



Drug information question: Does vortioxetine (Trintellix®) improve cognitive functioning in people with major depressive disorder?

**Conclusion: It is unclear whether vortioxetine meaningfully improves cognitive functioning in people with major depressive disorder.**

The BC Provincial Academic Detailing (PAD) Service's 2020-2021 topic [Antidepressants: Drug Information](#) addresses:

- How the efficacy of antidepressants is measured in clinical trials and reported in meta-analyses
- The quality and quantity of evidence that informs conclusions regarding antidepressant comparisons and combinations
- Drug information relevant to the prescribing, deprescribing and monitoring of antidepressants

[Vortioxetine](#) (Trintellix®) was approved by Health Canada in 2014 for the treatment of major depressive disorder in adults.<sup>1</sup> It is a serotonergic antidepressant that differs pharmacologically from serotonin reuptake inhibitors (SSRIs).<sup>1,2</sup> Similar to other antidepressants, its mechanism of antidepressant effect is not known.<sup>1,2</sup>

In 2016, the US Food and Drug Administration (FDA) reviewed vortioxetine as a potential treatment for cognitive dysfunction for people with major depressive disorder.<sup>3</sup> The [complete FDA review](#) is publicly accessible, but here are a few key points:<sup>3</sup>

- The FDA review included two pivotal 8-week trials, enrolling 1204 participants, where the principal efficacy measure included the Digit Symbol Substitution Test (DSST).
- The DSST is a timed task requiring that participants correctly match nine geometric symbols with corresponding numbers as provided on an answer key. Their scores reflect the number of correct matches achieved in 90 seconds.
- In the two trials, DSST scores at baseline indicated 42-43 correct matches on average out of a maximum of 133.
- The first trial enrolled participants with recurrent major depressive disorder. The number of correct matches improved by approximately four more in the vortioxetine group compared to placebo.
- The second trial enrolled participants with recurrent major depressive disorder who also reported difficulty concentrating, slow thinking, difficulty learning or remembering new things. The number of correct matches improved by approximately two more in the vortioxetine group compared to placebo.

The FDA did not approve the manufacturer's claim for vortioxetine as a treatment for cognitive dysfunction in major depressive disorder.<sup>4</sup> A principal issue raised during the review was uncertainty regarding whether DSST is a relevant measure of cognitive functioning in major depressive disorder.<sup>3</sup> The review also identified a lack of agreement on the minimal clinically-important change on the DSST score.<sup>3</sup>

Subsequent to the FDA's 2016 assessment of vortioxetine, a 2020 review by the [Canadian Agency for Drugs in Technology and Health](#) also concluded that:<sup>5</sup>

- The effects of vortioxetine on cognitive function are unclear.
- Current evidence is not sufficient to draw conclusions regarding the comparative effects of vortioxetine to other antidepressants.

In British Columbia, vortioxetine costs approximately \$95-105 a month compared to commonly-prescribed SSRIs which cost approximately \$5-20 a month.<sup>6</sup>

<sup>1</sup>[Health Canada Vortioxetine](#); <sup>2</sup>[ZHANG J Clin Psychiatry 2015 \(PMID 25562777\)](#); <sup>3</sup>[US FDA 2016 Review Vortioxetine Cognitive Dysfunction](#); <sup>4</sup>[Fierce Pharma March 29, 2016](#); <sup>5</sup>[CADTH 2020 Common Drug Review Vortioxetine](#); <sup>6</sup>[BC PAD Antidepressants: Drug Information](#)