QUILLIVANT XR- methylphenidate hydrochloride suspension, extended release
NextWave Pharmaceuticals, Inc

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use QUILLIVANT XR® safely and effectively.
See full prescribing information for QUILLIVANT XR®.
QUILLIVANT XR® (methylphenidate hydrochloride) for extended-release oral suspension, CII
Initial U.S. Approval: 1955

WARNING: ABUSE, MISUSE, AND ADDICTION

See full prescribing information for complete boxed warning.

QUILLIVANT XR has a high potential for abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Misuse and abuse of CNS stimulants, including QUILLIVANT XR, can result in overdose and death (5.1, 9.2, 10):

- **Before prescribing QUILLIVANT XR, assess each patient's risk for abuse, misuse, and addiction.**
- **Educate patients and their families about these risks, proper storage of the drug, and proper disposal of any unused drug.**
- **Throughout treatment, reassess each patient's risk and frequently monitor for signs and symptoms of abuse, misuse, and addiction.**

RECENT MAJOR CHANGES

Indications and Usage (1)	09/2025
Warnings and Precautions (5.7)	09/2025

INDICATIONS AND USAGE

QUILLIVANT XR is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). (1)

Limitations of Use

The use of QUILLIVANT XR is not recommended in pediatric patients younger than 6 years of age because they had higher plasma exposure and a higher incidence of adverse reactions (e.g., weight loss) than patients 6 years and older at the same dosage (5.7, 8.4).

DOSAGE AND ADMINISTRATION

- Before administering the dose, vigorously shake bottle for at least 10 seconds. (2.2)
- May be taken with or without food. (2.3)
- For patients 6 years and above, recommended starting dose is 20 mg given orally once daily in the morning. Dosage may be increased weekly in increments of 10 mg to 20 mg per day. Daily dosage above 60 mg is not recommended. (2.2)
- Reconstitution instructions for the pharmacist: Tap bottle until powder flows freely. Remove bottle cap, add specified amount of water for reconstitution. Insert bottle adapter into neck of bottle. Replace bottle cap. Shake with vigorous back and forth motion for at least 10 seconds to prepare suspension. (2.6)

DOSAGE FORMS AND STRENGTHS

Extended-release oral suspension (after reconstitution with water): 25 mg per 5 mL (5 mg per mL). (3)

CONTRAINDICATIONS

- Known hypersensitivity to methylphenidate or product components. (4.1)
- Concurrent treatment with a monoamine oxidase inhibitor (MAOI), or use of an MAOI within the preceding 14 days. (4.2, 7.1)

WARNINGS AND PRECAUTIONS

- *Risks to Patients with Serious Cardiac Disease:* Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmias, coronary artery disease, or other serious cardiac disease. (5.2)
- *Increased Blood Pressure and Heart Rate:* Monitor blood pressure and pulse. (5.3)

- *Psychiatric Adverse Reactions:* Prior to initiating QUILLIVANT XR, screen patients for risk factors for developing a manic episode. If new psychotic or manic symptoms occur, consider discontinuing QUILLIVANT XR. (5.4)
- *Priapism:* If abnormally sustained or frequent and painful erections occur, patients should seek immediate medical attention. (5.5)
- *Peripheral Vasculopathy, including Raynaud's Phenomenon:* Careful observation for digital changes is necessary during QUILLIVANT XR treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for patients who develop signs or symptoms of peripheral vasculopathy. (5.6)
- *Long-Term Suppression of Growth in Pediatric Patients:* Closely monitor growth (height and weight) in pediatric patients. Pediatric patients not growing or gaining height or weight as expected may need to have their treatment interrupted. (5.7)
- *Acute Angle Closure Glaucoma:* QUILLIVANT XR -treated patients considered at risk for acute angle closure glaucoma (e.g., patients with significant hyperopia) should be evaluated by an ophthalmologist. (5.8)
- *Increased Intraocular Pressure (IOP) and Glaucoma:* Prescribe QUILLIVANT XR to patients with open-angle glaucoma or abnormally increased IOP only if the benefit of treatment is considered to outweigh the risk. Closely monitor patients with a history of increased IOP or open angle glaucoma. (5.9)
- *Motor and Verbal Tics, and Worsening of Tourette's Syndrome:* Before initiating QUILLIVANT XR, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor patients for the emergence or worsening of tics or Tourette's syndrome. Discontinue treatment if clinically appropriate. (5.10)

ADVERSE REACTIONS

Based on accumulated data from other methylphenidate products, the most common (≥5% and twice the rate of placebo) adverse reactions are appetite decreased, insomnia, nausea, vomiting, dyspepsia, abdominal pain, weight decreased, anxiety, dizziness, irritability, affect lability, tachycardia, and blood pressure increased. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Tris Pharma, Inc. at 732-940-0358 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Antihypertensive Drugs: Monitor blood pressure. Adjust dosage of antihypertensive drug as needed. (7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 9/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: ABUSE, MISUSE, AND ADDICTION

QUILLIVANT XR has a high potential for abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Misuse and abuse of CNS stimulants, including QUILLIVANT XR, can result in overdose and death *[see Overdosage (10)]*, and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.
Before prescribing QUILLIVANT XR, assess each patient's risk for abuse, misuse, and addiction. Educate patients and their families about these risks, proper storage of the drug, and proper disposal of any unused drug. Throughout QUILLIVANT XR treatment, reassess each patient's risk of abuse, misuse, and addiction and frequently monitor for signs and symptoms of abuse, misuse, and addiction *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9.2)].*

1 INDICATIONS AND USAGE

QUILLIVANT XR is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) *[see Clinical Studies (14)].*

Limitations of Use

The use of QUILLIVANT XR is not recommended in pediatric patients younger than 6 years of age because they had higher plasma exposure and a higher incidence of adverse reactions (e.g., weight loss) than patients 6 years and older at the same dosage *[see Warnings and Precautions (5.7), Use in Specific Populations (8.4)].*

2 DOSAGE AND ADMINISTRATION

2.1 Pretreatment Screening

Prior to treating patients with QUILLIVANT XR, assess:

- for the presence of cardiac disease (i.e., perform a careful history, family history of sudden death or ventricular arrhythmia, and physical exam) *[see Warnings and Precautions (5.2)].*
- the family history and clinically evaluate patients for motor or verbal tics or Tourette's syndrome before initiating QUILLIVANT XR *[see Warnings and Precautions (5.10)].*

2.2 Recommended Dosage

Before administering the dose, **VIGOROUSLY SHAKE** the bottle of QUILLIVANT XR for at least 10 seconds, to ensure that the proper dose is administered.

The recommended starting dose of QUILLIVANT XR for patients 6 years and above is 20 mg once daily in the morning. The dose may be titrated weekly in increments of 10 mg to 20 mg. Daily doses above 60 mg have not been studied and are not recommended. As with any CNS stimulant, during titration of QUILLIVANT XR, the prescribed dose should be adjusted, if necessary, until a well-tolerated, therapeutic dose is achieved.

Patients should be advised to avoid alcohol while taking QUILLIVANT XR *[see Clinical*

Pharmacology (12.3)].

2.3 Administration Instructions

QUILLIVANT XR should be orally administered once daily in the morning with or without food *[see Clinical Pharmacology (12.3)].*

2.4 Switching from other Methylphenidate Products

If switching from other methylphenidate products, discontinue that treatment, and titrate with QUILLIVANT XR using the above titration schedule.

Do not substitute for other methylphenidate products on a milligram-per-milligram basis, because of different methylphenidate base compositions and differing pharmacokinetic profiles *[see Description (11), Clinical Pharmacology (12.3)].*

2.5 Dose Reduction and Discontinuation

If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug. If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.

2.6 Reconstitution Instructions for the Pharmacist

QUILLIVANT XR is supplied as a powder for oral suspension which must be reconstituted with water prior to dispensing. Preparation instructions: Tap bottle until powder flows freely. Remove bottle cap, and add specified amount of water to the bottle (see Table 1 below). Fully insert bottle adapter into neck of bottle *[see Instructions for Use, Figures F and G]*. Replace bottle cap. Shake with vigorous back and forth motion for at least 10 seconds to prepare suspension.

Table 1: Product Reconstitution Instructions

Amount of drug in bottle	Amount of water to add to bottle	Final reconstituted volume (yield)
300 mg	53 mL	60 mL
600 mg	105 mL	120 mL
750 mg	131 mL	150 mL
900 mg	158 mL	180 mL

Store reconstituted QUILLIVANT XR at 25ºC (77ºF); excursions permitted from 15º to 30ºC (59º to 86ºF). Dispense in original packaging (bottle in carton) with bottle adapter inserted and with enclosed oral dosing dispenser. QUILLIVANT XR is stable for up to 4 months after reconstitution.

3 DOSAGE FORMS AND STRENGTHS

Extended-release oral suspension (after reconstitution with water): 25 mg per 5 mL (5 mg per mL).

4 CONTRAINDICATIONS

4.1 Hypersensitivity to Methylphenidate or other Components of QUILLIVANT XR

QUILLIVANT XR is contraindicated in patients known to be hypersensitive to methylphenidate, or other components of QUILLIVANT XR. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with other methylphenidate products *[see Adverse Reactions (6.2)].*

4.2 Monoamine Oxidase Inhibitors

QUILLIVANT XR is contraindicated during treatment with monoamine oxidase inhibitors (MAOIs), and also within 14 days following discontinuation of treatment with a monoamine oxidase inhibitor (MAOI), because of the risk of hypertensive crisis *[see Drug Interactions (7.1)].*

5 WARNINGS AND PRECAUTIONS

5.1 Abuse, Misuse, and Addiction

QUILLIVANT XR has a high potential for abuse and misuse. The use of QUILLIVANT XR exposes individuals to the risks of abuse and misuse, which can lead to the development of a substance use disorder, including addiction. QUILLIVANT XR can be diverted for non-medical use into illicit channels or distribution *[see Drug Abuse and Dependence (9.2)].* Misuse and abuse of CNS stimulants, including QUILLIVANT XR, can result in overdose and death *[see Overdosage (10)],* and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.

Before prescribing QUILLIVANT XR, assess each patient’s risk for abuse, misuse, and addiction. Educate patients and their families about these risks and proper disposal of any unused drug. Advise patients to store QUILLIVANT XR in a safe place, preferably locked, and instruct patients to not give QUILLIVANT XR to anyone else. Throughout QUILLIVANT XR treatment, reassess each patient’s risk of abuse, misuse, and addiction and frequently monitor for signs and symptoms of abuse, misuse, and addiction.

5.2 Risks to Patients with Serious Cardiac Disease

Sudden death has occurred in patients with structural cardiac abnormalities or other serious cardiac disease who were treated with CNS stimulants at the recommended ADHD dosage.

Avoid QUILLIVANT XR use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmias, coronary artery disease, or other serious cardiac disease.

5.3 Increased Blood Pressure and Heart Rate

CNS stimulants cause an increase in blood pressure (mean increase approximately 2 to

4 mm Hg) and heart rate (mean increase approximately 3 to 6 bpm). Some patients may have larger increases.

Monitor all QUILLIVANT XR-treated patients for hypertension and tachycardia.

5.4 Psychiatric Adverse Reactions

Exacerbation of Pre-Existing Psychosis

CNS stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Induction of a Manic Episode in Patients with Bipolar Disorder

CNS stimulants may induce a manic or mixed episode in patients. Prior to initiating QUILLIVANT XR treatment, screen patients for risk factors for developing a manic episode (e.g., comorbid or history of depressive symptoms or a family history of suicide, bipolar disorder, or depression).

New Psychotic or Manic Symptoms

CNS stimulants, at the recommended dosage, may cause psychotic or manic symptoms (e.g., hallucinations, delusional thinking, or mania) in patients without a prior history of psychotic illness or mania. In a pooled analysis of multiple short-term, placebo-controlled studies of CNS stimulants, psychotic or manic symptoms occurred in approximately 0.1% of CNS stimulant-treated patients, compared to 0% of placebo-treated patients. If such symptoms occur, consider discontinuing QUILLIVANT XR.

5.5 Priapism

Prolonged and painful erections, sometimes requiring surgical intervention, have been reported with methylphenidate use in both adults and pediatric male patients. Although priapism was not reported with methylphenidate initiation, it developed after some time on methylphenidate, often subsequent to an increase in dosage. Priapism also occurred during a methylphenidate withdrawal (drug holidays or during discontinuation).

QUILLIVANT XR-treated patients who develop abnormally sustained or frequent and painful erections should seek immediate medical attention.

5.6 Peripheral Vasculopathy, including Raynaud’s Phenomenon

CNS stimulants, including QUILLIVANT XR, used to treat ADHD are associated with peripheral vasculopathy, including Raynaud’s phenomenon. Signs and symptoms are usually intermittent and mild; however, sequelae have included digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud’s phenomenon, were observed in post-marketing reports and at the therapeutic dosage of CNS stimulants in all age groups throughout the course of treatment. Signs and symptoms generally improved after dosage reduction or discontinuation of the CNS stimulant.

Careful observation of digital changes is necessary during QUILLIVANT XR treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for QUILLIVANT XR-treated patients who develop signs or symptoms of peripheral vasculopathy.

5.7 Long-Term Suppression of Growth in Pediatric Patients

QUILLIVANT XR is not approved and is not recommended for use in pediatric patients below 6 years of age *[see Use in Specific Populations (8.4)].*

CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. Careful follow-up of weight and height in pediatric patients ages 7 to 10 years who were randomized to either methylphenidate or nonmedication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and nonmedication-treated pediatric patients over 36 months (to the ages of 10 to 13 years), suggests that pediatric patients who received methylphenidate for 7 days per week throughout the year had a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this development period.

Closely monitor growth (weight and height) in QUILLIVANT XR-treated pediatric patients. Pediatric patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

5.8 Acute Angle Closure Glaucoma

There have been reports of angle closure glaucoma associated with methylphenidate treatment.

Although the mechanism is not clear, QUILLIVANT XR -treated patients considered at risk for acute angle closure glaucoma (e.g., patients with significant hyperopia) should be evaluated by an ophthalmologist.

5.9 Increased Intraocular Pressure and Glaucoma

There have been reports of an elevation of intraocular pressure (IOP) associated with methylphenidate treatment *[see Adverse Reactions (6.2)]*.

Prescribe QUILLIVANT XR to patients with open-angle glaucoma or abnormally increased IOP only if the benefit of treatment is considered to outweigh the risk. Closely monitor QUILLIVANT XR -treated patients with a history of abnormally increased IOP or open angle glaucoma.

5.10 Motor and Verbal Tics, and Worsening of Tourette's Syndrome

CNS stimulants, including methylphenidate, have been associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette's syndrome has also been reported *[see Adverse Reactions (6.2)]*.

Before initiating QUILLIVANT XR, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor QUILLIVANT XR -treated patients for the emergence or worsening of tics or Tourette's syndrome, and discontinue treatment if clinically appropriate.

6 ADVERSE REACTIONS

The following are discussed in more detail in other sections of the labeling:

- Known hypersensitivity to methylphenidate products or other ingredients of QUILLIVANT XR *[see Contraindications (4)]*
- Hypertensive Crisis When Used Concomitantly with Monoamine Oxidase Inhibitors *[see Contraindications (4), Drug Interactions (7.1)]*
- Abuse, Misuse, and Addiction *[see Boxed Warning, Warnings and Precautions (5.1), Drug Abuse and Dependence (9.2, 9.3)]*
- Risks to Patients with Serious Cardiac Disease *[see Warnings and Precautions (5.2)]*
- Increased Blood Pressure and Heart Rate *[see Warnings and Precautions (5.3)]*
- Psychiatric Adverse Reactions *[see Warnings and Precautions (5.4)]*
- Priapism *[see Warnings and Precautions (5.5)]*
- Peripheral Vasculopathy, including Raynaud's phenomenon *[see Warnings and Precautions (5.6)]*
- Long-Term Suppression of Growth in Pediatric Patients *[see Warnings and Precautions (5.7)]*
- Acute Angle Closure Glaucoma *[see Warnings and Precautions (5.8)]*
- Increased Intraocular Pressure and Glaucoma *[see Warnings and Precautions (5.9)]*
- Motor and Verbal Tics, and Worsening of Tourette's Syndrome *[see Warnings and Precautions (5.10)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Adverse Reactions in Studies with Other Methylphenidate Products in Children, Adolescents, and Adults with ADHD

Commonly reported (≥2% of the methylphenidate group and at least twice the rate of the placebo group) adverse reactions from placebo-controlled trials of methylphenidate products include: appetite decreased, weight decreased, nausea, abdominal pain, dyspepsia, dry mouth, vomiting, insomnia, anxiety, nervousness, restlessness, affect lability, agitation, irritability, dizziness, vertigo, tremor, blurred vision, blood pressure increased, heart rate increased, tachycardia, palpitations, hyperhidrosis, and pyrexia.

Adverse Reactions in Studies with QUILLIVANT XR in Children and Adolescents with ADHD

There is limited experience with QUILLIVANT XR in controlled trials. Based on this limited experience, the adverse reaction profile of QUILLIVANT XR appears similar to other methylphenidate extended-release products. The most common (≥2% in the QUILLIVANT XR group and greater than placebo) adverse reactions reported in the Phase 3 controlled study conducted in 45 ADHD patients (ages 6 to 12 years) were affect lability, excoriation, initial insomnia, tic, decreased appetite, vomiting, motion sickness, eye pain, and rash.

Table 2: Common Adverse Reactions occurring in ≥2% of subjects on QUILLIVANT XR and greater than placebo during the controlled cross-over phase

Adverse reaction	**QUILLIVANT XR** N= 45	**Placebo** N= 45

Affect lability	9%	2%
Excoriation	4%	0
Initial Insomnia	2%	0
Tic	2%	0
Decreased appetite	2%	0
Vomiting	2%	0
Motion sickness	2%	0
Eye pain	2%	0
Rash	2%	0

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of methylphenidate products. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These adverse reactions are as follows:

Blood and Lymphatic System Disorders: Pancytopenia, Thrombocytopenia, Thrombocytopenic purpura

Cardiac Disorders: Angina pectoris, Bradycardia, Extrasystole, Supraventricular tachycardia, Ventricular extrasystole

Eye Disorders: Diplopia, Increased intraocular pressure, Mydriasis, Visual impairment

General Disorders: Chest pain, Chest discomfort, Hyperpyrexia

Hepatobiliary Disorders: Severe hepatocellular injury

Immune System Disorders: Hypersensitivity reactions such as Angioedema, Anaphylactic reactions, Auricular swelling, Bullous conditions, Exfoliative conditions, Urticarias, Pruritus NEC, Rashes, Eruptions, and Exanthemas NEC

Investigations: Alkaline phosphatase increased, Bilirubin increased, Hepatic enzyme increased, Platelet count decreased, White blood cell count abnormal

Musculoskeletal, Connective Tissue and Bone Disorders: Arthralgia, Myalgia, Muscle twitching, Rhabdomyolysis

Nervous System Disorders: Convulsion, Grand mal convulsion, Dyskinesia, Serotonin syndrome in combination with serotonergic drugs, Motor and Verbal Tics

Psychiatric Disorders: Disorientation, Hallucination, Hallucination auditory, Hallucination visual, Libido changes, Mania

Urogenital System: Priapism

Skin and Subcutaneous Tissue Disorders: Alopecia, Erythema

Vascular Disorders: Raynaud’s phenomenon

7 DRUG INTERACTIONS

7.1 Clinically Important Drug Interactions

MAOI Inhibitors
Do not administer QUILLIVANT XR concomitantly with monoamine oxidase inhibitors (MAOIs) or within 14 days after discontinuing MAOI treatment. Concomitant use of MAOIs and CNS stimulants can cause hypertensive crisis. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure.

Antihypertensive Drugs
QUILLIVANT XR may decrease the effectiveness of drugs used to treat hypertension. Monitor blood pressure and adjust the dosage of the hypertensive drug as needed *[see Warnings and Precautions (5.3)].*

Halogenated Anesthetics
Concomitant use of halogenated anesthetics and QUILLIVANT XR may increase the risk of sudden blood pressure and heart rate increase during surgery. Monitor blood pressure and avoid use of QUILLIVANT XR in patients being treated with anesthetics on the day of surgery.

Risperidone

Combined use of methylphenidate with risperidone when there is a change, whether an increase or decrease, in dosage of either or both medications, may increase the risk of extrapyramidal symptoms (EPS). Monitor for signs of EPS.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ADHD medications during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Psychostimulants at 1-866-961-2388 or visiting online at https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/othermedications/.

Risk Summary

There are limited published studies and small case series that report on the use of methylphenidate in pregnant women; however, the data are insufficient to inform any drug-associated risks. There are clinical considerations *[see Clinical Considerations]*. No teratogenic effects were observed in embryo-fetal development studies with oral administration of methylphenidate to pregnant rats and rabbits during organogenesis at doses 2 and 11 times, respectively, the maximum recommended human dose (MRHD). However, spina bifida was observed in rabbits at a dose 40 times the MRHD *[see Data].*

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.

Clinical Considerations

Fetal/Neonatal adverse reactions

CNS stimulant medications, such as QUILLIVANT XR, can cause vasoconstriction and thereby decrease placental perfusion. No fetal and/or neonatal adverse reactions have been reported with the use of therapeutic doses of methylphenidate during pregnancy; however, premature delivery and low birth weight infants have been reported in amphetamine-dependent mothers.

Data

Animal Data

In studies conducted in rats and rabbits, methylphenidate was administered orally at doses of up to 75 and 200 mg/kg/day, respectively, during the period of organogenesis. Teratogenic effects (increased incidence of fetal spina bifida) were observed in rabbits at the highest dose, which is approximately 40 times the maximum recommended human dose (MRHD) on a mg/m^2 basis. The no effect level for embryo-fetal development in rabbits was 60 mg/kg/day (11 times the MRHD on a mg/m^2 basis). There was no evidence of specific teratogenic activity in rats, although increased incidences of fetal skeletal variations were seen at the highest dose level (7 times the MRHD on a mg/m^2 basis), which was also maternally toxic. The no effect level for embryo-fetal development in rats was 25 mg/kg/day (2 times the MRHD on a mg/m^2 basis).

8.2 Lactation

Risk Summary

Limited published literature reports that methylphenidate is present in human milk, which resulted in infant doses of 0.16% to 0.7% of the maternal weight-adjusted dosage and a milk/plasma ratio ranging between 1.1 and 2.7. There are no reports of adverse effects on the breastfed infant and no effects on milk production. Long-term neurodevelopmental effects on infants from CNS stimulant exposure are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for QUILLIVANT XR and any potential adverse effects on the breastfed infant from QUILLIVANT XR or from the underlying maternal condition.

Clinical Considerations

Monitor breastfeeding infants for adverse reactions, such as agitation, insomnia, anorexia, and reduced weight gain.

8.4 Pediatric Use

The safety and effectiveness of QUILLIVANT XR have not been established in pediatric patients below the age of 6 years.

In studies evaluating extended-release methylphenidate products, patients 4 to <6 years of age had higher systemic methylphenidate exposures than those observed in older pediatric patients at the same dosage. Pediatric patients 4 to <6 years of age also had a higher incidence of adverse reactions, including weight loss.

The safety and effectiveness of QUILLIVANT XR have been established in pediatric patients ages 6 to 17 years. Use of QUILLIVANT XR in pediatric patients 6 to 12 years of age is supported by one adequate and well-controlled study *[see Clinical Studies (14)].* Use in 12 to 17 year old’s is supported by the adequate and well-controlled studies of

QUILLIVANT XR in younger pediatric patients and additional pharmacokinetic data in adolescents, along with safety information from other methylphenidate-containing products.

Long Term Suppression of Growth

Growth should be monitored during treatment with CNS stimulants, including QUILLIVANT XR. Children who are not growing or gaining weight as expected may need to have their treatment interrupted *[see Warnings and Precautions (5.7)].*

Juvenile Animal Data

Rats treated with methylphenidate early in the postnatal period through sexual maturation demonstrated a decrease in spontaneous locomotor activity in adulthood. A deficit in acquisition of a specific learning task was observed in females only. The doses at which these findings were observed are at least 6 times the maximum recommended human dose (MRHD) on a mg/m^2 basis.

In the study conducted in young rats, methylphenidate was administered orally at doses of up to 100 mg/kg/day for 9 weeks, starting early in the postnatal period (postnatal day 7) and continuing through sexual maturity (postnatal week 10). When these animals were tested as adults (postnatal weeks 13 to 14), decreased spontaneous locomotor activity was observed in males and females previously treated with 50 mg/kg/day (approximately 6 times the maximum recommended human dose [MRHD] on a mg/m^2 basis) or greater, and a deficit in the acquisition of a specific learning task was observed in females exposed to the highest dose (12 times the MRHD on a mg/m^2 basis). The no effect level for juvenile neurobehavioral development in rats was 5 mg/kg/day (half the MRHD on a mg/m^2 basis). The clinical significance of the long-term behavioral effects observed in rats is unknown.

8.5 Geriatric Use

QUILLIVANT XR has not been studied in patients over the age of 65 years.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

QUILLIVANT XR contains methylphenidate, a Schedule II controlled substance.

9.2 Abuse

QUILLIVANT XR has a high potential for abuse and misuse which can lead to the development of a substance use disorder, including addiction *[see Warnings and Precautions (5.1)]*. QUILLIVANT XR can be diverted for non-medical use into illicit channels or distribution.

Abuse is the intentional non-therapeutic use of a drug, even once, to achieve a desired psychological or physiological effect. Misuse is the intentional use, for therapeutic purposes, of a drug by an individual in a way other than prescribed by a health care provider or for whom it was not prescribed. Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use (e.g., continuing drug use despite harmful

consequences, giving a higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence.

Misuse and abuse of methylphenidate may cause increased heart rate, respiratory rate, or blood pressure; sweating; dilated pupils; hyperactivity; restlessness; insomnia; decreased appetite; loss of coordination; tremors; flushed skin; vomiting; and/or abdominal pain. Anxiety, psychosis, hostility, aggression, and suicidal or homicidal ideation have also been observed with CNS stimulants abuse and/or misuse. Misuse and abuse of CNS stimulants, including QUILLIVANT XR, can result in overdose and death *[see Overdosage (10)]*, and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.

9.3 Dependence

Physical Dependence

QUILLIVANT XR may produce physical dependence. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug.

Withdrawal signs and symptoms after abrupt discontinuation or dose reduction following prolonged use of CNS stimulants including QUILLIVANT XR include dysphoric mood; depression; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; and psychomotor retardation or agitation.

Tolerance

QUILLIVANT XR may produce tolerance. Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose).

10 OVERDOSAGE

Clinical Effects of Overdose

Overdose of CNS stimulants is characterized by the following sympathomimetic effects:

- Cardiovascular effects including tachyarrhythmias, and hypertension or hypotension. Vasospasm, myocardial infarction, or aortic dissection may precipitate sudden cardiac death. Takotsubo cardiomyopathy may develop.
- CNS effects including psychomotor agitation, confusion, and hallucinations. Serotonin syndrome, seizures, cerebral vascular accidents, and coma may occur.
- Life-threatening hyperthermia (temperatures greater than 104°F) and rhabdomyolysis may develop.

Overdose Management

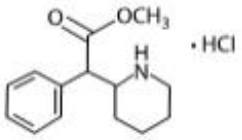
Consider the possibility of multiple drug ingestion. The pharmacokinetic profile of QUILLIVANT XR should be considered when treating patients with overdose. Because methylphenidate has a large volume of distribution and is rapidly metabolized, dialysis is not useful. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

11 DESCRIPTION

QUILLIVANT XR is a powder that, after reconstitution with water, forms an extended-release oral suspension formulation of methylphenidate intended for once daily oral administration. QUILLIVANT XR contains approximately 20% immediate-release and 80% extended-release methylphenidate. After reconstitution, QUILLIVANT XR is available in a 25 mg per 5 mL (5 mg per mL) extended-release oral suspension.

Methylphenidate HCl is a central nervous system (CNS) stimulant. The chemical name is methyl α-phenyl-2-piperidineacetate hydrochloride, and its structural formula is shown in Figure 1.

Figure 1: Methylphenidate HCl structure



$C_{14}H_{19}NO_2$•HCl Mol. Wt. 269.77

Methylphenidate HCl is a white, odorless crystalline powder. Its solutions are acid to litmus. It is freely soluble in water and in methanol, soluble in alcohol, and slightly soluble in chloroform and in acetone.

QUILLIVANT XR also contains the following inactive ingredients: sodium polystyrene sulfonate, povidone, triacetin, polyvinyl acetate, sucrose, anhydrous trisodium citrate, anhydrous citric acid, sodium benzoate, sucralose, poloxamer 188, corn starch, xanthan gum, talc, banana flavor, and silicon dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Methylphenidate HCl is a central nervous system (CNS) stimulant.

12.2 Pharmacodynamics

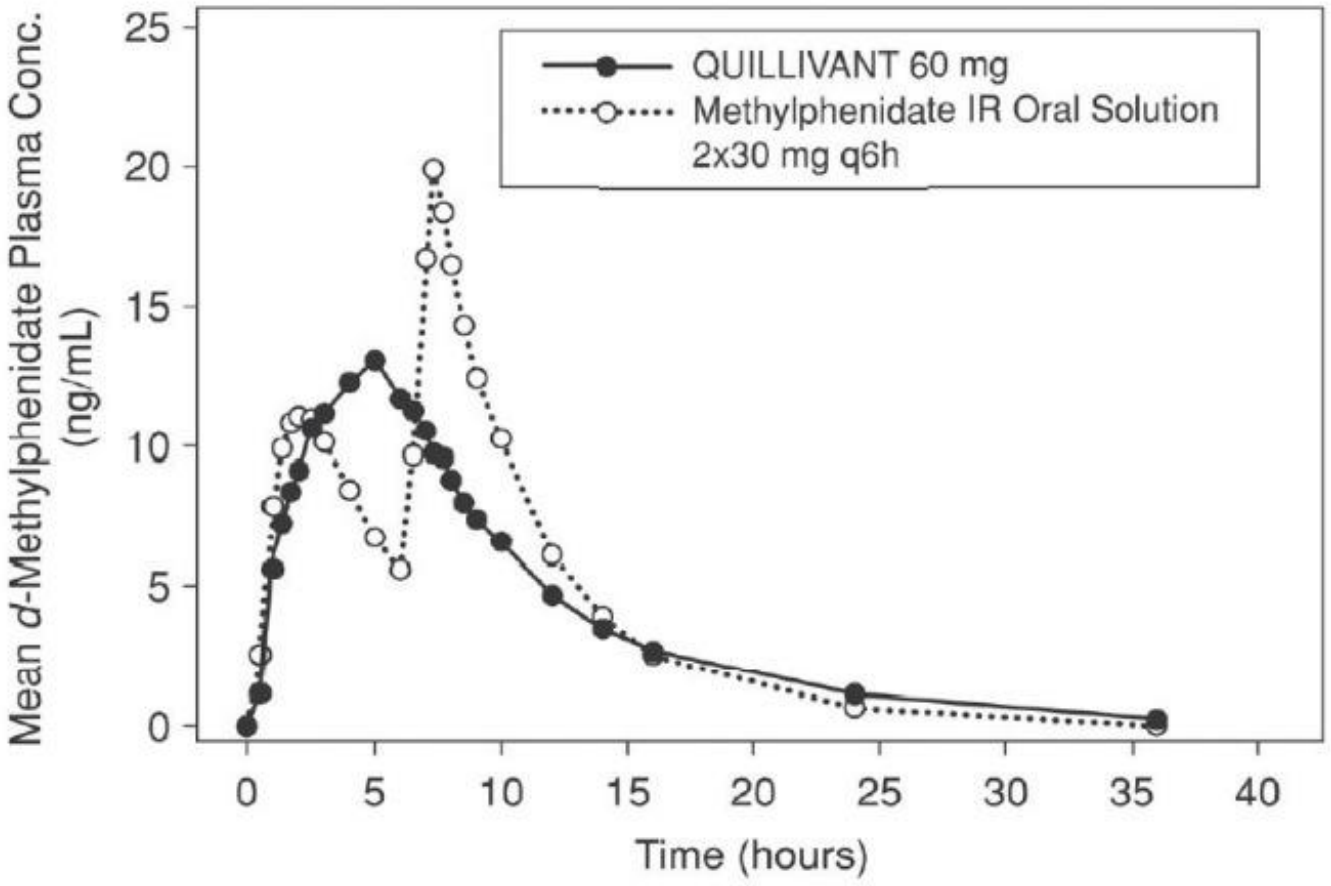
Methylphenidate is a racemic mixture comprised of the *d*- and *l*-isomers. The *d*-isomer is more pharmacologically active than the *l*-isomer. The mode of therapeutic action in ADHD is not known. Methylphenidate blocks the reuptake of norepinephrine and dopamine into the presynaptic neuron and increases the release of these monoamines into the extraneuronal space.

12.3 Pharmacokinetics

Absorption

Following a single, 60 mg oral dose of QUILLIVANT XR in 28 healthy adult subjects in a crossover study under fasting conditions, *d*-methylphenidate (*d*-MPH) mean (± SD) peak plasma concentrations of 13.6 (± 5.8) ng/mL occurred at a median time of 5 hours after dosing (Figure 2). The relative bioavailability of QUILLIVANT XR compared to Methylphenidate IR oral solution (2x30 mg, q6h) is 95%.

Figure 2: Mean *d*-Methylphenidate Plasma Concentration-Time Profiles



The single dose pharmacokinetics of *d*-MPH under fed conditions are summarized (Table 3) from studies in children and adolescents with ADHD, and healthy adults following an oral dose of 60 mg QUILLIVANT XR.

Table 3: d-MPH PK Parameters (mean ±SD) after 60 mg oral dosing of QUILLIVANT XR*

PK Parameter	Children† (n=3)	Adolescent† (n=4)	Adult (n=27)
T_{max} (hr)‡	4.05 (3.98-6.0)	2.0 (1.98-4.0)	4.0 (1.3-7.3)
$T_{1/2}$ (hr)	5.2±0.1	5.0±0.2	5.2±1.0
C_{max} (ng/mL)	34.4±14.0	21.1±5.9	17.0±7.7
AUC_{inf} (hr*ng/mL)	378±175	178±54.2	163.2±80.3
Cl (L/hr/kg)	4.27±0.70	5.06±1.42	5.66±2.15

* Breakfast was given 30 min prior to drug administration† total MPH measured in children (9 to 12 years old) and adolescents (13 to 15 years old), *l*-MPH <2% of *d*-MPH in circulation‡ data presented as median (range)

Food Effects

In a study in adult volunteers to investigate the effects of a high-fat meal on the bioavailability of QUILLIVANT XR at a dose of 60 mg, the presence of food reduced the time to peak concentration by approximately 1 hour (fed: 4 hours vs. fasted: 5 hours).

Overall, a high-fat meal increased the average C_{max} of QUILLIVANT XR by about 28% and the AUC by about 19%. These changes are not considered clinically significant.

Elimination

Following a single 60 mg oral dose of QUILLIVANT XR in 28 healthy adult subjects under fasting conditions, the mean plasma terminal elimination half-life of *d*-methylphenidate was 5.6 (± 0.8) hours.

Metabolism

In humans, methylphenidate is metabolized primarily via deesterification to alpha-phenyl-piperidine acetic acid (PPAA). The metabolite has little or no pharmacologic activity.

Excretion

After oral dosing of radiolabeled methylphenidate in humans, about 90% of the radioactivity was recovered in urine. The main urinary metabolite was PPAA, accounting for approximately 80% of the dose.

Alcohol Effect

An *in vitro* study was conducted to explore the effect of alcohol on the release characteristics of methylphenidate from QUILLIVANT XR Oral Suspension. At alcohol concentrations of 5% and 10%, there was no effect of alcohol on the release characteristics of methylphenidate. At 20% alcohol concentration, there was on average a 20% increase in drug exposure *[see Dosage and Administration (2.2)].*

Specific Populations

Sex

There is insufficient experience with the use of QUILLIVANT XR to detect gender variations in pharmacokinetics.

Race

There is insufficient experience with the use of QUILLIVANT XR to detect ethnic variations in pharmacokinetics.

Age

The pharmacokinetics of methylphenidate after QUILLIVANT XR administration were studied in pediatric patients with ADHD between 9 and 15 years of age. After a single oral dose of 60 mg QUILLIVANT XR, plasma concentrations of methylphenidate in children (9 to 12 years old; n=3) were approximately twice the concentrations observed in adults. The plasma concentrations in adolescent patients (13 to 15 years old; n=4) were similar to those in adults.

Renal Impairment

There is no experience with the use of QUILLIVANT XR in patients with renal insufficiency. After oral administration of radiolabeled methylphenidate in humans, methylphenidate was extensively metabolized and approximately 80% of the radioactivity was excreted in the urine in the form of PPAA. Since renal clearance is not an important route of methylphenidate clearance, renal insufficiency is expected to have little effect on the pharmacokinetics of QUILLIVANT XR.

Hepatic Impairment

There is no experience with the use of QUILLIVANT XR in patients with hepatic insufficiency.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

In a lifetime carcinogenicity study carried out in B6C3F1 mice, methylphenidate caused an increase in hepatocellular adenomas and, in males only, an increase in hepatoblastomas, at a daily dose of approximately 60 mg/kg/day. This dose is approximately 4 times the maximum recommended human dose on a mg/m^2 basis. Hepatoblastoma is a relatively rare rodent malignant tumor type. There was no increase in total malignant hepatic tumors. The mouse strain used is sensitive to the development of hepatic tumors, and the significance of these results to humans is unknown.

Methylphenidate did not cause any increase in tumors in a lifetime carcinogenicity study carried out in F344 rats; the highest dose used was approximately 45 mg/kg/day, which is approximately 5 times the maximum recommended human dose on a mg/m^2 basis.

Mutagenesis

Methylphenidate was not mutagenic in the *in vitro* Ames reverse mutation assay or in the *in vitro* mouse lymphoma cell forward mutation assay. Sister chromatid exchanges and chromosome aberrations were increased, indicative of a weak clastogenic response, in an *in vitro* assay in cultured Chinese Hamster Ovary (CHO) cells. Methylphenidate was negative in an *in vivo* mouse bone marrow micronucleus assay.

Impairment of Fertility

Methylphenidate did not impair fertility in male or female mice that were fed diets containing the drug in an 18-week Continuous Breeding study. The study was conducted at doses of up to 160 mg/kg/day, approximately 8-fold the maximum recommended human dose on a mg/m^2 basis.

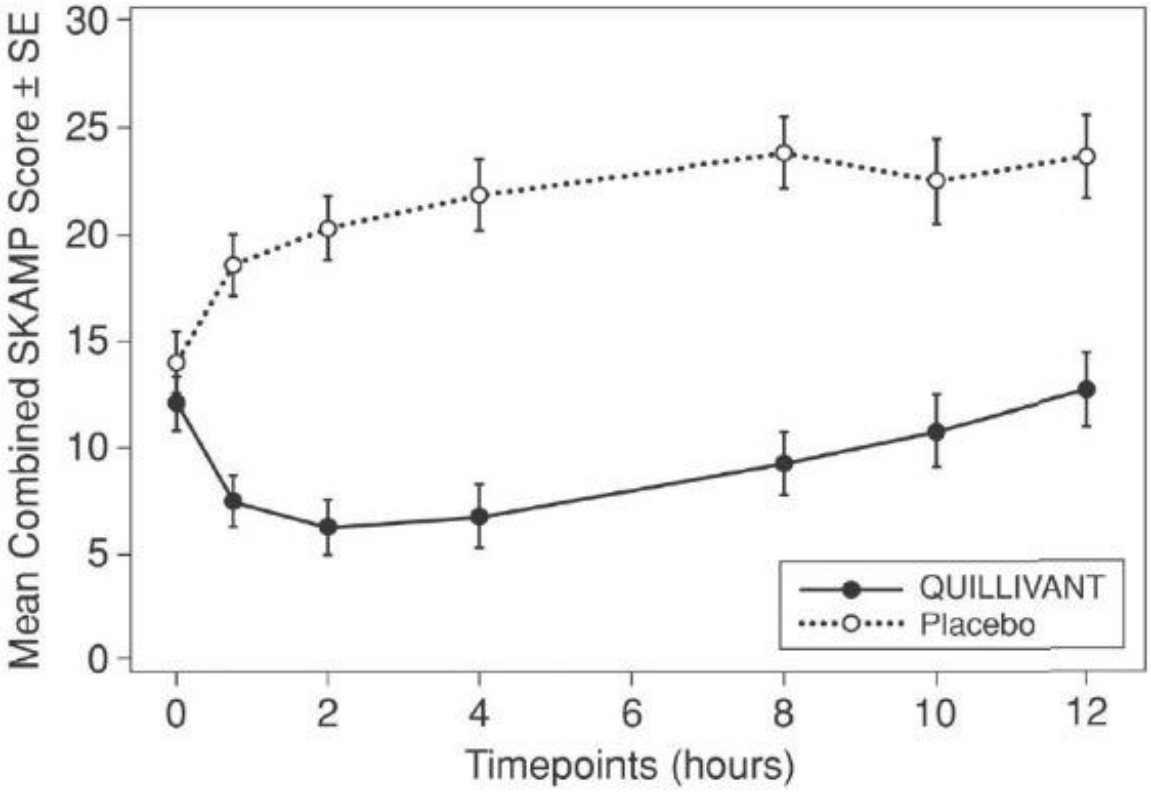
14 CLINICAL STUDIES

The efficacy of QUILLIVANT XR was evaluated in a laboratory classroom study conducted in 45 pediatric patients (ages 6 to 12 years) with ADHD. Patients in the trial met Diagnostic and Statistical Manual of Mental Diseases, 4th edition (DSM-IV®) criteria for ADHD. The study began with an open-label dose optimization period (4 to 6 weeks) with an initial QUILLIVANT XR dose of 20 mg once daily in the morning. The dose could be titrated weekly in increments of 10 or 20 mg until a therapeutic dose or the maximum dose of 60 mg/day was reached. At the end of the dose optimization period, approximately 5% of subjects were receiving 20 mg/day; 39%, 30 mg/day; 31%, 40 mg/day; 10%, 50 mg/day; and 15%, 60 mg/day. Subjects then entered a 2-week randomized, double-blind, crossover treatment with the individually optimized dose of QUILLIVANT XR or placebo. At the end of each week, school teachers and raters evaluated the attention and behavior of the subjects in a laboratory classroom using the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale. The primary efficacy

endpoint was the SKAMP-Combined score at 4 hours post-dosing. The key secondary efficacy endpoints were the SKAMP-Combined scores at 0.75, 2, 8, 10, and 12 hours post-dosing.

Results from the first double-blind, placebo-controlled week of the study are summarized in Figure 3. SKAMP-Combined scores were statistically significantly lower (improved) at all time points (0.75, 2, 4, 8, 10, 12 hours) post-dosing with QUILLIVANT XR compared to placebo.

Figure 3: Absolute SKAMP-Combined Score after treatment with QUILLIVANT XR or Placebo during Period 1.



16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

QUILLIVANT XR is supplied as powder that, after reconstitution with water, forms an extended-release oral suspension. The product is supplied in a carton. Each carton also contains one bottle, one oral dosing dispenser, and one bottle adapter.

The product must be reconstituted only by the pharmacist and not by the patient or caregiver. After reconstitution, the product is a light beige to tan viscous suspension containing 25 mg per 5 mL (5 mg per mL) of methylphenidate hydrochloride.

Bottles of 300 mg powder (to prepare 60 mL suspension)	NDC 24478-321-02
Bottles of 600 mg powder (to prepare 120 mL suspension)	NDC 24478-322-04
Bottles of 750 mg powder (to prepare 150 mL suspension)	NDC 24478-323-05
Bottles of 900 mg powder (to prepare 180 mL suspension)	NDC 24478-324-06

16.2 Storage and Handling

Store at 25ºC (77ºF); excursions permitted from 15ºC to 30ºC (59ºF to 86ºF). [See USP Controlled Room Temperature.]

Dispense in original container.

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Abuse, Misuse, and Addiction

Educate patients and their families about the risks of abuse, misuse, and addiction of QUILLIVANT XR, which can lead to overdose and death, and proper disposal of any unused drug *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9.2), Overdosage (10)]*. Advise patients to store QUILLIVANT XR in a safe place, preferably locked, and instruct patients to not give QUILLIVANT XR to anyone else.

Instructions for Using the Enclosed Oral Dosing Dispenser

Provide the following instructions on administration to the patient or caregiver:

- The pharmacist should provide this medicine in its original packaging (bottle within carton) with the bottle adapter fully inserted and the accompanying oral dosing dispenser. Use only with the oral dosing dispenser provided with this product.
- Check and make sure that the QUILLIVANT XR bottle contains liquid medicine. If QUILLIVANT XR is in powder form, do not use it. Return it to your pharmacist.
- **VIGOROUSLY SHAKE** the bottle of QUILLIVANT XR for at least 10 seconds before each dose, to ensure that the proper dose is administered.
- Remove the bottle cap. Confirm that the bottle adapter has been inserted into top of the bottle.
- Insert the tip of the oral dosing dispenser provided with this product into the bottle adapter.
- Turn bottle upside down and withdraw prescribed amount of QUILLIVANT XR into the oral dosing dispenser.
- Remove filled oral dosing dispenser from bottle and dispense QUILLIVANT XR directly into mouth.
- Replace bottle cap and store bottle as directed.
- Wash oral dosing dispenser after each use (components are dishwasher-safe).

Risks to Patients with Serious Cardiac Disease

Advise patients that there are potential risks to patients with serious cardiac disease, including sudden death with QUILLIVANT XR use. Instruct patients to contact a health care provider immediately if they develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease *[see Warnings and Precautions (5.2)].*

Increased Blood Pressure and Heart Rate

Advise patients that QUILLIVANT XR can elevate blood pressure and heart rate *[see Warnings and Precautions (5.3)].*

Psychiatric Adverse Reactions

Advise patients that QUILLIVANT XR, at recommended doses, can cause psychotic or manic symptoms, even in patients without a prior history of psychotic symptoms or mania *[see Warnings and Precautions (5.4)].*

Priapism

Advise patients, caregivers, and family members of the possibility of painful or prolonged penile erections (priapism). **Instruct the patient to seek immediate medical attention in the event of priapism** *[see Warnings and Precautions (5.5)].*

Circulation Problems in Fingers and Toes [Peripheral Vasculopathy, including Raynaud's Phenomenon]

- Instruct patients beginning treatment with QUILLIVANT XR about the risk of peripheral vasculopathy, including Raynaud's phenomenon, and associated signs and symptoms: fingers or toes may feel numb, cool, painful, and/or may change color from pale, to blue, to red.
- Instruct patients to report to their physician any new numbness, pain, skin color change, or sensitivity to temperature in fingers or toes.
- **Instruct patients to call their physician immediately with any signs of unexplained wounds appearing on fingers or toes while taking QUILLIVANT XR.**
- Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients *[see Warnings and Precautions (5.6)]*.

Long-Term Suppression of Growth in Pediatric Patients

Advise patients, families, and caregivers that QUILLIVANT XR can cause slowing of growth and weight loss *[see Warnings and Precautions (5.7)].*

Increased Intraocular Pressure (IOP) and Glaucoma

Advise patients that IOP and glaucoma may occur during treatment with QUILLIVANT XR *[see Warnings and Precautions (5.9)]*.

Motor and Verbal Tics, and Worsening of Tourette's Syndrome

Advise patients that motor and verbal tics and worsening of Tourette's Syndrome may occur during treatment with QUILLIVANT XR. Instruct patients to notify their healthcare provider if emergence of new tics or worsening of tics or Tourette's syndrome occurs *[see Warnings and Precautions (5.10)]*.

Pregnancy Registry

Advise patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to QUILLIVANT XR during pregnancy *[see Use in Specific Populations (8.1)]*.

Alcohol Effect

Patients should be advised to avoid alcohol while taking QUILLIVANT XR Oral Suspension. Consumption of alcohol while taking QUILLIVANT XR may result in a more rapid release of the dose of methylphenidate *[see Clinical Pharmacology (12.3)].*

This product's label may have been updated. For current full prescribing information, please visit www.trispharma.com.

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A subsidiary of Tris Pharma, Inc., Monmouth Junction, NJ 08852

Manufactured by:
Tris Pharma, Inc.
Monmouth Junction, NJ 08852

LB8529 Rev. 03

Medication Guide

QUILLIVANT XR® (\kwil-ə-vant\)
(methylphenidate hydrochloride) for extended-release oral suspension CII

What is the most important information I should know about QUILLIVANT XR?

QUILLIVANT XR may cause serious side effects, including:

- **Abuse, misuse, and addiction.** QUILLIVANT XR has a high chance for abuse and misuse and may lead to substance use problems, including addiction. Misuse and abuse of QUILLIVANT XR, other methylphenidate containing medicines, and amphetamine containing medicines, can lead to overdose and death. The risk of overdose and death is increased with higher doses of QUILLIVANT XR or when it is used in ways that are not approved, such as snorting or injection.

  - Your healthcare provider should check you or your child's risk for abuse, misuse, and addiction before starting treatment with QUILLIVANT XR and will monitor you or your child during treatment.

  - QUILLIVANT XR may lead to physical dependence after prolonged use, even if taken as directed by your healthcare provider.

  - Do not give QUILLIVANT XR to anyone else. See "**What is QUILLIVANT XR?**" for more information.

  - Keep QUILLIVANT XR in a safe place and properly dispose of any unused medicine. See "**How should I store QUILLIVANT XR?**" for more information.

  - Tell your healthcare provider if you or your child have ever abused or been dependent on alcohol, prescription medicines, or street drugs.

- **Risks for people with serious heart disease.** Sudden death has happened in people who have heart defects or other serious heart disease.
  - Your healthcare provider should check you or your child carefully for heart problems before starting treatment with QUILLIVANT XR.

Tell your health care provider if you or your child have any heart problems, heart disease, or heart defects.

Call your healthcare provider or go to the nearest hospital emergency room right away if you or your child has any signs of heart problems such as chest pain, shortness of breath, or fainting while taking QUILLIVANT XR.

- **Increased blood pressure and heart rate.**
  Your health care provider should check your or your child's blood pressure and heart rate regularly during treatment with QUILLIVANT XR.
- **Mental (Psychiatric) problems:**

  - new or worse behavior and thought problems
  - new or worse bipolar illness
  - new psychotic symptoms (such as hearing voices, believing things that are not true, are suspicious) or new manic symptoms

Tell your health care provider about any mental problems you or your child have, or about a family history of suicide, bipolar illness, or depression.

Call your health care provider right away if you or your child have any new or worsening mental symptoms or problems while taking QUILLIVANT XR, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

What is QUILLIVANT XR?

QUILLIVANT XR is a central nervous system stimulant prescription medicine. **QUILLIVANT XR is a liquid medicine** that you take by mouth.

It is used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). QUILLIVANT XR may help increase attention and decrease impulsiveness and hyperactivity in people with ADHD.

QUILLIVANT XR is not recommended for use in children under 6 years of age with ADHD.

QUILLIVANT XR is a federally controlled substance (CII) because it contains methylphenidate that can be a target for people who abuse prescription medicines or street drugs. Keep QUILLIVANT XR in a safe place to protect it from theft. Never give your QUILLIVANT XR to anyone else, because it may cause death or harm them. Selling or giving away QUILLIVANT XR may harm others and is against the law.

Do not take QUILLIVANT XR if you or your child:

- are allergic to methylphenidate hydrochloride, or any of the ingredients in QUILLIVANT XR. See the end of this Medication Guide for a complete list of ingredients in QUILLIVANT XR.
- are taking or have taken within the past 14 days a type of anti-depression medicine called a monoamine oxidase inhibitor (MAOI).

QUILLIVANT XR may not be right for you or your child. Before starting QUILLIVANT XR tell your or your child's health care provider about all health conditions (or a family history of) including:

- heart problems, heart disease, heart defects, or high blood pressure
- mental problems including psychosis, mania, bipolar illness, or depression
- circulation problems in fingers and toes

- have eye problems, including increased pressure in your eye, glaucoma, or problems with your close-up vision (farsightedness)
- have or had repeated movements or sounds (tics) or Tourette's syndrome, or have a family history of tics or Tourette's syndrome
- if you are pregnant or plan to become pregnant. It is not known if QUILLIVANT XR will harm your unborn baby. Talk to your health care provider if you are pregnant or plan to become pregnant.
    - There is a pregnancy registry for females who are exposed to ADHD medications during pregnancy. The purpose of the registry is to collect information about the health of females exposed to QUILLIVANT XR and their baby. If you or your child becomes pregnant during treatment with QUILLIVANT XR, talk to your healthcare provider about registering with the National Pregnancy Registry for Psychostimulants at 1-866-961-2388 or visit https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/othermedications/.
- if you are breastfeeding or plan to breast feed. QUILLIVANT XR passes into your breast milk. You and your healthcare provider should decide if you will take QUILLIVANT XR or breast feed.

Tell your health care provider about all of the medicines that you or your child take including prescription and nonprescription medicines, vitamins, and herbal supplements. QUILLIVANT XR and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be adjusted while taking QUILLIVANT XR.

Your health care provider will decide whether QUILLIVANT XR can be taken with other medicines.

Especially tell your health care provider if you or your child takes:
- anti-depression medicines including MAOIs

Know the medicines that you or your child takes. Keep a list of your medicines with you to show your health care provider and pharmacist. **Do not start any new medicine while taking QUILLIVANT XR without talking to your health care provider first.**

How should QUILLIVANT XR be taken?
- **Read the step-by-step instructions for using QUILLIVANT XR extended-release suspension at the end of this Medication Guide.**

- Take QUILLIVANT XR exactly as prescribed. Your health care provider may adjust the dose, if needed, until it is right for you or your child. During dose adjustment, you or your child may still have ADHD symptoms.
- QUILLIVANT XR should be used with the oral dosing dispenser provided with the product. If the oral dosing dispenser is missing or not provided, please contact your pharmacist for a replacement.
- Check and make sure that the QUILLIVANT XR bottle contains liquid medicine. If QUILLIVANT XR is in powder form, do not use it. Return it to your pharmacist.
- Check and make sure that the bottle adapter was fully inserted into the bottle by the pharmacist. If the bottle adapter is not fully inserted, insert the adapter into the bottle.

- Take QUILLIVANT XR 1 time each day in the morning. QUILLIVANT XR is an extended-release suspension. It releases medicine into your body throughout the day.
- QUILLIVANT XR can be taken with or without food. Taking QUILLIVANT XR with food may shorten the time it takes for the medicine to start working.
- Your health care provider may do regular checks of the blood, heart, and blood pressure while taking QUILLIVANT XR.
- Children should have their height and weight checked often while taking QUILLIVANT XR. QUILLIVANT XR treatment may be stopped if a problem is found during these check-ups.
- If a dose is missed, you or your child should talk to your health care provider about dosing.

If you or your child take too much QUILLIVANT XR, call your healthcare provider or Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away.

What should I avoid while taking QUILLIVANT XR?

- QUILLIVANT XR should not be taken with MAOI medicines. Do not start taking QUILLIVANT XR if you stopped taking an MAOI in the last 14 days.
- Do not drink alcohol while taking QUILLIVANT XR. This may cause a faster release of your methylphenidate dose.

What are the possible side effects of QUILLIVANT XR?

QUILLIVANT XR may cause serious side effects, including:

- **See "What is the most important information I should know about QUILLIVANT XR?"** for information on reported heart and mental problems.

Other serious side effects include:

- **Painful and prolonged erections (priapism)** have occurred with methylphenidate. If you or your child develop priapism, seek medical help right away. **Because priapism can cause long lasting damage, it should be checked by a health care provider right away.**
- **Circulation problems in fingers and toes (peripheral vasculopathy, including Raynaud's phenomenon):**
  Signs and symptoms may include:

  - fingers or toes may feel numb, cool, painful
  - fingers or toes may change color from pale, to blue, to red

Tell your healthcare provider if you or your child have numbness, pain, skin color change, or sensitivity to temperature in your fingers or toes, or if you or your child have any signs of unexplained wounds appearing on fingers or toes during treatment with QUILLIVANT XR.

- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with QUILLIVANT XR. QUILLIVANT XR treatment may be stopped if your child is not gaining weight or height.

- **Eye problems (increased pressure in the eye and glaucoma).** Call your healthcare provider right away if you or your child develop changes in your vision or

eye pain, swelling, or redness.

- **New or worsening tics or worsening Tourette's syndrome.** Tell your healthcare provider if you or your child get any new or worsening tics or worsening Tourette's syndrome during treatment with QUILLIVANT XR.

The most common side effects of QUILLIVANT XR include:

- decreased appetite
- trouble sleeping
- nausea
- vomiting
- indigestion
- stomach pain
- weight loss
- anxiety
- dizziness
- irritability
- mood swings
- fast heart beat
- increased blood pressure

These are not all the possible side effects of QUILLIVANT XR.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store QUILLIVANT XR?

- Store QUILLIVANT XR at 59°F to 86°F (15°C to 30°C).
- Store QUILLIVANT XR in a safe place, like a locked cabinet.
- Dispose of remaining, unused, or expired QUILLIVANT XR by a medicine take-back program at a U.S. Drug Enforcement Administration (DEA) authorized collection site. If no take-back program or DEA authorized collector is available, mix QUILLIVANT XR with an undesirable, nontoxic substance such as dirt, cat litter, or used coffee grounds to make it less appealing to children and pets. Place the mixture in a container such as a sealed plastic bag and throw away QUILLIVANT XR in the household trash. Visit http://www.fda.gov/drugdisposal for additional information on disposal of unused medicines.
- **Keep QUILLIVANT XR and all medicines out of the reach of children.**

General information about the safe and effective use of QUILLIVANT XR

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use QUILLIVANT XR for a condition for which it was not prescribed. Do not give QUILLIVANT XR to other people, even if they have the same condition. It may harm them.

You can ask your pharmacist or healthcare provider for information about QUILLIVANT XR that is written for healthcare professionals.

What are the ingredients in QUILLIVANT XR?

Active Ingredient: methylphenidate hydrochloride

Inactive Ingredients: sodium polystyrene sulfonate, povidone, triacetin, polyvinyl acetate, sucrose, anhydrous trisodium citrate, anhydrous citric acid, sodium benzoate, sucralose, poloxamer 188, corn starch, xanthan gum, talc, banana flavor, and silicon dioxide.

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Manufactured by:

Tris Pharma, Inc.

Monmouth Junction, NJ 08852

For more information, go to www.quillivantxr.com or call (732) 940-0358.

This product's label may have been updated. For current full prescribing information, please visit www.trispharma.com.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised:09/2025

Instructions for Use

QUILLIVANT XR® (\kwil-ə-vant\)
(methylphenidate hydrochloride)
for extended-release oral suspension CII

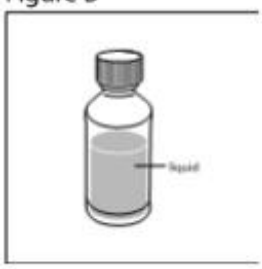
Read this Instructions for Use before using QUILLIVANT XR and each time you get a refill. There may be new information. This leaflet does not take the place of talking with the health care provider about your or your child's medical condition or treatment.

Step 1. Remove the QUILLIVANT XR bottle and oral dosing dispenser from the box **(See Figure A).** If the oral dosing dispenser is missing or not provided, please contact your pharmacist for a replacement.

Figure A

Step 2. Check and make sure that the QUILLIVANT XR bottle contains liquid medicine **(See Figure B).** If QUILLIVANT XR is still in powder form, **do not use it.** Return it to your pharmacist.

Figure B



Step 3. Shake the bottle well (up and down) for at least 10 seconds before each use **(See Figure C).**

Figure C

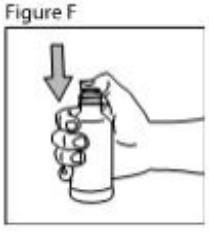
Step 4. Uncap the bottle and check that the bottle adapter has been fully inserted into the bottle **(See Figure D).**

Figure D

Step 4 (continued). If bottle adapter **(See Figure E)** has not been inserted by the pharmacist into the bottle, insert adapter into the bottle as shown **(See Figure E and Figure F).**

Figure E

Figure F

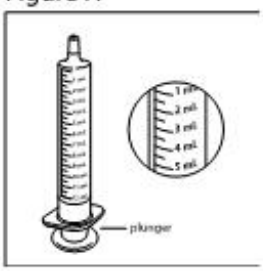


After the bottle adapter has been fully inserted into the bottle **(See Figure G)**, it should not be removed. If the bottle adapter has not been inserted and is missing from the box, contact your pharmacist.
The bottle adapter must be fully inserted and should be even with the mouth of the bottle and must remain in place to allow the child resistant cap to work the right way.

Figure G

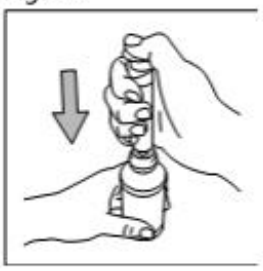
Step 5. Check the QUILLIVANT XR dose in milliliters (mL) as prescribed by your health care provider. Locate this number on the oral dosing dispenser **(See Figure H).**

Figure H



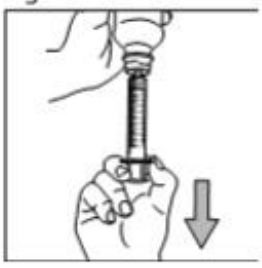
Step 6. Insert tip of the oral dosing dispenser into the upright bottle and push the plunger all the way down **(See Figure I).**

Figure I



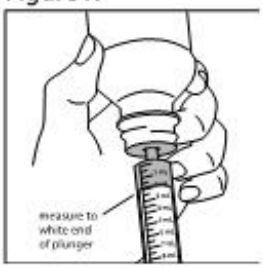
Step 7. With the oral dosing dispenser in place, turn the bottle upside down. Pull the plunger to the number of mL you need (the amount of liquid medicine in **Step 5 – See Figure J**).

Figure J



Step 7 (continued). Measure the number of mL of medicine from the white end of the plunger **(See Figure K).**

Figure K



Step 8. Remove the oral dosing dispenser from the bottle adapter.
Step 9. Slowly squirt QUILLIVANT XR directly into your or your child's mouth **(See Figure L).**

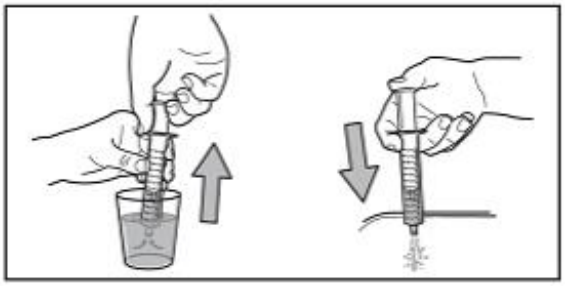
Figure L

Step 10. Cap the bottle tightly. Store the bottle upright at 59°F to 86°F (15°C to 30°C) **(See Figure M).**

Figure M

Step 11. Clean the oral dosing dispenser after each use by placing in the dishwasher, or by rinsing with tap water **(See Figure N).**

Figure N



These Instructions for Use have been approved by the U.S. Food and Drug Administration. Revised: 06/2021

This product's label may have been updated. For current full prescribing information, please visit www.trispharma.com.

