HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use RITALIN LA safely and effectively. See full prescribing information for RITALIN LA.

RITALIN LA® (methylphenidate hydrochloride) extended-release capsules for oral use, CII
Initial U.S. Approval: 1955

WARNING: ABUSE, MISUSE, AND ADDICTION

See full prescribing information for complete boxed warning.

Ritalin LA 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 Ritalin LA, can result in overdose and death (5.1, 9.2, 10).

- **Before prescribing Ritalin LA, 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)	10/2023
Warnings and Precautions (5.1, 5.2, 5.8, 5.9, 5.10)	10/2023

----------INDICATIONS AND USAGE----------

Ritalin LA is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 12 years of age (1).

----------DOSAGE AND ADMINISTRATION----------

- Administer orally once daily in the morning (2.2).
- Capsules may be swallowed whole or opened and the entire contents sprinkled on applesauce (2.2).
- Should not be crushed, chewed, or divided (2.2).
- Patients new to methylphenidate: Start at 20 mg daily, titrating the dose weekly in 10-mg increments. Doses above 60 mg daily are not recommended (2.3).
- For patients currently using Ritalin: Dosage is based on current dose regimen (2.4).
- If switching from other methylphenidate products, discontinue treatment and titrate with Ritalin LA (2.4).

----------DOSAGE FORMS AND STRENGTHS----------

Extended-release capsules: 10 mg, 20 mg, 30 mg, and 40 mg (3).

----------CONTRAINDICATIONS----------

- Known hypersensitivity to methylphenidate or product components (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 Patients with Serious Cardiac Disease:* Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac rhythm 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 Ritalin LA, screen patients for risk factors for developing a manic episode. If new psychotic or manic symptoms occur, consider discontinuing Ritalin LA (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 Ritalin LA 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 i*n 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:* Ritalin LA-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 Ritalin LA 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 abnormally increased IOP or open angle glaucoma (5.9).
- *Motor and Verbal Tics, and Worsening of Tourette's Syndrome*: Before initiating Ritalin LA, 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----------

Most common adverse reactions (greater than 5% during incidence) were headache, insomnia, upper abdominal pain, decreased appetite, and anorexia (6).

To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- *Antihypertensive Drugs:* Monitor blood pressure and heart. Adjust dosage of antihypertensive drug as needed (7.1).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 10/2023

FULL PRESCRIBING INFORMATION: CONTENTS* WARNING: ABUSE, MISUSE, AND ADDICTION

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE, MISUSE, AND ADDICTION

Ritalin LA 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 Ritalin LA, 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 Ritalin LA, 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 Ritalin LA 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

Ritalin LA® is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD), in pediatric patients 6 to 12 years of age *[see Clinical Studies (14)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Pretreatment Screening

Prior to treating patients with Ritalin LA, 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 Ritalin LA *[see Warnings and Precautions (5.10)]*.

2.2 General Dosing Information

The recommended starting dose for Ritalin LA is 20 mg once daily. Increase dosage gradually, in increments of 10 mg weekly. Daily dosage above 60 mg is not recommended. When a lower initial dose is appropriate, patients may begin treatment with 10 mg.

Administer Ritalin LA orally once daily in the morning. Ritalin LA may be swallowed as whole capsules or may be administered by sprinkling the capsule contents on a small amount of applesauce (see specific instructions below). Ritalin LA and/or their contents should not be crushed, chewed, or divided.

The capsules may be carefully opened and the beads sprinkled over a spoonful of applesauce. The applesauce should not be warm because it could affect the modified release properties of this formulation. The mixture of drug and applesauce should be consumed immediately in its entirety. The drug and applesauce mixture should not be stored for future use.

2.3 Patients Currently Using Ritalin

The recommended dose of Ritalin LA for patients currently taking Ritalin twice daily is provided below in Table 1.

Table 1: Recommended Dose Conversion from Ritalin

Previous Ritalin dose	Recommended Ritalin LA dose
5 mg Ritalin twice daily	10 mg once daily
10 mg Ritalin twice daily	20 mg once daily
15 mg Ritalin twice daily	30 mg once daily
20 mg Ritalin twice daily	40 mg once daily
30 mg Ritalin twice daily	60 mg once daily

2.4 Switching from Other Methylphenidate Products

If switching from other methylphenidate products, discontinue that treatment, and titrate with Ritalin LA using the titration schedule.

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

Clinical judgment should be used when selecting the starting dose. Daily dosage above 60 mg is not recommended.

