

## GUIDELINES FOR THE USE OF ARIPIPRAZOLE LONG-ACTING INJECTION (ABILIFY MAINTENA)

### Summary

Aripiprazole long-acting injection (LAI) is licensed for the maintenance treatment of adult patients with schizophrenia whose condition has been stabilised with oral aripiprazole.

It is **not indicated** for treatment-resistant schizophrenia nor for patients intolerant of oral aripiprazole.

KMPT has approved the use of aripiprazole LAI for the following unlicensed indications:

- Bipolar prophylaxis where oral aripiprazole has proven efficacy for the patient but long-term oral medication is not appropriate
- Schizoaffective disorder whose condition has been stabilised with oral aripiprazole

It may only be initiated by Consultant Psychiatrists following submission of the attached Named-Patient Request Form at the end of this document.

Aripiprazole LAI should be administered once monthly (**not 4 weekly**) by the intramuscular route into the gluteal or deltoid muscle. It should not be administered intravenously or subcutaneously.

The recommended dose is 400mg once per calendar month if there are no tolerability, metabolism or interaction issues.

Aripiprazole LAI does not require dose titration. The starting dose can be administered by following one of two regimens:

- One injection start: On the day of initiation, administer one injection of 400 mg Abilify Maintena and continue treatment with 10 mg to 20 mg oral aripiprazole per day for 14 consecutive days to maintain therapeutic aripiprazole concentrations during initiation of therapy.
- Two injection start: On the day of initiation, administer two separate injections of 400 mg Abilify Maintena at separate injection sites (see administration), along with one 20 mg dose of oral aripiprazole.

Aripiprazole LAI is supplied in single dose packs containing a vial of powder, together with a vial of solvent and product specific syringes. These will be available from the Trust's supplier (currently Lloyds Pharmacy), supplied to named individuals, following approval by the pharmacy team or the relevant Head of Psychiatry if it has been prescribed for an unlicensed indication, other than those defined above, on receipt of a valid prescription.

Aripiprazole LAI is expensive compared with typical depot antipsychotics, although less expensive than higher doses of risperidone consta or paliperidone palmitate. A dose of 400mg per month costs approximately £2640 per patient year.

### 1. Prescribing

- 1.1 Patients should have a history of response and tolerability to oral aripiprazole. Patients should be stabilised on oral aripiprazole for at least 14 days before initiating

aripiprazole LAI, if they do not have a recent history of tolerability and response to the drug.

1.2 In KMPT aripiprazole LAI is approved for the following indications only:

- Maintenance treatment of adult patients with schizophrenia (licensed use)
- Augmentation for treatment resistant depression where oral aripiprazole has proven efficacy for the patient but long-term oral medication is not appropriate (unlicensed use)
- Obsessive compulsive disorder where oral aripiprazole has proven efficacy for the patient but long-term oral medication is not appropriate (unlicensed use)
- Bipolar prophylaxis where oral aripiprazole has proven efficacy for the patient but long-term oral medication is not appropriate (unlicensed use)

The Trust's policy on prescribing unlicensed medication should be followed for all unlicensed use.

If it is being prescribed for an unlicensed indication, other than those defined above, the request must be approved by the relevant Head of Psychiatry.

1.3 **Recommended dosage regimen:**

1.3.1 **Switching from oral aripiprazole**

This should only occur in response to adherence issues in patients established on oral aripiprazole. The starting dose can be administered by following one of two regimens:

- **One injection start:** On the day of initiation, administer one injection of 400 mg Abilify Maintena and continue treatment with 10 mg to 20 mg oral aripiprazole per day for 14 consecutive days to maintain therapeutic aripiprazole concentrations during initiation of therapy.
- **Two injection start:** On the day of initiation, administer two separate injections of 400 mg Abilify Maintena at separate injection sites (see administration), along with one 20 mg dose of oral aripiprazole.

Consideration can be given to subsequently reducing the dose to 300mg per month in those patients previously stabilised on lower oral doses.

1.3.2 **Switching from other oral antipsychotics**

This should normally only occur in response to lack of efficacy, intolerability or adherence issues. Switching well-stabilised patients should not normally occur as this will carry the risk of relapse. Patients should be established on oral aripiprazole for at least 14 days before being switched to aripiprazole LAI. The one or two injection start regimen can be used.

1.3.3 **Switching from risperidone consta or paliperidone LAI**

There is no manufacturer's guidance on this. Prescribers should therefore not attempt a direct switch from either of these LAI's 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 as above.

