Supplemental Information for Long-Acting Amphetamine Stimulants

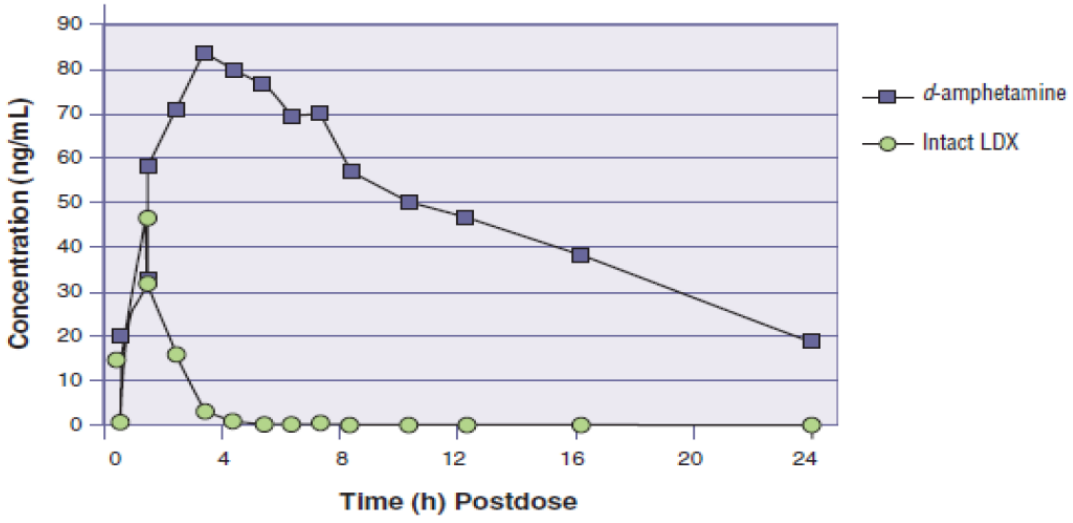
Educational Information:
The following is education and information on pertinent topics regarding long acting amphetamine stimulants, to assist in making the most appropriate decision for your patient(s).

Abuse Potential:
Vyvanse must be converted to its active form in the blood stream to exert its therapeutic effect. As there is no way to bypass the release mechanism to increase the absorption, it is considered to be an abuse-deterrent medication.

Adderall XR can be abused by crushing, melting, or dissolving the medication to ingest via the intranasal or injection route. This increases the absorption rate, which in turn can result in euphoria.

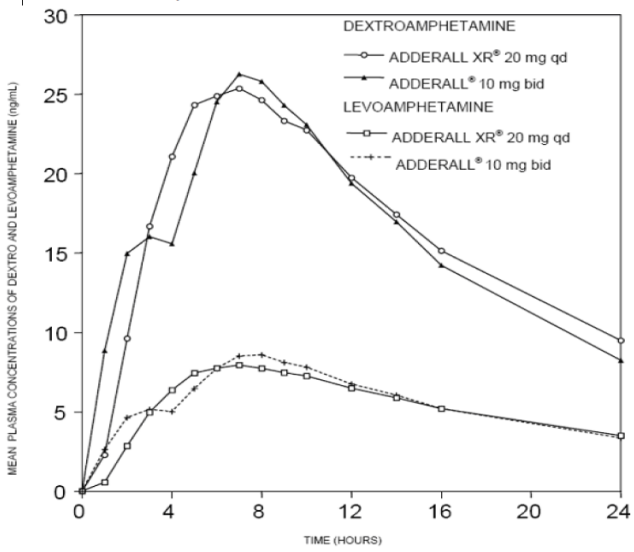
Length of Activity:
Vyvanse effect was first observed 2 hours post dose with peak plasma concentrations 4-5 hours post dose. This effect continued through the last measurement at 13 hours.

Figure 1. Concentration-time profile of *d*-amphetamine and intact Vyvanse (LDX) following day 7 administration of Vyvanse 70 mg (Krishnan and Kehner 2006)



Adderall XR effect was first observed at 1.5 hours post-dose with peak plasma concentrations 5-8 hours post dose. This effect continued through the last measurement at 12 hours.

Figure 1: Mean d-amphetamine and l-amphetamine plasma concentrations following administration of Adderall XR 20 mg (8 am) and Adderall (immediate-release) 10 mg twice daily (8 am and 12 noon) in the fed state



Mydayis effect was first observed at 2-4 hours post dose. This effect continued through the last measurement at 16 hours.

Figure 3. Mean *d*-Amphetamine Plasma Concentrations over Time after Seven Once-Daily Oral Doses of Mydayis in Healthy Adults (Shire Data on File SHP465-110)

