (if 3-monthly) or 4 years (if 6-monthly).
- Attend regularly for monitoring and review appointments with primary care and specialist. Be aware that medicines may be stopped if they do not attend appointments.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter medications to their prescriber and be aware they should discuss the use of paliperidone with their pharmacist before purchasing any OTC medicines.

Inform the specialist or primary care prescriber as soon as possible if they become pregnant or wish to become pregnant.

1. Background

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Long-Acting Injections (LAIs) form an important part of managing patients who have either expressed a preference for the associated convenience in dosing or through intentional or unintentional non-concordance with treatment, which increases the risk of relapse and may increase the frequency of hospital admission. Although the use of LAIs does not guarantee effective treatment adherence, for those who continue with LAIs, there may be some adherence advantage over oral antipsychotics which is demonstrated by a longer time to treatment discontinuation.[1]

There is established evidence for the use of antipsychotics in psychosis and schizophrenia[2] as well as in bipolar conditions[3]. First and second generation LAIs are considered to equally effective[4], however there is considerable variation in the adverse effect profiles, respectively.

Together with other factors such as patient preference, response, and compliance to treatment with oral antipsychotics, medical and drug history often determine the choice of LAIs.

According to NICE Guidelines for Schizophrenia[5], LAI antipsychotics should be offered to patients:

- who would prefer such treatment after an acute episode
- where avoiding covert non-adherence (either intentional or unintentional) to antipsychotic medication is a clinical priority within the treatment plan.

This shared care protocol applies to all adults aged 18 and older.

2. Indications

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Paliperidone 1-monthly injection is indicated for maintenance treatment of schizophrenia in adult patients stabilised with oral paliperidone or risperidone.

In selected adult patients with schizophrenia and previous responsiveness to oral paliperidone or risperidone, Paliperidone 1-monthly injection may be used without prior stabilisation with oral treatment if psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed.

Paliperidone 3-monthly injection is indicated for the maintenance treatment of schizophrenia in adult patients who are clinically stable on 1-monthly paliperidone palmitate injectable product.

Paliperidone 6-monthly injection is indicated for the maintenance treatment of schizophrenia in adult patients who are clinically stable on 1-monthly or 3-monthly paliperidone palmitate injectable products

3. Locally agreed off-label use

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N/A

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4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after at least 24 weeks, and when the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

6. Pharmaceutical aspects

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Route of administration:	The initiation doses using the 1-monthly formulation must be administered into the deltoid muscle only. Thereafter, the 1-monthly formulation may be administered into either the deltoid or the gluteal muscle. The 3-monthly or deep into the deltoid or gluteal muscle. The 6-monthly formulation must be administered by gluteal intramuscular injection only.
Formulation:	Long acting intramuscular injection

Administration details:	The recommended needle size for initial and maintenance administration of the 1-monthly and 3-monthly injection into the deltoid muscle is determined by the patient's weight. For those ≥ 90 kg, a 1½ inch, 22-gauge needle (38.1 mm x 0.72 mm) is recommended. For those < 90 kg, a 1-inch, 23-gauge needle (25.4 mm x 0.64 mm) is recommended. Deltoid injections should be alternated between the two deltoid muscles. The recommended needle size for maintenance administration of the 1-monthly and 3-monthly injection into the gluteal muscle is a 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. The needle for administration of the 6-monthly injection is a thin wall 1½ inch, 20-gauge (0.9 mm × 38 mm) needle, regardless of body weight. The required needles are provided with the product.
Other important information:	

7. Significant medicine interactions

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The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

Caution is advised when prescribing paliperidone with medicinal products known to prolong the QT interval.

Paliperidone is not expected to be involved in clinically important pharmacokinetic interactions with medicinal products that are metabolised by, or inducers or inhibitors of, cytochrome P450 isozymes.

Plasma levels of *oral* paliperidone may be reduced with concomitant use of carbamazepine due to induction of renal P-gp. The clinical significance of this with the long-acting injection formulation has not been established but should be considered.

Paliperidone may antagonise the effect of levodopa and other dopamine agonists. If this combination is deemed necessary, particularly in end-stage Parkinson's disease, the lowest effective dose of each treatment should be prescribed.

Caution should be used when paliperidone is prescribed in combination with other centrally acting medicinal products, e.g., anxiolytics, most antipsychotics, hypnotics, opiates, etc. or alcohol.

Because of its potential for inducing orthostatic hypotension, an additive effect may be observed when paliperidone is administered with other medicinal products that have this potential.

Caution is advised if paliperidone is combined with other medicinal products known to lower the seizure threshold (i.e., phenothiazines or butyrophenones, tricyclics or SSRIs (Selective Serotonin Reuptake Inhibitors), tramadol.

The combined use of psychostimulants (e.g. methylphenidate) with paliperidone can lead to extrapyramidal symptoms upon change of either or both treatments.

8. Baseline investigations, initial monitoring, and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

Baseline Monitoring

- HbA_{1C} (or fasting glucose, if appropriate)
- Lipids
- FBC
- LFTs
- U&Es including eGFR.
- Creatine Phosphokinase (CPK)
- Prolactin
- ECG - Recommended if:
  - Physical examination shows specific cardiovascular risk.
  - Personal history of CVD (cardiovascular disease)
  - Admitted as inpatient.
- BP & Pulse
- Weight & BMI
- Waist Circumference

9. Ongoing monitoring requirements to be undertaken by primary care Back to top

See section 10 for further guidance on management of adverse effects/responding to monitoring results.

