MMG008 GUIDELINES FOR INITIATION AND USE OF RISPERIDONE LONG-ACTING INJECTION AND PALIPERIDONE LONG-ACTING INJECTION
Table of Contents

Why we need this Policy ........................................................................................................3
What the Policy is trying to do .................................................................................................3
Which stakeholders have been involved in the creation of this Policy ..................................3
Any required definitions/explanations .....................................................................................3
Key duties ..................................................................................................................................3
  Medicines Management Committee .......................................................................................3
  Medical Director .......................................................................................................................3
  Clinical Directors ..................................................................................................................3
  Heads of Hospitals and Locality Managers ..........................................................................3
  Consultants ..............................................................................................................................3
  Chief Pharmacist ..................................................................................................................3

Use Of Risperidone Long acting injection and Paliperidone Long acting injection ...............4
Licensed indications: ......................................................................................................................4
When to consider using Risperidone LAI or Paliperidone LAI ...............................................4
Additional information to consider when initiating Risperidone Long acting injection ..........5
Additional information to consider when initiating Paliperidone Long acting injection ........6
Converting from oral treatment to Paliperidone LAI (Xeplion) ..............................................6
Converting from Risperidone long acting injection to Paliperidone LAI ................................6
Application process ..................................................................................................................7
Patient monitoring .....................................................................................................................7
Training requirements associated with this Policy .................................................................8
  Mandatory Training ...............................................................................................................8
  Specific Training not covered by Mandatory Training ..........................................................8
How this Policy will be monitored for compliance and effectiveness ..................................8
Equality considerations ..............................................................................................................8
Document control details .........................................................................................................9
Appendix 1 APPLICATION FOR USE OF RISPERDAL CONSTA INJECTION ..................10
Appendix 2 APPLICATION FOR USE OF XEPLION INJECTION ......................................12
Appendix 3 APPLICATION FOR USE OF TREVICTA INJECTION ....................................14
**Why we need this Policy**

Risperidone long-acting injection (Risperdal Consta®) and Paliperidone Long acting injection (Xeplion®) are high cost medicines, and it has been agreed by the Medicines Management Committee that to ensure use is targeted towards the most appropriate patients that the following guidelines should be followed when initiating treatment.

**What the Policy is trying to do**

To provide guidance on the use of Risperidone LAI and Paliperidone LAI.

**Which stakeholders have been involved in the creation of this Policy**

Medicines Management Committee

**Any required definitions/explanations**

LAI - Long acting injection

NHFT  - Northamptonshire Healthcare NHS Foundation Trust

**Key duties**

**Medicines Management Committee**

Will approve and review these guidelines

Will review any applications for Risperidone LAI or Paliperidone LAI the Chief pharmacist submits for consideration.

**Medical Director**

Is responsible for the dissemination of this guideline to their Clinical Directors and Clinical Tutors.

**Clinical Directors**

Are responsible for the dissemination and implementation of the guideline in their service areas.

**Heads of Hospitals and Locality Managers**

Are responsible for the dissemination and implementation of the guideline in their service areas.

**Consultants**

Are responsible for completing the application form for Risperidone LAI or Paliperidone LAI and submitting to the Chief pharmacist for approval.

**Chief Pharmacist**

- Is responsible for
- reviewing and approving, as appropriate, applications for Risperidone LAI or Paliperidone LAI. (In the absence of the chief pharmacist this task will be delegated to the Medical
Director, Chairman of MMC, deputy medical director (Mental Health) or deputy Chief Pharmacist

- maintaining a database of all applications for Risperidone LAI and Paliperidone LAI

Use Of Risperidone Long acting injection and Paliperidone Long acting injection

An application system for use of Risperidone long acting injection/Paliperidone long acting Injection is in place, and prior to prescribing an application form must be completed and signed by the patient’s consultant and forwarded to the Chief pharmacist for consideration and approval.

Licensed indications:
Risperidone Long acting Injection (LAI) is indicated for the maintenance treatment of schizophrenia in patients currently stabilised with oral antipsychotics.

Paliperidone long acting injection (LAI) is licensed / indicated for the maintenance treatment of adult patients with schizophrenia, whose condition has been stabilised with oral risperidone or paliperidone. In selected patients with previous responsiveness to oral risperidone (or paliperidone), Paliperidone LAI may be used without prior stabilisation with oral treatment if psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed. (Note – oral paliperidone is not included in the Trust Formulary) This is available in two preparations, Xeplion which is the monthly injection and Trevicta which is administered every 3 months.

Physical health checks should be undertaken at baseline in accordance with Trust standards (See Physical Health Policy CLP070) and then annually.

