DEXMETHYLPHENIDATE HYDROCHLORIDE- dexmethylphenidate hydrochloride tablet
Lupin Pharmaceuticals,Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DEXMETHYLPHENIDATE HYDROCHLORIDE TABLETS safely and effectively. See full prescribing information for DEXMETHYLPHENIDATE HYDROCHLORIDE TABLETS.

DEXMETHYLPHENIDATE HYDROCHLORIDE tablets, for oral use, CII
Initial U.S. Approval: 2001

WARNING: ABUSE AND DEPENDENCE

See full prescribing information for complete boxed warning.

Dexmethylphenidate hydrochloride tablets 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 dexmethylphenidate hydrochloride tablets, can result in overdose and death (5.1, 9.2, 10):

- **Before prescribing dexmethylphenidate hydrochloride tablets, 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

Boxed Warning	10/2023
Dosage and Administration (2.1, 2.2)	10/2023
Warnings and Precautions (5.1, 5.2, 5.8, 5.9, 5.10)	10/2023

INDICATIONS AND USAGE

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

DOSAGE AND ADMINISTRATION

- Administer orally twice daily, 4 hours apart with or without food (2)
- For patients new to methylphenidate: Recommend starting dose of 5 mg once daily (2.5 mg twice daily) (2.2).
- For patients currently taking methylphenidate: Initiate dexmethylphenidate hydrochloride therapy with half (1/2) the current total daily dose of methylphenidate (2.2).
- Titrate weekly in increments of 2.5 to 5 mg to a maximum of 20 mg/day (10 mg twice daily) (2.2).

DOSAGE FORMS AND STRENGTHS

Tablets: 2.5 mg, 5 mg, and 10 mg (3)

CONTRAINDICATIONS

- Known hypersensitivity to methylphenidate or other components of dexmethylphenidate hydrochloride tablets (4).
- Concurrent treatment with a monoamine oxidase inhibitor (MAOI), or use of an MAOI within the preceding 14 days (4).

WARNINGS AND PRECAUTIONS

- *Risks to Patient 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 dexmethylphenidate hydrochloride tablets, screen patients for risk factors for developing a manic episode. If new psychotic or manic symptoms occur, consider discontinuing dexmethylphenidate hydrochloride tablets (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 dexmethylphenidate hydrochloride tablets 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*: dexmethylphenidate hydrochloride tablets -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 dexmethylphenidate hydrochloride tablets 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 dexmethylphenidate hydrochloride tablets, 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

The most common adverse reactions (greater than or equal to 5% and twice the rate of placebo) in pediatric patients 6 to 17 years were abdominal pain, fever, nausea, and anorexia (6.1).
To report SUSPECTED ADVERSE REACTIONS, contact Lupin Pharmaceuticals, Inc. at 1-866-403-7592 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 (7.1).
- Halogenated Anesthetics: Avoid use of dexmethylphenidate hydrochloride tablets on the day of surgery if halogenated anesthetics will be used (7.1).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 12/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE AND DEPENDENCE

Dexmethylphenidate hydrochloride tablets 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 dexmethylphenidate hydrochloride tablets, 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 dexmethylphenidate hydrochloride tablets, 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 dexmethylphenidate hydrochloride tablets 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) and Drug Abuse and Dependence (9.2)].

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Pretreatment Screening

Prior to treating patients with dexmethylphenidate hydrochloride tablets, 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 dexmethylphenidate hydrochloride tablets [*see Warnings and Precautions (5.10)]*.

2.2 Pediatric Patients with Attention Deficit Hyperactivity Disorder

Patients New to Methylphenidate

The recommended starting dose of dexmethylphenidate hydrochloride tablet for pediatric patients who are not currently taking racemic methylphenidate, or for patients who are on stimulants other than methylphenidate, is 5 mg daily (2.5 mg twice daily) with or without food.

Patients Currently on Methylphenidate

The recommended starting dose of dexmethylphenidate hydrochloride tablet for pediatric patients currently using methylphenidate is half (1/2) the total daily dose of racemic methylphenidate.

Titration Schedule

The dose may be titrated weekly in increments of 2.5 to 5 mg to a maximum of 20 mg daily (10 mg twice daily). The dose should be individualized according to the needs and response of the patient.

Maintenance/Extended Treatment

Pharmacological treatment of ADHD may be needed for extended periods. Periodically reevaluate the long-term use of dexmethylphenidate hydrochloride tablets and adjust dosage as needed.

2.3 Administration Instructions

Dexmethylphenidate hydrochloride tablets is administered orally twice daily, at least 4 hours apart.

2.4 Dose Reduction and Discontinuation

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

3 DOSAGE FORMS AND STRENGTHS

Dexmethylphenidate hydrochloride tablets are as follows:
• 2.5 mg: blue, round, flat-faced, beveled-edge tablets, debossed with “862” on the one side and “n” on the other side
• 5 mg: yellow, round, flat-faced, beveled-edge tablets, debossed with “860” on the one side and “n” on the other side
• 10 mg: white, round, flat-faced, beveled-edge tablets, debossed with “861” on the one side and “n” on the other side

4 CONTRAINDICATIONS

- Hypersensitivity to methylphenidate or other components of dexmethylphenidate hydrochloride tablets. Hypersensitivity reactions, such as angioedema and anaphylactic reactions have been reported in patients treated with methylphenidate *[see Adverse Reactions (6.1)]*.
- Concomitant treatment with monoamine oxidase inhibitors (MAOIs), or within 14 days following discontinuation of treatment with an MAOI, because of the risk of hypertensive crises *[see Drug Interactions (7.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Potential for Abuse and Dependence

Dexmethylphenidate hydrochloride tablet has a high potential for abuse and misuse. The use of dexmethylphenidate hydrochloride tablet exposes individuals to the risks of abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Dexmethylphenidate hydrochloride tablet 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 dexmethylphenidate hydrochloride tablet, 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 dexmethylphenidate hydrochloride tablet 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 dexmethylphenidate hydrochloride tablet in a safe place, preferably locked, and instruct patients to not give dexmethylphenidate hydrochloride tablet to anyone else. Throughout dexmethylphenidate hydrochloride tablet 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 Patient With Serious Cardiac Disease

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

Avoid dexmethylphenidate hydrochloride tablets use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmia, 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 mmHg) and heart rate (mean increase approximately 3 to 6 beats per minute). Some patients may have larger increases.

Monitor all dexmethylphenidate hydrochloride tablets- treated patients for hypertension and tachycardia.

