NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Loxapine inhalation for the treatment of acute agitation with schizophrenia or bipolar disorder

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of loxapine inhalation within its licensed indication for the treatment of acute agitation in people with schizophrenia or bipolar disorder.

Background

Agitation is described as excessive motor activity associated with a feeling of inner tension. Acutely agitated patients often have an underlying major psychiatric disorder. Severe agitation occurs most often in psychotic illnesses, such schizophrenia and the manic phase of bipolar disorder.

Schizophrenia is a major psychiatric disorder, or cluster of disorders, characterised by psychotic symptoms that alter a person's perception, thoughts, affect and behaviour. Over a lifetime, about 1% of the population will develop schizophrenia. The first symptoms tend to start in young adulthood, but can occur at any age. Bipolar disorder is a chronic, cyclical mood disorder which is characterised by episodes of significantly altered mood, which may be manic (elated mood), depressive or mixed (manic and depressive episodes simultaneously). The prevalence of bipolar disorder in the UK was estimated to be 1% of the general population in 2009. Bipolar disorder can occur at any age, although it often develops in people who are aged between 18-24 years. More than 90% of people with either schizophrenia or bipolar disorder will experience agitation in their lifetime, experiencing an average of 11 to 12 episodes of acute agitation each year.

Activity which characterises an episode of agitation is usually non-productive and repetitious. Agitation may escalate over time, and the behaviour of some patients may be perceived as being threatening. People with lesser degrees of agitation can be treated with psychological methods to ease anxiety and tension. When agitation becomes more severe, pharmacological treatment may be required. Such treatment may be adjunctive to that used to treat the underlying psychiatric disorders.

The clinical guidelines on treatment of schizophrenia and bipolar disorder do not make specific recommendations for the treatment of agitation. Current UK clinical practice includes the use of typical antipsychotics (such as haloperidol) and benzodiazepines (such as lorazepam), given either alone or

in combination, for the treatment of acute agitation. Atypical antipsychotics (such as risperidone and olanzapine) are also used.

The technology

Loxapine inhalation (Staccato loxapine, Alexza Pharmaceuticals) is a breath-actuated, hand-held disposable inhaler which delivers a single dose of loxapine. Loxapine is a dopamine-2 and serotonin-2a receptor antagonist which acts as a tranquiliser.

Loxapine inhalation does not have a UK marketing authorisation for the treatment of acute agitation. Loxapine inhalation is intended to rapidly treat acute agitation as a substitute for currently available parenteral or oral therapies. It has been studied in clinical trials compared with placebo in adults with acute agitation associated with schizophrenia or bipolar I disorder.

Intervention(s)	Loxapine inhalation
Population(s)	Adults with acute agitation associated with schizophrenia or bipolar disorder
Comparators	Oral and intramuscular preparations of : • Benzodiazepines (such as lorazepam) • Antipsychotics (such as haloperidol, risperidone and olanzapine)
Outcomes	The outcome measures to be considered include: • agitation level • 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: Proposed Technology Appraisal, 'Asenapine for the first or second line acute and maintenance treatment of schizophrenia', Publication TBC. Proposed Technology Appraisal, 'Asenapine for the treatment of moderate to severe manic episodes associated with bipolar I disorder', Publication TBC. Related Guidelines: Clinical Guideline No. 82, Mar 2009, 'Core interventions in the treatment and management of schizophrenia in primary and secondary care (update),' Expected review date Mar 2012. Clinical Guideline No. 38, Jul 2006, 'The management of bipolar disorder in adults, children and adolescents in primary and secondary care', Expected review date Jul 2011. Clinical Guideline No. 25, Feb 2005, 'Violence: The short-term management of disturbed/violent behaviour in in-patient psychiatric settings and emergency Departments', Expected review date TBC.

Questions for consultation

How should acute agitation be defined?

Have the most appropriate comparators for loxapine inhalation for the treatment of acute agitation in people with schizophrenia or bipolar disorder been included in the scope?

In which treatment setting is loxapine inhalation expected to be used?

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

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might

improve the way that current need is met (is this a ‘step-change’ in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits

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)