METHYLPHENIDATE HYDROCHLORIDE EXTENDED-RELEASE- methylphenidate hydrochloride capsule, extended release
SpecGx LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use METHYLPHENIDATE HCl EXTENDED-RELEASE CAPSULES safely and effectively. See full prescribing information for METHYLPHENIDATE HCl EXTENDED-RELEASE CAPSULES.
METHYLPHENIDATE HCl extended-release capsules, CII
Initial U.S. Approval: 1955

WARNING: ABUSE AND DEPENDENCE

See full prescribing information for complete boxed warning.

- **CNS stimulants, including methylphenidate HCl extended-release capsules, other methylphenidate containing products, and amphetamines, have a high potential for abuse and dependence (5.1, 9.2, 9.3)**
- **Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy (5.1, 9.2)**

INDICATIONS AND USAGE

Methylphenidate HCl extended-release capsules are a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 15 years of age (1)

DOSAGE AND ADMINISTRATION

- Take orally once daily in the morning, before breakfast (2.3)
- Swallow whole with the aid of liquids, or sprinkle contents onto a small amount of applesauce and give immediately (2.3)
- Do not crush or chew the capsule or capsule contents (2.3)
- Recommended starting dose is 20 mg once daily. Dosage may be increased 10-20 mg at weekly intervals; do not exceed 60 mg per day (2.2)

DOSAGE FORMS AND STRENGTHS

Extended-release capsules: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg (3)

CONTRAINDICATIONS

- Known hypersensitivity to methylphenidate or other components of methylphenidate HCl extended-release capsules (4)
- Concurrent treatment with a monoamine oxidase inhibitor (MAOI), or use of an MAOI within the preceding 14 days (4)
- Use in patients with patients with hereditary problems of fructose intolerance, glucose-galactose malabsorption, or sucrase-isomaltase insufficiency (4)

WARNINGS AND PRECAUTIONS

- *Serious Cardiovascular Reactions:* Sudden death has been reported in association with CNS stimulant treatment at recommended doses in pediatric patients with structural cardiac abnormalities or other serious heart problems. In adults, sudden death, stroke, and myocardial infarction have been reported. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious heart problems (5.2)
- *Blood Pressure and Heart Rate Increases:* Monitor blood pressure and pulse. Consider the benefits and risks in patients for whom an increase in blood pressure or heart rate would be problematic (5.3)
- *Psychiatric Adverse Reactions:* Use of CNS stimulants may cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychiatric illness. Evaluate for bipolar disorder prior to methylphenidate HCl extended-release capsules use (5.4)
- *Priapism:* Cases of painful and prolonged penile erections and priapism have been reported with methylphenidate products. Immediate medical attention should be sought if signs or symptoms of painful or prolonged penile erections or priapism are observed (5.5)
- *Peripheral Vasculopathy, including Raynaud's Phenomenon:* Stimulants used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Careful observation for digital changes is necessary during treatment with ADHD stimulants (5.6)
- *Long-Term Suppression of Growth:* Monitor height and weight at appropriate intervals in pediatric patients (5.7)

ADVERSE REACTIONS

The most common adverse reactions (≥ 5% and twice the rate of placebo) were anorexia and insomnia (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Mallinckrodt at 1-800-778-7898 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

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

See 17 for Medication Guide.

Revised: 8/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
- 2.1 Pretreatment Screening
- 2.2 Dosage Recommendations
- 2.3 Administration Instructions
- 2.4 Dose Reduction and Discontinuation

3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
- 5.1 Potential for Abuse and Dependence
- 5.2 Serious Cardiovascular Reactions
- 5.3 Blood Pressure and Heart Rate Increases
- 5.4 Psychiatric Adverse Reactions
- 5.5 Priapism
- 5.6 Peripheral Vasculopathy, including Raynaud's Phenomenon
- 5.7 Long-Term Suppression of Growth

6 ADVERSE REACTIONS
- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
- 8.1 Pregnancy
- 8.2 Lactation
- 8.4 Pediatric Use
- 8.5 Geriatric Use

9 DRUG ABUSE AND DEPENDENCE
- 9.1 Controlled Substance
- 9.2 Abuse
- 9.3 Dependence

10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY
- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE AND DEPENDENCE

CNS stimulants, including methylphenidate HCl extended-release capsules, other methylphenidate-containing products, and amphetamines, have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9.2, 9.3)]*.

1 INDICATIONS AND USAGE

Methylphenidate HCl extended-release capsules are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 15 years of age.

2 DOSAGE AND ADMINISTRATION

2.1 Pretreatment Screening

Prior to initiating treatment with methylphenidate HCl extended-release capsules, assess for the presence of cardiac disease (i.e., perform a careful history including family history of sudden death or ventricular arrhythmia, and physical examination) *[see Warnings and Precautions (5.2)]*.

