Vortioxetine tablets for treating major depressive episodes in adult population

Summary

Background and licensed indication

Vortioxetine is licensed for the treatment of major depressive episodes in adults. \(^1\) It is described as a multimodal antidepressant as it inhibits the serotonin (5-HT) transporter and modulates 5-HT receptor activity (it is a 5-HT, 5-HT, and 5-HT, receptor antagonist, 5-HT receptor partial agonist and a 5-HT receptor agonist). \(^1\)

Dosing

Recommended starting dose of 10mg, increased to maximum 20mg once daily in adults. In adults aged ≥ 65 years the starting dose is 5mg and caution is advised when using doses greater than 10mg once daily.

Alternatives

Venlafaxine, TCAs, duloxetine (non-formulary), agomelatine (non-formulary)

NICE

NICE TA and depression guidelines

Safety

No major safety concerns. Current evidence shows a potentially better overall safety profile than other antidepressants in short-term studies. No long-term safety data.

Convenience

Once daily dosing regimen with/without food.

Budget impact

The anticipated incremental prescribing cost of vortioxetine to the NHS per 100,000 population is approximately £1,100 in 2016.

Funding

Likely funded via CCGs.

Suggested place in therapy

Third line treatment for major depressive episodes as an alternative to venlafaxine, TCAs, agomelatine (non-formulary in CNWL & NWL) or duloxetine (non-formulary in CNWL & NWL).

Background and introduction

Vortioxetine is licensed for the treatment of major depressive episodes in adults. \(^1\) It is described as a multimodal antidepressant as it inhibits the serotonin (5-HT) transporter and modulates 5-HT receptor activity (it is a 5-HT, 5-HT, and 5-HT, receptor antagonist, 5-HT receptor partial agonist and a 5-HT receptor agonist). \(^1\) Current options for treating major depressive disorder, such as venlafaxine and duloxetine, are associated with an increased likelihood of stopping treatment due to adverse events. \(^4\) It has been recognized that having a range of treatment options would allow a flexible approach for treating major depressive disorder. \(^7\)

1. Proposed place in therapy

In its technology appraisal NICE advocates vortioxetine as an option for treating major depressive episodes in adults whose condition has responded inadequately to two antidepressants within the current episode. \(^2\)

2. Evidence selected for inclusion

NICE published a technology appraisal on Vortioxetine in November 2015. It was felt that this document provided sufficient evidence for a new Drug Review. NICE Technology Appraisal – Vortioxetine for treating major depressive episodes (TA367). http://www.nice.org.uk/guidance/ta367. NICE only accepted the evidence submitted for third-line use in this TA and no evidence was submitted comparing vortioxetine to first line antidepressants.

3. Critical evaluation

3.1 Clinical application

Doses of vortioxetine ranging from 5 to 20mg were generally more effective than placebo in improving depression and resulted in a clinically relevant decrease in depression scores. \(^3\) The conclusion from the NICE technical appraisal is that vortioxetine is likely to be similar in efficacy to other antidepressants but may be superior to agomelatine and inferior to duloxetine. \(^2\) The company’s indirect treatment comparison was not sufficiently robust for estimating the clinical effectiveness of vortioxetine compared with other antidepressants for second-line treatment (those who had not tolerated initial antidepressant treatment or whose condition had responded inadequately to it, and who needed further antidepressant therapy). \(^2\) NICE concluded that further exploration of relapse rates were required. \(^2\)

