Aripiprazole Long-Acting Injection (Abilify Maintena®)
Guidelines for Prescribing and Administration
(Version 5.3 – August 2017)

1. Key Points.
   1.1 Aripiprazole long acting injection (LAI) is licensed / indicated for the maintenance treatment of adult patients with schizophrenia, whose condition has been stabilised with oral aripiprazole.
   1.2 Aripiprazole LAI is not indicated for treatment-resistant schizophrenia, unlicensed indications or patients intolerant to oral aripiprazole.
   1.3 Aripiprazole LAI 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.
   1.4 Aripiprazole LAI is intended for once-monthly injection (ie. once per calendar month, rather than 4-weekly), by intramuscular route into the gluteal or deltoid muscle and the injection site should be rotated between the two body sides.
   1.5 The recommended starting and maintenance dose of aripiprazole LAI is 400mg once per calendar month if there are no tolerability, metabolism or interaction issues.
   1.6 Aripiprazole LAI does not require any dose titration. However, patients should be treated with 10mg to 20mg of oral aripiprazole for 14 consecutive days from the date of the first injection in order to maintain therapeutic plasma levels during the initiation period.
   1.7 Aripiprazole LAI is supplied in single dose packs, either of pre-filled syringes® or containing a vial of powder, together with a vial of solvent and product specific syringes. These will be supplied to inpatient units by Western Sussex Hospitals Trust’s pharmacy departments. Supply to community teams will be via FP10 prescriptions dispensed by a nominated community pharmacy in each locality, which the patient needs to consent to using. See Protocol for Direct Delivery of Aripiprazole Injection at the link: http://www.sussexpartnership.nhs.uk/node/1457/attachment # (Pre-filled syringes need to be specifically requested / prescribed in the community).
   1.8 Aripiprazole LAI is expensive when compared to conventional antipsychotic depots but is less expensive than some doses of paliperidone LAI. At 400mg per month, it costs approximately £2,640 per patient year. (See section 6 for comparative prices).

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(Text Relay calls welcome).
2. Prescribing Treatment

2.1 Patients should have a history of response and tolerability to oral aripiprazole. The Trust recommends that patients be stabilised on oral aripiprazole for at least 14 days before initiating aripiprazole LAI, if they do not have a past recent history of response and tolerability to the drug. (See 1.1 above).

2.2 Recommended Dose Schemes:

2.2.1 Switching from oral aripiprazole
This should normally only occur in response to adherence issues in patients established on oral aripiprazole. The starting dose of aripiprazole LAI is 400mg per month regardless of the dose of oral aripiprazole being taken and the oral dose must be continued for 14 days from the date of the first injection. Consideration can be given to subsequently reducing the dose of aripiprazole LAI to 300mg per month in those patients previously stabilised on low oral doses.

2.2.2 Switching from other antipsychotics to aripiprazole LAI should normally only occur in response to inefficacy, intolerability or adherence issues. Switching well-stabilised patients should not generally occur as this will always carry a risk of destabilisation.

2.2.3 Switching form oral antipsychotics
Under the terms of the product licence, patient tolerability to (oral) aripiprazole must be established before being prescribed aripiprazole LAI, the (Trust) recommendation being that this be for at least 14 days. In addition, oral aripiprazole must be continued for 14 days from the date of the first injection in order to establish / maintain therapeutic plasma levels during initiation.

2.2.4 Switching from risperidone LAI or from paliperidone LAI
There is currently no manufacturer’s guidance on this. Prescribers should therefore not attempt a direct switch from either of these LAIs to aripiprazole LAI. Instead patients should first be changed to oral aripiprazole, (preferably for at least 14 days), stabilised and then, if there is a suitable response, changed to aripiprazole LAI.

2.2.5 Switching from traditional depot injections
There is currently no manufacturer’s guidance on this. Prescribers should therefore not attempt a direct switch from a traditional depot injection to aripiprazole LAI. Instead patients should first be changed to oral aripiprazole (preferably for at least 14 days), stabilised and then, if there is a suitable response, changed to aripiprazole LAI.

2.3 The recommended initiation and maintenance dose is 400mg per month. However, a maintenance dose of 300mg per month is also considered therapeutic and may be more suitable for patients who have some degree of intolerance to the larger dose or have responded well to low doses of oral aripiprazole. However, all patients should be initiated at 400mg per month.

2.4 The maximum licensed maintenance dose is 400mg per month and this should not be exceeded. Doses should be scheduled at once per calendar month but on no occasion should two doses be given with less than 26 days between them. It is recommended that patients receive the injection on a set day of the month, e.g. the second Monday of every month. This will mean that occasionally there is a five week gap between injections but will ensure that 12 injections are administered annually.

3. Other Dosing Recommendations / Considerations

3.1 The elderly: The product is not recommended in patients over 65 years of age as efficacy and safety has not been established. In addition, the product is not indicated for dementia-related psychosis. The product should not be initiated in patients aged over 65
years and use in patients becoming 65 years of age during the course of their treatment must be kept under regular review.

3.2 **Children & Adolescents:** The product is **not licensed** for use in patients less than 18 years of age as efficacy and safety has not been established.

3.3 **Renal impairment:** No dosage adjustment is needed in patients with renal impairment.

3.4 **Hepatic impairment:** No dosage adjustment is needed patients with mild or moderate hepatic impairment. Use in severe impairment should be avoided.