5.4 Psychiatric Adverse Reactions

Exacerbation of Preexisting Psychosis

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

Induction of a Manic Episode in Patients With Bipolar Disorder

CNS stimulants may induce a manic or mixed mood episode in patients. Prior to initiating dexmethylphenidate hydrochloride tablets 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 dosages, 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 dexmethylphenidate hydrochloride tablets.

5.5 Priapism

Prolonged and painful erections, sometimes requiring surgical intervention, have been reported with methylphenidate use in both adult and pediatric male patients. Although priapism was not reported with methylphenidate initiation, it developed after some time on the drug, often subsequent to an increase in dose. Priapism has also appeared during a period of drug withdrawal (drug holidays or during discontinuation). 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 dexmethylphenidate hydrochloride tablets, 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 dosages 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 for digital changes is necessary during dexmethylphenidate hydrochloride tablets treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for dexmethylphenidate hydrochloride tablets -treated patients who develop signs or symptoms of peripheral vasculopathy

5.7 Long-Term Suppression of Growth in Pediatric Patients

CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients.
Careful follow-up of weight and height in patients ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated 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 dexmethylphenidate hydrochloride tablets -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, dexmethylphenidate hydrochloride tablets -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 dexmethylphenidate hydrochloride tablets to patients with open-angle glaucoma or abnormally increased IOP only if the benefit of treatment is considered to outweigh the risk. Closely monitor dexmethylphenidate hydrochloride tablets -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 dexmethylphenidate hydrochloride tablets, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor dexmethylphenidate hydrochloride tablets -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:

- Abuse, Misuse, and Addiction *[see Boxed Warning, Warnings and Precautions (5.1), Drug Abuse and Dependence (9.2, 9.3)]*
- Known hypersensitivity to methylphenidate or other ingredients of dexmethylphenidate hydrochloride tablet *[see Contraindications (4)]*
- Hypertensive crisis with Concomitant Use of Monoamine Oxidase Inhibitors *[see Contraindications (4), Drug Interactions (7.1)]*
- 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.

Clinical Trials Experience with Dexmethylphenidate Hydrochloride in Pediatric Patients with ADHD

The safety data in this section is based on data related to dexmethylphenidate hydrochloride exposure during the premarketing development program in a total of 696

participants in clinical trials (684 patients, 12 healthy adult subjects). These participants received dexmethylphenidate hydrochloride 5, 10, or 20 mg/day. The 684 ADHD patients (ages 6 to 17 years) were evaluated in 2 controlled clinical studies, 2 clinical pharmacology studies, and 2 open-label long-term safety studies.

Most Common Adverse Reactions (incidence of greater than or equal to 5% and at least twice placebo): abdominal pain, fever, anorexia, and nausea

Adverse Reactions Leading to Discontinuation: Overall, 50 of 684 (7.3%) pediatric patients treated with dexmethylphenidate hydrochloride experienced an adverse reaction that resulted in discontinuation. The most common reasons for discontinuation were twitching (described as motor or vocal tics), anorexia, insomnia, and tachycardia (approximately 1% each).

Table 1 enumerates adverse reactions for two, placebo-controlled, parallel group studies in pediatric patients with ADHD taking dexmethylphenidate hydrochloride tablet doses of 5, 10, and 20 mg/day. The table includes only those reactions that occurred in patients treated with dexmethylphenidate hydrochloride tablet for which the incidence was at least 5% and twice the incidence among placebo-treated patients.

Table 1: Common Adverse Reactions in Pediatric Patients (6 to 17 years of age) with ADHD*

System Organ Class	Adverse Reactions	Dexmethylphenidate hydrochloride tablets (N = 79)	Placebo (N = 82)
Body as a Whole	Abdominal pain	15%	6%
	Fever	5%	1%
Digestive System	Anorexia	6%	1%
	Nausea	9%	1%

Abbreviation: ADHD, attention deficit hyperactivity disorder

6.2 Postmarketing Experience

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

Musculoskeletal: rhabdomyolysis

Immune System Disorders: hypersensitivity reactions, such as angioedema, anaphylactic reactions

Adverse Reactions Reported with all Ritalin and Dexmethylphenidate Hydrochloride Formulations

The following adverse reactions associated with the use of all Ritalin and dexmethylphenidate hydrochloride formulations were identified in clinical trials, spontaneous reports, and literature. Because these reactions were reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or to establish a causal relationship to drug exposure.

Infections and Infestations: nasopharyngitis

Blood and the Lymphatic System Disorders: leukopenia, thrombocytopenia, anemia

Immune System Disorders: hypersensitivity reactions, including angioedema and anaphylaxis

Metabolism and Nutrition Disorders: decreased appetite, reduced weight gain, and suppression of growth during prolonged use in pediatric patients

Psychiatric Disorders: insomnia, anxiety, restlessness, agitation, psychosis (sometimes with visual and tactile hallucinations), depressed mood, depression

Nervous System Disorders: headache, dizziness, tremor, dyskinesia, including choreoatheetoid movements, drowsiness, convulsions, cerebrovascular disorders (including vasculitis, cerebral hemorrhages, and cerebrovascular accidents), serotonin syndrome in combination with serotonergic drugs

Eye Disorders: blurred vision, difficulties in visual accommodation

Cardiac Disorders: tachycardia, palpitations, increased blood pressure, arrhythmias, angina pectoris

Respiratory, Thoracic, and Mediastinal Disorders: cough

Gastrointestinal Disorders: dry mouth, nausea, vomiting, abdominal pain, dyspepsia

Hepatobiliary Disorders: abnormal liver function, ranging from transaminase elevation to severe hepatic injury

Skin and Subcutaneous Tissue Disorders: hyperhidrosis, pruritus, urticaria, exfoliative dermatitis, scalp hair loss, erythema multiforme rash, thrombocytopenic purpura

Musculoskeletal and Connective Tissue Disorders: arthralgia, muscle cramps, rhabdomyolysis, trismus

Investigations: weight loss (adult ADHD patients)

Vascular Disorders: peripheral coldness, Raynaud's phenomenon

Additional Adverse Reactions Reported with Other Methylphenidate-Containing Products

The list below shows adverse reactions not listed with Ritalin and dexmethylphenidate hydrochloride formulations that have been reported with other methylphenidate products based on clinical trials data and post-marketing spontaneous reports.

Blood and Lymphatic Disorders: pancytopenia

Immune System Disorders: hypersensitivity reactions, such as auricular swelling

Psychiatric Disorders: affect lability, mania, disorientation, libido changes

Nervous System Disorders: migraine

Eye Disorders: diplopia, mydriasis

Cardiac Disorders: sudden cardiac death, myocardial infarction, bradycardia, extrasystole, supraventricular tachycardia, ventricular extrasystole

Respiratory, Thoracic, and Mediastinal Disorders: pharyngolaryngeal pain, dyspnea

Gastrointestinal Disorders: diarrhea, constipation

Skin and Subcutaneous Tissue Disorders: angioneurotic edema, erythema, fixed drug eruption

Musculoskeletal, Connective Tissue, and Bone Disorders: myalgia, muscle twitching

Renal and Urinary Disorders: hematuria

Reproductive System and Breast Disorders: gynecomastia

General Disorders: fatigue

Urogenital Disorders: priapism

7 DRUG INTERACTIONS

7.1 Clinically Important Drug Interactions with Dexmethylphenidate Hydrochloride Tablet

Table 2 presents clinically important drug interactions with dexmethylphenidate hydrochloride tablet.

Table 2: Clinically Important Drug Interactions with Dexmethylphenidate Hydrochloride Tablet

Monoamine Oxidase Inhibitors (MAOI)	
Clinical Impact	Concomitant use of MAOIs and CNS stimulants, including dexmethylphenidate hydrochloride , can cause hypertensive crisis. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure *[see Contraindications (4)]*.
Intervention	Concomitant use of dexmethylphenidate hydrochloride with MAOIs or within 14 days after discontinuing MAOI treatment is contraindicated.
Antihypertensive Drugs	
Clinical Impact	Dexmethylphenidate hydrochloride may decrease the effectiveness of drugs used to treat hypertension *[see Warnings and Precautions (5.3)]*.
Intervention	Adjust the dosage of the antihypertensive drug as needed.
Halogenated Anesthetics	
Clinical Impact	Concomitant use of halogenated anesthetics and dexmethylphenidate hydrochloride may increase the risk of sudden blood pressure and heart rate increase during surgery.
Intervention	Monitor blood pressure and avoid use of dexmethylphenidate hydrochloride in patients being treated with anesthetics on the day of surgery.
Risperidone	
	Combined use of methylphenidate with risperidone when

Clinical Impact	there is a change, whether an increase or decrease, in dosage of either or both medications, may increase the risk of extrapyramidal symptoms (EPS)
Intervention	Monitor for signs of EPS

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Dexmethylphenidate is the *d-threo* enantiomer of racemic methylphenidate. Published studies and postmarketing reports on methylphenidate use during pregnancy have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. There may be risks to the fetus associated with the use of CNS stimulants use during pregnancy *(see Clinical Considerations)*. Embryo-fetal development studies in rats showed delayed fetal skeletal ossification at doses up to 5 times the maximum recommended human dose (MRHD) of 20 mg/day given to adults based on plasma levels. A decrease in pup weight in males was observed in a pre- and post-natal development study with oral administration of methylphenidate to rats throughout pregnancy and lactation at doses 5 times the MRHD of 20 mg/day given to adults based on plasma levels. Plasma levels in adults were comparatively similar to plasma levels in adolescents *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies 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.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

CNS stimulants such as dexmethylphenidate hydrochloride, 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 embryo-fetal development studies conducted in rats and rabbits, dexmethylphenidate was administered orally at doses of up to 20 and 100 mg/kg/day, respectively, during the period of organogenesis. No evidence of malformations was found in either the rat or rabbit study; however, delayed fetal skeletal ossification was observed at the highest dose level in rats. When dexmethylphenidate was administered to rats throughout pregnancy and lactation at doses of up to 20 mg/kg/day, post-weaning body weight gain was decreased in male offspring at the highest dose, but no other effects on postnatal development were observed. At the highest doses tested, plasma levels [area under the curves (AUCs)] of dexmethylphenidate in pregnant rats and rabbits were approximately

5 and 1 times, respectively, those in adults dosed with the MRHD of 20 mg/day.

Racemic methylphenidate has been shown to cause malformations (increased incidence of fetal spina bifida) in rabbits when given in doses of 200 mg/kg/day throughout organogenesis.

8.2 Lactation

Risk Summary

Dexmethylphenidate is the *d-threo* enantiomer of racemic methylphenidate. Limited published literature, based on milk sampling from seven mothers 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 stimulant exposure are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for dexmethylphenidate hydrochloride and any potential adverse effects on the breastfed infant from dexmethylphenidate hydrochloride 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 dexmethylphenidate hydrochloride have been established in pediatric patients ages 6 to 17 years in two adequate and well-controlled clinical trials *[see Clinical Studies (14)].*

The safety and effectiveness of dexmethylphenidate hydrochloride in pediatric patients less than 6 years have not been established.

The long-term efficacy of dexmethylphenidate hydrochloride in pediatric patients has not been established.

Long Term Suppression of Growth

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

Juvenile Animal Toxicity Data

Rats treated with racemic 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 MRHD of 60 mg/day given to children on a mg/m^2 basis.

In a study conducted in young rats, racemic 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 4 times the MRHD of 60 mg of racemic methylphenidate given to children on a mg/m^2 basis) or greater, and a deficit in the acquisition of a specific learning task was seen in females exposed to the highest dose (8 times the MRHD given to children on a mg/m^2 basis). The no effect level for juvenile neurobehavioral development in rats was 5 mg/kg/day (approximately 0.5 times the MRHD given to children on a mg/m^2 basis). The clinical significance of the long-term behavioral effects observed in rats is unknown.

8.5 Geriatric Use

Dexmethylphenidate hydrochloride has not been studied in the geriatric population.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Dexmethylphenidate hydrochloride tablet contains dexmethylphenidate hydrochloride, a Schedule II controlled substance.

9.2 Abuse

Dexmethylphenidate hydrochloride tablet 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)*]. Dexmethylphenidate hydrochloride tablet 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 ofCNS stimulants, including dexmethylphenidate hydrochloride tablets, 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

Dexmethylphenidate hydrochloride tablets 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 dexmethylphenidate hydrochloride tablets include dysphoric mood; depression; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; and psychomotor retardation or agitation.

Tolerance

Dexmethylphenidate hydrochloride tablets 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

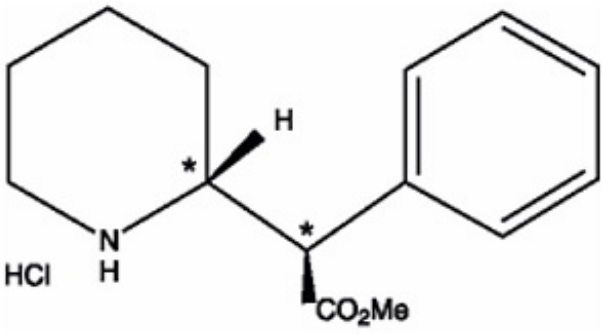
Consider the possibility of multiple drug ingestion. Because methylphenidate has a large volume of distribution and is rapidly metabolized, dialysis is not useful. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

11 DESCRIPTION

Dexmethylphenidate hydrochloride tablets contains dexmethylphenidate hydrochloride, a CNS stimulant. Dexmethylphenidate hydrochloride is the *d-threo* enantiomer of racemic methylphenidate hydrochloride. Dexmethylphenidate hydrochloride tablets are available as 2.5 mg, 5 mg, and 10 mg strength tablets for oral administration.

Chemically, dexmethylphenidate hydrochloride is methyl α-phenyl-2-piperidineacetate hydrochloride, (R,R')-(+)-.

Its structural formula is:



$C_{14}H_{19}NO_2$•HCl M.W. 269.77 g/mol

Note: * = asymmetric carbon centers

Dexmethylphenidate hydrochloride is a white 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. Its molecular weight is 269.77 g/mol.

Inactive ingredients: citric acid anhydrous, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinized starch, sodium starch glycolate, and FD&C Blue No.1 (2.5 mg tablets), D&C Yellow #10 (5 mg tablets); the 10 mg tablet contains no dye.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Dexmethylphenidate hydrochloride is a CNS stimulant. The mode of therapeutic action in ADHD is not known.

12.2 Pharmacodynamics

Pharmacodynamics

Dexmethylphenidate is the more pharmacologically active d-enantiomer of racemic methylphenidate. Methylphenidate blocks the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

Cardiac Electrophysiology

A formal QT study has not been conducted in patients taking dexmethylphenidate hydrochloride tablet; however, a large QT effect is not expected. At the recommended maximum total daily dosage of 40 mg, dexmethylphenidate hydrochloride extended-release capsule does not prolong the QTc interval to any clinically relevant extent.

12.3 Pharmacokinetics

Absorption

Dexmethylphenidate hydrochloride is readily absorbed following oral administration of dexmethylphenidate hydrochloride. In patients with ADHD, plasma dexmethylphenidate concentrations increase rapidly, reaching a maximum in the fasted state at about 1 to

1.5 hours postdose. No differences in the pharmacokinetics of dexmethylphenidate hydrochloride were noted following single and repeated twice daily dosing, thus indicating no significant drug accumulation in children with ADHD.

After single dose administration of dexmethylphenidate hydrochloride to pediatric patients, dexmethylphenidate exposure (C_{max} and $AUC_{0\text{-}inf}$) showed dose-proportional increase in the range of 2.5 mg to 10 mg. Comparable plasma dexmethylphenidate levels were achieved following single *dl-threo*-methylphenidate HCl doses given as capsules in twice the total mg amount (equimolar with respect to dexmethylphenidate hydrochloride).

Approximately 90% of the dose is absorbed after oral administration of radiolabeled racemic methylphenidate. However, due to first pass metabolism the mean absolute bioavailability of dexmethylphenidate when administered in various formulations was 22% to 25%.

Effect of Food

High fat breakfast did not significantly affect C_{max} or $AUC_{0\text{-}inf}$ of dexmethylphenidate when two 10 mg dexmethylphenidate hydrochloride tablets were administered, but delayed T_{max} from 1.5 hours post dose to 2.9 hours post dose.

Distribution

The plasma protein binding of dexmethylphenidate is not known; racemic methylphenidate is bound to plasma proteins by 12% to 15%, independent of concentration. Dexmethylphenidate shows a volume of distribution of 2.65 ± 1.11 L/kg.

Elimination

Plasma dexmethylphenidate concentrations declined exponentially following oral administration of dexmethylphenidate hydrochloride tablets. Intravenous dexmethylphenidate was eliminated with a mean clearance of 0.40 ± 0.12 L/hr/kg. The mean terminal elimination half-life of dexmethylphenidate was approximately 2.2 hours.

Metabolism

In humans, dexmethylphenidate is metabolized primarily via de-esterification to *d*-α-phenyl-piperidine acetic acid (also known as *d*-ritalinic acid). This metabolite has little or no pharmacological activity. There is little or no *in vivo* interconversion to the *l-threo*-enantiomer.

Excretion

After oral dosing of radiolabeled racemic methylphenidate in humans, about 90% of the radioactivity was recovered in urine. The main urinary metabolite of racemic *dl*-methylphenidate was *dl*-ritalinic acid, accountable for approximately 80% of the dose. Urinary excretion of parent compound accounted for 0.5% of an intravenous dose.

Studies in Special Populations

Male and Female Patients

Pharmacokinetic parameters were similar for boys and girls (mean age 10 years).

In a single dose study conducted in adults, the mean dexmethylphenidate $AUC_{0\text{-}inf}$ values (adjusted for body weight) following single two 10 mg doses of dexmethylphenidate hydrochloride were 25% to 35% higher in adult female volunteers

(n = 6) compared to male volunteers (n = 9). Both T_{max} and $t_{1/2}$ were comparable for males and females.

Racial or Ethnic Groups

There is insufficient experience with the use of dexmethylphenidate hydrochloride to detect ethnic variations in pharmacokinetics.

Pediatric Patients

The pharmacokinetics of dexmethylphenidate after dexmethylphenidate hydrochloride tablets administration have not been studied in children less than 6 years of age. When single doses of dexmethylphenidate hydrochloride tablet were given to children between the ages of 6 to 12 years and healthy adult volunteers, C_{max} of dexmethylphenidate was similar, however, pediatric patients showed somewhat lower AUCs compared to the adults.

Patients with Renal Impairment

There is no experience with the use of dexmethylphenidate hydrochloride tablet in patients with renal impairment. Since renal clearance is not an important route of methylphenidate clearance, renal impairment is expected to have little effect on the pharmacokinetics of dexmethylphenidate hydrochloride tablet.

Patients with Hepatic Impairment

There is no experience with the use of dexmethylphenidate hydrochloride tablet in patients with hepatic impairment.