3.2 Safety

3.2.1. Key adverse events

The most common adverse effects with vortioxetine during short term or long term treatment are nausea and headache. Nausea was experienced in more than 1 in 10 people. \(^3\) The SPC also lists the following as “common” and “very common” adverse reactions: abnormal dreams, constipation, diarrhea, dizziness, itching and vomiting. \(^5\) Side effects were usually mild or moderate, short-lasting and occurred in the first two weeks of treatment. \(^1\) Effects on the gut, such as nausea, are more common in women than in men. \(^5\)
NICE found that the long-term adverse effect profile of vortioxetine compared with commonly used antidepressants in England was uncertain. However, it accepted that the available evidence suggested vortioxetine leads to a lower probability of stopping treatment and fewer adverse effects than most other antidepressants in the short term. They concluded that, based on the available (albeit sparse) evidence, vortioxetine may have a better overall safety profile than other antidepressants. Tolerability is comparable with other antidepressants categorised in the NICE guideline on depression in adults as “better-tolerated newer generation antidepressants.” NICE accepted the company’s evidence that vortioxetine improved sexual function in people with sexual dysfunction more than escitalopram. This is an advantage, as improvements in sexual function is one of the outcomes which contribute to treatment success. However, the 20 mg dose of vortioxetine was associated with an increase in treatment-emergent sexual dysfunction (TESD). NICE noted the manufacturer’s view that vortioxetine is innovative because of it reduces cognitive dysfunction, a factor which is associated with stopping treatment. The committee acknowledged that it may be a valuable treatment option for people with a major depressive disorder experiencing cognitive dysfunction. This is not a licensed indication.

3.3 Potential advantages and disadvantages over existing technologies

3.3.1 Convenience

Convenient dosing schedule of once daily either with or without food. There is no specificity around timing of doses. Tablets are the only dosage form available. This limits use in patients with swallowing difficulties or where a more staggered dosing regimen is required. Patients treated with Brintellix can abruptly stop taking the medicinal product without the need for a gradual reduction in dose unlike many existing anti-depressants. Vortioxetine is metabolised by cytochrome 2D6, 3A4/5 and C9 so there is potential for drug interactions.

3.3.2 Healthcare resource utilisation

There should be little impact on resources. There are no specific monitoring requirements. The once daily dosing schedule, either with or without food, may allow flexibility in administration times. The ability to discontinue treatment abruptly has the potential to reduce time spent switching medications.

3.3.3 Suitability for shared care

Vortioxetine should be suitable for shared care especially as GPs often manage depression in people for whom third-line treatment is needed. It is anticipated that vortioxetine will be added to the North West London CCG formulary.

3.3.4 Drug cost and likely budgetary impact

The acquisition cost of vortioxetine is £27.72/28 days for 5mg, 10mg or 20mg film-coated tablets. The budget impact of vortioxetine compares the antidepressant spending in two scenarios: one where vortioxetine is not available and one where it is.

| Estimated budget impact per 100,000 population over the next four years (acquisition cost only) |
|----------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 2016                                   | 2017            | 2018            | 2019            | Total           |
| Vortioxetine unavailable               | £40,536         | £40,536         | £40,536         | £40,536         | £217,136        |
| Vortioxetine available                 | £41,608         | £43,424         | £47,344         | £51,676         | £239,098        |
| Difference in budget                   | £1,073          | £2,888          | £6,808          | £11,141         | £21,962         |
| Total patients treated                 | 5,150           | 1,030           | 1,030           | 1,030           | 5,150           |
| Vortioxetine patients                  | 5               | 14              | 34              | 56              | 110             |

NICE estimates that about 28,000 people are eligible for treatment with vortioxetine each year.

4 Health Economics

Based on assuming equal efficacy for the purposes of assessing the cost effectiveness, NICE has concluded that treatment with vortioxetine is a cost-effective use of NHS resources. The incremental cost effectiveness ratios (ICERs) for vortioxetine compared with other antidepressants is £9000 per quality-adjusted life year (QALY) gained or below. Refer to the NICE Technology Appraisal for a full evaluation of cost effectiveness.

5 Likely commissioning and funding pathway

Likely funded via CCGs.

6 Suggested place in therapy

Third line treatment for major depressive episodes as an alternative to venlafaxine, TCAs, agomelatine or duloxetine. Please note that duloxetine and agomelatine are non-formulary in CNWL and NWL.

References:


