Overview of Viloxazine ER (Qelbree®) Clinical Peer-Reviewed Publications

Phase 1	
QTC[1]	Supratherapeutic doses of viloxazine ER had no effect on cardiac repolarization or other ECG parameters in healthy adults.
DDI- MPH[2]	Coadministration of viloxazine ER (700 mg) and methylphenidate (36 mg) did not impact the PK of either drug; the combination was safe and well tolerated in healthy adults.
DDI- AMP[3]	Coadministration of viloxazine ER (700 mg) and lisdexamfetamine (50 mg) did not impact the PK of either drug; the combination was safe and well tolerated in healthy adults.
DDI-Paroxetine[4]	Coadministration of viloxazine ER (metabolized by CYP2D6) and paroxetine (a strong CYP2D6 inhibitor) had a minimal impact on viloxazine ER PK in healthy adults.
Bioavailability[5]	Viloxazine ER can be sprinkled or taken as whole capsule, with or without meals.
Pharmacokinetics[6]	Viloxazine ER is a strong CYP1A2 inhibitor and a weak CYP2D6 and CYP3A4 inhibitor.
Phase 2	
Dose Selection 812P202[7]	Viloxazine ER (200, 300, or 400 mg/day, fixed dose) significantly improved ADHD symptoms in children (6-12 yrs) in an 8-week, double-blind placebo-controlled study
Phase 3 Pivotal Trials	
Children- Low dose 812P301[8]	Viloxazine ER (100, 200 mg/day, fixed dose) significantly improved ADHD symptoms in children (6-11 yrs) in a 6-week, double-blind placebo-controlled study
Children- High dose 812P302[9]	Viloxazine ER (200, 400 mg/day, fixed dose) significantly improved ADHD symptoms in adolescents (12-17 yrs) in a 6-week, double-blind placebo-controlled study
Adolescent- Low dose 812P303[10]	Viloxazine ER (200, 400 mg/day, fixed dose) significantly improved ADHD symptoms in children (6-11 yrs) in an 8-week, double-blind placebo-controlled study
Adolescent- High dose 812P304[11]	Viloxazine ER (400 mg but not 600 mg/day, fixed dose) significantly improved ADHD symptoms in adolescents (12-17 yrs) in a 7-week, double-blind placebo-controlled study
Adult- Flexible Dose 812P306[12]	Viloxazine ER (200-600 mg/day, flexible dose) significantly improved ADHD symptoms (AISRS) in adults (18-65 yrs) in a 6-week, double-blind placebo-controlled study
Phase 3 Open Label Extension (OLE)	
Adult 812P311[13]	Open-label, long-term use of viloxazine ER (200-600 mg/day) in adults with ADHD was generally safe and well-tolerated, with no new safety findings.
Children & Adolescent 812P310*	Open-label, long-term use of viloxazine ER (200-400 mg/day) in children and adolescents with ADHD was generally safe and well-tolerated, with no new safety findings.
Phase 4	
Viloxazine ER + Stimulant Coadministration 812P412*	In children and adolescents with ADHD experiencing partial response to stimulants, viloxazine ER added to their regimen was safe and well-tolerated. As early as week 1, there was significant improvement in ADHD symptoms and sleep problems relative to baseline stimulant monotherapy.

Abbreviations: ER: Extended-release; **PK:** pharmacokinetics; **CYP:** CYP P450 enzymes; **ADHD:** Attention-deficit/hyperactivity disorder

References: 1. Nasser, A. J Clin Psychiatry. 2020;81(6): 20m13395. **2.** Faison, SL. *Clin Drug Investig.* 2021;41(2):149-159. **3.** Faison, SL. *J Clin Psychopharmacol.* 2021 Mar-Apr 01;41(2):155-162. **4.** Wang, Z. *Clin Pharmacol Drug Dev.* 2021;10(11): 1365-1374. **5.** Wang, Z. Eur J Drug Metab Pharmacokinet. 2022; 47(1):69-79. **6.** Wang, Z. *Clin Drug Investig.* 2024;44:303-317. **7.** Johnson, JK. *J Atten Disord*. 2020;24(2):348-358. **8.** Nasser, A. *Clin Ther.* 2020;42(8):1452-1466. **9.** Nasser, A. *J Clin Psychopharmacol.* 2021;41(4):370-380. **10.** Nasser, A. *Clin Ther.* 2021;43(4):684-700. **11.** Nasser, A. *Psychopharmacol Bull.* 2021;51(2):43-64. **12.** Nasser, A. *CNS Drugs.* 2022;36(8):897-915. **13.** Childress, A. *CNS Drugs.* 2024; https://doi.org/10.1007/s40263-024-01120-0. *Publication in final draft

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