Distributed by:

NextWave Pharmaceuticals, Inc
A subsidiary of Tris Pharma, Inc., Monmouth Junction, NJ 08852

Manufactured by:
Tris Pharma, Inc.
Monmouth Junction, NJ 08852

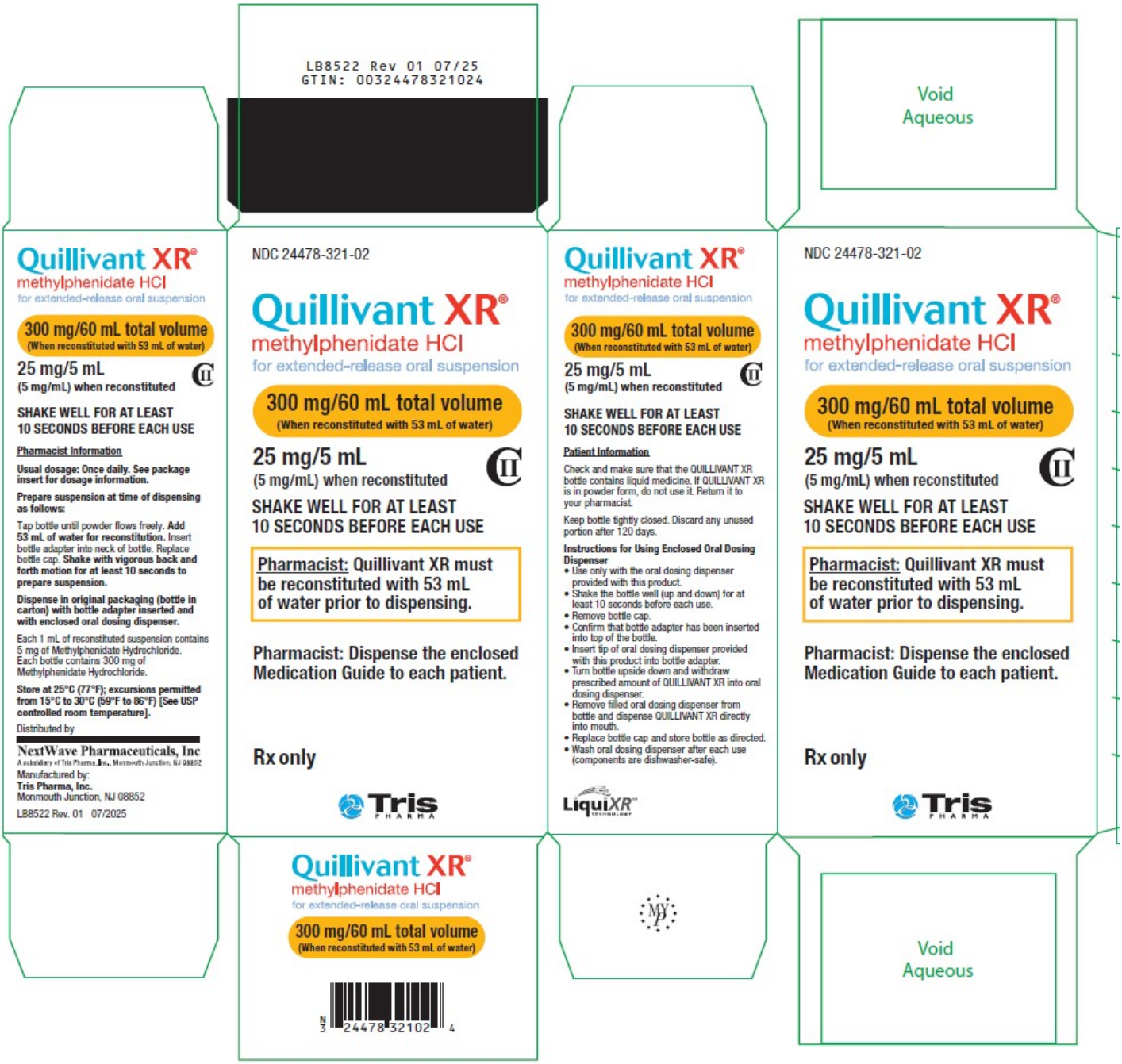
LB8529

Rev. 01

06/2021

PRINCIPAL DISPLAY PANEL

NDC 24478-321-02
QUILLIVANT XR®
methylphenidate HCl
for extended-release oral suspension
300 mg/ 60 mL total volume
(When reconstituted with 53 mL of water)
25 mg/5 mL
(5 mg/mL) When reconstituted
Rx Only



PRINCIPAL DISPLAY PANEL

NDC 24478-322-04
QUILLIVANT XR®
methylphenidate HCl
for extended-release oral suspension
600 mg/ 120 mL total volume
(When reconstituted with 105 mL of water)
25 mg/5 mL
(5 mg/mL) When reconstituted
Rx Only

PRINCIPAL DISPLAY PANEL

NDC 24478-323-05
QUILLIVANT XR®
methylphenidate HCl
for extended-release oral suspension
750 mg/ 150 mL total volume
(When reconstituted with 131 mL of water)
25 mg/5 mL
(5 mg/mL) When reconstituted
Rx Only

PRINCIPAL DISPLAY PANEL

NDC 24478-324-06
QUILLIVANT XR®
methylphenidate HCl
for extended-release oral suspension
900 mg/ 180 mL total volume
(When reconstituted with 158 mL of water)
25 mg/5 mL
(5 mg/mL) When reconstituted
Rx Only

QUILLIVANT XR

methylphenidate hydrochloride suspension, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:24478-321
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	300 mg in 60 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
TRIACETIN (UNII: XHX3C3X673)	
SUCROSE (UNII: C151H8M554)	
ANHYDROUS TRISODIUM CITRATE (UNII: RS7A450LGA)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
SODIUM BENZOATE (UNII: OJ245FE5EU)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
POLOXAMER 188 (UNII: LQA7B6G8JG)	
STARCH, CORN (UNII: O8232NY3SJ)	
XANTHAN GUM (UNII: TTV12P4NEE)	
TALC (UNII: 7SEV7J4R1U)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
POLYVINYL ACETATE PHTHALATE (UNII: 58QVG85GW3)	

Product Characteristics			
Color		**Score**	
Shape		**Size**	
Flavor	BANANA	**Imprint Code**	
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:24478-321-02	1 in 1 CARTON	10/01/2012	
1		60 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA202100	10/01/2012	

QUILLIVANT XR

methylphenidate hydrochloride suspension, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:24478-322
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	600 mg in 120 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
TRIACETIN (UNII: XHX3C3X673)	
SUCROSE (UNII: C151H8M554)	
ANHYDROUS TRISODIUM CITRATE (UNII: RS7A450LGA)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
SODIUM BENZOATE (UNII: OJ245FE5EU)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
POLOXAMER 188 (UNII: LQA7B6G8JG)	
STARCH, CORN (UNII: O8232NY3SJ)	
XANTHAN GUM (UNII: TTV12P4NEE)	
TALC (UNII: 7SEV7J4R1U)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
POLYVINYL ACETATE PHTHALATE (UNII: 58QVG85GW3)	

Product Characteristics

Color		**Score**	
Shape		**Size**	
Flavor	BANANA	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:24478-322-04	1 in 1 CARTON	10/01/2012	
1		120 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA202100	10/01/2012	

QUILLIVANT XR

methylphenidate hydrochloride suspension, extended release

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:24478-323
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	750 mg in 150 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
TRIACETIN (UNII: XHX3C3X673)	
SUCROSE (UNII: C151H8M554)	
ANHYDROUS TRISODIUM CITRATE (UNII: RS7A450LGA)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
SODIUM BENZOATE (UNII: OJ245FE5EU)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
POLOXAMER 188 (UNII: LQA7B6G8JG)	
STARCH, CORN (UNII: O8232NY3SJ)	
XANTHAN GUM (UNII: TTV12P4NEE)	
TALC (UNII: 7SEV7J4R1U)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
POLYVINYL ACETATE PHTHALATE (UNII: 58QVG85GW3)	

Product Characteristics

Color		**Score**	
Shape		**Size**	
Flavor	BANANA	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:24478-323-05	1 in 1 CARTON	10/01/2012	
1		150 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA202100	10/01/2012	

QUILLIVANT XR

methylphenidate hydrochloride suspension, extended release

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:24478-324
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	900 mg in 180 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
TRIACETIN (UNII: XHX3C3X673)	
SUCROSE (UNII: C151H8M554)	
ANHYDROUS TRISODIUM CITRATE (UNII: RS7A450LGA)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
SODIUM BENZOATE (UNII: OJ245FE5EU)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
POLOXAMER 188 (UNII: LQA7B6G8JG)	
STARCH, CORN (UNII: O8232NY3SJ)	
XANTHAN GUM (UNII: TTV12P4NEE)	
TALC (UNII: 7SEV7J4R1U)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
POLYVINYL ACETATE PHTHALATE (UNII: 58QVG85GW3)	

Product Characteristics

Color		**Score**	
Shape		**Size**	
Flavor	BANANA	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:24478-324-	1 in 1 CARTON	01/04/2013	

1	06	1 in 1 CARTON	01/04/2013	
1		180 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA202100	01/04/2013	

Labeler - NextWave Pharmaceuticals, Inc (008816703)

Revised: 9/2025 NextWave Pharmaceuticals, Inc