NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Vortioxetine for the treatment of major depressive disorder

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of vortioxetine within its licensed indication for the treatment of major depressive disorder.

Background

Major depressive disorder is a broad and heterogeneous condition associated with a range of cognitive, behavioural, emotional, and physical symptoms. Central to major depressive disorder is low mood and/or loss of pleasure in most activities. The severity of the disorder may vary from mild to severe depending on both the number of symptoms and the degree of functional impairment. In severe cases, psychotic symptoms such as hallucination or delusion may be present. Major depressive disorder often has a remitting and relapsing course, and symptoms may persist between episodes.

In the UK, the prevalence of major depressive disorder ranges from 5% to 10% of people seen in primary care settings and 10% to 14% of medical inpatients. The risk of relapse is 50%, 70%, and 90% after the first, second, and third episodes of major depressive disorder respectively. The rate of major depressive disorder in women is two times the rate in men. In older adults, major depressive disorder is relatively rare although between 10% and 15% of older people have depressive symptoms.

NICE clinical guideline 90 advocates a stepwise approach for the management of major depressive disorder. The routine use of antidepressants to treat mild major depressive disorder is not recommended except for those who have a past history of moderate or severe major depressive disorder or who have mild major depressive disorder that persists after other interventions. For people with moderate or severe depression, the guideline recommends a combination of antidepressant medication and a high-intensity psychological intervention (cognitive behavioural therapy or interpersonal psychotherapy). When an antidepressant is being prescribed, it should normally be a selective serotonin reuptake inhibitor (SSRI). If the person with depression develops side effects or is not getting an adequate response, switching to an alternative SSRI or an antidepressant of a different class (for example venlafaxine, a tricyclic antidepressant, or a monoamine oxidase inhibitor) may be considered. Antidepressants may then be combined or augmented with other pharmacological treatments.

The technology

Vortioxetine (brand name unknown, Lundbeck and Takeda) is a bimodal oral antidepressant that is thought to work through a combination of reuptake inhibition of serotonin and modulation of serotonin receptor activity.

Vortioxetine does not have a UK marketing authorisation for the treatment of major depressive disorder. It has been studied in clinical trials as a first line treatment, and in people whose depression did not respond adequately to SSRIs or serotonin noradrenaline reuptake inhibitors (SNRIs). The comparators for vortioxetine in the clinical trials include duloxetine, agomelatine, venlafaxine and placebo.

Intervention(s)	Vortioxetine
Population(s)	Adults with major depressive disorder.
Comparators	• Selective serotonin reuptake inhibitors (for example citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) • Tricyclic antidepressants (for example clomipramine, doxepin, imipramine, lofepramine, nortriptyline, trimipramine, and amitriptyline) • Tricyclic-related antidepressants (for example mianserin and trazodone) • Serotonin and noradrenaline reuptake inhibitors (for example venlafaxine and duloxetine) • Other antidepressant drugs (for example mirtazapine and reboxetine)

Outcomes	The outcome measures to be considered include: • change from baseline severity of depression • remission of symptoms • anxiety • response to treatment (including response rate and time to response) • relapse (including relapse rate and time from remission to relapse) • hospitalisation • mortality • adverse effects of treatment (including adverse effects of treatment discontinuation) • 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	If evidence allows the following subgroups will be considered: • by the severity of depression (mild, moderate or severe) If evidence allows the clinical and cost effectiveness of vortioxetine may be considered in different positions in the treatment pathway. Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Terminated Technology Appraisal No. 231, Jul 2011, 'Agomelatine for the treatment of major depressive episodes' Related Guidelines: Clinical Guideline No. 90, Oct 2009, 'Depression: the treatment and management of depression in adults' Review proposal date Oct 2012 Clinical Guideline No. 91, Oct 2009, 'The treatment and management of depression in adults with chronic physical health problems' Review proposal date Oct 2012 Clinical Guideline No. 123, May 2011, 'Common mental health disorders: identification and pathways to care' Review proposal date May 2014. Related Quality Standards: Published Quality Standard, 'Depression in adults'

Questions for consultation

What is the likely place of vortioxetine in the treatment pathway for the treatment of major depressive disorder (that is, the line of therapy and whether it would be used alone or in combination with other treatments)?

- Is vortioxetine likely to be used to treat mild, moderate or severe depression?
- How would the relevant population in which vortioxetine is likely to be used be defined?

Have the most appropriate comparators for vortioxetine for the treatment of major depressive disorder been included in the scope? Are the comparators listed routinely used in clinical practice?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other 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?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which vortioxetine will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

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)