QELBREE®

——— DOSAGE AND ADMINISTRATION ————

older (1)

Qelbree is a selective norepinephrine reuptake inhibitor indicated for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older.

2.1 Important Considerations Prior to Initiating Treatment

Prior to initiating treatment with Qelbree, screen patients for a personal or family history of suicide, bipolar disorder, and depression [see Warnings and Precautions (5.3)].

2.2 Recommended Dosage

Pediatric patients

The recommended starting dosage for pediatric patients 6 to 11 years of age is 100 mg orally once daily. Dosage may be titrated in increments of 100 mg daily, depending on response and tolerability.

Adult patients

The recommended starting dosage for adults is 200 mg orally once daily. Dosage may be titrated in increments of 100 mg weekly to the maximum recommended dosage of 600 mg once daily (2.4, 8.6).

2.3 Administration Information

In clinical studies, higher rates of suicidal thoughts and behavior were reported in patients treated with Qelbree than in patients treated with placebo. Closely monitor for worsening and emergence of suicidal thoughts and behaviors (5.1).

2.4 Recommended Dose

Initiate dosage as follows:

- Pediatric patients 6 to 11 years of age: Recommended starting dosage is 100 mg once daily. May titrate in increments of 100 mg weekly to the maximum recommended dosage of 400 mg once daily (2.2).
- Pediatric patients 12 to 17 years of age: Recommended starting dosage is 200 mg once daily. May titrate after 1 week, by an increment of 200 mg, to the maximum recommended dosage of 400 mg once daily (2.2).
- Adult patients: Recommended starting dosage is 200 mg once daily. May titrate in increments of 200 mg weekly, to maximum recommended dosage of 600 mg once daily (2.2).

2.5 Dosing in Specific Populations

- Patients with Renal Impairment: Dose reduction may be warranted (7.1).

3. DOSAGE FORMS AND STRENGTHS

Extended-release capsules: 100 mg, 150 mg, and 200 mg (3).

4. CONTRAINDICATIONS

- Concomitant administration of monoamine oxidase inhibitors (MAOIs), or dosing within 14 days after discontinuing an MAOI (4, 7.1).
- Concomitant administration of sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range (4, 7.1).

5. WARNINGS AND PRECAUTIONS

- Blood Pressure and Heart Rate Increases: Assess heart rate and blood pressure prior to initiating treatment, following increases in dosage, and periodically while on therapy (5.2).
- Activation of Mania or Hypomania: Screen patients for bipolar disorder (5.3).
- Somnolence and Fatigue: Advise patients to use caution when driving or operating hazardous machinery due to potential somnolence (including sedation and lethargy) and fatigue (5.4).

6. ADVERSE REACTIONS

Most commonly observed adverse reactions (≥5% and at least twice the rate of placebo) were:

- Pediatric patients 6 to 17 years of age: somnolence, decreased appetite, fatigue, nausea, vomiting, insomnia, and irritability (6.1).
- Adult patients: insomnia, headache, somnolence, fatigue, nausea, decreased appetite, dry mouth and constipation (6.1).

8. USE IN SPECIFIC POPULATIONS

- Pregnancy: May cause maternal harm; discontinue when pregnancy is recognized (8.1).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

* Sections or subsections omitted from the full prescribing information are not listed.
In pediatric patients 12 to 17 years of age, 52/205 (25%) of patients treated with Qelbree had a ≥20 bpm increase in heart rate at any time point in the clinical trial, compared to 3% of placebo-treated patients. Table 1 data reflect exposure to Qelbree in 826 pediatric patients (6 to 17 years) who participated in randomized, double-blind, placebo-controlled trials with doses ranging from 100 mg to 400 mg. The population (N=826) was 65% male, 35% female, 54% White, 41% Black, 3% multiracial, and 1% other races.

Adverse Reactions Leading to Discontinuation of Qelbree Treatment Approximately 3% (n=27) of 826 patients receiving Qelbree in clinical studies discontinued treatment due to an adverse reaction. The adverse reactions most commonly associated with discontinuation of Qelbree were somnolence (n=5), nausea (n=3), headache (n=2), irritability (n=2), tachycardia (n=2), fatigue (n=2), and decreased appetite (n=2).

Most Common Adverse Reactions occurring at ≥2% and at least twice the placebo rate for any dose: somnolence, decreased appetite, fatigue, nausea, vomiting, insomnia, and irritability.

Table 1 lists adverse reactions that occurred in at least 2% of patients treated with Qelbree and more frequently in Qelbree-treated patients than in placebo-treated patients. Table 1 data also reflects pooled data from pediatric patients 6 to 17 years of age who were enrolled in randomized, placebo-controlled trials of Qelbree.
Effects on Weight: In short-term, controlled studies (6 to 8 weeks), Qelbree-treated patients 6 to 11 years of age gained an average of 0.2 kg, compared to a gain of 1 kg in same-aged patients who received placebo. Qelbree-treated patients 12 to 17 years of age lost an average of 0.2 kg, compared to a weight gain of 1.5 kg in same-aged patients who received placebo. In a long-term, open-label extension safety trial, 197 patients received at least 1 dose of Qelbree. Among the 338 patients evaluated at 12 months, the mean change from baseline in weight-for-age z-score was -0.2 (standard deviation of 0.5). In the absence of a control group, it is unclear whether the weight change observed in the long-term open-label extension was attributable to the effect of Qelbree.

Adults
The data described below reflect exposure to Qelbree in 189 adults with ADHD who participated in the flexible-dose, randomized, double-blind, placebo-controlled trial with doses ranging from 200 mg to 600 mg. The population (N=189) was 56% male, 44% female, 81% White, 12% Black, 3% Asian, 3% other races and 1% multiracial.

Adverse Reactions Leading to Discontinuation of Qelbree Treatment: Approximately 9% of the 189 patients receiving Qelbree in clinical studies discontinued treatment due to an adverse reaction. The adverse reactions most commonly associated with discontinuation of Qelbree were nausea, headache, somnolence, fatigue, constipation, and dry mouth.

Most Common Adverse Reactions (occurring at ≥5% and at least twice the placebo rate of Qelbree): insomnia, headache, somnolence, fatigue, nausea, decreased appetite, dry mouth, and constipation.

Table 2 lists adverse reactions that occurred in at least 2% of patients treated with Qelbree and more frequently in Qelbree-treated patients than in placebo-treated patients. Table 2 represents data from adults with ADHD who were enrolled in a flexible-dose, randomized, placebo-controlled trial of Qelbree at doses of 200 mg to 600 mg.

Table 2: Adverse Reactions Reported in ≥2% of Adults Treated with Qelbree and at a Rate Greater than Placebo-Treated Patients in a Flexible-Dose Placebo-Controlled ADHD Study

<table>
<thead>
<tr>
<th>Body System</th>
<th>Adverse Reaction</th>
<th>Placebo (N=183) (%)</th>
<th>Qelbree (200 mg to 600 mg) N=189 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric disorders</td>
<td>Insomnia</td>
<td>7</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Irritability</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headache</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Somnolence</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Gastrointestinal system disorders</td>
<td>Nausea</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Dry mouth</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Gastroesophageal reflux disease</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Body as a Whole - General disorders</td>
<td>Fatigue</td>
<td>3</td>
</tr>
<tr>
<td>Metabolic and nutritional disorders</td>
<td>Decreased appetite</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td>Tachycardia</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

The following terms were combined:

Somnolence: somnolence, lethargy, sedation
Headache: headache, migraine, migraine with aura, tension headache
Insomnia: initial insomnia, insomnia, middle insomnia, poor quality sleep, sleep disorder, terminal insomnia

7. DRUG INTERACTIONS

7.1 Drugs Having Clinically Important Drug Interactions with Qelbree

Table 3: Clinically Important Drug Interactions with Qelbree

<table>
<thead>
<tr>
<th>Monamine Oxidase Inhibitors (MAOI)</th>
<th>Clinical Impact</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concomitant use of Qelbree with an MAOI may lead to a potentially life-threatening hypertensive crisis.</td>
<td>Concomitant use of Qelbree with an MAOI or within 2 weeks after discontinuing an MAOI is contraindicated [see Contraindications (4)].</td>
<td></td>
</tr>
</tbody>
</table>

Sensitive CYP1A2 Substrates or CYP1A2 Substrates with a Narrow Therapeutic Range

Clinical Impact: Viloxazine is a strong CYP1A2 inhibitor. Concomitant use of viloxazine significantly increases the total exposure, but not peak exposure, of sensitive CYP1A2 substrates [see Clinical Pharmacology (12.3)], which may increase the risk of adverse reactions associated with these CYP1A2 substrates.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry
There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed Qelbree during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Psychiatric Medications at 1-866-961-2388 or visiting online at www.womensmentalhealth.org/preg.

Risk Summary
Based on findings from animal reproduction studies, viloxazine may cause maternal harm when used during pregnancy. Discontinue Qelbree when pregnancy is recognized unless the benefits of therapy outweigh the potential risk to the mother. Available data from case series with viloxazine use in pregnant women are insufficient to determine a drug-associated risk of major birth defects, miscarriage or adverse maternal outcomes.

In animal reproduction studies, oral administration of viloxazine during the period of organogenesis caused fetal toxicities and delayed fetal development in the rat and maternal toxicities in the rabbit at doses approximately equal to the maximum recommended human dose (MRHD) of 600 mg in adults, based on mg/m². Oral administration of viloxazine to pregnant rats and mice during pregnancy and lactation caused maternal toxicities and deaths and fetal toxicities at doses equal to or less than the MRHD of 600 mg in adults, based on mg/m², respectively (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnant women have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data
Viloxazine was administered orally to pregnant rats during the period of organogenesis at doses of 13, 33, and 82 mg/kg/day. The high dose is approximately equal to the MRHD of 600 mg in adults, based on mg/m². Viloxazine did not cause maternal toxicity up to the high dose. Viloxazine at the high dose induced early and late resorption, delayed fetal development, and possibly caused low incidences of fetal malformations or anomalies (craniorachischisis, missing cervical vertebrae, and morphological changes associated with hydranencephaly). The NOAEL for fetal toxicity and malformation is 33 mg/kg/day, which is less than the MRHD of 600 mg in adults, based on mg/m².

Viloxazine was administered orally to pregnant rabbits during the period of organogenesis at doses of 43, 87, and 217 mg/kg/day, which are approximately 1, 3, and 4 times the MRHD of 600 mg in adults, based on mg/m². Viloxazine caused maternal toxicity of decreased body weight, weight gain, and food consumption at doses ≥ 87 mg/kg/day but did not cause fetal toxicity at doses up to 130 mg/kg/day. The NOAELs for maternal and fetal toxicity are 43 mg/kg/day and 130 mg/kg/day, respectively, which is approximately 1 and 4 times the MRHD, based on mg/m², respectively. Viloxazine was administered orally to pregnant rats during gestation and lactation at doses of 43, 87, and 217 mg/kg/day, which are less than, equal to, and 4 times the MRHD of 600 mg in adults, based on mg/m², respectively. Viloxazine caused maternal toxicity of decreased body weight, weight gain, and food consumption at doses ≥ 87 mg/kg/day and maternal deaths near term at 217 mg/kg/day. At these maternally toxic doses, viloxazine caused lower live birth, decreased viability, and delayed growth and sexual maturation without affecting learning and memory in the offspring. The NOAEL for maternal and developmental toxicity is 43 mg/kg/day, which is less than the MRHD of 600 mg in adults, based on mg/m².

Viloxazine was administered orally to pregnant mice during gestation and lactation at doses of 13, 33, and 82 mg/kg/day, which are less than the MRHD of 600 mg in adults, based on mg/m². Viloxazine treatment at 82 mg/kg/day during the gestation period caused maternal deaths and decreased body weight and food consumption in the offspring. The NOAEL for both maternal and developmental toxicity is 33 mg/kg/day, which is less than the MRHD of 600 mg in adults, based on mg/m².

