

Marder negative factor (KarXT, -3.8; placebo, -1.8 [LSM difference, -2.0; 95% CI, -2.8 to -1.2;  $P < 0.0001$ ; Cohen's  $d$ , 0.42]), and CGI-S scores (KarXT, -1.1; placebo, -0.5 [LSM difference, -0.6; 95% CI, -0.8 to -0.4;  $P < 0.0001$ ; Cohen's  $d$ , 0.63]).

**Conclusions.** In pooled analyses from the EMERGENT trials, KarXT demonstrated statistically significant improvements across efficacy measures with consistent and robust effect sizes. These findings support the potential of KarXT to be first in a new class of medications to treat schizophrenia based on muscarinic receptor agonism and without any direct dopamine D<sub>2</sub> receptor blocking activity.

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## A Review of the Delivery Technologies used in Attention-Deficit/Hyperactivity Disorder Stimulant Medications

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**Introduction.** Multiple pharmaceutical technologies have been developed over the years and applied in the Attention-Deficit/Hyperactivity Disorder (ADHD) treatment space. While the base drugs are either the same or similar, these technologies lead to differences in the medications' properties – including mechanism of release, timing of active drug release, and pharmacokinetic profiles. The technology differences also bring up clinical considerations applicable to patients, including delayed- or extended-release properties so that once daily dosing can be achieved.

This review seeks to make side-by-side comparisons of the technical features of the different technologies used in ADHD medications, not an efficacy comparison. The publication will focus on stimulant medications that use methylphenidate or amphetamine formulations. Gaining an understanding of the technologies' properties and their implications will help clinicians to make more informed decisions when developing their patients' treatment plans to fit their individual needs, and potentially improve adherence.

**Methods.** Sources including published literature, company websites, filed patents, and prescribing information were reviewed to extract data on the technology used for different ADHD medications. The comparison of the technology in ADHD medications included the drug delivery system, mechanism of drug release, and technology components such as use of resins, beads, complexes, coating or layers. Special considerations that come from these properties were elucidated and framed into a broader clinical context.

**Results.** Although the medications evaluated were all stimulants containing methylphenidate or amphetamine as the active ingredient, they vary significantly in the technology used to deliver medication to patients. Differences in the technologies used to deliver the stimulants are significant and provide the platform to

meet individual patient needs. This side-by-side comparison, describing the specific features and benefits of each technology, will better inform prescribers, leading to better treatment of patients' ADHD.

**Conclusions.** Clarifying the technologies available among ADHD pharmacotherapies and discussing their implications on patient care may help healthcare professionals better understand the treatment landscape and assist them in clinical decision-making for appropriate ADHD treatment. Knowledge of the mechanism of the technology could improve patients' medication adherence. Additionally, understanding the applications of the technology could also benefit research and clinical programs.

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## Efficacy of Viloxazine ER (Qelbree) for ADHD in Adults Based on Prior Stimulant Exposure

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**Introduction.** Although many patients respond equally well to both stimulant and nonstimulant medications for ADHD, some patients respond preferentially to one class over another. Currently, most patients receive a stimulant as first-line therapy; however, nonstimulants present fewer obstacles for prescribers and patients and have low abuse/misuse potential. Still, when patients have suboptimal response to stimulants, physicians may be reticent to switch to a nonstimulant medication due to concerns that the nonstimulant response will be less robust or less preferable for patients. Viloxazine ER (viloxazine extended-release capsules; Qelbree®) is a nonstimulant, FDA-approved treatment for ADHD in children (≥6 years) and adults. This post-hoc analysis of adult Phase 3 trial data (NCT04016779) evaluates response to viloxazine ER (200-600 mg/day) based on whether or not patients reported a history of previous stimulant use.

**Methods.** For patients randomized to viloxazine in this Phase 3, double-blind, placebo-controlled trial, the change from baseline (CFB) in Adult ADHD Investigator Symptom Rating Scale (AISRS) score (primary trial outcome) was analyzed for prior stimulant users vs. nonusers using MMRM. Prior stimulant use was based on patient-reported medication history recorded upon enrollment. Subjects using stimulants at the time of study screening were required to undergo a ≥1-week washout period prior to randomization.

**Results.** Of 372 patients treated, 189 received viloxazine ER. Of the patients who received viloxazine ER, 40 reported prior stimulant use and 149 did not. Mean (SD) baseline AISRS scores for prior stimulant users and nonusers were 38.5 (7.40) and 38.3