Qelbree (viloxazine extended-release)

NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Qelbree
- **Generic name:** Viloxazine
- **Pharmacologic class:** Selective norepinephrine reuptake inhibitor (SNRI)
- **Strength and Formulation:** 100mg, 150mg, 200mg; extended-release capsules
- **Manufacturer:** Supernus Pharmaceuticals
- **How supplied:** Caps—30, 60, 90, 100
- **Legal Classification:** Rx

Indication

- Treatment of **attention deficit hyperactivity disorder (ADHD)** in pediatric patients 6 to 17 years of age.

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Dosage and Administration

- Assess heart rate and blood pressure prior to initiating treatment, following dose increases, and periodically during therapy.
- Screen patients for a personal or family history of suicide, bipolar disorder, and depression prior to initiating treatment.

Dosage and Administration

- Swallow whole or sprinkle contents of capsule onto a teaspoonful of applesauce and consume within 2 hours.
- **Patients 6 to 11 years of age**: Initially 100mg once daily; may titrate in increments of 100mg at weekly intervals to a maximum dose of 400mg once daily, based on response and tolerability.
- **Patients 12 to 17 years of age**: Initially 200mg once daily; after 1 week, may increase by an increment of 200mg to a maximum dose of 400mg once daily, based on response and tolerability.
- **Severe renal impairment (eGFR <30mL/min/1.73m^2)**: Initially 100mg once daily; may titrate in weekly increments of 50–100mg once daily to a maximum dose of 200mg once daily.

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Considerations for Specific Populations

- **Pregnancy:** May cause maternal harm; available data is insufficient to determine a drug-associated risk of major birth defects, miscarriage, or adverse maternal outcomes.
- **Nursing mothers:** No data on the presence of viloxazine in human milk, effects on breastfed infant, or effects on milk production; consider benefits of breastfeeding along with mother's clinical need and potential adverse effects.
- **Pediatric**: <6 years: not established.
- **Geriatrics**: Clinical trial did not include sufficient numbers to determine difference from younger patients.
- **Renal impairment**: Patients with severe renal impairment (eGFR <30mL/min/1.73 m^2): reduce dose (see *Dosage and Administration*).
- **Hepatic impairment**: Not recommended.

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Contraindications

- Concomitant use with **monoamine oxidase inhibitors** (MAOI) or within 14 days of discontinuing an MAOI (eg, selegiline, isocarboxazid, phenelzine, tranylcypromine, safinamide, rasagiline) because of an increased risk of hypertensive crisis.
- Concomitant use with **sensitive CYP1A2 substrates** or CYP1A2 substrates with a narrow therapeutic range (eg, alosetron, duloxetine, ramelteon, tasimelteon, tizanidine, theophylline).

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Warnings and Precautions

- Increased risk of suicidal thoughts and behavior in children (**Boxed Warning**).
- Closely monitor all patients for clinical worsening and emergence of suicidal thoughts/behaviors esp. during the first few months, and at times of dosage changes.
- Assess heart rate and blood pressure prior to initiating treatment, following dose increases, and periodically during therapy.
- Screen patients for a personal or family history of suicide, bipolar disorder, and depression prior to initiating treatment.
- Can cause somnolence and fatigue; caution with performing activities that require mental alertness.

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Interactions

- *Contraindicated* with MAOIs, sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range.
- *Potentiates moderate sensitive CYP1A2 substrates* (eg, clozapine, pirfenidone): not recommended.
- *Potentiates CYP2D6 substrates* (eg, atomoxetine, desipramine, dextromethorphan, nortriptyline, metoprolol, nebivolol, perphenazine, tolterodine, venlafaxine, risperidone) and CYP3A4 substrates (eg, alfentanil, avanafil, buspirone, conivaptan, darifenacin, darunavir, ebastine, everolimus, ibrutinib, lomitapide, lovastatin, midazolam, naloxegol, nisoldipine, saquinavir, simvastatin, sirolimus, tacrolimus, tipranavir, triazolam, vardenafil, lurasidone); monitor and adjust dose of substrates as clinically indicated.

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Adverse Reactions

- **Most common** (≥5% and at least twice the rate of placebo): Somnolence, decreased appetite, fatigue, nausea, vomiting, insomnia, irritability.
- **Others**: Increased blood pressure, increased heart rate, mania/hypomania.

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Mechanism of Action

- The mechanism of action of **viloxazine** in the treatment of ADHD is unclear; however, it is thought to be through inhibiting the reuptake of norepinephrine.

Pharmacokinetics

- **Absorption**: Median time to peak plasma concentration is ~5 hours (range, 3-9 hours), following a single 200mg dose.
- **Effect of food**: Administration of viloxazine 200mg with a high-fat meal decreased C_{max} and AUC by about 9% and 8%, respectively; T_{max} increased by about 2 hours. Sprinkling contents of capsule on applesauce decreased C_{max} and AUC by about 10% and 5%, respectively.
- **Metabolism**: CYP2D6, UGT1A9, and UGT2B15.
- **Excretion**:
  - Mean (± SD) half-life: 7.02 hours ± (4.74 hours).
  - Renal excretion is the primary route.

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Clinical Trials

- Approval was based on 3 short-term, randomized, placebo-controlled monotherapy trials (Studies 1, 2, and 3) that evaluated the efficacy and safety of Qelbree in pediatric patients 6 to 17 years of age with ADHD.
- In Study 1, patients were randomly assigned to receive Qelbree 100mg, 200mg, or placebo once daily.
- In Studies 2 and 3, patients were randomly assigned to receive Qelbree 200mg, 400mg, or placebo once daily.

Clinical Trials

- The **primary endpoint** for all studies was the change from baseline to the end of the study on the total score on the ADHD Rating Scale (ADHD-RS-5), an 18- question scale that assesses hyperactivity, impulsivity, and inattentive symptoms.
- The key **secondary endpoint** was the Clinical Global Impression-Improvement (CGI-I) score.

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Clinical Trials

- Findings from all 3 studies showed that treatment with Qelbree led to statistically significantly greater reductions in ADHD-RS-5 total score compared with placebo.
- A statistically significantly greater reduction in CGI-I score was also observed in patients treated with Qelbree compared with placebo.

Clinical Trials

Primary Efficacy Measure: ADHD-RS-5 Total Score				
Study Number (Age range)	Treatment Group	Mean Baseline Score (SD)	Least-Squares Mean Change from Baseline (Standard Error)	Placebo-subtracted Difference (95% CI)
Study 1 (6 to 11 years)	100mg/day	45.0 (6.53)	-16.6 (1.16)	-5.8 (-8.9, -2.6)
	200mg/day	44.0 (6.80)	-17.7 (1.12)	-6.9 (-10.0, -3.8)
	Placebo	43.6 (7.05)	-10.9 (1.14)	--
Study 2 (6 to 11 years)	200mg/day	43.8 (6.54)	-17.6 (1.43)	-6.0 (-10.0, -1.9)
	400mg/day	45.0 (6.55)	-17.5 (1.52)	-5.8 (-9.9, -1.7)
	Placebo	43.5 (6.79)	-11.7 (1.48)	--
Study 3 (12 to 17 years)	200mg/day	39.9 (7.22)	-16.0 (1.45)	-4.5 (-8.4, -0.6)
	400mg/day	39.4 (7.59)	-16.5 (1.38)	-5.1 (-8.9, -1.3)
	Placebo	40.5 (6.79)	-11.4 (1.37)	--

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New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/qelbree/