Assess the risk of abuse prior to prescribing, and monitor for signs of abuse and dependence while on therapy. Maintain careful prescription records, educate patients about abuse, monitor for signs of abuse and overdose, and periodically re-evaluate the need for methylphenidate HCl extended-release capsules use *[see Boxed Warning, Warnings and Precautions (5.1), Drug Abuse and Dependence (9)]*.

2.2 Dosage Recommendations

The recommended starting dose of methylphenidate HCl extended-release capsules is 20 mg once daily. Dosage may be adjusted in weekly 10 mg to 20 mg increments to the maximum recommended dose of 60 mg per day.

Dosage should be individualized according to the needs and responses of the patient.

Pharmacological treatment of ADHD may be needed for extended periods. Periodically re-evaluate the long-term use of methylphenidate HCl extended-release capsules, and adjust the dosage as needed.

2.3 Administration Instructions

Administer methylphenidate HCl extended-release capsules orally once daily in the morning, before breakfast.

Swallow the capsule whole with the aid of liquids. Alternatively, open the capsule and sprinkle the contents onto a small amount (tablespoon) of applesauce and administer immediately. Do not store for future use. Drink fluids following the intake of the sprinkled capsule contents with applesauce. The capsules and the capsule contents must not be crushed or chewed.

2.4 Dose Reduction and Discontinuation

If paradoxical aggravation of symptoms or other adverse reactions occur, reduce dosage or, if necessary, discontinue methylphenidate HCl extended-release capsules. If improvement is not observed after appropriate dosage adjustment over a one-month period, discontinue methylphenidate HCl extended-release capsules.

3 DOSAGE FORMS AND STRENGTHS

Methylphenidate HCl extended-release capsules are available in the following dosage strengths (see Table 1):

Table 1: Strengths and Identifying Characteristics of Methylphenidate HCl Extended-Release Capsules

Strength	Capsule Color (cap/body)	Imprinting on Capsule Cap	Imprinting on Capsule Body
10 mg	dark green/white	“M” in a box over “1810” in white letters	“10 mg” in black letters
20 mg	medium blue/white	“M” in a box over “1820” in white letters	“20 mg” in black letters
30 mg	maroon/white	“M” in a box over “1830” in white letters	“30 mg” in black letters
40 mg	yellow ivory/white	“M” in a box over “1840” in black letters	“40 mg” in black letters
50 mg	purple/white	“M” in a box over “1850” in white letters	“50 mg” in black letters
60 mg	white/white	“M” in a box over “1860” in black letters	“60 mg” in black letters

4 CONTRAINDICATIONS

Methylphenidate HCl extended-release capsules are contraindicated in patients with:

- Known hypersensitivity to methylphenidate or other component of methylphenidate HCl extended-release capsules. Angioedema has been reported in patients treated with methylphenidate HCl extended-release capsules. Anaphylactic reactions have been reported in patients treated with other methylphenidate products *[see Adverse*

Reactions (6)].
- Concomitant treatment with monoamine oxidase inhibitors (MAOIs), or within 14 days following discontinuation of treatment with an MAOI, because of the risk of hypertensive crisis *[see Drug Interactions (7)]*.
- Methylphenidate HCl extended-release capsules contain sucrose. Therefore, patients with hereditary problems of fructose intolerance, glucose-galactose malabsorption, or sucrase-isomaltase insufficiency should not take this medicine.

5 WARNINGS AND PRECAUTIONS

5.1 Potential for Abuse and Dependence

CNS stimulants, including methylphenidate HCl extended-release capsules, other methylphenidate-containing products, and amphetamines, have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing, and monitor for signs of abuse and dependence while on therapy *[see Drug Abuse and Dependence (9.2, 9.3)]*.

5.2 Serious Cardiovascular Reactions

Sudden death, stroke and myocardial infarction have been reported in adults with CNS stimulant treatment at recommended doses. Sudden death has been reported in pediatric patients with structural cardiac abnormalities and other serious heart problems taking CNS stimulants at recommended doses for ADHD. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, and other serious heart problems. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during methylphenidate HCl extended-release capsules treatment.

5.3 Blood Pressure and Heart Rate Increases

CNS stimulants cause an increase in blood pressure (mean increase approximately 2 to 4 mmHg) and heart rate (mean increase approximately 3 to 6 bpm). Individuals may have larger increases. Monitor all patients for hypertension and tachycardia.

5.4 Psychiatric Adverse Reactions

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

Induction of a Manic Episode in Patients with Bipolar Disorder
CNS stimulants may induce a manic or mixed episode in patients. Prior to initiating 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 recommended doses, may cause psychotic or manic symptoms (e.g., hallucinations, delusional thinking, or mania) in patients without a prior history of psychotic illness or mania. If such symptoms occur, consider discontinuing methylphenidate HCl extended-release capsules. 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 in placebo-treated patients.

5.5 Priapism

Prolonged and painful erections, sometimes requiring surgical intervention, have been reported with methylphenidate products in both pediatric and adult patients. Priapism was not reported with drug initiation but 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 methylphenidate HCl extended-release capsules, used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; however, very rare sequelae include digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud's phenomenon, were observed in postmarketing reports at different times and at therapeutic doses in all age groups throughout the course of treatment. Signs and symptoms generally improve after reduction in dose or discontinuation of drug. Careful observation for digital changes is necessary during treatment with ADHD stimulants. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients.