In addition to this, the SPC for Paliperidon e Long Acting Injection states the following:

Events of leucopenia, neutropenia, and agranulocytosis have been reported with Xeplion. Agranulocytosis has been reported very rarely (< 1/10,000 patients) during post-marketing surveillance.

Patients with a history of a clinically significant low white blood cell count (WBC) or a drug-induced leucopenia/neutropenia should be monitored during the first few months of therapy and discontinuation of Xeplion should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors. Patients with clinically significant neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count < 1 x 10⁹/L) should discontinue Xeplion and have their WBC followed until recovery.

When to consider using Risperidone LAI or Paliperidone LAI
Use of Risperidone LAI or Paliperidone LAI may be considered in the following circumstances:

Patients presently prescribed an oral atypical with compliance problems or where patient choice and clinical need favour the use of a depot
Every effort should be made to establish any reasons for non-compliance. If it is because of side-effects an alternative atypical with a different side-effect profile should be tried.
If the non-compliance cannot be addressed by changing to another oral medicine or by increased support, use of Risperidone long-acting injection or Paliperidone long acting injection may be considered with monitoring as listed below.

**Patients presently on typical depots**

If they are not suffering from extrapyramidal side effects (EPSEs), patients presently on typical depots should continue on them.

If a patient is experiencing unacceptable EPSEs and has not recently been offered the alternative of an oral atypical antipsychotic, this should be considered. Non-compliance in the past may no longer be an issue and if agreeing to take regular oral medication is an alternative to suffering from EPSEs patients may agree to the change. Any issues of support should be addressed.

If a patient is experiencing unacceptable EPSEs and changing to an oral atypical has been unsuccessful in the past because of non-compliance, the reasons should be reviewed. If it was due to other side effects, consideration should then be given to changing to another oral atypical with a different side effect profile. If, however, a patient is unlikely to comply with any oral medication and is suffering unacceptable EPSEs a trial of Risperidone long-acting injection or Paliperidone long acting injection may be considered.

**Additional information to consider when initiating Risperidone Long acting injection**

Risperidone long-acting injection is not appropriate for patients who have not tolerated or responded to the oral form in the past.

The manufacturers recommend that patients with no previous history of risperidone use should be pre-treated with oral risperidone for several days as clinically feasible to assess tolerability before the first injection. Supplementation with the previously used dose of oral risperidone or previous antipsychotic should be provided during the first three weeks after the first injection. This is to ensure coverage until the main release phase of risperidone from the injection site has begun. Oral risperidone or previous antipsychotic should then be tapered and discontinued.

Only small quantities (<1% of the dose) are released in the first 3 weeks. The main release starts from week 3 onwards and is maintained in weeks 4 to 6. Because of this, no dose increase should be made until after three injections have been given at two weekly intervals.

No additional benefits were observed with a dose of 75 mg in clinical trials and doses above 50 mg every 2 weeks are not recommended. If, in a rare case, it is considered that increasing the dose to 75 mg every 2 weeks would be beneficial to an individual patient the **Policy for Unlicensed Medicines – MMP006** should be followed. Where a dose of 75mg is used this should be given as 2 injections in 2 sites (see also information on Paliperidone long acting injection below).

Although risperidone is classed as an atypical antipsychotic, EPSEs do still occur.

Weight gain is also a commonly reported side-effect.

Symptoms of hyperprolactinaemia occur but are uncommon.
Tardive dyskinesia and seizures have occasionally been reported.

The entire pack must be stored in a refrigerator at 2º-8ºC. If refrigeration is unavailable, RISPERDAL CONSTA can be stored at temperatures not exceeding 25ºC for no more than 7 days prior to administration. If this happens write expiry date on the box and do not return to refrigerator.


Additional information to consider when initiating Paliperidone Long acting injection.
Paliperidone LAI is not indicated for treatment-resistant schizophrenia, unlicensed indications or patients intolerant to oral risperidone or paliperidone.

Paliperidone LAI (Xeplion)is intended for once-monthly injection (i.e. once per calendar month, rather than 4-weekly), by intramuscular route into the deltoid or gluteal muscle. However, initial loading doses must be given into the deltoid muscle. Teams may wish to consider fixing the administration to a specific day of the month e.g. the first Tuesday etc. to facilitate monthly administration. Whilst this will mean that there is a five week interval between injections on some occasions this will not affect efficacy but will result in the intended 12 injections per year

Paliperidone long-acting injection has a higher acquisition cost than Risperidone long acting injection and if the recommended monthly injection regime is not followed this will have major cost implications for the Trust.