2.5 Dosage Reduction and Discontinuation

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

3 DOSAGE FORMS AND STRENGTHS

- 10 mg extended-release capsules white/light brown, (imprinted "NVR R10")
- 20 mg extended-release capsules white, (imprinted "NVR R20")
- 30 mg extended-release capsules yellow, (imprinted "NVR R30")
- 40 mg extended-release capsules light brown, (imprinted "NVR R40")

4 CONTRAINDICATIONS

- Hypersensitivity to methylphenidate or other components of Ritalin LA. 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 Abuse, Misuse, and Addiction

Ritalin LA has a high potential for abuse and misuse. The use of Ritalin LA exposes individuals to the risks of abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Ritalin LA 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 Ritalin LA, 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 Ritalin LA, 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 Ritalin LA in a safe place, preferably locked, and instruct patients to not give Ritalin LA to anyone else. Throughout Ritalin LA 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 been reported in patients with structural cardiac abnormalities or other serious cardiac disease who are treated with CNS stimulants at the recommended ADHD dosage.

Avoid Ritalin LA 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 Ritalin LA-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 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 Ritalin LA 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 Ritalin LA.

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 methylphenidate, often subsequent to an increase in dosage. Priapism also occurred during methylphenidate withdrawal (drug holidays or during discontinuation).

Ritalin LA-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 Ritalin LA, 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 the CNS stimulant.

Careful observation for digital changes is necessary during Ritalin LA treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for Ritalin LA-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 pediatric 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 to13 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 Ritalin LA-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, Ritalin LA-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 Ritalin LA to patients with open-angle glaucoma or abnormally increased IOP only if the benefit of treatment is considered to outweigh the risk. Closely monitor Ritalin LA-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 Ritalin LA, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor Ritalin LA-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 Ritalin LA *[see Contraindications (4)]*
- Hypertensive crisis when used concomitantly with 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 practice.

The clinical program for Ritalin LA consisted of 6 studies: 2 controlled clinical studies conducted in children with ADHD aged 6 to 12 years and 4 clinical pharmacology studies conducted in healthy adult volunteers. These studies included a total of 256 subjects; 195 children with ADHD and 61 healthy adult volunteers. The subjects received Ritalin LA in doses of 10 to 40 mg per day. Safety of Ritalin LA was assessed by evaluating frequency and nature of adverse events, routine laboratory tests, vital signs, and body weight. A placebo-controlled, double-blind, parallel-group study was conducted to evaluate the efficacy and safety of Ritalin LA in children with ADHD aged 6 to 12 years. All subjects received Ritalin LA for up to 4 weeks, and had their dose optimally adjusted, prior to entering the double-blind phase of the trial. In the 2-week double-blind treatment phase of this study, patients received either placebo or Ritalin LA at their individually-titrated dose (range, 10 mg to 40 mg).

Adverse reactions with an incidence greater than 5% during the initial 4-week single-blind Ritalin LA titration period of this study were headache, insomnia, upper abdominal pain, appetite decreased, and anorexia.

Adverse reactions with an incidence greater than 2% among Ritalin LA-treated subjects, during the 2-week double-blind phase of the clinical study, are shown in Table 2.

Table 2: Adverse Reactions in Greater Than 2% Ritalin LA-Treated Subjects in the 2-Week Double-Blind Phase

Preferred Term	Ritalin LA N = 65 N (%)	Placebo N = 71 N (%)
Anorexia	2 (3.1)	0 (0.0)
Insomnia	2 (3.1)	0 (0.0)

Adverse Reactions Associated with Discontinuation of Treatment

In the 2-week double-blind treatment phase of a placebo-controlled parallel-group study in children with ADHD, one Ritalin LA-treated subject (1/65, 1.5%) discontinued due to an adverse event (depressed mood).

In the single-blind titration period of this study, subjects received Ritalin LA for up to 4 weeks. During this period a total of 6 subjects (6/161, 3.7%) discontinued due to adverse events. The adverse events leading to discontinuation were anger (2 patients), hypomania, anxiety, depressed mood, fatigue, migraine, and lethargy.

6.2 Postmarketing Experience

The following adverse reactions have been identified during the post approval use of methylphenidate products. 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.

Adverse Reactions Reported with Ritalin and Ritalin LA

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 children

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

Nervous System Disorders: headache, dizziness, tremor, dyskinesia, including choreoathetoid 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

Adverse Reactions Reported with Other Methylphenidate-Containing Products

The list below shows adverse reactions not listed with Ritalin, or Ritalin LA formulations that have been reported with other methylphenidate-containing products.

Blood and Lymphatic Disorders: pancytopenia

Immune System Disorders: hypersensitivity reactions, such as auricular swelling, bullous conditions, eruptions, exanthemas

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

Nervous System Disorders: migraine, motor and verbal tics

Eye Disorders: diplopia, increased intraocular pressure, mydriasis

Cardiac Disorders: sudden cardiac death, myocardial infarction, bradycardia, 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, hyperpyrexia

Urogenital Disorders: priapism

7 DRUG INTERACTIONS

7.1 Clinically Important Drug Interactions with Ritalin LA

Table 3 presents clinically important drug interactions with Ritalin LA.

Table 3: Clinically Important Drug Interactions with Ritalin LA

Monoamine Oxidase Inhibitors (MAOI)	
Clinical impact	Concomitant use of MAOIs and CNS stimulants, including Ritalin LA, 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 Ritalin LA with MAOIs or within 14 days after discontinuing MAOI treatment is contraindicated.
Antihypertensive Drugs	
Clinical impact	Ritalin LA may decrease the effectiveness of drugs used to treat hypertension *[see Warnings and Precautions (5.3)]*.
Intervention	Monitor blood pressure and adjust the dosage of the antihypertensive drug as needed.
Halogenated Anesthetics	
Clinical impact	Concomitant use of halogenated anesthetics and Ritalin LA may increase the risk of sudden blood pressure and heart rate increase during surgery.
Intervention	Avoid use of Ritalin LA in patients being treated with anesthetics on the day of surgery.
Risperidone	
Clinical impact	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)
Intervention	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, including Ritalin LA during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for ADHD medications at 1-866-961-2388 or visiting https://womensmentalhealth.org/adhd-medications/.

Risk Summary

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)*. No effects on morphological development were observed in embryo-fetal development studies with oral administration of methylphenidate to pregnant rats and rabbits during organogenesis at doses up to 10 and 15 times, respectively, the maximum recommended human dose (MRHD) of 60 mg/day given to adolescents on a mg/m^2 basis. However, spina bifida was observed in rabbits at a dose 52 times the MRHD given to adolescents. A decrease in pup body weight was observed in a pre- and post-natal development study with oral administration of methylphenidate to rats throughout pregnancy and lactation at doses 6 times the MRHD given to 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 Ritalin LA, 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, methylphenidate was administered orally at doses of up to 75 and 200 mg/kg/day, respectively, during the period of organogenesis. Malformations (increased incidence of fetal spina bifida) were observed in rabbits at the highest dose, which is approximately 52 times the MRHD of 60 mg/day given to adolescents on a mg/m^2 basis. The no effect level for embryo-fetal development in rabbits was 60 mg/kg/day (15 times the MRHD given to adolescents on a mg/m^2 basis). There was no evidence of morphological development effects in rats, although increased incidences of fetal skeletal variations were seen at the highest dose level (10 times the MRHD of 60 mg/day given to adolescents 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 (3 times the MRHD on a mg/m^2 basis). When methylphenidate was administered to rats throughout pregnancy and lactation at doses of up to 45 mg/kg/day, offspring body weight gain was decreased at the highest dose (6 times the MRHD of 60 mg/day given to adolescents on a mg/m^2 basis), but no other effects on postnatal development were observed. The no effect level for pre- and post-natal development in rats was 15 mg/kg/day (approximately 2 times the MRHD given to adolescents on a mg/m^2 basis).

8.2 Lactation

Risk Summary

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 Ritalin LA and any potential adverse effects on the breastfed infant from Ritalin LA 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 Ritalin LA for the treatment of ADHD have been established in pediatric patients aged 6 to 12 years.

The safety and effectiveness of Ritalin LA in pediatric patients aged less than 6 years have not been established.

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

Long-Term Suppression of Growth

Growth should be monitored during treatment with stimulants, including Ritalin LA. 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 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 4 times the MRHD of 60 mg/day given to children on a mg/m^2 basis.

In a 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 4 times the MRHD of 60 mg/day 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

Ritalin LA has not been studied in the geriatric population.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Ritalin LA contains methylphenidate hydrochloride, a Schedule II controlled substance.

9.2 Abuse

Ritalin LA 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)]*. Ritalin LA 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 hydrochloride 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 Ritalin LA, 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

Ritalin LA 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 Ritalin LA include dysphoric mood; depression; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; and psychomotor retardation or agitation.

