

If lisdexamfetamine (Vyvanse®) is a prodrug of dextroamphetamine (Dexedrine®), are there any important differences between them?

Conclusion: Lisdexamfetamine and dextroamphetamine immediate-release tablets may provide similar amphetamine blood levels when dosed once a day. Differences in important patient outcomes, such as efficacy and safety, are unknown.

The BC Provincial Academic Detailing (PAD) service is now delivering the topic <u>Medications for Attention Deficit</u> <u>Hyperactivity Disorder (ADHD)</u>. This includes comparisons of different methylphenidate and amphetamine formulations.

Methylphenidate (Ritalin®) has a half-life of 2-3 hours. Modified (longer-acting) formulations prolong medication release to provide a drug effect for an estimated 8-16 hours.¹

Dextroamphetamine is the active drug in both lisdexamfetamine dimesylate (Vyvanse®) and dextroamphetamine sulfate tablets (Dexedrine®).^{2,3} Immediate-release dextroamphetamine is often perceived as a short-acting medication; however, its half-life is relatively long: 8-12 hours.¹ Lisdexamfetamine is an inactive prodrug that is converted in red blood cells to dextroamphetamine.

A small pharmacokinetic study compared dextroamphetamine (d-amphetamine) to lisdexamfetamine in compounded capsules at equivalent doses given once a day. The figure below illustrates that amphetamine blood levels are similar. One difference is that lisdexamfetamine reaches peak blood level approximately one hour later than dextroamphetamine.

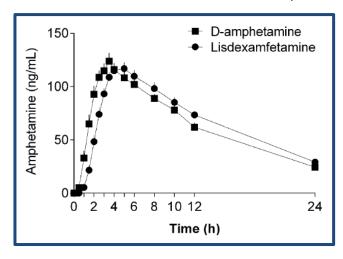


Figure reproduced under open access from P Dolder et al. Front Pharmacol 2017;8:617 (PMID: 23936175)⁴

Plasma concentrations of d-amphetamine in 24 healthy adults (ages 21-34; 50% male) receiving single oral doses of dextroamphetamine sulfate 40 mg and lisdexamfetamine dimesylate 100 mg (providing equivalent dose of dextroamphetamine, 29.6 mg) on separate days⁴

The US Food and Drug Administration's pharmacology review of Vyvanse found that animal studies show a similar pattern when comparing the pharmacokinetics of Vyvanse and dextroamphetamine.² It is unknown if there are differences in important patient outcomes (such as efficacy or safety) between dextroamphetamine and lisdexamfetamine.⁵

Under the BC PharmaCare formulary, Dexedrine is a regular benefit, while Vyvanse is a limited coverage benefit.

¹BC Provincial Academic Detailing Service: Medications for ADHD (October 2022); ²US FDA 2007 Pharmacology Review Vyvanse; ³Health Canada Drug Product Database; ⁴DOLDER Front Pharmacol 2017:8:617 (PMID: 23936175); ⁵CORTESE Lancet Psychiatry 2018;5:727-35.