BNSSG Shared Care Guidance

Amber Three Months

Section 1: Heading

Trust(s)	Avon and Wiltshire Mental Health Partnership NHS Trust
Speciality / Department	Mental Health
Drug	Aripiprazole (oral)
Indication	The treatment of schizophrenia in adults and in adolescents aged 15 years and older. The treatment of moderate to severe manic episodes in Bipolar I Disorder and for the prevention of a new manic episode in adults who experienced predominantly manic episodes and whose manic episodes responded to aripiprazole treatment See NICE TA213 'Aripiprazole for schizophrenia in people aged 15-17 years.' Link, click here.

Section 2: Treatment Schedule

Usual dose and frequency of administration	Usual range is 10mg to 30 mg once daily depending on age and indication. Schizophrenia: Child 15 – 18 years Gradual titration from 2mg to 10mg; increased if needed by 5mg increments to max 30mg daily. Adult over 18 years - 10-15mg once daily; usual maintenance 15mg once daily; max 30mg daily. Mania: Adult over 18 years – 15mg once a day increased if necessary to max 30mg once daily.
Route and formulation	Oral. Available for shared care as: Tablets - 5mg, 10mg, 15mg & 30mg Liquid - 1mg / ml
Duration of treatment	Depends on response & tolerability. Long term (at least 3 years)

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate Pre-treatment by AWP Specialist team: Weight (waist size and BMI if possible), blood pressure, ECG, Creatinine Phosphokinase, prolactin, HbA1c or fasting blood glucose, LFTs, U&Es, FBC and lipid profile (cholesterol and triglycerides), *VTE risk assessment including e.g. reduced mobility. Please also refer to NICE CG92. *MHRA: Antipsychotic use may be associated with an increased risk of VTE. At present there are insufficient data available to determine any difference in risk between atypical and conventional antipsychotics, or between individual drugs. All possible risk factors for VTE should be identified before and during antipsychotic treatment and preventative measures taken.
Subsequent tests - where appropriate There are no mandatory monitoring requirements for aripiprazole but it is recommended monitoring is done nonetheless as prevalence of metabolic disorders is high in this group of patients. Annual review by Primary Care: 1. Weight (waist size and BMI if possible), 2. HbA1c or fasting blood glucose, 3. LFTs, 4. FBC and lipid profile (cholesterol and triglycerides), If possible, assess patient for VTE risk and consider preventative measures.

Section 4: Side Effects

Please list the most common side effects and management. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	Common (1/100 to < 1/10) Akathisia and nausea are the most commonly reported side effects for aripiprazole Psychiatric disorders: Common: restlessness, insomnia, anxiety Nervous system disorders Common: extrapyramidal disorder, akathisia, tremor, dizziness, somnolence, sedation, headache Eye disorders Common: Blurred vision Gastrointestinal disorders Common: Dyspepsia, vomiting, nausea, constipation, salivary hypersecretion General Common: Fatigue Management of other side effects:

	1. Weight gain: > 5% over baseline Antipsychotics are associated with weight gain especially in first 6 to 9 months of treatment (average 2 to 10lb or ~0.9Kg to 4.5Kg). Encourage healthy balanced diet and regular exercise. 2. Signs / symptoms of hyperglycaemia e.g. polydipsia, polyuria, polyphagia and weakness, or worsening of glucose control. Raised blood glucose or HbA1C from upper threshold. May indicate Impaired Fasting Glucose. 3. Raised blood lipids. Consultant AWP for advice. 4. Abnormal ECG / Cardiac disorders (SPC – frequency unknown): QTc prolongation and arrhythmias. Consult AWP Specialist for advice. GPs should also be aware of non-psychotropic drugs which are associated with QT prolongation. Some examples include: Erythromycin, clartithromycin, ampicillin, co-trimoxazole, some quinolones Quinidine, amiodarone, sotalol, Chloroquine, mefloquine, Quinine Methadone, tamoxifen, diphenhydramine. 5. Raised prolactin: In women: Amenorrhoea, menstrual disorders, galactorrhoea and reduced libido. In men: reduced libido, impotence & gynaecomstia: The longer the patient is exposed to hyperprolactinaemia, the greater the risk of reduced bone density and hypogonadism. Treatment with calcium and vitamin D should be considered and started by the GP for these patients. 6. Suspected neuroleptic malignant syndrome (NMS) - Raised creatinine phosphokinase: Development of symptoms such as fever, sweating, rigidity, confusion, fluctuating blood pressure, tachycardia (see special warnings): If Neuroleptic Malignant Syndrome (NMS) is suspected stop aripiprazole and call for ambulance immediately. Inform AWP Specialist.
Referral back to specialist	Persistent side effects unresolved by reducing dose or which are intolerable to the service user or of concern..