Tolerance

Ritalin LA 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

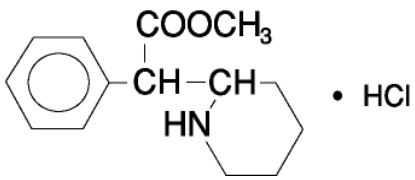
Consider the possibility of multiple drug ingestion. The pharmacokinetic profile of Ritalin LA should be considered when treating patients with overdose. Because methylphenidate has a large volume of distribution and is rapidly metabolized, dialysis is not useful. Consider contacting the Poison Help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

11 DESCRIPTION

Ritalin LA contains methylphenidate hydrochloride, a CNS stimulant.

Ritalin LA extended-release capsules is an extended-release formulation of methylphenidate for oral administration with a bi-modal release profile. Each bead-filled Ritalin LA capsule contains half the dose as immediate-release beads and half as enteric-coated beads, thus providing an immediate release of methylphenidate and a second delayed release of methylphenidate.

The active substance in Ritalin LA is methyl α-phenyl-2-piperidineacetate hydrochloride, and its structural formula is



Methylphenidate hydrochloride USP is a white, odorless, fine 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: ammonio methacrylate copolymer, black iron oxide (10 and 40 mg capsules only), gelatin, methacrylic acid copolymer, polyethylene glycol, red iron oxide (10 and 40 mg capsules only), sugar spheres, talc, titanium dioxide, triethyl citrate, and yellow iron oxide (10, 30, and 40 mg capsules only).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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

12.2 Pharmacodynamics

Methylphenidate is a racemic mixture comprised of the *d*- and *l-threo* enantiomers. The *d-threo* enantiomer is more pharmacologically active than the *l-threo* enantiomer. Methylphenidate blocks the reuptake of norepinephrine and dopamine into the presynaptic neuron and increases the release of these monoamines into the extraneuronal space.

Cardiac Electrophysiology

A formal QT study has not been conducted in patients taking Ritalin LA.

The effect of dexmethylphenidate, the pharmacologically active *d*-enantiomer of Ritalin, on the QT interval was evaluated in a double-blind, placebo- and open-label active (moxifloxacin)-controlled study following single doses of dexmethylphenidate XR 40 mg (maximum recommended adult total daily dosage) in 75 healthy volunteers. Electrocardiograms were collected up to 12 hours postdose. Frederica's method for heart rate correction was employed to derive the corrected QT interval (QTcF). The maximum mean prolongation of QTcF intervals was less than 5 ms, and the upper limit of the 90% confidence interval was below 10 ms for all time matched comparisons versus placebo. This was below the threshold of clinical concern and there was no evident-exposure response relationship.

12.3 Pharmacokinetics

Ritalin LA produces a bi-modal plasma concentration-time profile (i.e., 2 distinct peaks approximately 4 hours apart) when administered orally to children diagnosed with ADHD and healthy adults.

No accumulation of methylphenidate is expected following multiple once daily oral dosing with Ritalin LA, however, there is a slight upward trend in the methylphenidate area under the curve and peak plasma concentrations (C_{max1} and C_{max2}) after oral administration of Ritalin LA 20 mg and 40 mg capsules to adults.

Absorption

The absolute oral bioavailability of methylphenidate in children was 22% ± 8% for d-methylphenidate and 5% ± 3% for l- methylphenidate. The relative bioavailability of Ritalin LA given once daily is comparable to the same total dose of Ritalin tablets given in 2 doses 4 hours apart in both children and adults.

The initial rate of absorption for Ritalin LA is similar to that of Ritalin tablets as shown by the similar rate parameters between the 2 formulations, i.e., initial lag time (T_{lag}), first peak concentration (C_{max1}), and time to the first peak (T_{max1}), which is reached in 1 to 3 hours. The mean time to the interpeak minimum (T_{minip}), and time to the second peak (T_{max2}) are also similar for Ritalin LA given once daily and Ritalin tablets given in 2 doses 4 hours apart (see Figure 1 and Table 1), although the ranges observed are greater for Ritalin LA.

Ritalin LA given once daily exhibits a lower second peak concentration (C_{max2}), higher interpeak minimum concentrations (C_{minip}), and less peak and trough fluctuations than Ritalin tablets given in 2 doses given 4 hours apart. This is due to an earlier onset and more prolonged absorption from the delayed-release beads (see Figure 1 and Table 4).