Monitoring and actions	Frequency
Weight & BMI	Weekly for first 6 weeks (Specialist)
HbA_{1C} (or fasting glucose, if appropriate) Lipids BP & Pulse Weight & BMI	At first 3 months of treatment (Specialist)
HbA1C (or fasting glucose, if appropriate) Lipids BP & Pulse Weight & BMI Waist Circumference Prolactin (if appropriate) ECG - Recommended if: ○ Physical examination shows specific cardiovascular risk. ○ Personal history of CVD	Annually (GP)
Note: Paliperidone is known to cause weight gain, dyslipidaemia, 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. **(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.**	

10. Adverse effects and other management

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Any serious adverse reactions should be reported to the MHRA (Medicines & Healthcare products Regulatory Agency) via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For information on incidence of ADRs (Adverse Drug Reactions) see relevant summaries of product characteristics

Result	Action for primary care
As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance	
Neuroleptic Malignant Syndrome, although very rare, is a medical emergency – signs and symptoms include hyperthermia, fever, sweating, muscle rigidity, autonomic instability, altered consciousness, confusion, fluctuating blood pressure, tachycardia, raised creatinine kinase.	Urgent Medical Attention required

11. Advice to patients and carers

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The specialist will counsel the patient about the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

See also https://www.choiceandmedication.org/sabp/printable-leaflets/patient-information-leaflets/109/ALL/

12. Pregnancy, paternal exposure, and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

Pregnancy:

Since paliperidone is released from the long acting injection up to 4 months after the administration of the 1-monthly injection, 18 months after the 3-monthly injection, and since

plasma levels are still detectable up to 4 years after the last injection of the 6-monthly injection, consideration should be given to the long-acting nature of this formulation as maternal exposure before and during pregnancy may lead to adverse reactions in the newborn child.

Breastfeeding:

Paliperidone is excreted in the breast milk to such an extent that effects on the breast-fed infant are likely if therapeutic doses are administered to breast-feeding women. Consideration should be given to the long-acting nature of paliperidone injections as breastfed infants may be at risk even from administration long before breast-feeding. The manufacturer advises that paliperidone long-acting injection should not be used while breast-feeding.

Paternal exposure:

The manufacturer reports that there were no relevant effects observed on fertility in the non-clinical studies. They do not specifically mention paternal exposure.

13. Specialist contact information

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Name: *[insert name]*
Role and specialty: *[insert role and specialty]*
Daytime telephone number: *[insert daytime telephone number]*
Email address: *[insert email address]*
Alternative contact: *[insert contact information, e.g. for clinic or specialist nurse]*
Out of hours contact details: *[insert contact information, e.g. for duty doctor]*

14. Additional information

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Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

Missed or delayed doses

In cases of missed or delayed doses, the manufacturer offers specific advice on restarting treatment, depending on the time elapsed since the last injection, and the usual frequency of administration.

- If the patient does not attend the planned appointment, then the practice nurse will call patient and establish reason and rebook if agreeable within a timescale appropriate to the schedule set out by the manufacturer.
- Ensure repeat LAI administered within the timescale set out by the manufacturer for the specific frequency of injections that the person is receiving.
- If the person is refusing treatment or shows or signs of relapse or did not attend their appointment without successful follow up, then escalate to the Community Mental Health Team duty worker to action. The injection due will then be administered by the Community Mental Health Team.
- The Community Mental Health Team to keep a list of people under shared care with primary care.
- Assessment to be completed and outcome to be communicated to GP via the practice manager.
- Outcome will either be:
    a. that there is a reasonable explanation for non-attendance and to continue with shared care with primary care
    b. or the person needs to be reallocated a care coordinator and prescribing and administration responsibility to return to SABP.

15. References

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Summary of product characteristics. Available via www.medicines.org.uk.

Taylor D, Barnes T, Young AH. The Maudsley® Prescribing Guidelines in Psychiatry. 14th Edition. 2021. Available online via https://onlinelibrary.wiley.com/doi/10.1002/9781119870203.ffirs

16. Other relevant national guidance

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Psychosis and schizophrenia in adults: prevention and management. [CG178]. Last updated: 01 March 2014. https://www.nice.org.uk/guidance/cg178

17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

To be agreed and completed locally

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*:* *[insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed *[insert APC name]*shared care protocol for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care, and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened regarding this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
The last long-acting injection of paliperidone was administered on	
The next long-acting injection of paliperidone will be due to be administered on	
I have arranged a follow up with this patient in the following timescale	

Treatment was started on, *[insert date started]* and the current dose is *[insert dose and frequency]*.

The next injection is due on *[insert date]*

If you agree, please undertake monitoring and treatment from *[insert date]* NB: date must be at least 1 month from initiation of treatment.

The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

Please respond to this request for shared care, in writing, within 14 days of the request being made where possible.

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*
Patient *[insert Patient's name]*
NHS Number *[insert NHS Number]*
Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment.

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: _____Date: _____

Primary Care Prescriber address/practice stamp

Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

Re:

Patient	*[insert Patient's name]*
NHS Number	*[insert NHS Number]*
Identifier	*[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety NHS *[insert CCG name]***,** in conjunction with local acute trusts have classified *[insert medicine name]*as a Shared Care drug and requires a few conditions to be met before transfer can be made to primary care.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

		Tick which applies
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care.** As the patients' primary care prescriber, I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.**	
2.	**The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement.** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	

3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible to provide them with the medication that you have recommended. ***Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.***	
5.	**Shared Care Protocol not received.** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed***.*** For this reason, I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England ‘Responsibility for prescribing between Primary & Secondary/Tertiary care’ guidance (2018) states that “when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs

would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs." In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible.

Yours sincerely

Primary Care Prescriber signature: _____
Date: _____

Primary Care Prescriber address/practice stamp