

What evidence exists for using lisdexamfetamine (Vyvanse®) in binge eating disorder in adults and how does this relate to weight loss?

Conclusion: Lisdexamfetamine is approved for use in adults with moderate to severe binge eating disorder where evidence indicates it can reduce binge eating frequency and secondarily results in ~6% body weight loss. However, lisdexamfetamine is not approved for use, or recommended in any guidelines, for people without binge eating disorder.

The BC Provincial Academic Detailing (PAD) service's topic <u>Medications for Weight Loss in Adults</u> looks at the evidence for tirzepatide, semaglutide, liraglutide, naltrexone-bupropion and orlistat.¹ We received this question during PAD sessions: What about using lisdexamfetamine (Vyvanse®) for weight loss?

- what are the indications for lisdexamfetamine? In addition to ADHD, lisdexamfetamine is indicated for moderate to severe binge eating disorder (BED) in adults.² Diagnosis of BED is not based on body weight, it is based on DSM-5 criteria which includes recurrent episodes of excess food intake accompanied by a sense of lack of control which occur at least weekly for three months or more.^{3,4} People experiencing BED often report marked emotional distress about these episodes. Eating disorder focused cognitive behavioural or interpersonal therapy are recommended as the first line treatment for BED.⁴
- b) How was the efficacy of lisdexamfetamine measured in BED trials? The primary efficacy measure in the two pivotal trials was the number of binge eating days per week.⁵ The starting dose was 30 mg per day, titrated at weekly intervals up to 50-70 mg per day. From a baseline of approximately 5 binge days per week, lisdexamfetamine resulted in 1.35 and 1.66 fewer binge days per week compared with placebo, in the two 12-week pivotal trials. Percent change in body weight was one of the secondary outcomes and lisdexamfetamine resulted in approximately a 6% reduction in body weight.
- c) Why is lisdexamfetamine not recommended as a weight loss medication? For weight loss, the US Food and Drug Administration and Health Canada require pivotal trials that are at least one year in duration with at least 3000 patients randomized to the drug.⁶ The two pivotal BED trials were 12 weeks in length with less than 400 participants randomized to the drug.⁵ The Vyvanse Product monograph specifies that it "is not indicated or recommended for weight loss" and Obesity Canada does not recommend lisdexamfetamine as a weight loss treatment outside of managing BED.^{2,6}
- d) What adverse events are expected? The most common adverse events in the lisdexamfetamine BED trials were dry mouth (36% of participants), insomnia (20%), decreased appetite (8%), increased heart rate (7%), constipation (6%) and anxiety (5%). Lisdexamfetamine is contraindicated in moderate to severe hypertension, advanced atherosclerosis and symptomatic cardiovascular disease. These contraindications may have additional clinical relevance for the BED population as compared to the ADHD population. Participants with cardiovascular risk factors other than smoking or obesity were excluded from the BED efficacy trials and long-term cardiovascular safety trials were not required as part of the drug approval process.

¹BC Provincial Academic Detailing Service: Medications for Weight Loss; ²Health Canada Drug Product Database Vyvanse; ³American Psychiatry Association DSM-V 2022; ⁴American Psychiatry Association 2023 Eating Disorders Guideline; ⁵US FDA Review 2015 Vyvanse Binge Eating Disorder; ⁶US FDA 2007 Guidance for Industry Developing Products for Weight Management; ⁶Obesity Canada 2022 Pharmacotherapy Update