Drug Interaction Studies

Methylphenidate is not metabolized by cytochrome P450 (CYP) isoenzymes to a clinically relevant extent. Inducers or inhibitors of CYPs are not expected to have any relevant impact on methylphenidate pharmacokinetics. Conversely, the d- and l-enantiomers of methylphenidate did not relevantly inhibit CYP1A2, 2C8, 2C9, 2C19, 2D6, 2E1, or 3A. Clinically, methylphenidate coadministration did not increase plasma concentrations of the CYP2D6 substrate desipramine.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

Carcinogenesis

Lifetime carcinogenicity studies have not been carried out with dexmethylphenidate. In a lifetime carcinogenicity study carried out in B6C3F1 mice, racemic methylphenidate caused an increase in hepatocellular adenomas, and in males only, an increase in hepatoblastomas was seen at a daily dose of approximately 60 mg/kg/day. This dose is approximately 2 times the MRHD of 60 mg/day of racemic methylphenidate given to children 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.

Racemic 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 4 times the MRHD (children) of 60 mg/day of racemic methylphenidate on a mg/m^2 basis.

In a 24-week carcinogenicity study with racemic methylphenidate in the transgenic mouse strain p53+/-, which is sensitive to genotoxic carcinogens, there was no evidence of carcinogenicity. Male and female mice were fed diets containing the same concentrations as in the lifetime carcinogenicity study; the high-dose group was exposed to 60-74 mg/kg/day of racemic methylphenidate.

Mutagenesis

Dexmethylphenidate was not mutagenic in the *in vitro* Ames reverse mutation assay, in the *in vitro* mouse lymphoma cell forward mutation assay, or in the *in vivo* mouse bone marrow micronucleus test. In an *in vitro* assay using cultured Chinese Hamster Ovary cells treated with racemic methylphenidate, sister chromatid exchanges and chromosome aberrations were increased, indicative of a weak clastogenic response.

Impairment of Fertility

No human data on the effect of methylphenidate on fertility are available.

Fertility studies have not been conducted with dexmethylphenidate. Racemic 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 10 times the MRHD of 60 mg/day of racemic methylphenidate given adolescents on a mg/m^2 basis.

14 CLINICAL STUDIES

The efficacy of dexmethylphenidate hydrochloride tablet for the treatment of ADHD was established in two double-blind, parallel-group, placebo-controlled trials in untreated or previously treated patients (ages 6 to 17 years old) who met The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for ADHD inattentive, hyperactive-impulsive, or combined inattentive/hyperactive-impulsive subtypes. The sample was predominantly younger (ages 6 to 12 years); thus, the findings are most pertinent to this age group.

In Study 1, patients were randomized to receive either dexmethylphenidate hydrochloride tablet (5, 10, or 20 mg/day total dose), racemic methylphenidate HCl (10, 20, or 40 mg/day total dose), or placebo in a multicenter, 4-week, parallel group study in 132 pediatric patients. Patients received study medication twice daily separated by a 3.5 to 5.5 hours interval. Treatment was initiated with the lowest dose, and doses could be doubled at weekly intervals, depending on clinical response and tolerability, up to the maximum dose. The primary outcome was change from baseline to week 4 of the average score (an average of 2 ratings during the week) of the teacher’s version of the Swanson, Nolan and Pelham (SNAP)-ADHD Rating Scale. This 18 item scale measures ADHD symptoms of inattention and hyperactivity/impulsivity, rated on a scale of 0 (Not at All) to 3 (Very Much). Patients treated with dexmethylphenidate hydrochloride tablet showed a statistically significant improvement in symptom scores from baseline over patients who received placebo (Table 3).

Table 3: Summary of Efficacy Results From ADHD Acute-Phase Study in Pediatric Patients (6 - 17 years) (Study 1)

Study Number	Treatment Group	Primary Efficacy Measure: Teacher SNAP-ADHD Total Score[a]	
		Mean Baseline Score (SD)	Mean Change from Baseline Week 4 Score (SD)
Study 1	Dexmethylphenidate hydrochloride tablets 5 to 20 mg/day[b] (n = 44)	1.4 (0.7) (n = 42)	- 0.7 (0.7) (n = 42)
	Placebo (n = 42)	1.6 (0.7) (n = 41)	- 0.2 (0.7) (n = 39)

Abbreviation: ADHD, Attention Deficit Hyperactivity Disorder; SD: standard deviation; SNAP, Swanson, Nolan and Pelham; n = number of patients available at the assessment time point.
[a]Average of two ratings.
[b]Statistically significantly different from placebo.

Study 2 was a multicenter, placebo-controlled, double-blind, 2-week treatment withdrawal study in 75 children (ages 6 to 12 years) who were responders during a 6-week, open-label initial treatment period. Children took study medication twice a day separated by a 3.5 to 5.5 hour interval. The primary outcome was proportion of treatment failures at the end of the 2-week withdrawal phase, where treatment failure was defined as a rating of 6 (much worse) or 7 (very much worse) on the Investigator Clinical Global Impression - Improvement (CGI-I). Patients continued on dexmethylphenidate hydrochloride tablet showed a statistically significant lower rate of failure over patients who received placebo (Table 4).

Table 4: Summary of Efficacy Results From ADHD Randomized Withdrawal Study in Pediatric Patients (6 to 17 years) (Study 2)

Study Number	Treatment Group	Primary Efficacy Measure: Proportion of Treatment Failure[a]	
		Number of Treatment Failures/Number of Randomized Patients	Percentage
Study 2	Dexmethylphenidate hydrochloride tablets 5 to 20 mg/day[b]	6/35	17.1%
	Placebo	25/40	62.5%

Abbreviation: ADHD, attention deficit hyperactivity disorder.
[a]One patient did not have the value at Visit 10 and hence not included in this analysis.
[b]Statistically significantly different from placebo.

16 HOW SUPPLIED/STORAGE AND HANDLING

2.5 mg Tablets: blue, round, flat-faced, beveled-edge tablets, debossed with “862” on the one side and “n” on the other side.
Bottles of 30……NDC 43386-862-03
Bottles of 100……NDC 43386-862-01
Bottles of 1000……NDC 43386-862-10

5 mg Tablets: yellow, round, flat-faced, beveled-edge tablets, debossed with “860” on the one side and “n” on the other side.
Bottles of 30……NDC 43386-860-03
Bottles of 100……NDC 43386-860-01
Bottles of 1000……NDC 43386-860-10

10 mg Tablets: white, round, flat-faced, beveled-edge tablets, debossed with “861” on the one side and “n” on the other side.
Bottles of 30……NDC 43386-861-03
Bottles of 100……NDC 43386-861-01
Bottles of 1000……NDC 43386-861-10

Store at 20°C to 25°C (68°F to 77°F), with excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature].
Dispense in tight, light-resistant container (USP).