Converting from oral treatment to Paliperidone LAI (Xeplion)
Paliperidone LAI requires the administration of two loading doses, (on day 1 and on day 8), but does not require any oral supplementation thereafter.

Recommended Dose Scheme:

- Day 1 - 150mg into the deltoid muscle.
- Day 8 (+/- 4 days) - 100mg into the deltoid muscle.
- Day 36 (+/- 7 days) - Maintenance dose into deltoid or gluteal muscle

The recommended maintenance dose is 75mg per month although some patients may benefit from lower or higher doses.

A maintenance (maximum) dose of 150mg per month is also within the terms of the Product Licence.

Converting from Risperidone long acting injection to Paliperidone LAI
No loading dose is required and the equivalent dose of Paliperidone LAI should be given on the date the Risperidone LAI is next due.

Trevicta®. The MMC have agreed that Trevicta may be considered for patients who are adequately treated with 1-monthly paliperidone palmitate (Xeplion) injectable (preferably for four months or more) and do not require dose adjustment.

TREVICTA should be initiated in place of the next scheduled dose of 1-monthly paliperidone palmitate injectable (± 7 days). The TREVICTA dose should be based on the previous 1-monthly paliperidone palmitate injectable dose using a 3.5-fold higher dose shown in the following table:

<table>
<thead>
<tr>
<th>TREVICTA doses for patients adequately treated with 1-monthly paliperidone palmitate injectable</th>
<th>Initiate TREVICTA at the following dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>If the last dose of 1-monthly paliperidone palmitate injectable is</td>
<td></td>
</tr>
<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>
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</tbody>
</table>

**Application process**

Completed application forms for Risperidone long-acting injection and both Paliperidone long-acting injections may be submitted to the Chief Pharmacist who has been authorised by the MMC to approve applications which fulfil the agreed criteria. The deputy Chief Pharmacist may approve applications in the absence of the Chief Pharmacist. In an emergency situation when neither the Chief Pharmacist nor the deputy Chief Pharmacist are available applications may be made to the MMC Chairman or, in his absence, the Medical Director or the Deputy Medical Director (Mental Health), who may give approval for its use.

Forms are available from Berrywood Pharmacy

Berrywood Pharmacy will maintain a record of all applications for use of Risperidone LA injection and both Paliperidone LAI injections. The NHFT Chief Pharmacist will hold a master list of all Risperidone LAI and Paliperidone LAI patients.

Prescriptions will only be dispensed where an application has been received and approved or where it can be shown that an individual has been transferred back to the care of NHFT stabilised on Risperidone long acting injection or paliperidone long acting injection e.g. copy of discharge information from transferring Trust.

**Patient monitoring**

To help confirm the effectiveness of the injection for individual patients and for audit purposes HoNOS rating scales should be completed at suitable intervals.
Training requirements associated with this Policy

Mandatory Training
There is no mandatory training associated with this guideline

Specific Training not covered by Mandatory Training
Ad hoc training sessions based on an individual’s training needs as defined within their annual appraisal or job description.

How this Policy will be monitored for compliance and effectiveness

<table>
<thead>
<tr>
<th>Aspect of compliance or effectiveness being monitored</th>
<th>Method of monitoring</th>
<th>Individual responsible for the monitoring</th>
<th>Monitoring frequency</th>
<th>Group or committee who receive the findings or report</th>
<th>Group or committee or individual responsible for completing any actions</th>
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</thead>
<tbody>
<tr>
<td>Duties</td>
<td>To be addressed by the monitoring activities below.</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Process followed for use of Risperidone LAI and Paliperidone LAI</td>
<td>Section to be included in MMC annual report detailing number of applications received and approved and current patient numbers at year end</td>
<td>Chief Pharmacist</td>
<td>Annual</td>
<td>Medicines Management Committee</td>
<td>Medicines Management Committee</td>
</tr>
</tbody>
</table>

Where a lack of compliance is found, the identified group, committee or individual will identify required actions, allocate responsible leads, target completion dates and ensure an assurance report is represented showing how any gaps have been addressed.

Equality considerations
See MMP001 Control of Medicines Policy.