Figure 1: Mean Plasma Concentration Time-profile of Methylphenidate After a Single Dose of Ritalin LA 40 mg and Ritalin 20 mg Given in Two Doses 4 Hours Apart

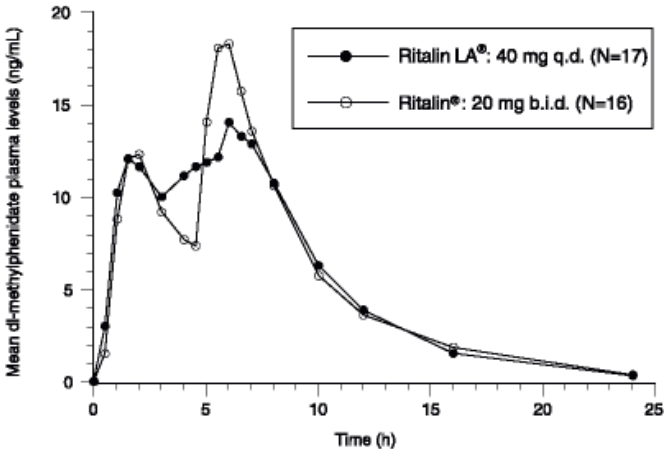


Table 4: Mean ± SD and Range of Pharmacokinetic Parameters of Methylphenidate After a Single Dose of Ritalin LA and Ritalin Given in Two Doses 4 Hours Apart

Population	Children		Adult males	
Formulation dose	**Ritalin 10 mg & 10 mg**	**Ritalin LA 20 mg**	**Ritalin 10 mg & 10 mg**	**Ritalin LA 20 mg**
N	**21**	**18**	**9**	**8**
T_{lag} (h)	0.24 ± 0.44	0.28 ± 0.46	1.0 ± 0.5	0.7 ± 0.2
	0 - 1	0 - 1	0.7 - 1.3	0.3 - 1.0
T_{max1} (h)	1.8 ± 0.6	2.0 ± 0.8	1.9 ± 0.4	2.0 ± 0.9
	1 - 3	1 - 3	1.3 - 2.7	1.3 - 4.0
C_{max1} (ng/mL)	10.2 ± 4.2	10.3 ± 5.1	4.3 ± 2.3	5.3 ± 0.9
	4.2 - 20.2	5.5 - 26.6	1.8 - 7.5	3.8 - 6.9
T_{minip} (h)	4.0 ± 0.2	4.5 ± 1.2	3.8 ± 0.4	3.6 ± 0.6
	4 - 5	2 - 6	3.3 - 4.3	2.7 - 4.3
C_{minip} (ng/mL)	5.8 ± 2.7	6.1 ± 4.1	1.2 ± 1.4	3.0 ± 0.8
	3.1 - 14.4	2.9 - 21.0	0.0 - 3.7	1.7 - 4.0
T_{max2} (h)	5.6 ± 0.7	6.6 ± 1.5	5.9 ± 0.5	5.5 ± 0.8
	5 - 8	5 - 11	5.0 - 6.5	4.3 - 6.5
C_{max2} (ng/mL)	15.3 ± 7.0	10.2 ± 5.9	5.3 ± 1.4	6.2 ± 1.6
	6.2 - 32.8	4.5 - 31.1	3.6 - 7.2	3.9 - 8.3
$AUC_{(0-\infty)}$	102.4 ± 54.6	86.6 ± 64.0[a]	37.8 ± 21.9	45.8 ± 10.0
(ng/mL x h-1)	40.5 - 261.6	43.3 - 301.44	14.3 - 85.3	34.0 - 61.6
$t_{1/2}$ (h)	2.5 ± 0.8	2.4 ± 0.7[a]	3.5 ± 1.9	3.3 ± 0.4
	1.8 - 5.3	1.5 - 4.0	1.3 - 7.7	3.0 - 4.2

[a]N = 15.

Effect of Food

Administration times relative to meals and meal composition may need to be individually titrated.

When Ritalin LA was administered with a high-fat breakfast to adults, Ritalin LA had a longer lag time until absorption began and variable delays in the time until the first peak concentration, the time until the interpeak minimum, and the time until the second peak. The first peak concentration and the extent of absorption were unchanged after food relative to the fasting state, although the second peak was approximately 25% lower. The effect of a high fat lunch was not examined.

There were no differences in the pharmacokinetics of Ritalin LA when administered with applesauce, compared to administration in the fasting condition. There is no evidence of dose dumping in the presence or absence of food.

Effect of Alcohol

An *in vitro* study was conducted to explore the effect of alcohol on the release characteristics of methylphenidate from the Ritalin LA 40 mg capsule dosage form. At an alcohol concentration of 40% there was a 98% release of methylphenidate in the first hour. The results with the 40 mg capsule are considered to be representative of the other available capsule strengths.

Distribution

Binding to plasma proteins is low (10% to 33%). The volume of distribution was 2.65 ± 1.11 L/kg for d-methylphenidate and 1.80 ± 0.91 L/kg for l-methylphenidate.

Elimination

The systemic clearance is 0.40 ± 0.12 L/h/kg for d-methylphenidate and 0.73 ± 0.28 L/h/kg for l-methylphenidate. In studies with Ritalin LA and Ritalin tablets in adults, methylphenidate from Ritalin tablets is eliminated from plasma with an average half-life of about 3.5 hours, (range, 1.3 to 7.7 hours). In children the average half-life is about 2.5 hours, with a range of about 1.5 to 5.0 hours. The rapid half-life in both children and adults may result in un-measurable concentrations between the morning and mid-day doses with Ritalin tablets. No accumulation of

methylphenidate is expected following multiple once a day oral dosing with Ritalin LA. The half-life of ritalinic acid is about 3 to 4 hours.

Metabolism

The absolute oral bioavailability of methylphenidate in children was 22% ± 8% for d-methylphenidate and 5% ± 3% for l- methylphenidate, suggesting pronounced presystemic metabolism. Biotransformation of methylphenidate by the carboxylesterase CES1A1 is rapid and extensive leading to the main, de-esterified metabolite α-phenyl-2-piperidine acetic acid (ritalinic acid), which has little or no pharmacologic activity. Only small amounts of hydroxylated metabolites (e.g., hydroxymethylphenidate and hydroxyritalinic acid) are detectable in plasma. Therapeutic activity is principally due to the parent compound.

Excretion

After oral administration of an immediate release formulation of methylphenidate, 78% to 97% of the dose is excreted in the urine and 1% to 3% in the feces in the form of metabolites within 48 to 96 hours. Only small quantities (less than 1%) of unchanged methylphenidate appear in the urine. Most of the dose is excreted in the urine as ritalinic acid (60% to 86%), the remainder being accounted for by minor metabolite.

Studies in Specific Populations

Male and Female Patients

There were no apparent gender differences in the pharmacokinetics of methylphenidate between healthy male and female adults when administered Ritalin LA.

Racial or Ethnic Groups

There is insufficient experience with the use of Ritalin LA to detect ethnic variations in pharmacokinetics.

Pediatric Patients

The pharmacokinetics of Ritalin LA was examined in 18 children with ADHD between 7 and 12 years of age. Fifteen of these children were between 10 and 12 years of age. The time until the between peak minimum, and the time until the second peak were delayed and more variable in children compared to adults. After a 20-mg dose of Ritalin LA, concentrations in children were approximately twice the concentrations observed in 18- to 35-year-old adults. This higher exposure is almost completely due to the smaller body size and total volume of distribution in children, as apparent clearance normalized to body weight is independent of age.

Patients with Renal Impairment

Ritalin LA has not been studied in renally-impaired patients. Renal impairment is expected to have minimal effect on the pharmacokinetics of methylphenidate since less than 1% of a radiolabeled dose is excreted in the urine as unchanged compound, and the major metabolite (ritalinic acid), has little or no pharmacologic activity.

Patients with Hepatic Impairment

Ritalin LA has not been studied in patients with hepatic impairment. Hepatic impairment is expected to have minimal effect on the pharmacokinetics of methylphenidate since it is metabolized primarily to ritalinic acid by nonmicrosomal hydrolytic esterases that are widely distributed throughout the body.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and 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 2 times the MRHD of 60 mg/day 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.

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) on a mg/m^2 basis.

In a 24-week carcinogenicity study 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 concentration of methylphenidate as in the lifetime carcinogenicity study; the high-dose groups were exposed to 60 to 74 mg/kg/day of methylphenidate.

Mutagenesis

Methylphenidate 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 vitro* chromosomal aberration assay using human lymphocytes. Sister chromatid exchanges and chromosome aberrations were increased, indicative of a weak clastogenic response, in an *in vitro* assay in cultured Chinese Hamster Ovary cells. Methylphenidate was negative *in vivo* in males and females in the mouse bone marrow micronucleus assay.