8.2 Lactation

Risk Summary
There are no data on the presence of viloxazine in human milk, the effects on the breastfed infant, or the effects on milk production. Viloxazine is likely present in rat milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Qelbree and any potential adverse effects on the breastfed child from Qelbree or from the underlying maternal condition.

8.4 Pediatric Use
The safety and effectiveness of Qelbree in pediatric patients 6 to 17 years of age with ADHD have been established based on randomized, placebo-controlled studies in pediatric patients [see Adverse Reactions (6.1) and Clinical Studies (14)].
The safety and effectiveness of Qelbree have not been established in pediatric patients younger than 6 years old.

Patients treated with Qelbree should be monitored for suicidal thoughts and behavior [see Warnings and Precautions (5.1)] and for changes in weight [see Adverse Reactions (6.1)].

Juvenile Animal Toxicity Data
Viloxazine was administered orally to juvenile rats from postnatal day (PND) 23 through PND 79 at doses of 45, 130, and 217 mg/kg/day, which are approximately 1, 2, and 3 times the MRHD of 400 mg in children, based on mg/m², respectively. Viloxazine decreased body weight, weight gain, and food consumption in both sexes at 217 mg/kg/day. Sexual maturation, reproductive capacity, and learning and memory were not affected. The NOAE for juvenile toxicity is 130 mg/kg/day, which is approximately 2 times the MRHD of 400 mg in children, based on mg/m².

8.5 Geriatric Use
Clinical trials of Qelbree in the treatment of ADHD did not include sufficient numbers of patients aged 65 and older to determine whether or not they respond differently from younger patients.

8.6 Renal Impairment
Dosage reduction is recommended in patients with severe (eGFR of < 30 mL/min/1.73m² [MDRD]) renal impairment [see Dosage and Administration (2.4)].

No dosage adjustment of Qelbree is recommended in patients with mild to moderate (eGFR of 30 to 89 mL/min/1.73m² [MDRD]) renal impairment.

The exposure of viloxazine increases in patients with renal impairment [see Clinical Pharmacology (12.3)].

10 OVERDOSAGE
Human Experience
The pre-market clinical trials with Qelbree do not provide information regarding symptoms of overdose.

Literature reports from post marketing experience with immediate-release viloxazine include cases of overdose from 1000 mg to 6500 mg (1.7 to 10.8 times the maximum recommended daily dose). The most reported symptom was drowsiness. Impaired consciousness, diminished reflexes, and increased heart rate have also been reported.

Treatment and Management
There is no specific antidote for Qelbree overdose. Administer symptomatic and supportive treatment as appropriate. In case of overdose, consult a Certified Poison Control Center (1-800-222-1222 or www.poison.org).

11 DESCRIPTION
Qelbree contains viloxazine, a selective norepinephrine reuptake inhibitor, in the form of viloxazine hydrochloride which is (±)-2-[(2-ethoxyphenoxy)methyl]morpholine hydrochloride. The molecular formula is C₂₁H₂₆ClNO₂ and its molecular weight is 273.8 (HCl salt) with the following structural formula:

\[
\text{CH}_3\text{H}_2\text{N}-\text{CH}-(\text{CHOH})_2\text{CH}-(\text{CHOH})_2\text{CH}-(\text{Cl})\text{NO}_2
\]

Viloxazine hydrochloride is a white to off-white powder. Viloxazine hydrochloride is soluble in water, 0.1N HCl and aqueous solutions of pH 9.5 and lower. Viloxazine hydrochloride is sparingly soluble in methanol, very slightly soluble in acetonitrile, acetic acid and isopropyl alcohol, and practically insoluble in ethyl acetate.

Qelbree extended-release capsules are intended for oral administration. Each extended-release capsule contains 100 mg, 150 mg, and 200 mg of viloxazine free base equivalent to 115mg, 175mg, and 231mg, respectively, of viloxazine hydrochloride salt.