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Abuse, Misuse, and Addiction

Educate patients and their families about the risks of abuse, misuse, and addiction of dexmethylphenidate hydrochloride tablets, 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 dexmethylphenidate hydrochloride tablets in a safe place, preferably locked, and instruct patients to not give dexmethylphenidate hydrochloride tablets to anyone else.

Risks to Patient with Serious Cardiac Disease

Advise patients that there are potential risks to patients with serious cardiac disease, including sudden death, with dexmethylphenidate hydrochloride tablets use. Instruct patients to contact a healthcare 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

Instruct patients that dexmethylphenidate hydrochloride tablet can cause elevations of their blood pressure and pulse rate *[see Warnings and Precautions (5.3)].*

Psychiatric Adverse Reactions

Advise patients that dexmethylphenidate hydrochloride tablet, at recommended doses, can cause psychotic or manic symptoms, even in patients without prior history of

psychotic symptoms or mania *[see Warnings and Precautions (5.4)].*

Priapism

Advise patients of the possibility of painful or prolonged penile erections (priapism). Instruct them 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 dexmethylphenidate hydrochloride tablet 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 dexmethylphenidate hydrochloride tablet. 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 that dexmethylphenidate hydrochloride tablet may 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 dexmethylphenidate hydrochloride tablet [*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 dexmethylphenidate hydrochloride tablet. 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)*].

Manufactured for:
Lupin Pharmaceuticals, Inc.
Baltimore, MD 21202

Manufactured by:
Novel Laboratories, Inc.
Somerset, NJ 08873

SAP code: 274932
Rev: 11/2023

MEDICATION GUIDE

Dexmethylphenidate (dex'' meth il fen' i date) Hydrochloride (hye''droe klor' ide) Tablets CII

What is the most important information I should know about dexmethylphenidate hydrochloride tablet?

Dexmethylphenidate hydrochloride tablet may cause serious side effects, including:

- Abuse, misuse, and addiction. Dexmethylphenidate hydrochloride tablet has a high chance for abuse and misuse and may lead to substance use problems, including addiction. Misuse and abuse of dexmethylphenidate hydrochloride tablet, 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 dexmethylphenidate hydrochloride tablet 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 dexmethylphenidate hydrochloride tablet and will monitor you or your child during treatment.
- dexmethylphenidate hydrochloride tablet may lead to physical dependence after prolonged use, even if taken as directed by your healthcare provider.
- Do not give dexmethylphenidate hydrochloride tablet to anyone else. See "**What is dexmethylphenidate hydrochloride tablet?**" for more information.

o Keep dexmethylphenidate hydrochloride tablet in a safe place and properly dispose of any unused medicine. See "**How should I store dexmethylphenidate hydrochloride tablet?**" for more information.
o 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 dexmethylphenidate hydrochloride tablet. Tell your healthcare 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 dexmethylphenidate hydrochloride tablet.

• **Increased blood pressure and heart rate**. Your healthcare provider should check you or your child's blood pressure and heart rate regularly during treatment with dexmethylphenidate hydrochloride tablet.

• Mental (psychiatric) problems:

All Patients

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

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

Call your healthcare provider right away if you or your child have any new or worsening mental symptoms or problems while taking dexmethylphenidate hydrochloride tablet, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

What are dexmethylphenidate hydrochloride tablets?

- Dexmethylphenidate hydrochloride tablets are a central nervous system stimulant (CNS) prescription medicine. **It is used for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD).** Dexmethylphenidate hydrochloride tablets may help increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.
- Dexmethylphenidate hydrochloride tablets should be used as a part of a total treatment program for ADHD that may include counseling or other therapies.

Who should not take dexmethylphenidate hydrochloride tablets: Dexmethylphenidate hydrochloride tablets should not be taken if you or your child:

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

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

Dexmethylphenidate hydrochloride tablets may not be right for you or your child. Before starting dexmethylphenidate hydrochloride tablets, tell your or your child's doctor 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 or toes
- have eye problems, including increased pressure in your eye, glaucoma, or problems with your close-up vision (farsightedness)
- have or had repeated movements
- if you are pregnant or plan to become pregnant. It is not known if dexmethylphenidate hydrochloride tablets will harm your unborn baby.
- if you are breastfeeding or plan to breastfeed. Dexmethylphenidate hydrochloride tablets passes into your breast milk. Talk to your healthcare provider about the best way to feed the baby during

treatment with dexmethylphenidate hydrochloride tablets.

Tell your healthcare provider about all of the medicines that you or your child takes including prescription and over-the-counter medicines, vitamins, and herbal supplements. Dexmethylphenidate hydrochloride tablets 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 dexmethylphenidate hydrochloride tablets. Your healthcare provider will decide whether dexmethylphenidate hydrochloride tablets can be taken with other medicines.

Especially tell your healthcare provider if you or your child takes:

- blood pressure medicines (anti-hypertensive)
  Know the medicines that you or your child takes. Keep a list of your medicines with you to show your healthcare provider and pharmacist.
- You should not take dexmethylphenidate hydrochloride tablets on the day of your operation if a certain type of anesthetic is used. This is because there is a chance of a sudden rise in blood pressure and heart rate during the operation.

Do not start any new medicine while taking dexmethylphenidate hydrochloride tablets without talking to your healthcare provider first.

How should dexmethylphenidate hydrochloride tablets be taken?

- Take dexmethylphenidate hydrochloride tablets exactly as prescribed. Your healthcare provider may adjust the dose until it is right for you or your child.
- Take dexmethylphenidate hydrochloride tablets twice daily, at least 4 hours apart.
- Dexmethylphenidate hydrochloride tablets may be taken with or without food.
- Your healthcare provider may do regular checks of the blood, heart, and blood pressure while taking dexmethylphenidate hydrochloride tablets.
- Children should have their height and weight checked often while taking dexmethylphenidate hydrochloride tablets. Dexmethylphenidate hydrochloride tablets treatment may be stopped if a problem is found during these check-ups.

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

What are the possible side effects of dexmethylphenidate hydrochloride tablets?