Impairment of Fertility

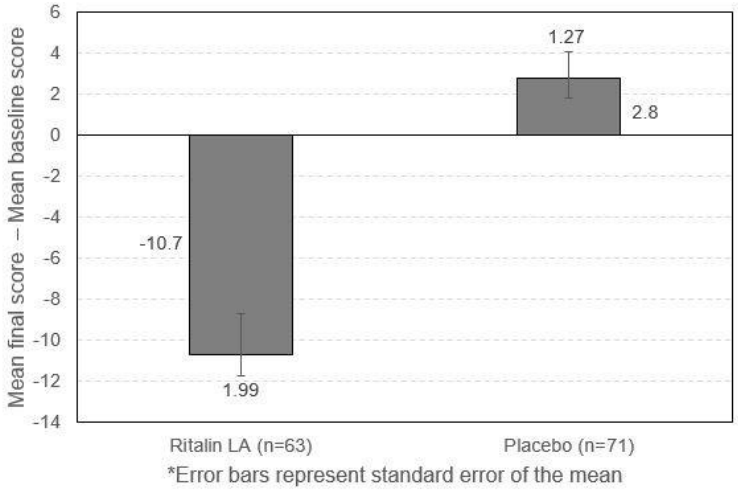
Methylphenidate did not impair fertility in male or female mice that were fed diets containing the drug in an 18-week continuous breeding study. The study was conducted at doses up to 160 mg/kg/day, approximately 10 times the maximum recommended dose of 60 mg/day given to adolescents on a mg/m^2 basis.

14 CLINICAL STUDIES

14.1 Children and Adolescents

Ritalin LA was evaluated in a randomized, double-blind, placebo-controlled, parallel group clinical study in which 134 children, ages 6 to 12 years, with DSM-IV diagnoses of ADHD received a single morning dose of Ritalin LA in the range of 10 to 40 mg/day, or placebo, for up to 2 weeks. The doses used were the optimal doses established in a previous individual dose titration phase. In that titration phase, 53 of 164 patients (32%) started on a daily dose of 10 mg and 111 of 164 patients (68%) started on a daily dose of 20 mg or higher. The patient's regular schoolteacher completed the Conners ADHD/DSM-IV Scale for Teachers (CADS-T) at baseline and the end of each week. The CADS-T assesses symptoms of hyperactivity and inattention. The change from baseline of the (CADS-T) scores during the last week of treatment was analyzed as the primary efficacy parameter. Patients treated with Ritalin LA showed a statistically significant improvement in symptom scores from baseline [Mean (final score - baseline) = -10.7 points] over patients who received placebo [Mean (final score - baseline) = +2.8 points]. The lower the final score on the CADS-T scale from baseline, the less severe the disease is. This demonstrates that a single morning dose of Ritalin LA exerts a treatment effect in ADHD.

Figure 2: CADS-T Total Subscale - Mean Change from Baseline*



16 HOW SUPPLIED/STORAGE AND HANDLING

- 10 mg extended-release capsules (NDC 0078-0424-05) white/light brown, (imprinted "NVR R10") supplied in bottles of 100
- 20 mg extended-release capsules (NDC 0078-0370-05) white, (imprinted "NVR R20") supplied in bottles of 100
- 30 mg extended-release capsules (NDC 0078-0371-05) yellow, (imprinted "NVR R30") supplied in bottles of 100
- 40 mg extended-release capsules (NDC 0078-0372-05) light brown, (imprinted "NVR R40") supplied in bottles of 100

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [See USP controlled room temperature].

Dispense in tight 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 Ritalin LA, 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 Ritalin LA in a safe place, preferably locked, and instruct patients to not give Ritalin LA to anyone else.

Risks to Patients with Serious Cardiac Disease

Advise patients that there are potential risks to patients with serious cardiac disease, including sudden death, with Ritalin LA 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 Ritalin LA can cause elevations of their blood pressure and pulse rate *[see Warnings and Precautions (5.3)]*.

Psychiatric Adverse Reactions

Advise patients that Ritalin LA, 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 Ritalin LA 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 Ritalin LA. 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 Ritalin LA 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 Ritalin LA *[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 Ritalin LA. 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)]*.

Alcohol Effect

Advise patients to avoid alcohol while taking Ritalin LA. Consumption of alcohol while taking Ritalin LA may result in a more rapid release of the dose of methylphenidate *[see Clinical Pharmacology (12.3)]*.

Pregnancy Registry

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

Distributed by:
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936

MEDICATION GUIDE

RITALIN LA® (rit-ah-lin LA)

(methylphenidate hydrochloride)

extended-release capsules for oral use, CII

What is the most important information I should know about RITALIN LA?

RITALIN LA may cause serious side effects, including:

- **Abuse, misuse, and addiction.** RITALIN LA has a high chance for abuse and misuse and may lead to substance use problems, including addiction. Misuse and abuse of RITALIN LA, 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 RITALIN LA 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 RITALIN LA and will monitor you or your child during treatment.
  - RITALIN LA may lead to physical dependence after prolonged use, even if taken as directed by your healthcare provider.
  - Do not give RITALIN LA to anyone else. See "**What is RITALIN LA?**" for more information.
  - Keep RITALIN LA in a safe place and properly dispose of any unused medicine. See "**How should I store RITALIN LA?**" 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 RITALIN LA.

