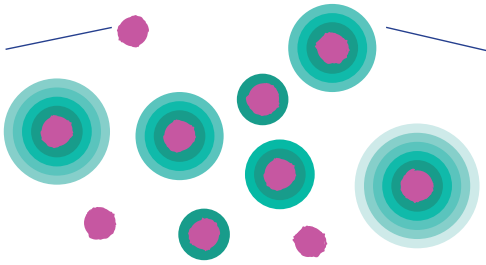
For the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older

Discover advanced drug delivery

Driven by diffusion[1,2]

DYANAVEL® XR
(amphetamine) extended-release
tablets 5 mg • 10 mg • 15 mg • 20 mg | oral suspension 2.5 mg/mL

Active drug bound to **uncoated** and **coated** carrier particles



Immediate release from **uncoated** particles

Extended release through **coatings** of various thicknesses for continuous diffusion

Continuous Release & Smooth PK Profile[1-3]

- ☐ AMP is released through ion-exchange and diffusion
- ☐ AMP complexed to micron-sized carrier particles
- ☐ XR particles have coatings of various thicknesses
- ☐ Drug takes longer to diffuse through thicker coatings; different thicknesses ensure drug releases continuously over time
- ☐ Each dose has millions of drug particle complexes

Consistent Delivery Under Variable Conditions[1-5]

- ☐ AMP is protected within coating until released in GI tract
- ☐ Coatings are non-degrading; not affected by chewing or gastric acid
- ☐ Diffusion not affected by food timing or type
- ☐ Diffusion not affected by where AMP is released in the GI tract
- ☐ Diffusion not affected by pH of GI tract

AMP = amphetamine

INDICATION

DYANAVEL® XR (amphetamine) is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older.

IMPORTANT SAFETY INFORMATION

WARNING: ABUSE, MISUSE, AND ADDICTION

DYANAVEL XR has a high potential for abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Misuse and abuse of CNS stimulants, including DYANAVEL XR, can result in overdose and death. Before prescribing DYANAVEL XR, assess each patient's risk for abuse, misuse, and addiction. Educate patients and their families about these risks, proper storage of the drug, and proper disposal of any unused drug. Throughout treatment, reassess each patient's risk and frequently monitor for signs and symptoms of abuse, misuse, and addiction.

Please see additional Important Safety Information on the next page and product Full Prescribing Information, including Boxed Warning regarding Abuse, Misuse, and Addiction.

To learn more, visit trisadhdhcp.com/dyanavel-xr-tablet

DYANAVEL® XR (II)
(amphetamine) extended-release
tablets 5 mg • 10 mg • 15 mg • 20 mg | oral suspension 2.5 mg/mL

IMPORTANT SAFETY INFORMATION (CONT'D)