Dexmethylphenidate hydrochloride tablets may cause serious side effects, including:

- See **"What is the most important information I should know about dexmethylphenidate hydrochloride tablets?"** for information on reported heart and mental problems.
- **painful and prolonged erections (priapism)** have occurred with methylphenidate. If you or your child develops priapism, seek medical help right away. Because of the potential for lasting damage, priapism

should be evaluated by a healthacre provider immediately.
- **circulation problems in fingers and toes** (peripheral vasculopathy, Including Raynaud's phenomenon):

  - 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 the fingers or toes.
- **Call your healthcare provider right away if you have or your child has any signs of unexplained wounds appearing on fingers or toes while taking dexmethylphenidate hydrochloride tablets.**
- **slowing of growth (height and weight) in children.**Children should have their height and weight checked often during treatment with dexmethylphenidate hydrochloride tablet. Dexmethylphenidate hydrochloride tablet treatment may be stopped if your child is not growing or gaining weight.
- **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 dexmethylphenidate hydrochloride tablet.

Common side effects include:
- abdominal pain
- fever
- anorexia
- nausea

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

How should I store dexmethylphenidate hydrochloride tablets?
- Store dexmethylphenidate hydrochloride tablets in a safe place and in a tightly closed container at room temperature between 68°F to 77°F (20°C to 25°C).
- Protect from light.
- Dispose of remaining, unused, or expired dexmethylphenidate hydrochloride tablet 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 dexmethylphenidate hydrochloride tablet 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 dexmethylphenidate hydrochloride tablet in the household trash. Visit www.fda.gov/drugdisposal for additional information on disposal of unused medicines. Keep dexmethylphenidate hydrochloride tablet and all medicines out of the reach of children

- **Keep dexmethylphenidate hydrochloride tablets and all medicines out of the reach of children.**

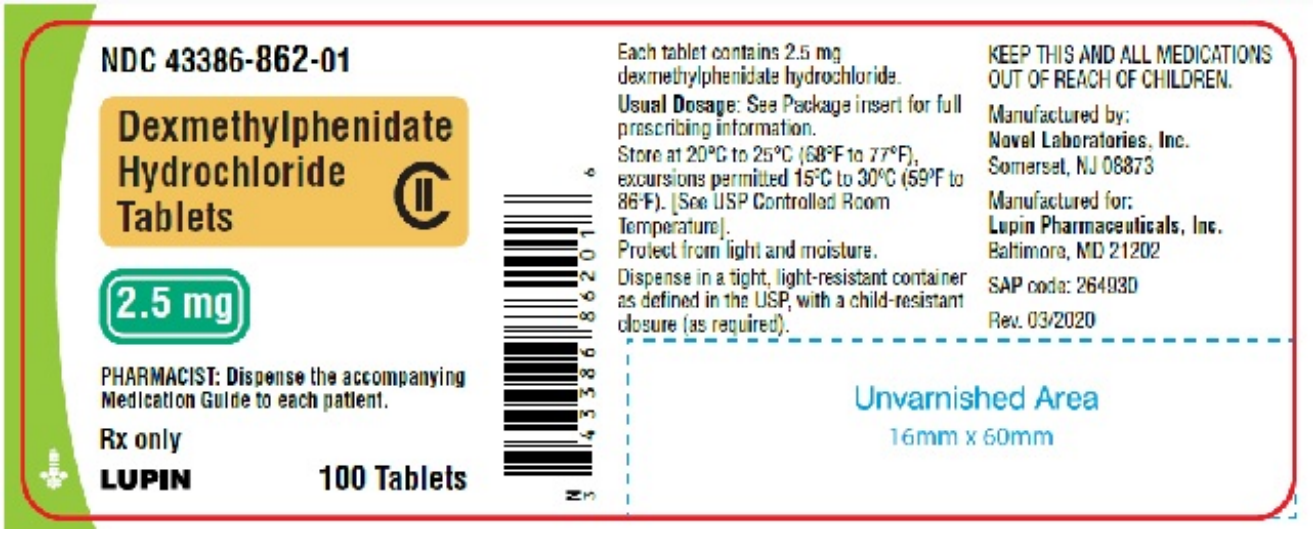
General information about the safe and effective use of dexmethylphenidate hydrochloride tablets.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about dexmethylphenidate hydrochloride tablets that is written for healthcare professionals. Do not use dexmethylphenidate hydrochloride tablets for a condition for which they were not prescribed. Do not give dexmethylphenidate hydrochloride tablets to other people, even if they have the same symptoms that you have. It may harm them and it is against the law.

What are the ingredients in dexmethylphenidate hydrochloride tablets?
Active ingredient: dexmethylphenidate hydrochloride
Inactive ingredients: citric acid anhydrous, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinized starch, sodium starch glycolate, and FD&C Blue No.1 (2.5 mg tablets), D&C Yellow #10 (5 mg tablets); the 10 mg tablet contains no dye.
Manufactured for:
Lupin Pharmaceuticals, Inc.
Baltimore, MD 21202
Manufactured by:
Novel Laboratories, Inc.
Somerset, NJ 08873
SAP code: 274932
Rev: 11/2023

