Paliperidone palmitate 3-monthly Long-Acting Injection (Trevicta®) Guidelines for Prescribing and Administration (Version 2)

1. Key Points

1.1 Paliperidone palmitate 3-monthly long-acting injection (paliperidone 3-monthly) is licensed / indicated for the maintenance treatment of schizophrenia in adult patients who are clinically stable on 1-monthly paliperidone long-acting injection, (Xeplion®). In relation to this product the Trust defines clinically stable patients as those that have been stable on the same dose of 1-monthly paliperidone long-acting injections for at least 6 months, i.e. patients that have received at least six 1-monthly injections at a consistent, stable dose.

1.2 To ensure the patient is on the lowest effective dose before transferring to a 3-monthly injection, the patient should be reviewed to ensure each previous dose increase only took place after at least 3 months on the previous dose. This is because patients only get to a steady state dose after three 1-monthly injections. If the increase in dose occurred before the dose was stabilized, serious consideration should be given to trying to stabilize the patient on a lower dose of 1-monthly injection before moving to the 3-monthly preparation.

1.3 Patients on the maximum 150mg dose per month must receive a full MDT review and this review should include a pharmacist. Consideration should be given to lowering the dose before a final decision is made to transfer to the 3-monthly injection. Note that 100mg monthly doses of paliperidone injection are equivalent to 50mg fortnightly doses of risperidone injection, a dose that is usually not exceeded. Monthly doses of paliperidone exceeding 100mg should only occur in exceptional cases.

1.4 Paliperidone 3-monthly is not indicated for treatment-resistant schizophrenia, unlicensed indications or patients intolerant to paliperidone.

1.5 Before prescribing paliperidone 3-monthly, consideration must be given to the suitability of a three-monthly injection schedule for the individual patient and whether additional contacts with the patient will be required on a more frequent basis.

1.6 A baseline prolactin level should be obtained prior to prescribing paliperidone 3-monthly.

1.7 Paliperidone 3-monthly may only be newly prescribed by doctors of specialist registrar grade or above. Other grades may not initiate therapy or adjust dose without direct instruction from their consultant. It is not expected that patients will require hospital admission for initiation of this injection.

1.8 Paliperidone 3-monthly is intended for administration once every three calendar months, (ie. 4 times a year), by slow, deep intramuscular injection into the deltoid or gluteal muscle, using only the thin-walled needles from the Trevicta® packs. (See section 4).

1.9 When switching from paliperidone 1-monthly injections, paliperidone 3-monthly should be initiated in place of the next scheduled dose (+/- 7 days) and the dose based on the stabilised 1-monthly dose multiplied by a factor of 3.5 (See section 2).

1.10 Paliperidone 3-monthly is supplied as pre-filled syringes and available to community teams via Polar Speed direct delivery using Polar Speed prescription / order stationery.
1.11 **Paliperidone 3-monthly is very expensive** when compared to conventional antipsychotic depots but equivalent to the cost of paliperidone 1-monthly long-acting injection on an equivalent dose basis over the course of a year. At 525mg 3-monthly, (maximum dose, equivalent to paliperidone injection 150mg per month), it costs approximately £4,700 per patient year. (See section 7).

1.12 Paliperidone 3-monthly has not been approved by local CCGs for GP prescribing; therefore referral cannot be made to primary care for continuation of treatment unless a drug specific local arrangement is in place.

2. **Prescribing Treatment.**

2.1 Patients may only be prescribed paliperidone 3-monthly if they are already clinically stable on 1-monthly paliperidone long-acting injection, (Xeplion®). (See section 1).

2.2 When switching from paliperidone 1-monthly injections, paliperidone 3-monthly should be initiated in place of the next scheduled dose (+/- 7 days) and the dose based on the stabilised 1-monthly dose multiplied by a factor of 3.5 (See below).

2.3 **Switching from other long-acting injections, (other than paliperidone 1-monthly), or from traditional depot injections must not occur.**

2.4 **Switching from oral antipsychotic drugs must not occur.**

2.5 Switching from paliperidone 1-monthly long-acting injection – dose equivalents in those patients stabilised on paliperidone 1-monthly injections for at least 6 months:

<table>
<thead>
<tr>
<th>Stable dose of 1-monthly paliperidone injection:</th>
<th>Initiate paliperidone 3-monthly at the following dose:</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 mg</td>
<td>175 mg</td>
</tr>
<tr>
<td>75 mg</td>
<td>263 mg</td>
</tr>
<tr>
<td>100 mg</td>
<td>350 mg</td>
</tr>
<tr>
<td>150 mg - (must be fully reviewed)</td>
<td>525 mg</td>
</tr>
</tbody>
</table>

2.6 The licensed maximum dose of paliperidone 3-monthly is 525mg per 3 months, which should not be exceeded. This dose is equivalent to administering 1-monthly paliperidone long-acting injections at a dose of 150mg per month.

