Tees, Esk and Wear Valleys NHS
NHS Foundation Trust

Shared care guidelines

Drug	**ARIPIPRAZOLE** long-acting injection (Abilify Maintena®)
Specialty	ALL SPECIALTIES (excluding Children & Young People's Services)
Indication	SCHIZOPHRENIA
Overview	Aripiprazole is a dopamine D_2 partial agonist with weak 5-HT_{1a} partial agonism and 5-HT_{2A} receptor antagonism. Abilify Maintena® is indicated for maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole. It should be initiated by a specialist with expertise in schizophrenia as part of a comprehensive treatment plan but prescribing, administration & monitoring responsibility can transfer to GPs under these shared care guidelines.

Specialist responsibilities

Pre-treatment: *(see SPC) for full details of contra-indications & cautions)*

Assess suitability for treatment with Abilify Maintena® by reviewing the patient's medical history, completing a physical examination and completing the baseline monitoring as detailed in appendix 1. It should be noted that the safety and efficacy of Abilify Maintena in the treatment of schizophrenia in patients 65 years or older has not been established.

Initial prescription - dosage and administration: *(see BNF, SPC) and North of England Guidance for prescribing LAI for full details)*

For patients who have never taken aripiprazole, tolerability with oral aripiprazole must be established prior to initiating treatment with Abilify Maintena.

The recommended starting and maintenance dose of Abilify Maintena is 400 mg.

Titration of the dose is not required. It should be administered **once every calendar month** as a single injection (no sooner than 26 days after the previous injection).

After the first injection, treatment with 10 mg to 20 mg oral aripiprazole should be continued for 14 consecutive days to maintain therapeutic aripiprazole concentrations during initiation of therapy (then stopped)

If there are adverse reactions with the 400 mg dose, reduction of the dose to 300 mg once per calendar month should be considered.

Dose adjustments may be necessary due to interacting drugs (see SPC & appendix 2)

Monitoring – see appendix 1:
The baseline efficacy and tolerability of antipsychotic medication should be established by the use of objective and validated measures.

- **Side effects** – use LUNSERS or GASS to assess tolerability at each review
- **Physical Health monitoring** – for the first 12 months of treatment, then at each review (at least annually); see physical parameters in appendix 1
- **Clinical response** – use an appropriate measures, e.g. PANSS (positive and negative syndrome scale), CGI (clinical global impressions) and GAF (global assessment of functioning), to assess response prior to transfer and at each review.

Where tolerability or clinical response is not demonstrated, the LAI should not continue to be prescribed. The on-going clinical need and patient preference for a LAI should be reviewed at least annually.

Transfer of prescribing / communication
Prescribing, administration and monitoring responsibility may be transferred to the patient's GP after 3 months or once the treatment has been stabilised, whichever is the longer. The request must be made using the attached form with a covering clinic letter and a copy of this guideline (with contact details added) – the following details should be clearly communicated at transfer, and after each subsequent review:

Specialist responsibilities *(continued)*

- **Diagnosis**
- **Dose** of aripiprazole LAI
- **Date** and **site** of last administration, and **date when next dose is due**
- Completed and required **monitoring**
- **Discontinued medication** for same diagnosis
- **Date** of next specialist review

The transfer request should be sent one month in advance of the patient needing their next dose. Acceptance should not be assumed until the GP responds positively using the attached form (faxed or scanned & e-mailed to the specialist team)

GP responsibilities

Transfer of prescribing / communication:
Notify specialist immediately (within 2 weeks) if transfer of prescribing and monitoring responsibility is not accepted so that alternative arrangements can be put in place. Contact specialist if communication of prescribing, administration & monitoring requirements is not clear.

Maintenance (repeat) prescription:
Stop any repeat prescriptions for oral aripiprazole

Prescribe Abilify Maintena® (Aripiprazole) in accordance with specialist advice received on transfer and following reviews:

The recommended maintenance dose of Abilify Maintena® is 400 mg.

It should be administered each calendar month as a single injection (no sooner than 26 days after the previous injection).

If there are adverse reactions with the 400 mg dose, reduction of the dose to 300 mg will be considered and advised by the specialist team.

Dose adjustments may be necessary due to interacting drugs (see *SPC* & appendix 2)

Administration:
Abilify Maintena® can be administered into either the deltoid or gluteal muscle. See *SPC* and appendix 2 for detailed information regarding administration and action to take in response to missed or delayed doses.