- DYANAVEL® XR (amphetamine) is contraindicated:
  - in patients known to be hypersensitive to amphetamine, or other components of DYANAVEL XR. Hypersensitivity reactions, such as angioedema and anaphylactic reactions, have been reported with other amphetamines.
  - in patients taking monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOIs (including MAOIs such as linezolid or intravenous methylene blue), because of increased risk of hypertensive crisis.
- Sudden death has been reported in patients with structural cardiac abnormalities or other serious cardiac disease who were treated with CNS stimulants at the recommended ADHD doses. Serious cardiovascular effects with overdose may precipitate sudden cardiac death. Prior to treating patients with DYANAVEL XR, assess for the presence of cardiac disease. Avoid DYANAVEL XR use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmia, coronary artery disease, or other serious cardiac disease. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during DYANAVEL XR treatment.
- CNS stimulants cause increase in blood pressure (mean increase about 2 to 4 mm Hg) and heart rate (mean increase about 3 to 6 bpm). Monitor all patients for potential tachycardia and hypertension.
- Use of CNS stimulants may cause exacerbation of pre-existing psychosis and may induce a manic or mixed episode in patients with bipolar disorder. In patients without prior history of psychotic illness or mania, CNS stimulants may cause new psychotic or manic symptoms (e.g., hallucinations, delusional thinking, or mania) at the recommended dosage. Prior to initiating DYANAVEL XR treatment, screen patients for risk factors for developing a manic episode. If new psychotic or manic symptoms occur, consider discontinuing DYANAVEL XR.
- CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients with ADHD; monitor weight and height during treatment with DYANAVEL XR. Treatment may need to be interrupted in children not growing as expected.
- CNS stimulants, including DYANAVEL XR, are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; very rare sequelae include digital ulceration and/or soft tissue breakdown. Careful observation for digital changes is necessary during treatment with ADHD stimulants. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for DYANAVEL XR-treated patients who develop signs or symptoms of peripheral vasculopathy.
- Serotonin syndrome risk is increased when co-administered with serotonergic agents (e.g., SSRIs, SNRIs, triptans), MAOIs, and during overdosage situations. If it occurs, discontinue DYANAVEL XR and any concomitant serotonergic agents immediately, and initiate supportive treatment.
- CNS stimulants, including amphetamine, have been associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette's syndrome has also been reported. Before initiating DYANAVEL XR, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor DYANAVEL XR-treated patients for the emergence or worsening of tics or Tourette's syndrome and discontinue treatment if clinically appropriate.
- Most common adverse reactions observed with amphetamine products: dry mouth, anorexia, weight loss, abdominal pain, nausea, insomnia, restlessness, emotional lability, dizziness, and tachycardia. Based on limited experience with DYANAVEL XR in controlled trials, the adverse reaction profile of DYANAVEL XR appears similar to other amphetamine extended-release products. The most common (≥2% in the DYANAVEL XR group and greater than placebo) adverse reactions reported in the Phase 3 controlled study conducted in 108 patients with ADHD (aged 6 to 12 years) were: epistaxis (DYANAVEL XR 4%, placebo 0%), allergic rhinitis (4%, 0%) and upper abdominal pain (4%, 2%).
- DYANAVEL XR use during pregnancy may cause fetal harm. To monitor pregnancy outcomes in women exposed to DYANAVEL XR during pregnancy, healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Psychostimulants at 1-866-961-2388 or visiting online at **https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/othermedications/**.
- Because of the potential for serious adverse reactions in a breastfed infant, breastfeeding is not recommended during treatment with DYANAVEL XR.
- **To report SUSPECTED ADVERSE REACTIONS, contact Tris Pharma, Inc. at 1-732-940-0358 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**.

Please see Full Prescribing Information including Boxed Warning regarding Abuse, Misuse, and Addiction.

References: 1. Kando JC, King TR, Pardo A. A novel, modified release drug delivery technology containing amphetamine and methylphenidate ion-exchange complexes. Poster presented at: American Psychiatric Association Annual Meeting; May 1-3, 2021. **2.** Pardo A, Kando JC, King TR, et al. Single-dose pharmacokinetics of amphetamine extended-release tablets compared with amphetamine extended-release oral suspension. *CNS Spectrums.* 25(6): 774-781. https://doi.org/10.107/S1092852919001676. **3.** Cutler AJ, Childress AC, Pardo A, et al. Randomized, double-blind, placebo-controlled, fixed-dose study to evaluate the efficacy and safety of amphetamine extended-release tablets in adults with attention-deficit/hyperactivity disorder. *J Clin Psychiatry.* 2022;83(5):22m14438. **4.** Powell JJ, Greenfield SM, Thompson RP. Concentrations of metals in gastric juice in health and peptic ulcer disease. *Gut.*1992;33(12):1617-1620. **5.** Childress AC, Wigal SB, Brams MN, et al. Efficacy and safety of amphetamine extended-release oral suspension in children with attention-deficit/hyperactivity disorder. *J Child Adolesc Psycholpharmacol.* 2018;28(5):306-313.

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