PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
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NHS Pan Mersey Area Prescribing Committee

VORTIOXETINE tablets (Brintellix®▼)

GREEN

The Pan Mersey Area Prescribing Committee recommends the prescribing of VORTIOXETINE tablets (Brintellix®▼) as a third line option for treating major depressive episodes in adults whose condition has responded inadequately to two antidepressants within the current episode, in accordance with NICE TA367 [November 2015]

The Pan Mersey Area Prescribing Committee recommends that if vortioxetine is considered clinically appropriate, it should be prescribed as a third line or later option following an inadequate response to two or more antidepressants.

People whose treatment with vortioxetine is not recommended in NICE TA367[1], but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

Vortioxetine has UK marketing authorisation for the treatment of major depressive episodes in adults[2]. However, the original evidence submission for NICE TA367 was restricted to a subset of the licensed population i.e. adults with a moderate to severe major depressive episode that have responded inadequately in terms of efficacy and/or tolerability to initial antidepressant treatment and require alternative treatment.

NICE TA367 found no convincing evidence to show that vortioxetine was more or less effective than other antidepressants, but agreed that based on the available evidence, it may have a better overall safety profile than other antidepressants. NICE recommended vortioxetine as a possible treatment option for adults having a first or recurrent major depressive episode, if the current episode has not responded to two antidepressants.

Current NICE guidelines for the pharmacological treatment of depression in adults [CG90; 2009][3] recommend a generic selective serotonin reuptake inhibitor (SSRI) as first line treatment. If there is an inadequate response, a different SSRI or a better tolerated 'newer-generation antidepressant' is recommended as second-line treatment. If another antidepressant is subsequently needed, a drug from a different class may be considered. If there is no improvement from switching antidepressants, augmentation strategies or combination antidepressant treatment may be considered by specialists.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

VORTIOXETINE tablets (Brintellix®▼)

EFFECTIVENESS

Vortioxetine is a first in class multimodal antidepressant that is thought to produce its clinical effects through direct modulation of serotonergic receptor activity and inhibition of the serotonin transporter[4].

One efficacy study (REVIVE[5]) was directly relevant to the evidence submission for NICE TA367. In this 12 week non-inferiority randomised controlled clinical trial (RCT), a total of 501 patients with an inadequate response to initial SSRI or SNRI treatment were randomised 1:1 to flexible doses of either vortioxetine 10 or 20 mg/day or agomelatine 25 or 50 mg/day. The mean change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at week 8 was -16.5 and -14.4 points for vortioxetine versus agomelatine respectively, giving a mean difference of -2.16 points in favour of vortioxetine (95% CI: -3.51 to -0.81; p = 0.002). Vortioxetine was non-inferior to agomelatine based on the pre-specified non-inferiority margin.

A further study (SOLUTION[6]) in patients with recurrent major depressive disorder provided evidence of vortioxetine efficacy for NICE TA367. In this 8-week RCT, 410 patients were randomised 1:1 to fixed doses of vortioxetine 10 mg daily or venlafaxine XR 150 mg daily. Vortioxetine was found to be non-inferior to venlafaxine. The mean change from baseline in MADRS total scores at week 8 was −19.4 points for vortioxetine and −18.2 points for venlafaxine, giving a mean difference of −1.2 points (95% CI −3.0 to 0.6) in favour of vortioxetine.

In addition, two meta-analyses (Pae et al. 2015[7]; Llorca et al 2014[8]) provided evidence that the relative effectiveness of vortioxetine was comparable with that of other antidepressants.

NICE TA367 concluded that based on the totality of the evidence, vortioxetine is likely to be of similar efficacy to other antidepressants.

SAFETY

Vortioxetine is contraindicated in combination with non-selective monoamine oxidase inhibitors (MAOIs) or selective MAO-A inhibitors due to a risk of serotonin syndrome[4].

Vortioxetine was generally well tolerated in clinical trials. Adverse reactions were generally transient, mild to moderate in nature and occurred within the first two weeks of treatment. They did not generally lead to cessation of treatment.

The summary of product characteristics (SPC)[4] lists the following 'common' and 'very common' adverse reactions: nausea, vomiting, constipation, diarrhoea, dizziness, abnormal dreams and itching. Gastrointestinal adverse reactions, such as nausea, occurred more frequently in women than men. Class precautions include suicidal ideation and behaviour, bone fractures, convulsions, serotonin syndrome and neuroleptic malignant syndrome, hyponatraemia and haemorrhage. For full details of adverse reactions and contraindications, refer to the summary of product characteristics.

Any suspected adverse reactions to vortioxetine should be reported via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

COST

The basic NHS list price* of a 28-day pack is £27.72 excluding V.A.T. across all strengths of vortioxetine.

Annual cost (i.e. for 365 days) of vortioxetine 10 to 20mg/day is £361.35

* Costs may vary because of negotiated procurement discounts[1]

Annual costs** of alternative third line antidepressants

- Mirtazapine tablets 15 to 45mg/day: £14.00-£29.59
- Venlafaxine m/r tablets 75 to 225mg/day: £31.63 - £408.80 (Prices may differ if branded generics are used).
- Duloxetine capsules 60 to 120mg/day: £48.62 -£97.25
- Agomelatine tablets 25 to 50mg/day £391.07-£782.15

**Source: Feb 2018 Drug Tariff

The NICE TA367 costing statement states that it is unlikely that the guidance will result in a significant change in resource use in the NHS.

PATIENT FACTORS[4]

- The safety and efficacy of vortioxetine in children and adolescents less than 18 years old have not been established.
- Data for use of vortioxetine in pregnancy is limited.
- Caution is advised in severe renal or hepatic impairment and in adults aged 65 years or older treated with doses higher than 10 mg/day.
- Dose adjustment may be necessary if vortioxetine is concurrently prescribed with a strong CYP2D6 inhibitor (e.g. bupropion, quinidine, fluoxetine, paroxetine) or a broad cytochrome P450 inducer (e.g. rifampicin, carbamazepine, phenytoin)

PRESCRIBING INFORMATION

The recommended starting dosage of vortioxetine is 10 mg orally once daily in adults younger than 65 years, and 5 mg once daily in adults 65 years and older[4]. Depending on response, the dose may be increased to a maximum of 20 mg once daily or decreased to a minimum of 5 mg once daily. Treatment should continue for at least 6 months after the symptoms resolve. People with a history or recurrent depression may need antidepressants for at least 2 years[3].

IMPLEMENTATION NOTES

Vortioxetine is a treatment option alongside current standard third line treatments for major depressive disorder. Information on switching antidepressants is included in the NICE Clinical Knowledge Summary on Depression[9].

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