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 RITALIN LA.

- **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 RITALIN LA.

- **Mental (psychiatric) problems:**

  All Patients
  - 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 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 RITALIN LA, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

What is RITALIN LA?

RITALIN LA is a central nervous system (CNS) stimulant prescription medicine. **It is used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).** RITALIN LA may help increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.

RITALIN LA should be used as a part of a total treatment program for ADHD that may include counseling or other therapies.

It is not known if RITALIN LA is safe and effective in children under 6 years of age.

RITALIN LA 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 RITALIN LA in a safe place to protect it from theft. Never give your RITALIN LA to anyone else because it may cause death or harm them. Selling or giving away RITALIN LA may harm others and is against the law.

Who should not take RITALIN LA?

RITALIN LA should not be taken if you or your child:

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

RITALIN LA may not be right for you or your child. Before starting RITALIN LA, tell your or your child's healthcare 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 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 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 RITALIN LA will harm your unborn baby.
  - There is a pregnancy registry for females who are exposed to ADHD medications, including RITALIN LA during pregnancy. The purpose of the registry is to collect information about the health of females exposed to RITALIN LA and their baby. If you or your child becomes pregnant during treatment with RITALIN LA, talk to your healthcare provider about registering with the National Pregnancy Registry of ADHD medications at 1-866-961-2388 or visit online at https://womensmentalhealth.org/adhd- medications/.
- if you are breastfeeding or plan to breastfeed. RITALIN LA passes into your breast milk. Talk to your healthcare provider about the best way to feed the baby during treatment with RITALIN LA.

Tell your healthcare provider about all of the medicines that you or your child take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. RITALIN LA 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 RITALIN LA.

Your healthcare provider will decide whether RITALIN LA can be taken with other medicines.

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

- anti-depression medicines, including MAOIs
- blood pressure medicines (anti-hypertensive)
- risperidone

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 RITALIN LA 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 RITALIN LA without talking to your healthcare provider first.

How should RITALIN LA be taken?

- Take RITALIN LA exactly as prescribed. Your healthcare provider may adjust the dose until it is right for you or your child.
- Take RITALIN LA once a day in the morning. RITALIN LA is an extended-release capsule.
- **Do not chew or crush RITALIN LA capsules or the medicine inside the capsule.** Swallow RITALIN LA capsules whole with water or other liquids.
- If you cannot swallow the capsule whole, open it and sprinkle the medicine over a spoonful of applesauce.

Swallow the applesauce and medicine mixture without chewing. Follow with a drink of water or other liquid.

- You should avoid drinking alcohol during treatment with RITALIN LA. This may cause a faster release of RITALIN LA.

Your healthcare provider may do regular checks of the blood, heart, and blood pressure while taking RITALIN LA. Children should have their height and weight checked often while taking RITALIN LA. If you or your child take too much RITALIN LA, 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 possible side effects of RITALIN LA?

- see **"What is the most important information I should know about RITALIN LA?"** 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 healthcare 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 RITALIN LA.

- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with RITALIN LA. RITALIN LA 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 RITALIN LA.
- **Common side effects include:**
  - fast heartbeat
  - sweating a lot
  - abnormal heartbeat (palpitations)
  - decreased appetite
  - trouble sleeping
  - nausea
  - nervousness
  - stomach pain

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 RITALIN LA?

- Store RITALIN LA in a safe place and in a tightly closed container at room temperature, 68°F to 77°F (20°C to 25°C).
- Protect from moisture.
- Dispose of remaining, unused, or expired RITALIN LA 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 RITALIN LA 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 RITALIN LA in the household trash. Visit www.fda.gov/drugdisposal for additional information on disposal of unused medicines.
- **Keep RITALIN LA and all medicines out of the reach of children.**

General information about the safe and effective use of RITALIN LA.

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 RITALIN LA that is written for healthcare professionals. Do not use RITALIN LA for a condition for which it was not prescribed. Do not give RITALIN LA to other people, even if they have the same symptoms. It may harm them and it is against the law.

What are the ingredients in RITALIN LA?

Active ingredient: methylphenidate HCl

Inactive ingredients: ammonio methacrylate copolymer, black iron oxide (10 and 40 mg capsules only), gelatin, methacrylic acid copolymer, polyethylene glycol, red iron oxide (10 and 40 mg capsules only), sugar spheres, talc, titanium dioxide, triethyl citrate, and yellow iron oxide (10, 30, and 40 mg capsules).

Distributed by:
Novartis Pharmaceuticals Corporation East Hanover, New Jersey 07936

For more information, call 1-888-669-6682.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 10/2023