NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Aripiprazole for the treatment and prevention of acute manic and mixed episodes in bipolar disorder in children and adolescents

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of aripiprazole, within its licensed indication, for the treatment and prevention of acute manic and mixed episodes in bipolar disorder in children and adolescents.

Background

Bipolar disorder is a cyclical mood disorder which is characterised by both episodes of depressed mood and episodes of elated mood (mania or hypomania). In its more severe forms, bipolar disorder is associated with significant impairment of personal and social functioning.

Bipolar disorder is currently classified by the Diagnostic and Statistical Manual of Mental Disorders version four (DSM-IV) as a single episode of mania or a single episode of hypomania plus a single major depressive episode. In DSM-IV, a distinction is drawn between bipolar I disorder and bipolar II disorder. In bipolar I disorder, the patient suffers full-blown manic episodes, most commonly interspersed with episodes of major depression. In bipolar II disorder, the patient experiences depressive episodes and less severe manic episodes, classed as hypomanic episodes. The same criteria are used for the diagnosis of bipolar disorder in adolescents except that: mania must be present; euphoria must be present most days, most of the time (for at least 7 days); and irritability should not be used as a core criterion. The range and severity of symptoms may be assessed using rating scales such as the Young Mania Rating Scale, which includes assessment of irritability, disruptive/aggressive behaviour, sleep, elevated mood, speech, increased activity, sexual interest, language/thought disorder, thought content, appearance and insight. Other rating scales include the Clinical Global Impression-Bipolar Scale and the Children Depression Rating Score.

Recent estimates have suggested that bipolar affective disorder has a point prevalence of up to 5% of the general population, suggesting that up to 2.6 million individuals are affected in England and Wales. Bipolar affective disorder can severely limit quality of life and lead to suicide in 10–15% of sufferers.

Recent epidemiological surveys, report a mean age of onset of bipolar disorder of between 17.1 to 29 years, with a peak onset of occurring between

the ages of 15 to 19 years. Approximately 25% of people with bipolar disorder experience their first episode before the age of 18.

The current management for bipolar disorder depends on the phase of the disorder being experienced, preference for future prophylactic treatment and side effect profile. NICE clinical guideline CG38 states that the drug treatment of acute mania for adolescents should be the same as for adults, except treatment should be initiated at lower doses. Treatment options for patients who develop acute mania when not taking an antimanic medication therefore include an antipsychotic (normally olanzapine, quetiapine or risperidone), valproate or lithium. Lithium is the only drug with current UK marketing authorisation for bipolar disorder in patients younger than 18 years. If a patient already taking an antipsychotic experiences a manic episode, and there is a poor response from the antipsychotic, adding lithium or valproate should be considered, although valproate should be avoided in girls and young women of childbearing age.

The technology

Aripiprazole (Abilify, Otsuka Pharmaceuticals and Bristol-Myers Squibb) is a piperazine atypical antipsychotic that acts as a partial agonist of the dopamine D2 and serotonin 5-HT1a receptors, and as an antagonist of the 5-HT2a serotonin receptors of the dopamine serotonin system. Aripiprazole is administered orally.

Aripiprazole does not hold a UK marketing authorisation for the treatment or prevention of bipolar disorder in children and adolescents. It is currently being studied in clinical trials compared with placebo in children and adolescents with Bipolar 1 Disorder with manic or mixed episode with or without psychotic features. Aripiprazole is currently licensed for the treatment of adults with moderate to severe manic episodes in Bipolar I Disorder and for the prevention of a new manic episode in patients who experienced predominantly manic episodes and whose manic episodes responded to aripiprazole treatment. It is also licensed for adults with schizophrenia.

Intervention(s)	Aripiprazole for the treatment of children and adolescents with bipolar I disorder
Population(s)	Children and adolescents with bipolar I disorder
Comparators	• Typical antipsychotics • Atypical antipsychotics (such as olanzapine, quetiapine or risperidone) • Valproate • Lithium • Combination treatment with any of the above

Outcomes	The outcome measures to be considered include: • response rate • range and severity of symptoms of mania and depression • recurrence of manic episodes • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. TA59, April 2003, 'The clinical effectiveness and cost effectiveness of electroconvulsive Therapy (ECT) for depressive illness, schizophrenia, catatonia and mania.' Related Guidelines: Clinical Guideline No. CG38, July 2006, 'The management of bipolar disorder in adults, children and adolescents, in primary and secondary care'. Expected review date: July 2011. Clinical Guideline No. CG28, September 2005, 'Depression in children and young people: identification and management in primary, community and secondary care'. Expected review date: September 2010.

Questions for consultation

Have the most appropriate comparators for the treatment of acute manic and mixed episodes in bipolar disorder in children and adolescents been included in the scope?

Should carbamazepine be included as a comparator?

Which treatments are used in routine practice for the treatment and prevention of acute manic and mixed episodes in bipolar disorder in children and adolescents?

What outcome measures would be appropriate to assess the range and severity of symptoms of mania and depression? Should measures of psychotic symptoms be included as outcomes?

Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp