Medicines Information Bulletin

Oxford Health NHS Foundation Trust

Vol. 14 No. 2 **Vortioxetine (Brintellix) for depression** **January 2016**

DTG decision: Formulary Restricted

The Drugs and Therapeutics Group has included vortioxetine on the formulary as a restricted medicine. It should only be used according to the NICE technology appraisal guidance (TA367)[1], which recommends vortioxetine as an option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode.

Vortioxetine is as effective as other antidepressants, but may have a better overall safety profile.[1] Vortioxetine has pro-cognitive effects and NICE suggests that it may be a valuable treatment option for people experiencing cognitive dysfunction as part of their depression.[1]

Clinicians wishing to prescribe vortioxetine must make an entry in the patient's notes that clearly describes how the restriction criteria are met.

What is it?

Vortioxetine is thought to work through a combination of two pharmacological modes of action: reuptake inhibition and receptor activity. *In vitro* studies indicate that vortioxetine is an inhibitor of the serotonin transporter and also a 5-HT_3, 5-HT_7 and 5-HT_{1D} receptor antagonist, 5-HT_{1B} receptor partial agonist, and 5-HT_{1A} receptor agonist. *In vivo* non-clinical studies have demonstrated that vortioxetine modulates neurotransmission in several systems, including predominantly the serotonin but probably also the norepinephrine, dopamine, histamine, acetylcholine, GABA and glutamate systems.[2]

How much does it cost?

Vortioxetine has a flat based pricing structure – all strengths are £27.72 for a 28 day supply.

Annual treatment cost for comparison

	per year (MIMS[3]) £
Vortioxetine 10mg OD	361.35
Mirtazapine 30mg OD	17.72
Venlafaxine 112.5mg **BD**	63.88
Venlafaxine MR **TABLETS** 225mg OD	408.80
Venlafaxine MR **CAPSULES** 225mg OD	767.67

What is the dose?

- Adults <65 years of age: 10 mg once daily (starting and maintenance dose), increase to 20mg OD or reduce to 5mg OD depending on individual patient response.
- Elderly ≥ 65 years of age: 5mg once daily. Increase if necessary to 10mg OD. Data is limited for doses >10mg in this age group.
- Children <18 years of age: no data.

Continue treatment for at least 6 months after symptoms have resolved.[2]

What tablet strengths are available?
Film coated tablets are available in three strengths: 5mg, 10mg, and 20mg

How is it taken?
The tablets can be taken with or without food.

Are there any contraindications or precautions?

Vortioxetine is contraindicated in anyone who is allergic to the active substance or any of the excipients and in anyone taking a non-selective MAOI or moclobemide.[2]

The following are included as precautions: suicide/suicidal thoughts or clinical worsening; seizures; serotonin syndrome; neuroleptic malignant syndrome; mania/hypomania; hyponatraemia; renal impairment; hepatic impairment.[2] For more detail refer to the manufacturer's literature (SPC): http://www.medicines.org.uk/emc/medicine/30904

How does vortioxetine compare with other antidepressants?

Vortioxetine appears equally effective as other antidepressants but may have a better overall safety profile. It appears to have no effect on body weight; no effect on pulse, blood pressure or any ECG parameter, including no effect on the QT interval; it has not been associated with insomnia or somnolence; and the incidence of self-reported sexual dysfunction was low and similar to placebo.[2]

What adverse effects does it cause?

As with all new drugs, vortioxetine is a black triangle ▼ drug and all suspected adverse reactions should be reported to the MHRA via the yellow card scheme (www.mhra.gov.uk/yellowcard).

Very common (=/>10%)	Nausea.
Common (>/=1/100 to <1/10)	Abnormal dreams, dizziness, diarrhoea, constipation, vomiting, pruritus.
Uncommon (>/=1/1000 to <1/100)	Flushing, night sweats.
Unknown	Serotonin syndrome.

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Are there any drug interactions?