3.5 **Known CYP2D6 poor metabolisers:** The starting and maintenance dose should be reduced to 300mg in these patients.

3.6 **Concomitant treatment with a CYP3A4 inducer:** Carbamazepine, omeprazole, phenytoin, rifampicin, topiramate and St John’s Wort are potent inducers of CYP3A4 enzymes, (this list of drugs is not exhaustive). Aripiprazole LAI should not be prescribed in patients taking these drugs. Similarly, these drugs should not be prescribed for patients already established on aripiprazole LAI unless the aripiprazole LAI is stopped.

**Concomitant treatment with a potent CYP3A4 inhibitor:** Amiodarone (see below), erythromycin, fluconazole, itraconazole, ketoconazole, protease-inhibitors and trazodone are potent inhibitors of CYP3A4 enzymes, (this list of drugs is not exhaustive). The monthly dose of aripiprazole LAI should be reduced by 100mg if these drugs are co-prescribed. (See 4.8).

3.7 **Concomitant treatment with a potent CYP2D6 inhibitor:** Amiodarone (see below), fluoxetine, paroxetine and quinidine are potent inhibitors of CYP2D6 enzymes, (this list of drugs is not exhaustive). The monthly dose of aripiprazole LAI should be reduced by 100mg if these drugs are co-prescribed. (See 4.8)

3.9 **Concomitant treatment with a potent CYP3A4 inhibitor and a potent CYP2D6 inhibitor** (including amiodarone): 400mg doses of aripiprazole LAI should be reduced to 200mg, and 300mg doses reduced to 160mg. (See 4.8).

4. **Administration**

4.1 Administration of aripiprazole LAI must only be by slow intramuscular injection into the deltoid or gluteal muscle. (Note: ventrogluteal is preferred to the dorsogluteal and should be used if the administering nurse is trained and competent to do so). Package inserts provide guidance on recommended needle sizes / gauges for both obese and non-obese patients.

4.2 There is only one injection size available in the UK, 400mg/2ml. To administer smaller doses the injection must be reconstituted (non-prefilled syringe) to produce a 400mg injection and the excess discarded. (See 4.8).

4.3 The injections require reconstitution before use and once prepared should be administered immediately. Where immediate administration does not occur, the prepared injection may be stored in the vial, below 25°C, for up to two hours (prefilled syringe), or for up to four hours (non-prefilled syringe), after which if not used it must be safely discarded.

4.4 The starting and maintenance dose is usually 400mg per calendar month. No dose titration is required, but 10mg to 20mg of oral aripiprazole should be continued for 14 consecutive days from the day of the first injection.

4.5 The Trust recommends that where possible, patients be stabilised on oral aripiprazole for at least 14 days before initiating aripiprazole LAI, if they do not have a past recent history of response and tolerability to the drug.
4.6 Doses exceeding 400mg and administration of doses more frequently than once per calendar month are not licensed and should not be used.

4.7 Following administration of aripiprazole LAI there is no requirement for any enhanced level of patient monitoring. Patients should be monitored for post-injection events in the same way as for other long-acting antipsychotic injections.

4.8 Reconstituted volumes to inject:

<table>
<thead>
<tr>
<th>Dose</th>
<th>Volume</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>400mg</td>
<td>2.0ml</td>
<td>Prefilled or non-prefilled syringe</td>
</tr>
<tr>
<td>300mg</td>
<td>1.5ml</td>
<td>Non-prefilled syringe</td>
</tr>
<tr>
<td>200mg</td>
<td>1.0ml</td>
<td>Non-prefilled syringe</td>
</tr>
<tr>
<td>160mg</td>
<td>0.8ml</td>
<td>Non-prefilled syringe</td>
</tr>
</tbody>
</table>

5. Storage

Packs of aripiprazole LAI should be stored in a locked medicines cabinet, not in cold storage.

6. Cost Comparison of Long-Acting Antipsychotic Injections

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose</th>
<th>Cost per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole LAI (Abilify Maintena®)</td>
<td>400mg monthly (x12)</td>
<td>£2,645</td>
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<tr>
<td></td>
<td>300mg monthly (x12)</td>
<td>£2,645</td>
</tr>
<tr>
<td>Paliperidone LAI (Xeplion®)</td>
<td>50mg monthly (x12)</td>
<td>£2,207</td>
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<tr>
<td></td>
<td>75mg monthly (x12)</td>
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<td></td>
<td>100mg monthly (x12)</td>
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<tr>
<td></td>
<td>150mg monthly (x12)</td>
<td>£4,716</td>
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<tr>
<td>Risperidone LAI (Consta®)</td>
<td>25mg 2-weekly (x26)</td>
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<td></td>
<td>37.5mg 2-weekly (x26)</td>
<td>£2,894</td>
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<tr>
<td></td>
<td>50mg 2-weekly (x26)</td>
<td>£3,712</td>
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<tr>
<td>Flupentixol depot injection</td>
<td>200mg 2-weekly (x26)</td>
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<td>Fluphenazine depot injection</td>
<td>100mg 2-weekly (x26)</td>
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<tr>
<td>Haloperidol depot injection</td>
<td>200mg 4-weekly (x13)</td>
<td>£130</td>
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<td>Zuclopenthixol depot injection</td>
<td>500mg 2-weekly (x26)</td>
<td>£193</td>
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</tbody>
</table>

7. References


Guidelines prepared by:

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