The inactive ingredients are: Ammonium hydroxide, black iron oxide, butyl alcohol, corn starch, ethylcellulose, FD&C Blue #1, FD&C Red #28, FD&C Yellow #5, FD&C Yellow #6, FD&C Yellow #10, gelatin, hypromellose, isopropyl alcohol, lactose monohydrate, medium chain triglycerides, oleic acid, polyethylene glycol, potassium hydroxide, propylene glycol, shellac, strong ammonia solution, sucrose, t alc, triacetin, titanium dioxide.

12 CLINICAL PHARMACOLOGY
12.1 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.

12.2 Pharmacodynamics
Viloxazine binds to the norepinephrine transporter (NET, K_i=0.63 mM) and inhibits the reuptake of norepinephrine (IC₅₀=0.2 µM).

Cardiac Electrophysiology
At a dose 3 times the maximum recommended dose, Qelbree did not prolong the QT interval to any clinically relevant extent. There was no effect of Qelbree on the PR interval or QRS duration in healthy volunteers. However, nonclinical studies suggest the potential for Qelbree to inhibit cardiac sodium channels.

12.3 Pharmacokinetics
Viloxazine C_max and AUC increase proportionally over a dosage range from 100 mg to 600 mg once daily. Steady-state was reached after two days of once-daily administration, and no accumulation was observed.

Absorption
The relative bioavailability of viloxazine extended-release relative to an immediate-release formulation was about 88%. The median (range) time to peak plasma concentration of viloxazine (T_max) was approximately 5 hours, with a range of 3 to 9 hours, following a single 200 mg dose.

Effect of Food
Administration of 200 mg viloxazine extended-release with a high-fat meal (800 to 1000 calories) decreased viloxazine C_max and AUC by about 9% and 8%, respectively. Viloxazine T_max increased by about 2 hours after administration with a high-fat meal. Sprinkling the contents of a capsule on applesauce decreased viloxazine C_max and AUC by about 10% and 5%, respectively.

Distribution
Viloxazine is 76-82% bound to human plasma proteins over the blood concentration range of 0.5 mcg/mL to 10 mcg/mL.

Elimination
The mean (± SD) half-life of viloxazine was 7.02 ± 4.74 hours.

12.4 Effect of Other Drugs on Viloxazine Pharmacokinetics

CYP2D6 Metabolism
A multiple-dose study was conducted with Qelbree 900 mg once-daily in healthy volunteers to compare the effect of CYP2D6 poor metabolizers (PMs) and extensive metabolizers (EMs) on the PK of viloxazine. At steady state, viloxazine geometric means for C_max and AUC₀₋₂₄ were 21% and 26%, respectively, higher in CYP2D6 PMs compared to EMs.

Drug Interaction Studies
Alcohol: There was no significant effect on viloxazine C_max and AUC when 200 mg viloxazine ER was administered with orange juice containing 4% and 20% alcohol. However, when administered with orange juice containing 40% alcohol, C_max and AUC of viloxazine decreased by about 32% and 19%, respectively. The effect of other drugs on the pharmacokinetics of viloxazine is presented in Figure 2.

Figure 2: Effects of Other Drugs on Viloxazine Pharmacokinetics

The effect of viloxazine on the pharmacokinetics of other drugs is presented in Figure 3 [see Drug Interactions (7.1)].
A total of 477 patients were randomized in Study 1; 399 completed the study, and 78 discontinued. The change from baseline (reduction) in ADHD-RS-5 total score was statistically significantly greater in patients treated with Qelbree 200 mg or with Qelbree 400 mg than in patients on placebo (see Table 4). Compared with patients on placebo, a statistically significantly greater reduction (improvement) in CGI-I score at the end of the study was observed both in patients treated with Qelbree 200 mg and in patients treated with Qelbree 400 mg.