Monitoring – see appendix 1:
Efficacy and tolerability measures should be completed by the specialist team prior to transfer and at each review. Physical health monitoring should be completed by the specialist team for the first 12 months, then at each review (at least annually); any additional physical health monitoring by GP should be communicated to the specialist

Referral:
Refer back to the specialist should any of the following occur:

- Significant adverse reaction or intolerable side effects
- Lack of efficacy/ patient's condition deteriorates
- Development of co-morbidities/necessity to prescribe interacting drugs
- Pregnancy
- Failure to attend for administration of aripiprazole within permitted timeframe (26-35 days after last dose)

Adverse events

See BNF and SPC for full details of known adverse effects
Common side effects include anxiety, hypersalivation and malaise. Side effects commonly and uncommonly reported at the start of treatment usually wear off within the first few weeks.
Report any suspected adverse events to MHRA via the Yellow Card scheme

Specialist contact details
(to be added by specialist prescriber when transferring prescribing)

Name:

Base:

Telephone no:

E-mail address:

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GP details:

Patient details (name/address/DOB/NHS number):

Diagnosis:

Medication details:
The patient is stabilised on: (list dose, frequency and brand. Specify clinical indications if first line option not prescribed or non-standard formulation prescribed):

Discontinued medication (list details of any drugs discontinued when this AMBER treatment initiated):

Last Administration (details of date and site of administration and date next dose due):

Monitoring results:

Secondary care review frequency:

Actions requested of GP:
Please continue to issue prescriptions and administer monthly Abilify Maintena® until advised
The treatment has been explained to the patient and they understand they should contact you for future prescriptions.
You will be informed of any changes to treatment, if you are not required to issue prescriptions or if treatment is to be discontinued.
Please contact the prescriber on the number below if there is any change in the patient's condition, if the patient fails to regularly collect prescriptions, if non-compliance with treatment is suspected or you require advice.

Secondary care contacts:	Contact details (address/telephone no):
Care coordinator (name):	
Consultant (name):	
Prescriber (name):	
Signature & date:	

Fax back acceptance of prescribing responsibility by GP (or scan & e-mail)

Patient's name:	**NHS Number:**
Address:	
Medication:	
I confirm receipt of prescribing transfer information for the above patient and accept prescribing responsibility	
GP's name: *(Please print name in BLOCK CAPITALS)*	
Signature/ Practice Stamp:	
Date:	

Please fax back to:
Fax number:
or return as soon as possible to:

Appendix 1 Monitoring requirements for antipsychotic long-acting injections (from *North of England Guidance for prescribing LAI)*

Test/ Measurement	Why is it important?	Baseline	3 months after initiation	Annually
Weight (Waist measurement and BMI where possible)	Antipsychotic drugs can cause weight gain and this can contribute to an ↑ risk of cardiovascular and metabolic problems	√ Then weekly for the first 6 weeks	√	√
Urea and electrolytes, (including creatinine or estimated GFR)	Pateints with renal impairment may have reduced capacity to excrete drugs and dose reductions may be required. Hypolkaleamia is linked to QTc lengthening and other ECG abnormaliites	√		√
Lipids (Total cholesterol, HDL cholesterol, Total/ HDH-cholesterol ratio, Triglycerides - fasting sample if possible)	Some antipsychotics can cause small adverse changes in lipid profiles. Triglyceride levels can rise during periods of weight gain.	√	√	√
Liver function (Bilirubin, Alk Phos, ALT, Albumin, Total protein, Gamma-GT)	Patients with hepatic impairment may have reduced capacity to metabolise drugs and dose reductions may be required. Drug induced liver damage can be due to direct dose related hepatotoxicity or hypersensitivity reactions. Risk factors for drug induced hepatotoxicity include - ↑age, female gender, alcohol, prescribed enzyme inducing drugs, obesity	√		√
Full Blood Count (Hb, WBC, Platelets)	BNF advises caution when using antipsychotics in patients with blood dyscrasias Antipsychotics can cause blood dyscrasias including agranulocytosis and leucopenia	√		√
Blood Glucose FBG/HbA_{1c}	Antipsychotics can increase the risk of developing diabetes.	√	√	√
Blood Pressure (sitting / lying and standing) and pulse	Hypotension is a side effect of many antipscyhotics and it is important to monitor this during peiods of initation and stabilisation. Longer term it is important to montior and manage factors that inluence a patients CV risk	√	Frequently during dose titration (determined by clinical situation) and also after 12 weeks	√
Prolactin	Antipsychotics can increase prolactin levels. This can inhibit sex hormones – oestrogen and testosterone and may ↑ risk of osteoporosis	√	√	√

Test/ Measurement	Why is it important?	Baseline	Annually
ECG (QTc Interval)	Many antipsychotics are associated with ECG changes and some are linked to prolongation of the QT interval. All new inpatients should have an ECG on admission. For long stay patients and those in the community. When clinically indicated ECGs should be performed at baseline and annually. Factors that may determine if ECG monitoring is clinically indicated include: • If there is a personal history of cardiovascular disease (e.g. - known ischaemic / structural heart disease QT prolongation), • If physical examination identifies cardiovascular risk factors • If patients on antipsychotics that require ECG monitoring e.g. - haloperidol or pimozide (check summary of product characteristics for more information) • If a patient is on high dose antipsychotic therapy (HDAT) • If patient is on other drugs known to cause ECG abnormalities (e.g. Tricycylic antidepressants, erythromycin, anti-arrhythmics – see BNF for further information) • If the patient has Factors which may predispose to arrhythmias including: ○ Electrolyte abnormalities – hypokalaemia, hypocalcaemia, hypomagnesaemia ○ Systemic disease – liver disease, renal disease, hypothyroidism		
Pregnancy test		If there is any uncertainty about the possibility of pregnancy, a urine pregnancy test should be carried out	
Smoking status	Linked to CV risk	√	√
Drug screening		If indicated by history or clinical picture	
Review of the side effects of drug treatment, efficacy and adherence	Before treatment the side effects the patient is least willing to tolerate should be assessed. On review the treatment efficacy patient adherence and side effects experienced should be assessed. Including : • Extrapyramidal symptoms, akathisia, dystonia and tardive dyskinesia • Common side effects e.g. – sedation • Less common but serious adverse effects e.g. palpitations. An appropriate rating scale may be useful (e.g. GASS)	√	√
References	Maudsley Prescribing Guidelines 11th edition (2013) SPC of individual medicines, available at www.medicines.org.uk BNF 68, September 2014 Royal College of Psychiatrists Consensus Statement on high dose antipsychotic prescribing May 2006 Lester UK Adaptation Positive Cardiometabolic Health Resource June 2014 - www.rcpsych.ac.uk/quality/NAS/resources		

Appendix 2 – Administration Information

Administration

Abilify Maintena® (See SPC for further details and package insert for reconstitution details)

- Available as 300mg or 400mg of powder and solvent for prolonged release suspension for injection. The suspension should be injected immediately after reconstitution but can be stored below 25 °C for up to 4 hours in the vial.
- Available in pre-filled syringes of 300mg or 400mg of powder and solvent for prolonged release suspension for injection which must be kept in the outer container to protect from light. The suspension should be injected immediately after reconstitution but can be stored below 25 °C for up to 2 hours in the syringe.
- Do not freeze
- The injection should be administered slowly as a single injection into either the gluteal or the deltoid muscle. The injection sites should be rotated between the two gluteal or deltoid muscles. Care should be taken to avoid inadvertent injection into a blood vessel.

Deltoid muscle administration, recommended needle size is:
  - 25 mm (1 inch), 23 gauge hypodermic safety needle
  - For obese patients, a 38 mm (1.5 inch), 22 gauge hypodermic safety needle should be used.
- Deltoid injections should be alternated between the two deltoid muscles.

Gluteal muscle administration, recommended needle is:
  - 38 mm (1.5 inch), 22 gauge hypodermic safety needle;
  - For obese patients (Body mass index > 28 kg/m^2), a 51 mm (2 inch), 21 gauge hypodermic safety needle should be used.
- Gluteal injections should be alternated between the two gluteal muscles.

Missed doses

- Initiation will be carried out by the specialist service.
- After initiation, the recommended injection cycle is once per calendar month (no sooner than 26 days after previous injection), it is not necessary to give every 28 days
- If a monthly maintenance dose is missed after the third monthly injection, if less than 6 weeks have elapsed since last injection, the previously stabilised dose should be administered as soon as possible, followed by injections at monthly intervals.
- If more than 6 weeks have elapsed since last injection, concomitant oral aripiprazole should be restarted for 14 days with next administered injection, then resume monthly injection schedule.

Dose adjustment due to interactions

Dosage adjustments should be made in patients taking concomitant strong CYP3A4 inhibitors or strong CYP2D6 inhibitors for more than 14 days. If the CYP3A4 inhibitor or CYP2D6 inhibitor is withdrawn, the dosage may need to be increased to the previous dose. In case of adverse reactions despite dose adjustments of Abilify Maintena, the necessity of concomitant use of CYP2D6 or CYP3A4 inhibitor should be reassessed.

Concomitant use of CYP3A4 inducers with Abilify Maintena should be avoided for more than 14 days because the blood levels of aripiprazole are decreased and may be below the effective levels.

In patients who are known to be CYP2D6 poor metabolisers, the starting and maintenance dose should be 300 mg.

Dose adjustments of Abilify Maintena in patients who are taking concomitant strong CYP2D6 inhibitors, strong CYP3A4 inhibitors, and/or CYP3A4 inducers for more than 14 days

	Adjusted dose
Patients taking 400 mg of Abilify Maintena	
Strong CYP2D6 or strong CYP3A4 inhibitors	300 mg
Strong CYP2D6 and strong CYP3A4 inhibitors	200 mg*
CYP3A4 inducers	Avoid use
Patients taking 300 mg of Abilify Maintena	
Strong CYP2D6 or strong CYP3A4 inhibitors	200 mg*
Strong CYP2D6 and strong CYP3A4 inhibitors	160 mg*
CYP3A4 inducers	Avoid use

* 200 mg and 160 mg can be achieved via adjustment of the injection volume only by using Abilify Maintena powder and solvent for prolonged-release suspension for injection.

Examples:

CYP34A inducers - Carbamazepine, Rifampicin, Rifabutin, Phenytoin, Phenobarbital, Primidone, Efavirenz, Nevirapine and St. John's Wort

CYP34A Inhibitors - Ketoconazole, Itraconazole, HIV protease inhibitors, Diltiazem (weak inhibitor)

CYP2D6 inhibitors - Quinidine, Fluoxetine, Paroxetine, Escitalopram (weak inhibitor)