Vortioxetine is extensively metabolised in the liver, primarily through oxidation catalysed by CYP2D6 and to a minor extent CYP3A4/5 and CYP2C9. It is therefore liable to a number of interactions[2]:

Drug	Effect
Serotonergic medicines e.g. tramadol, triptans	**Caution.** Increased risk of serotonin syndrome
MAOIs, irreversible non-selective: phenelzine, isocarboxazid, tranylcypromine	**Contraindicated** due to risk of serotonin syndrome. Allow 14 days after stopping an MAOI before starting vortioxetine. Allow 14 days after stopping vortioxetine before starting an MAOI.
Linezolid (MAOI, reversible non-selective)	**Contraindicated** due to risk of serotonin syndrome. The manufacturer advises that if a combination of linezolid and vortioxetine proves necessary, the minimum dose should be used with close monitoring for serotonin syndrome.
Moclobemide (MAO-A inhibitor, reversible selective)	**Contraindicated** due to risk of serotonin syndrome. The manufacturer advises that if a combination of moclobemide and vortioxetine proves necessary, the minimum dose should be used with close monitoring for serotonin syndrome.
Selegiline and rasagaline (MAO-B inhibitors, irreversible, selective)	**Caution.** A lower risk of serotonin syndrome is expected with selective MAO-B inhibitors than with MAO-A inhibitors. None-the-less combining vortioxetine with MAO-B inhibitors such as selegiline or rasagiline should be done cautiously, with close monitoring for serotonin syndrome.
CYP2D6 inhibitors e.g. bupropion, quinidine, fluoxetine, paroxetine	Strong CYP2D6 inhibitors increase vortioxetine exposure and increase the risk of adverse effects. A lower dose of vortioxetine should be considered.
CYP3A4 inhibitors and CYP2C9 inhibitors e.g. ketoconazole, fluconazole	No dose adjustment necessary.
Broad CYP450 inducers e.g. rifampicin, carbamazepine, phenytoin	**Caution**. Reduced vortioxetine exposure is possible. Dose adjustment according to response may be necessary.
Drugs that lower the seizure threshold e.g. antidepressants, antipsychotics, mefloquine, bupropion, tramadol	**Caution** due to additive seizure threshold lowering effect.
Anticoagulants and antiplatelet drugs	**Caution**. No pharmacokinetic interactions, however caution is recommended due to an increased risk of bleeding as a result of a pharmacodynamic interaction.
Lithium and tryptophan.	**Caution**. Levels of lithium are not affected. However there are reports of enhanced effects when antidepressants with serotonergic effect have been given together with lithium or tryptophan.
Smoking	No effect.

How should patients be switched from their current antidepressant to vortioxetine?

FROM	TO VORTIOXETINE[4]
Bupropion, mirtazapine, reboxetine, trazodone	Cross taper cautiously
Clomipramine, fluvoxamine	Taper and stop then start low dose
Fluoxetine	Taper and stop, wait 4-7 days then start low dose
Citalopram, escitalopram, paroxetine, sertraline, duloxetine, venlafaxine	Cross taper cautiously starting with a low dose
Tricyclics (TCAs)	Halve dose, start vortioxetine, then slowly withdraw remainder of TCA
MAOIs	Taper and stop and wait for 2 weeks
Moclobemide	Taper and stop and wait for 24 hours

How should vortioxetine be stopped?

Vortioxetine is not associated with discontinuation symptoms, so it can be stopped abruptly without the need to taper the dose.

Need more information?

For more detailed prescribing information please refer to the SPC.

OR contact the Medicines Information Service on 01865 904365 or email: med.info@oxfordhealth.nhs.uk.

References

1. NICE. Vortioxetine for treating major depressive episoes. Technology appraisal guidance TA367, November 2015
2. Lundbeck Ltd. Vortioxetine Summary of Product Characteristics. Date of most recent revision of the text: 17 June 2015
3. Monthly Index of Medical Spciaties (accessed online on 26.1.16 www.mims.co.uk)
4. Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines in Psychiatry 12th edition, Wiley 2015