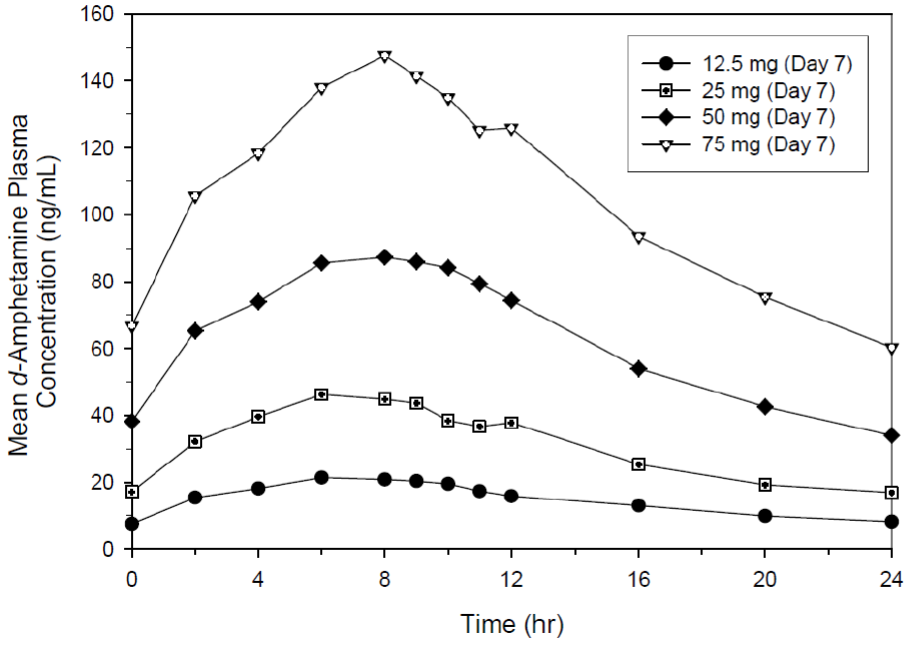
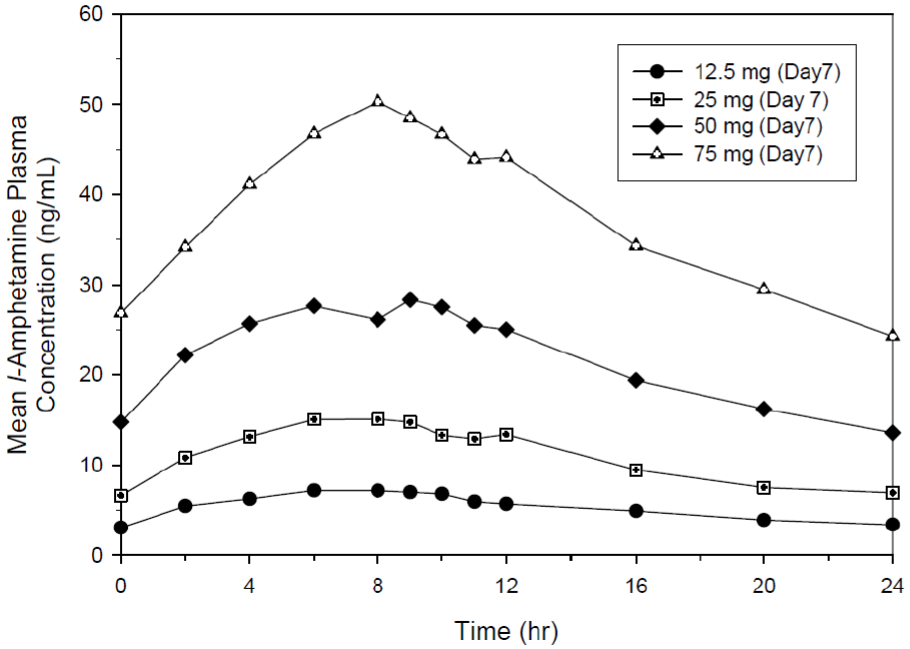


Figure 4. Mean *l*-Amphetamine Plasma Concentrations over Time after Seven Once-Daily Oral Doses of Mydayis in Healthy Adults (Shire Data on File SHP465-110)



Metabolism:

Vyvanse is a pro-drug and is converted to an active form via hydrolysis when it touches red blood cells. It is not dependent on the cytochrome P450 (CYP450) system for metabolism, leading to low metabolism variability and less need for higher/more frequent dosing.

Adderall XR is a mixture of 4 active amphetamine salts, with known metabolism via CYP2D6, leading to some possible metabolism variability in the population. There is not adequate evidence that doses greater than 20 mg/day confer additional benefit.

Mydayis is converted into its active forms, norphedrine and 4-hydroxy-amhetamine, the latter of which is formed via CYP2D6 metabolism. This may lead to some possible metabolism variability in the population. There is no evidence that doses beyond 50mg/day demonstrate additional clinical benefit.

Insomnia risk:

All amphetamine products cause insomnia. If this is an issue for your patient, you may want to consider a methylphenidate product which has between 2% and 5% occurrence of insomnia in clinical trials.

Vyvanse: 23% of adults and 13-23% of children in clinical trials reported insomnia.

Adderall XR: 27% of adults and 12-17% of children in clinical trials reported insomnia.

Mydayis: 31% of adults and 8% of adolescents in clinical trials reported insomnia.

References:

Vyvanse [package insert]. Lexington, MA: Shire US Inc; 2017

Adderall XR [package insert]. Lexington, MA: Shire US Inc; 2017

Mydayis [package insert] Lexington, MA Shire US, Inc 2017

Shari N. Allen (*2014*) Adderall XR® and Vyvanse™. Mental Health Clinician: January 2014, Vol. 4, No. 1, pp. 8-10. http://mhc.cpnp.org/doi/abs/10.9740/mhc.n186948 Accessed July 27, 2017