#### 1.3.4 **Switching from typical depot antipsychotics**

There is no manufacturer's guidance on this. Prescribers should therefore not attempt a direct switch from a typical depot to aripiprazole. Instead patients should first be switched to oral aripiprazole for at least 14 days, stabilised, and then if there is a suitable response, changed to aripiprazole LAI as above.

1.4 The recommended initiation and maintenance dose is 400mg per calendar month. However a maintenance dose of 300mg per calendar month is also considered therapeutic and may be more suitable for patients who cannot tolerate higher doses or who have responded well to lower doses of oral aripiprazole.

1.5 The maximum licensed maintenance dose is 400mg per calendar month and this should not be exceeded. Doses should be scheduled once per calendar month but on no occasion should two doses be given less than 26 days apart. It is recommended that the injection be given on a set day each month so that 12 injections are given in annually. E.g. 2nd Wednesday of each month.

## 2. **Other dosing recommendations**

2.1 Aripiprazole Lai is not licensed in patients over 65 years as efficacy and safety has not been established. In addition, the drug is not indicated for dementia-related psychosis. The product should not be initiated in patients over 65 years, and use in patients who attain the age of 65 during the course of treatment must be kept under regular review.

2.2 Aripiprazole is not licensed for use in patients under 18 years as efficacy and safety has not been established.

2.3 No dosage adjustment is required in renal impairment

2.4 No dosage adjustment is required in patients with mild to moderate hepatic impairment. Use in severe hepatic impairment should be avoided.

2.5 Known CYP2D6 poor metabolisers

### **In patients who are known to be CYP2D6 poor metabolisers:**

- One injection start: The starting dose should be 300 mg Abilify Maintena and continue treatment with prescribed dose of oral aripiprazole per day for 14 consecutive days.
- Two injection start: The starting dose should be 2 separate injections of 300 mg Abilify Maintena (see administration) along with one single dose of the previous prescribed dose of oral aripiprazole.

### **In patients who are known to be CYP2D6 poor metabolisers and concomitantly use a strong CYP3A4 inhibitor:**

- The one injection start: The starting dose should be reduced to 200 mg and continue treatment with the prescribed dose of oral aripiprazole per day for 14 consecutive days.
  - Two injection start is not to be used in patients who are known to be CYP2D6 poor metabolisers and concomitantly use a strong CYP3A4 inhibitor.
- After the injection start, see table below for the recommended maintenance dose of Abilify Maintena. Abilify Maintena should be administered once monthly as a single injection (no sooner than 26 days after the previous injection).

**2.6 Dose adjustments of aripiprazole LAI in patients who are taking concomitant strong CYP2D6 inhibitors, strong CYP3A4 inhibitors, and/or CYP3A4 inducers for more than 14 days**

<b>Patient taking 400mg aripiprazole LAI</b>	<b>Adjusted dose</b>
Strong CYP2D6 or strong CYP3A4 inhibitors	300mg
Strong CYP2D6 and strong CYP3A4 inhibitors	200mg
CYP3A4 inducers	Avoid use
<b>Patients taking 300mg aripiprazole LAI</b>	
Strong CYP2D6 or strong CYP3A4 inhibitors	200mg
Strong CYP2D6 and strong CYP3A4 inhibitors	160mg
CYP3A4 inducers	Avoid use

**3. Administration**

- 3.1 Administration of aripiprazole LAI must be by slow intramuscular injection into the deltoid or gluteal muscle. (Note the ventrogluteal site is preferred to the dorsogluteal and should be used if the nurse administering is trained and competent to do so). For most patients a 38mm, 21G needle should be used. For obese (BMI>28) patients, a 50mm 21G needle should be used.
- 3.2 If initiating with the two injection start, inject into two different sites in two different muscles. DO NOT inject both injections concomitantly into the same deltoid or gluteal muscle. For known CYP2D6 poor metabolisers administer in either two separate deltoid muscles or one deltoid and one gluteal muscle. DO NOT inject into two gluteal muscles.
- 3.3 There is only one injection size available in UK – 400mg/2ml. To administer smaller doses the injection must be reconstituted to produce a 400mg/2ml injection and the excess discarded.
- 3.4 Aripiprazole LAI requires 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 4 hours, after which it should be safely discarded.
- 3.5 The starting dose can be administered by following one of two regimens:

- One injection start: On the day of initiation, administer one injection of 400 mg Abilify Maintena and continue treatment with 10 mg to 20 mg oral aripiprazole per day for 14 consecutive days to maintain therapeutic aripiprazole concentrations during initiation of therapy.