### Table 5. Primary Efficacy Results for Change from Baseline AISR S Total Score in Adults (18 to 60 years of age) with ADHD (Study 4)

<table>
<thead>
<tr>
<th>Study Number (Population)</th>
<th>Treatment Group</th>
<th>n Mean Baseline Score (SD)</th>
<th>LS Mean Change from Baseline (SE)</th>
<th>Placebo-subtracted Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 4 (Adults)</td>
<td>Qelbree</td>
<td>200 mg to 600 mg</td>
<td>175</td>
<td>38.5 (6.56)</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>179</td>
<td>37.9 (6.62)</td>
<td>-11.7 (0.90)</td>
</tr>
</tbody>
</table>
| AISR S: Attention-Deficit/Hyperactivity Disorder Investigator Symptom Rating Scale; n: sample size; SD: standard deviation; SE: standard error; LS Mean: least-squares mean; CI: confidence interval, not adjusted for multiple comparisons
* Difference (drug minus placebo) in least-squares mean change from baseline
† Treatment is statistically significantly superior to placebo

## 16 HOW SUPPLIED/STORAGE AND HANDLING

**How Supplied**

Qelbree (viloxazine extended-release capsules) are available in the following strengths and colors:

- 100 mg (yellow capsule printed with "SPN" on capsule cap and “100” on capsule body with edible black ink).

**Bottles of**

- 100 capsules: NDC 17772-131-01
- 90 capsules: NDC 17772-131-90
- 60 capsules: NDC 17772-131-60
- 30 capsules: NDC 17772-131-30

**150 mg (lavender capsule printed with "SPN" on capsule cap and “150” on capsule body with edible black ink).**

**Bottles of**

- 100 capsules: NDC 17772-132-01
- 90 capsules: NDC 17772-132-90
- 60 capsules: NDC 17772-132-60
- 30 capsules: NDC 17772-132-30
200mg (light green capsule printed with “SPN” on capsule cap and “200” on capsule body with edible black ink).
Bottles of 100 capsules NDC 17772-133-01
Bottles of 90 capsules NDC 17772-133-90
Bottles of 60 capsules NDC 17772-133-60
Bottles of 30 capsules NDC 17772-133-30

Storage and Handling
Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F).

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Suicidal Thoughts and Behaviors
Advise patients and caregivers to monitor for the emergence of suicidal thoughts or behaviors or symptoms that might be precursors to emerging suicidal ideation or behavior, especially early during treatment and when the dosage is adjusted up or down. Instruct patients and caregivers to report such symptoms to the healthcare provider [see Boxed Warning and Warnings and Precautions (5.1)].

Concomitant Use with Monoamine Oxidase Inhibitors (MAOI)
Caution patients about the concomitant use of Qelbree and monoamine oxidase inhibitors (MAOIs), or within 14 days after discontinuing an MAOI, because of an increased risk of hypertensive crisis [see Contraindications (4) and Drug Interactions (7.1)].

Blood Pressure and Heart Rate Increases
Instruct patients that Qelbree can cause elevations of their blood pressure and pulse rate and they should be monitored for such effects [see Warnings and Precautions (5.2)].

Activation of Mania/Hypomania
Advise patients and their caregivers to look for signs of activation of mania/hypomania [see Warnings and Precautions (5.3)].

Somnolence and Fatigue
Advise patients about the potential for somnolence (including sedation and lethargy) and fatigue. Advise patients to use caution when performing activities requiring mental alertness, such as driving a motor vehicle or operating hazardous machinery, until they know how they will be affected by Qelbree [see Warnings and Precautions (5.4)].

Effects on Weight
Advise patients and their caregivers that Qelbree may affect weight and that weight should be monitored while using Qelbree [see Adverse Reactions (6.1)].

Pregnancy
Advise patients that there is a pregnancy registry that monitors pregnancy outcomes in women exposed to Qelbree during pregnancy. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy to discuss if Qelbree should be discontinued [see Use in Specific Populations (8.1)].

Administration Instructions
Advise patients to take the capsule whole or sprinkled over a teaspoonful or tablespoonful of applesauce or pudding and consume within 15 minutes when mixed with pudding or within 2 hours when mixed with applesauce. Do not cut, chew or crush the capsule [see Dosage and Administration (2.3)].

Qelbree is manufactured by: Catalent Pharma Solutions, LLC, 1100 Enterprise Drive Winchester, KY 40391.

Distributed by: Supernus Pharmaceuticals, Inc. Rockville, MD 20850 USA

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