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Rev. 11/2023

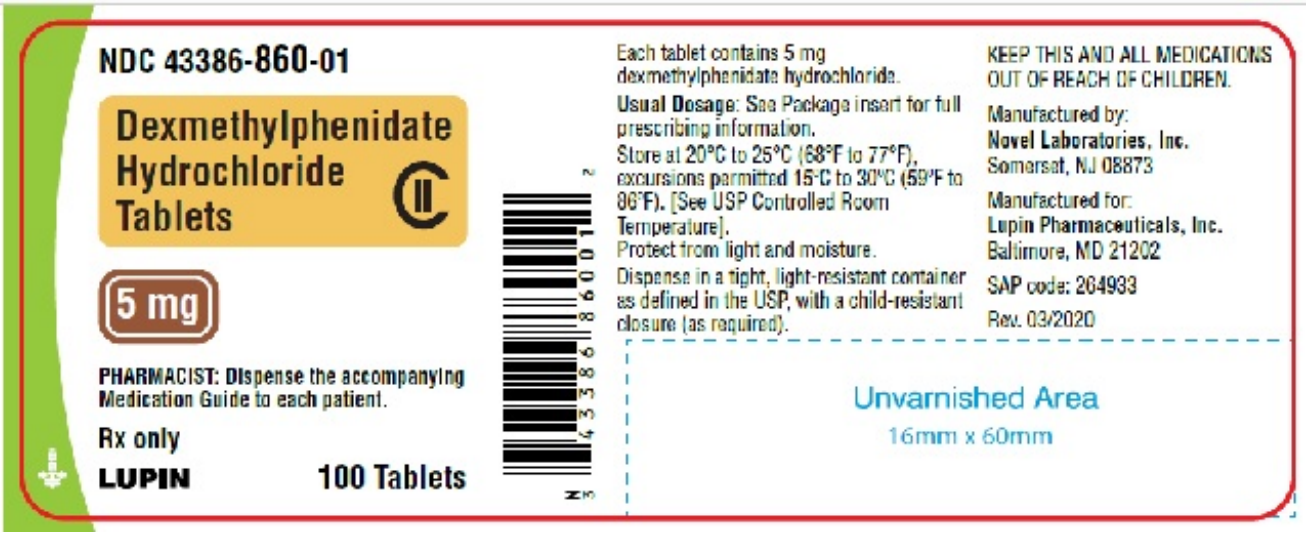
2.5 mg Tablets

100 count



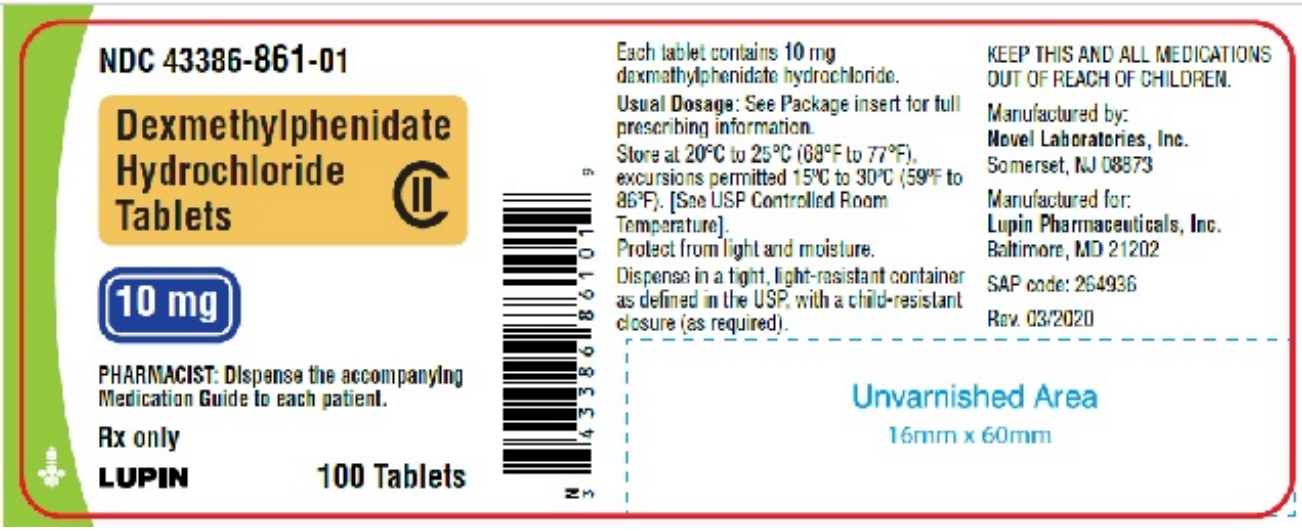
5 mg Tablets

100 count



10 mg Tablets

100 count



DEXMETHYLPHENIDATE HYDROCHLORIDE

dexmethylphenidate hydrochloride tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:43386-862
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
DEXMETHYLPHENIDATE HYDROCHLORIDE (UNII: 1678OK0E08) (DEXMETHYLPHENIDATE - UNII:M32RH9MFGP)	DEXMETHYLPHENIDATE HYDROCHLORIDE	2.5 mg

Inactive Ingredients	
Ingredient Name	**Strength**
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
STARCH, CORN (UNII: O8232NY3SJ)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	

Product Characteristics			
Color	BLUE	**Score**	no score
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	862;n
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:43386-862-03	30 in 1 BOTTLE; Type 0: Not a Combination Product	01/31/2040	
2	NDC:43386-862-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	12/04/2015	
3	NDC:43386-862-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	01/31/2040	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA204534	12/04/2015	

DEXMETHYLPHENIDATE HYDROCHLORIDE

dexmethylphenidate hydrochloride tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:43386-860
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
DEXMETHYLPHENIDATE HYDROCHLORIDE (UNII: 1678OK0E08) (DEXMETHYLPHENIDATE - UNII:M32RH9MFGP)	DEXMETHYLPHENIDATE HYDROCHLORIDE	5 mg

Inactive Ingredients	
Ingredient Name	**Strength**
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
STARCH, CORN (UNII: O8232NY3SJ)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	

Product Characteristics			
Color	YELLOW	**Score**	no score
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	860;n
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:43386-860-03	30 in 1 BOTTLE; Type 0: Not a Combination Product	01/31/2040	
2	NDC:43386-860-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	12/04/2015	
3	NDC:43386-860-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	01/31/2040	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA204534	12/04/2015	

DEXMETHYLPHENIDATE HYDROCHLORIDE

dexmethylphenidate hydrochloride tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:43386-861
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
DEXMETHYLPHENIDATE HYDROCHLORIDE (UNII: 1678OK0E08) (DEXMETHYLPHENIDATE - UNII:M32RH9MFGP)	DEXMETHYLPHENIDATE HYDROCHLORIDE	10 mg

Inactive Ingredients

Ingredient Name	Strength
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
STARCH, CORN (UNII: O8232NY3SJ)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	

Product Characteristics

Color	WHITE	**Score**	no score
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	861;n
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43386-861-03	30 in 1 BOTTLE; Type 0: Not a Combination Product	01/31/2040	
2	NDC:43386-861-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	12/04/2015	
3	NDC:43386-861-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	01/31/2040	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA204534	12/04/2015	

Labeler - Lupin Pharmaceuticals,Inc. (089153071)

Registrant - Novel Laboratories, Inc. (793518643)

Establishment

Name	Address	ID/FEI	Business Operations
Novel Laboratories, Inc.		793518643	manufacture(43386-860, 43386-861, 43386-862) , analysis(43386-860, 43386-861, 43386-862) , pack(43386-860, 43386-861, 43386-862)

Revised: 1/2024 Lupin Pharmaceuticals,Inc.