- **Thank you for the opportunity to make a few comments regarding Qelbree.**
- *Please Refer to complete Prescribing Information for full product details:*
  https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aedf408d-0f84-418d-9416-7c39ddb0d29a

- **WARNING: SUICIDAL THOUGHTS AND BEHAVIORS In clinical studies, higher rates of suicidal thoughts and behaviors were reported in pediatric patients with ADHD treated with Qelbree than in patients treated with placebo. Closely monitor all Qelbree-treated patients for clinical worsening and for emergence of suicidal thoughts and behaviors.**

- While there (31) drugs approved for the treatment of ADHD, all but 3 of them are formulations of just 2 stimulant molecules, methylphenidate and amphetamine.[1]
- The diagnosis of ADHD in children is complex, and patients require more than just new stimulant delivery systems. Moreover, there are only 3 FDA nonscheduled options with two of these medicines with similar mechanisms of action. Physicians have indicated there is need for additional nonscheduled options.[1]
- Whether for considerations of stimulant abuse and diversion, patient intolerance to stimulants or nonstimulants, or inability to swallow pills, Qelbree offers an important option for the treatment of ADHD.[1-4]
- Qelbree is a new chemical entity, nonscheduled, once-daily medication approved by the FDA in April of last year for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6-17 years of age.[5]
- Qelbree is a new molecular entity (NME) and is the first NME approved for ADHD in over 10 years[5-6]
- 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. Additional data from animal models and *in vitro* research suggests that viloxazine increases dopamine, norepinephrine, and serotonin in the prefrontal cortex. The increase in serotonin is not through reuptake inhibition, but through other mechanisms. This combined pharmacology makes viloxazine distinct from any FDA medicine used to treat ADHD.[5-6]
- The most common adverse reactions (≥ 5% and at least twice the rate of placebo for any dose) were somnolence, decreased appetite, fatigue, nausea, vomiting, insomnia, and irritability.[5]
- Qelbree is contraindicated with monoamine oxidase inhibitors and sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range.[5]
- Warnings and Precautions with Qelbree: possible effect on blood pressure and heart rate; activation of mania or hypomania; potential somnolence and fatigue.[5]
- Additional clinical data that indirectly highlight areas unique to Qelbree that differentiate it from Strattera:
  - No evidence of hepatic injury as evidenced by minimal AST and ALT elevations in liver enzymes across all trials. No drug-Induced Liver Injury (DILI). [5, 8]
  - Qelbree has multiple metabolic routes of elimination and is unlikely to have an interaction with other drugs metabolized by CYP2D6. Strattera has warnings for concomitant use of potent CYP2D6 inhibitors.[5, 13]
  - Phenotypic CYP2D6 metabolizer status appears to have only a minimal impact on Qelbree metabolism with only a 1.5-fold increase in poor metabolizers vs. extensive metabolizers. Poor metabolizers using Strattera may have a 10-fold higher AUC and a 5-fold higher Cmax.[5,8, 13]
  - Qelbree has minimal impact on the cardiovascular system, with supratherapeutic doses producing no clinically significant effects on cardiac repolarization or other ECG parameters in healthy adults, suggesting that it is not associated with a risk for cardiac arrhythmias. Sudden death, stroke, and myocardial infarction have been reported in associated with Strattera treatment [8-9,13]
  - Medication adherence can also be negatively impacted due to pill swallowing difficulties. Qelbree is the only non-stimulant that is designed to be swallowed whole or the capsules can be opened and sprinkled on a spoonful of soft food.

For these reasons we ask for Qelbree to be added to the preferred drug list.

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