- Two injection start: On the day of initiation, administer two separate injections of 400 mg Abilify Maintena at separate injection sites along with one 20 mg dose of oral aripiprazole.

3.6 The maintenance dose is usually 400mg per calendar month.

3.7 Consideration can be given to subsequently reducing the dose to 300mg per month in those patients previously stabilised on lower oral doses.

3.8 Patients should be stabilised on oral aripiprazole before being started on aripiprazole LAI for at least 14 days before initiating aripiprazole LAI, if they do not have a recent history of response and tolerability to the drug.

3.9 Doses exceeding 400mg and administration of doses more frequently than once per calendar month (no sooner than 26 days after the last injection) are not licensed and should not be used.

3.10 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 any other long-acting antipsychotic injection.

3.11 **Reconstituted volumes to inject**

<b>400mg vial</b>	
Dose	Volume
400mg	2ml
300mg	1.5ml
200mg	1.0ml
160mg	0.8ml

3.12 Missed doses

<b>If 2<sup>nd</sup> or 3<sup>rd</sup> dose is missed and time since last injection is</b>	<b>Action</b>
>4 weeks and <5 weeks	The injection should be administered as soon as possible and then resume monthly injection schedule
>5 weeks	Concomitant oral aripiprazole should be restarted for 14 days with next administered injection or two separate injections given at one time, along with a single dose of 20 mg oral aripiprazole. Monthly injection schedule should then resume.
<b>If 4<sup>th</sup> or subsequent doses are missed (i.e. After attainment of steady state) and time since last injection is:</b>	<b>Action</b>

>4 weeks and <6 weeks	The injection should be administered as soon as possible and then resume monthly injection
>6 weeks	Concomitant oral aripiprazole should be restarted for 14 days with next administered injection or two separate injections given at one time, along with a single dose of 20 mg oral aripiprazole. Monthly injection schedule should then resume.

#### 4. Storage

Packs of aripiprazole LAI should be stored in a locked drug cupboard. There is no requirement to store in a fridge

#### 5. Cost comparison of antipsychotic long-acting injections

Drug	Dose	Cost per year (£)
Aripiprazole LAI	400mg monthly	2640
	300mg monthly	2640
Paliperidone palmitate LAI	50mg monthly	2207
	75mg monthly	2939
	100mg monthly	3769
	150mg monthly	4711
Risperidone consta	25mg two weekly	2072
	37.5mg two weekly	2894
	50mg two weekly	3712
Flupentixol decanoate	200mg two weekly	468
Fluphenazine decanoate	100mg two weekly	234
Haloperidol decanoate	200mg four weekly	130
Pipotiazine palmitate	200mg four weekly	624
Zuclopenthixol decanoate	500mg two weekly	182

These prices are a guideline only. The doses are not meant to be comparable with each other.

**ARIPIPRAZOLE LONG-ACTING INJECTION NAMED PATIENT REQUEST FORM**  
**This form must be completed for each patient initiated on aripiprazole LAI**

Patient Name			
Date of Birth			
Previous Psychotropic Medication including Dose and Route			
Name of Ward/Team			
Name of Initiating Consultant		Consultant Signature	
Date of Request			
Name of Care Coordinator			
Telephone Number for Care Coordinator			
Indication for use (Delete to leave the actual indication only)	<ul style="list-style-type: none"> <li>Maintenance treatment of adult patients with schizophrenia (licensed use)</li> <li>Bipolar prophylaxis where oral aripiprazole has proven efficacy for the patient but long-term oral medication is not appropriate (unlicensed use)</li> <li>Schizoaffective disorder whose condition has been stabilised with oral aripiprazole (unlicensed use)</li> <li>Other (Use must be approved by the Head of Psychiatry)</li> </ul> Specify indication		

- I confirm that arrangements are in place for the administration of aripiprazole LAI to take place on a **monthly** basis in accordance with the guidelines above
- I confirm that the patient will be closely monitored for efficacy and tolerability, using the Glasgow Antipsychotic Rating Scale (GASS) and that a full assessment will be carried out at 3 months, 6 months and regularly thereafter, which will be documented in the patient record
- I confirm that the patient is non-compliant with oral medication

**Please scan and email completed form to: [kmpt.lai-authorisation@nhs.net](mailto:kmpt.lai-authorisation@nhs.net)**

**LAI Approval**

Pharmacist 1	Signature	Date
Pharmacist 2	Signature	Date
Head of Psychiatry (other unlicensed use only)	Signature	Date

**If the prescribing of Aripiprazole LAI is being continued from another Trust please email the clinical lead pharmacist in your locality for approval and this form will not need to be completed.**