3. **Other Dosing Recommendations / Considerations.**

3.1 **The elderly:** In general, recommended dosing for elderly patients with normal renal function is the same as for younger adult patients with normal renal function. As elderly patients may have reduced renal function, see Renal impairment below for dosing recommendations in patients with renal impairment.

3.2 **Children & Adolescents:** The product is not licensed for use in patients less than 18 years of age, so it should not be used. No efficacy or safety data are available.

3.3 **Renal impairment:** The product has not been studied in patients with renal impairment. For patients with mild renal impairment, (creatinine clearance ≥ 50 to < 80 ml/min), the dose of paliperidone monthly long-acting injection should have been adjusted accordingly and consideration must be given to the likelihood of further renal deterioration. **Paliperidone 3-monthly should not be used in those with moderate or severe renal impairment, (creatinine clearance < 50 ml/min).**

3.4 **Hepatic impairment:** The product has not been studied in patients with hepatic impairment. However, based on experience with oral paliperidone, no dose adjustment is
required in patients with mild or moderate hepatic impairment. It should be used with caution in those with severe hepatic impairment (see SPC - https://www.medicines.org.uk/emc/search?q=%22Trevicta%22)

3.5 Switching from paliperidone 3-monthly: Switching to another long-acting injection or to an oral antipsychotic should not generally occur until 3 months have elapsed since the last administration of paliperidone 3-monthly. Please refer to your local pharmacy team or to the manufacturer’s data for further advice.

4. Administration.

4.1 Paliperidone 3-monthly pre-filled syringes must be vigorously shaken for at least 15 seconds no more than 5 minutes prior to administration of the injection to ensure a homogenous solution and accurate dosage.

4.2 Paliperidone 3-monthly is intended for administration once every 3 calendar months, (+/- 2 weeks). Administering the product at greater or lesser intervals than this has not been studied and should not occur.

4.3 If the dose is delayed to between 3.5 months and 4 months then the injection should be administered as soon as possible and then resume the 3-monthly injection schedule.

4.4 If the dose is delayed to between 4 months and 9 months then the injection should be administered using the recommended re-initiation regimen shown in the table in the Trevicta SPC. https://www.medicines.org.uk/emc/search?q=%22Trevicta%22

4.5 If the dose is delayed more than 9 months, then re-initiate treatment with 1-monthly paliperidone palmitate injectable as described in the prescribing information for that product. Paliperidone 3-monthly can then be resumed after the patient has been adequately treated with paliperidone 1-monthly, preferably for six months or more.

4.6 Patients on paliperidone 3-monthly need to be scheduled to attend clinic or to be visited for injection, once every three months. For example, administration could be scheduled for a certain date on each of those months, (adjusted for weekends if necessary). Applying this sort of schedule will mean doses are suitably spaced out so that efficacy is maximised.

4.7 The packs of paliperidone 3-monthly offer two needle options for intramuscular administration only. Other needles and other routes must not be used.

For deltoid administration:
- A thin-wall 1½ inch, 22 gauge (yellow hub) needle for patients ≥ 90kg.
- A thin-wall 1 inch, 22 gauge (pink hub) needle for patients < 90 kg.

For gluteal administration:
- The thin wall 1½ inch, 22 gauge (yellow hub) needle, regardless of weight.

4.8 Following administration of paliperidone 3-monthly, there is no requirement for any enhanced level of patient monitoring and patients should be monitored for post-injection events in the same way as for paliperidone monthly injection or for traditional depots. However, clinicians should remain aware that anaphylactic reactions in response to monthly paliperidone injection have been reported, rarely, in patients that have previously tolerated oral risperidone or oral paliperidone.

4.9 Great care must be taken to avoid wastage of this product as each individual injection is extremely expensive, ranging in price from £550 to £1,180 depending on dose.
5. **Storage.**

5.1 Packs of paliperidone 3-monthly should be stored in a locked medicines cabinet; there is no requirement for fridge storage.

5.2 Paliperidone 3-monthly is supplied in pre-filled syringes; there is no need for any reconstitution or dilution. Each pack contains one pre-filled syringe and two needles. Only full syringe doses may be used as the accuracy of a dose administered from less than a full syringe cannot be assured.

6. **References:**

  [https://www.medicines.org.uk/emc/search?q=%22Trevicta%22](https://www.medicines.org.uk/emc/search?q=%22Trevicta%22)

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