Vortioxetine

Traffic light classification- Amber 3
Information sheet for Primary Care Prescribers

Licensed Indications[1]

- Vortioxetine is licensed for the treatment of more severe depression in adults
- Vortioxetine is recommended in patients ≥ 65 years of age with a lower starting dose
- Vortioxetine is not recommended in patients < 18 years of age

Therapeutic Summary

Vortioxetine predominantly modulates serotonergic receptor activity and inhibits the reuptake of serotonin. It also modulates the norepinephrine, dopamine, histamine, acetylcholine, GABA, and glutamate systems[1,2].

Medicines Initiation

Vortioxetine is an option for treating more severe depression in adults whose condition has responded inadequately to two antidepressants within the current episode[3]. Primary care may initiate vortioxetine as per this guideline.

Products Available

Vortioxetine 5mg, 10mg, 20mg tablets. Cost x 28 tablets = £27.72[4]

Dosages and Route of Administration[1,2]

- The starting dose is 10mg once daily for adults and 5mg once daily for patients ≥ 65 years of age.
- Dose can be increased, if necessary, up to 20mg once daily. Caution in patients ≥ 65 years of age with doses higher than 10mg due to limited clinical data.
- Vortioxetine tablets may be taken with or without food. Taking it with, or just after, food may minimise nausea.
- Vortioxetine should be taken in the morning. It can affect sleep if taken at night.

Duration of Treatment

NICE guideline 222[5] advises to support and encourage a person who has benefited from taking an antidepressant to continue medication for at least 6 months after remission of an episode of depression; this greatly reduces the risk of relapse. Review the need for continued antidepressant treatment beyond 6 months after remission considering the likelihood of relapse and the potential risks of continuing with antidepressants long term. For people who have been assessed as being at higher risk of relapse, consider continuing with antidepressant medication maintaining the dose that led to full or partial remission, unless there is good reason to reduce it. Review treatment with antidepressant medication at least every 6 months thereafter.

Treatment Discontinuation

No gradual reduction in dose is required on treatment discontinuation[1]. Vortioxetine has not been associated with withdrawal symptoms in clinical trials[1]. However, unless there is a clinical reason to stop suddenly, it may be better to reduce the dose gradually over several weeks.

Use in Pregnancy

There are limited data from the use of vortioxetine in pregnant women. Vortioxetine should only be administered in pregnancy if the expected benefits outweigh the potential risk to the foetus[1].

If used during the later stages of pregnancy, there is a risk of neonatal withdrawal symptoms and persistent pulmonary hypertension in the newborn[2].

In January 2021, the MHRA published a drug safety update on the small increased risk of postpartum haemorrhage when SSRIs, SNRIs, or vortioxetine were used in the month before delivery[6]. Therefore, prescribers should consider this risk in the context of individual patient's susceptibility to bleeding or thrombotic events during the peripartum period, and the benefits of vortioxetine for the patient's mental health during this time. Anticoagulant medication prescribed for women at high risk of thrombotic events should not be stopped in reaction to these data but be aware of the risk identified.

Side effects
The most common side effect is nausea. This is generally mild or moderate and occurs within the first 2 weeks of treatment. It is usually transient[1]. Taking vortioxetine with or after food may help to reduce nausea.

For a comprehensive list of side effects, refer to the SPC.

Contraindications[1]
- Hypersensitivity to the active substance or to any of the excipients
- Concomitant use of non-selective monoamine oxidase inhibitors (MAOIs) or selective MAO-A inhibitors

Precautions[1,2]
- Bleeding disorders**,** liver cirrhosis**,** renal impairment**,** history of mania/hypomania**,** history of suicide-related events or a current significant degree of suicidal ideation**,** history of seizures, unstable epilepsy, and susceptibility to angle-closure glaucoma.

Clinically Relevant Medicine Interactions and Their Management[1,2]
Vortioxetine is metabolised primarily by cytochrome P450 2D6 (CYP2D6) and to a minor extent CYP3A4/5 and CYP2C9. Medicines that interact with these isoenzymes may decrease or increase the bioavailability of vortioxetine.

- Concomitant use of broad CYP450 inducers (rifampicin, carbamazepine, phenytoin) – higher dose of vortioxetine may be considered.
- Concomitant use of strong CYP2D6 inhibitors (bupropion, quinidine, fluoxetine, and paroxetine) – lower dose of vortioxetine may be considered.
- Concomitant use of CYP3A4/5 and CYP2C9 inhibitors (ketoconazole and fluconazole) – no dose adjustment is needed.
- Poor CYP2D6 metabolisers: Concomitant use of strong CYP3A4 inhibitors (itraconazole, voriconazole, clarithromycin, and many of the HIV protease inhibitors) and CYP2C9 inhibitors (fluconazole and amiodarone) – lower dose of vortioxetine may be considered.

- Vortioxetine is contraindicated with the following due to the risk of serotonin syndrome:
  - Irreversible non-selective MAOIs (e.g. phenelzine, isocarboxazid and tranylcypromine)
  - Reversible selective MAO-A inhibitors (moclobemide)
  - Reversible, non-selective MAOI (linezolid)

- Vortioxetine should be used with caution alongside irreversible selective MAO-B inhibitors (selegiline and rasagiline). Close monitoring for serotonin syndrome is necessary.
- Caution with concomitant use of serotonergic medicines (e.g. tramadol and triptans) and herbal remedies (St. John's wort) due to risk of serotonin syndrome.

- Caution with concomitant use of serotonergic medicines that can lower the seizure threshold (antidepressants, neuroleptics, mefloquine, bupropion, tramadol).
- Caution with NSAIDs, oral anticoagulants and antiplatelet medicines due to a potential increased risk of bleeding.

For a comprehensive list of interactions, refer to the SPC and BNF.

Patient information

- Patients should be informed of the effects on driving and performing skilled tasks especially when starting treatment or changing the dose[1]
- Patient information leaflets for vortioxetine, other medicines and mental health conditions can be found at: https://www.mind.org.uk/information-support/drugs-and-treatments/antidepressants-a-z/vortioxetine/

Pharmacy Contacts - Nottinghamshire Healthcare NHS Foundation Trust
Mental Health Medicines Pharmacist Advice Line: 0300 303 5808
Wells Road Centre Pharmacy 01159 555 357
Email MI@nottshc.nhs.uk

References and Version Control

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3. Vortioxetine for Treating Major Depressive Episodes. NICE Technology Appraisal Guidance 367 (November 2015). https://www.nice.org.uk/guidance/ta367. [Accessed on 12/10/2022]
4. The Electronic Drug Tariff https://www.drugtariff.nhsbsa.nhs.uk/#/00798052-DC/DC00798043/Home [Accessed on 12/10/2022].
5. Depression in Adults: Treatment and Management. NICE Guideline 222 (June 2022). https://www.nice.org.uk/guidance/ng222. [Accessed on 12/10/2022].
6. SSRI/SNRI Antidepressant Medicines: small increased risk of postpartum haemorrhage when used in the month before delivery. MHRA Drug Safety Update (January 2021). https://www.gov.uk/drug-safety-update/ssri-slash-snri-antidepressant-medicines-small-increased-risk-of-postpartum-haemorrhage-when-used-in-the-month-before-delivery [Accessed on 12/10/2022].

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Version	Author(s)	Date	Changes
1.0	Kay Goh, Senior Clinical Pharmacist, Nottinghamshire Healthcare NHS Foundation Trust Hannah Godden, Principal Pharmacist, Adult Mental Health Community Teams, Nottinghamshire Healthcare NHS Foundation Trust	January 2023	