Reference Guide
1 Risperdal Consta SPC 1.09.2015 emc [www.medicines.org.uk](http://www.medicines.org.uk)
### Document control details

<table>
<thead>
<tr>
<th>Version No.</th>
<th>Date Ratified/Amended</th>
<th>Date of Implementation</th>
<th>Next Review Date</th>
<th>Reason for Change (e.g. full rewrite, amendment to reflect new legislation, updated flowchart, minor amendments, etc.)</th>
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<tr>
<td>1.0</td>
<td>21.11.17</td>
<td>21.11.17</td>
<td>30.11.19</td>
<td>Review</td>
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<tr>
<td>2.0</td>
<td>19.03.19</td>
<td>19.03.19</td>
<td>31.03.22</td>
<td>Addition of Trevicta to preparations available; monitoring information updated Review</td>
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</table>
# APPLICATION FOR USE OF RISPERDAL CONSTA INJECTION

**Patient’s Name:**

**Date of Birth:**
**NHS No.:**

**Ward (if in-patient):**

**PCRT:**

**Diagnosis:**

**Current Therapy:**

**Previous Medication History:**

**Has patient had EPSEs on typical antipsychotics?**
- Yes
- No
- Not applicable

**Has patient responded to oral risperidone?**
- Yes
- No
- Too early to assess
- Not applicable

**Is patient considered treatment resistant?**
- Yes
- No

**Is patient compliant?**
- Yes
- No

CONTINUED OVERLEAF…
Brief Clinical Summary:

<table>
<thead>
<tr>
<th>Is patient at risk of relapse?</th>
<th>Yes</th>
<th>No</th>
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</thead>
</table>

Reasons why patient may benefit from use of Risperdal Consta

Consultant’s name

Consultant’s Signature

Date

Please return form to Michaela Cox, Pharmacy, Berrywood Hospital

For MMC use only

<table>
<thead>
<tr>
<th>APPROVED BY AUTHORISED PHARMACIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
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</table>

Comments

Signature Date

<table>
<thead>
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<th>APPROVED BY MMC CHAIRMAN</th>
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</thead>
<tbody>
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<td>Yes</td>
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Comments

Signature Date
## Appendix 2 APPLICATION FOR USE OF XEPLION INJECTION

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<tr>
<th>Patient’s Name:</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Date of Birth:</td>
<td>NHS no:</td>
<td></td>
</tr>
<tr>
<td>Ward (if in-patient):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCRT:</td>
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<tr>
<td>Diagnosis:</td>
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<td></td>
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<tr>
<td>Current Therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous Medication History:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Is the patient currently stabilised on risperidone?**
- Yes
- No

**If not currently stabilised on risperidone has patient previously tolerated and responded to oral risperidone?**
- Yes
- No

**Has patient had EPSEs on typical antipsychotics?**
- Yes
- No
- Not applicable

**Is patient considered treatment resistant?**
- Yes
- No

**Is patient compliant?**
- Yes
- No

CONTINUED OVERLEAF…
Brief Clinical Summary:

Is patient at risk of relapse?  
<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>

Reasons why patient may benefit from use of Xeplion Injection

Consultant’s name

Consultant’s Signature

Date

Please return form to Michaela Cox, Pharmacy, Berrywood Hospital

For MMC use only

APPROVED BY AUTHORISED PHARMACIST

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Referred for Chairman’s action</th>
<th>Referred to MMC</th>
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Comments

Signature  Date

APPROVED BY MMC CHAIRMAN

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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</table>

Comments

Signature  Date
**APPLICATION FOR USE OF TREVICTA® INJECTION**

<table>
<thead>
<tr>
<th>Patient’s Name:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Birth:</td>
<td>NHS no:</td>
</tr>
<tr>
<td>Ward (if in-patient):</td>
<td></td>
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<tr>
<td>PCART:</td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
</tr>
</tbody>
</table>

**Current Therapy:**

Has the patient been on paliperidone palmitate long acting monthly injection (Xeplion*) for at least 6 months?  
Yes/No

If “yes” has the patient received paliperidone palmitate long acting monthly injection (Xeplion) at the same dose for at 3 months?  
Yes/No

Has the patient been stable mentally for at least 3 months?  
Yes/No

**Previous Medication History:**

**Reasons for considering Trevicta**:  

Has patient had EPSEs on typical antipsychotics?

Yes ☐ No ☐ Not applicable ☐

Is patient considered treatment resistant?

Yes ☐ No ☐

Is patient compliant?

Yes ☐ No ☐

Brief Clinical Summary:

Did the patient experience side effects to the Xeplion (paliperidone once monthly) depot? Yes/No

If yes please describe:

How was improvement on paliperidone depot measured?

Is patient at risk of relapse?

Yes ☐ No ☐

Reasons why patient may benefit from use of Trevicta Injection

Consultant’s name

Signature

Date

Please return form to Michaela Cox, Pharmacy, Berrywood Hospital

For MMC use only

APPROVED BY AUTHORISED PHARMACIST

Yes ☐ No ☐ Referred for Chairman’s action ☐ Referred to MMC ☐

Comments

Signature Date

APPROVED BY MMC CHAIRMAN

Yes ☐ No ☐

Comments

Signature Date