Section 5: Drug Interactions

Please list clinically significant drug interactions (eMC link please click here)

Significant Drug Interactions	Due to its α1-adrenergic receptor antagonism, aripiprazole has the potential to enhance the effect of some antihypertensive agents. Enhanced sedation likely when taken with other centrally acting drugs e.g. alcohol. Potent inhibitors of CYP2D6 e.g. fluoxetine, paroxetine (and quinidine) may increase levels of aripiprazole so dose

	reductions of aripiprazole are advised. Potent inhibitors of CYP3A4 e.g. itraconzaole & ketoconazole can also increase aripiprazole levels, requiring dose reduction of aripiprazole Upon discontinuation of the CYP2D6 or 3A4 inhibitor, the dosage of aripiprazole should be increased to the level prior to the initiation of the concomitant therapy. Potent inducers of CYP3A4 e.g. carbamazepine likely to reduce levels of aripiprazole; dose of Aripiprazole should be doubled when taken concomitantly with carbamazepine. Same applies with other potent inducers of CYP3A4 e.g. rifampicin, rifabutin, phenytoin, phenobarbital, primidone, efavirenz, nevirapine and St. John's Wort. Upon discontinuation of potent CYP3A4 inducers, the dosage of aripiprazole should be reduced to the level prior to the initiation of the concomitant therapy. Please also refer to Appendix 1 of the current BNF - 'bulleted points' denote significant interactions
Reminder to ask patient about specific problems	

Section 6: Contra-indications, Cautions and Special Recommendations

Please list

Hypersensitivity to aripiprazole or to any of the excipients.

Special warnings and precautions for use:

1. Suicidal behaviour: The occurrence of suicidal behaviour is inherent in psychotic illnesses and in some cases has been reported early after initiation or switch of antipsychotic therapy. Close supervision of high-risk patients should accompany antipsychotic therapy.
2. Cardiovascular disorders: Aripiprazole should be used with caution in patients with known cardiovascular disease (history of myocardial infarction or ischaemic heart disease, heart failure, or conduction abnormalities), cerebrovascular disease, conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medicinal products) or hypertension, including accelerated or malignant.
3. Tardive dyskinesia: in clinical trials of one year or less duration, there were uncommon reports of treatment emergent dyskinesia during treatment with aripiprazole. If signs and symptoms of tardive dyskinesia appear in a patient on aripiprazole, dose reduction or discontinuation should be considered. These symptoms can temporarily deteriorate or can even arise after discontinuation of treatment
4. Neuroleptic malignant syndrome (NMS): NMS has been associated with antipsychotic treatment. Clinical manifestations include hyperpyrexia, muscle rigidity, altered mental status, evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia) and elevated creatinine phosphokinase. If a patient develops signs and symptoms indicative of NMS, or has unexplained high fever, all antipsychotic medicinal products must be discontinued.
5. Seizure: in clinical trials, uncommon cases of seizure were reported during treatment with aripiprazole. Therefore, aripiprazole should be used with caution in patients who have a history of seizure disorder or have conditions associated with seizures.
6. Hyperglycaemia and diabetes mellitus: Hyperglycaemia has been reported during treatment with aripiprazole. Patients with diabetes mellitus or with risk factors for diabetes mellitus (e.g. obesity or family history of diabetes) should be monitored regularly for signs and symptoms (e.g. polydipsia, polyuria, polyphagia and weakness) for hyperglycaemia or worsening of glucose control.
7. Weight gain: Weight gain has been reported post-marketing among patients prescribed

aripiprazole; usually in those with significant risk factors such as history of diabetes, thyroid disorder or pituitary adenoma. In clinical trials aripiprazole has not been shown to induce clinically relevant weight gain.

8. Venous thromboembolism: Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with aripiprazole and preventive measures undertaken.

Section 7: Advice to the patient

Advice for prescribing clinician to inform patient

1. Agitation, insomnia and restlessness may be present when treatment is started. This usually improves after a few weeks – a benzodiazepine used short term may help with these symptoms.

Section 8: Responsibilities for Secondary Care

Core responsibilities

1. Initiating treatment and prescribing the First Three Months of treatment
2. Undertaking the clinical assessment and monitoring for the First Three Months of treatment.
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of Aripiprazole.
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1 Assess patient, establish diagnosis and develop care plan. Ensure care plan contains correct contact details for care co-ordinator/ key worker and specialist consultant psychiatrist. Forward a copy of the care plan to the GP.

2 To undertake physical health screen and assessment when patient is admitted to mental health services, including screening for possible risk factors for venous thromboembolism (VTE) before and during treatment with aripiprazole and preventive measures undertaken. VTE assessment tool can be found here. Please also see NICE CG 92.

3 The choice and formulation of aripiprazole should be a joint decision between the patient (discuss with carer where patients lack capacity) and the specialist taking into consideration the risks and benefits of the treatment (including the relative potential of individual antipsychotics to cause side-effects such as extrapyramidal side effects (EPS) and metabolic side-effects, including weight gain) including the action to be taken should side effects occur.

4 To provide the patient with information on drug prescribed including a patient information leaflet (PIL). Information on mental health conditions, treatments and medication can be found at: http://www.choiceandmedication.org/awp/

5 Ensure patient is fully informed about their treatment including any plans of pregnancy. Aripiprazole should only be given to pregnant women when, in the judgement of the attending physician the potential benefits outweigh the possible risk.

6 Ensure that arrangements of appropriate blood tests has been made. Blood tests may be taken at the GP surgery providing appropriate communication with the GP and the GP is in agreement with this. Secondary care is responsible for the interpretation and monitoring of these blood test results for the first 3 months of treatment.

7 Review results of any baseline tests and relay any abnormal findings to the GP with appropriate advice.

8 Discuss the proposal of shared care agreement with the patient. If possible obtain consent (verbal is fine) and document in notes. If patient declines SCA, then please document this too.

9 Ask the GP whether s/he is willing to participate in shared care once patient has been stabilised on treatment. This must be done using the shared care agreement signature sheet for aripiprazole.

10 Ensure that the GP has a copy of the shared care agreement and a signed copy of the shared care agreement form.

11 Communicate promptly with the GP when treatment is changed.

12 Inform GP of concurrent therapy (as this may interact with other medication patient gets from GP)

13 Advise the GP on when and how to adjust the dose or stop treatment (assuming no relapse in patients condition) according to clinical parameters, and consult with the specialist.

14 To review patient / provide advice as requested via the GP or Primary Care Liaison Service as necessary

15 To review the patient and treatment at least once a year until the patient is discharged from the mental health service where this is possible

16 Ensure that clear backup arrangements exist for GPs to obtain advice and support.

17 Any verbal communication between primary and secondary care should be confirmed in writing.

Section 9: Responsibilities for Primary Care

Core responsibilities

1. Responsible for taking over prescribing after the First Three Months of treatment
2. Responsible for the clinical assessment and monitoring after the First Three Months of treatment.
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. Reply to the request for shared care within 3 weeks of receipt of request using the shared care agreement signature sheet for aripiprazole.

2. If the GP decides not to prescribe aripiprazole, it should still be added to the patients repeat medication as a “non issued’ item for information and safety purposes. For EMIS systems: The quantity should be set to *0 or 1. On the dose line it should read: ‘Hospital prescribing only. Do not prescribe’.

This process should also be done during the stabilisation period before the GP takes over the prescribing.

3. Adjust the dose / stop drug as advised by the specialist.

4. Inform specialist team of any change in the patient’s medication that may interact with medication patient receives from secondary care.

5. To request specialist review or seek specialist advice when necessary.

6. Once the patient has been discharged from specialist Mental Health services, advice may be sought from the Primary Care Liaison Service on any aspect of the patient’s mental health that is of concern to the GP.

7. Monitor patients overall health and compliance with medication and ask about side effects.

Section 10: Contact Details

Name	Organisation	Telephone Number	E mail address
Dr Specialist Consultant Psychiatrist	AWP Mental Health NHS Trust		
Care co-ordinator	AWP Mental Health NHS Trust		
Bethan Shepherd Formulary Pharmacist	AWP Mental Health NHS Trust		
Primary Care Liaison Service: Bristol Intensive and Primary Care Liaison – interim to Speedwell then to Callington Road	AWP Mental Health NHS Trust	Phone: 0117 9195670 Fax: 0117 9195625	
Primary Care Liaison Service: North Somerset Intensive and Primary Care Liaison – Long Fox Unit	AWP Mental Health NHS Trust	Phone: 01934 836406 Fax: 01934 836405	
Primary Care Liaison Service: South Gloucestershire Intensive and Primary Care Liaison – Bybrook Lodge, Blackberry Hill Hospital	AWP Mental Health NHS Trust	Phone: 01173 787960 Fax: 0117 3787941	

Section 11: Document Details

Date prepared	AWP version approved at AWP MMG on 22nd February 2013 for dissemination to local formulary groups. Approved at JFG December 2013
Prepared by	Bethan Shepherd, Formulary Pharmacist, AWP Mental Health Trust
Date of review	2 years or sooner if guidance changes
Document Identification	Aripiprazole SCA (BNSSG) V2 December 2013

Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

1. This Shared Care Agreement has been developed by the Formulary Pharmacist with feedback from members of the AWP Medicines Management Group – includes consultants, senior nursing staff, pharmacists, clinical risk manager, Head of Medicines Management and occasionally representatives from finance.

Section 13: References

Please list references

1. Summary of product characteristics for aripiprazole www.medicines.org.uk

2. MTRAC VS04/20 / Verdict & Summary plus ESCA (schizophrenia) and ESCA (bipolar) accessed via http://www.keele.ac.uk/pharmacy/mtrac/mtracverdictsheetsescas

3. NICE Clinical Guideline 82 Schizophrenia: Core interventions in the treatment and management of schizophrenia in adults in primary and secondary care guidance.nice.org.uk/cg82

4. D Taylor et al. Maudsley Prescribing Guidelines 11th Edition (latest edition)

5. Leicestershire Medicines Strategy Group Shared Care Agreement for Atypical Antipsychotics January 2008.

6. Shared care Guidance for Aripiprazole for BNSSG Dec 2009 Theresa Turner Clinical Specialist Pharmacist

7. MHRA PUBLIC ASSESSMENT REPORT The risk of venous thromboembolism associated with antipsychotics June 2009