

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Loxapine inhalation for the treatment of acute agitation and disturbed behaviours associated with schizophrenia or bipolar disorder

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of loxapine inhalation within its licensed indication for the treatment of acute agitation and disturbed behaviours 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 as schizophrenia and the manic phase of bipolar disorder.

Schizophrenia is a cluster of major psychiatric 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 (elevated 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.

NICE clinical guidelines on treatment of schizophrenia and bipolar disorder do not make specific recommendations for the treatment of agitation and disturbed behaviours. Current UK clinical practice includes the use of antipsychotics (such as haloperidol, olanzapine, risperidone and aripiprazole) and benzodiazepines (such as lorazepam), given either alone or in combination, for the treatment of acute agitation.

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. 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 or disturbed behaviours associated with schizophrenia or bipolar disorder
Comparators	Oral and intramuscular preparations of : <ul style="list-style-type: none"> • Benzodiazepines (such as lorazepam) • Antipsychotics (such as haloperidol, risperidone, aripiprazole and olanzapine)
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none"> • level of agitation and/or disturbed behaviour • 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.

<p>Related NICE recommendations</p>	<p>Related Technology Appraisals: None</p> <p>Related Clinical Guidelines: Clinical Guideline No. 82, Mar 2009, 'Core interventions in the treatment and management of schizophrenia in primary and secondary care (update)', Currently under review. Expected date of publication TBC.</p> <p>Clinical Guideline No. 38, Jul 2006, 'The management of bipolar disorder in adults, children and adolescents in primary and secondary care'. Currently under review. Expected date of publication TBC.</p> <p>Clinical Guideline No. 25, Feb 2005, 'Violence: The short-term management of disturbed/violent behaviour in in-patient psychiatric settings and emergency Departments'. Currently under review. Expected date of publication TBC.</p>
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