5.7 Long-Term Suppression of Growth

CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients.

Careful follow-up of weight and height in children 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 children over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have 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 period of development.

Closely monitor growth (weight and height) in pediatric patients treated with CNS stimulants, including methylphenidate HCl extended-release capsules. **Patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.**

6 ADVERSE REACTIONS

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

- Abuse and Dependence *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9.2, 9.3)]*
- Hypersensitivity to Methylphenidate and Other Component of Methylphenidate HCl Extended-Release Capsules *[see Contraindications (4)]*
- Hypertensive Crisis when Used Concomitantly with MAOIs *[see Contraindications (4) and Drug Interactions (7)]*
- Serious Cardiovascular Reactions *[see Warnings and Precautions (5.2)]*
- Blood Pressure and Heart Rate Increases *[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 *[see Warnings and Precautions (5.7)]*

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.

Clinical trials experience with methylphenidate HCl extended-release capsules included 188 pediatric patients 6 to 15 years old with ADHD exposed to methylphenidate HCl extended-release capsules. Patients received methylphenidate HCl extended-release capsules 20 mg, 40 mg, and/or 60 mg per day. The 188 patients were evaluated in the following studies: Study 1, a 3-week placebo-controlled clinical study consisting of a total of 314 pediatric patients (ages 6 to 15 years; methylphenidate HCl extended-release capsules n=155); Study 2, a placebo-controlled, crossover clinical study consisting of 25 pediatric patients (ages 7 to 12 years); and Study 3, an uncontrolled clinical study consisting of 8 pediatric patients (ages 6 to 10 years).

Adverse Reactions Leading to Discontinuation of Treatment
In the 3-week placebo-controlled, parallel-group trial, two methylphenidate HCl extended-release capsules-treated patients (1%) and no placebo-treated patients discontinued due to an adverse reaction (rash and pruritus; and headache, abdominal pain, and dizziness, respectively).

Most Common Adverse Reactions
The most common adverse reactions that occurred in 5% or more of patients treated with methylphenidate HCl extended-release capsules in a pool of Studies 1, 2 and 3 (ages 6 to 15 years) where the incidence in patients treated with methylphenidate HCl extended-release capsules was at least twice the incidence in placebo-treated patients were anorexia and insomnia.

Adverse reactions that occurred in ≥5% of patients treated with methylphenidate HCl extended-release capsules and greater than placebo in pooled Studies 1, 2, and 3 are presented in Table 2:

Table 2: Adverse Reactions (≥5% and Greater than Placebo) in Pediatric Patients Ages 6 to 15 Years Receiving Methylphenidate HCl Extended-Release Capsules in Pooled Three to Four Week Trials

Body System	Preferred Term	Methylphenidate HCl Extended-Release Capsules (n=188) %	Placebo (n=190) %
General	Headache	12	8
	Abdominal Pain (stomachache)	7	4
Digestive System	Anorexia	9	2
Nervous System	Insomnia	5	2

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of methylphenidate HCl extended-release capsules and other methylphenidate HCl products. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Adverse Reactions with Methylphenidate HCl Extended-Release Capsules
Blood and the lymphatic system disorders: thrombocytopenia

Cardiac disorders: cardiac arrest, sudden death

Immune system disorders: angioedema

Musculoskeletal and connective tissue disorders: rhabdomyolysis

Psychiatric disorders: abnormal behavior, aggression, anxiety, irritability, obsessive-compulsive disorder, suicidal behavior (including completed suicide), libido changes, serotonin syndrome in combination with serotonergic drugs

Nervous system disorders: migraine, reversible ischemic neurological deficit, bruxism

Skin and subcutaneous tissue disorders: fixed drug eruption

Vascular disorders: peripheral coldness, Raynaud's phenomenon

Adverse Reactions with Other Methylphenidate HCl Products
Blood and the lymphatic system disorders: leukopenia, anemia, pancytopenia

Cardiac disorders: palpitations, increased blood pressure, tachycardia, angina pectoris, cardiac arrhythmia, myocardial infarction, bradycardia, extrasystole

Eye disorders: blurred vision, difficulties in visual accommodation, diplopia, mydriasis

Gastrointestinal disorders: nausea, abdominal pain, dry mouth, vomiting, dyspepsia, diarrhea, constipation

General disorders: fatigue, hyperpyrexia

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

Immune system disorders: hypersensitivity, including anaphylaxis, auricular swelling, bullous conditions, eruptions, exanthemas

Infections and infestations: nasopharyngitis

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

Musculoskeletal and connective tissue disorders: arthralgia, muscle cramps, myalgia, muscle twitching

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

Psychiatric disorders: depressed mood, restlessness, agitation, psychosis (sometimes with visual and tactile hallucinations), affect liability, mania, disorientation

Renal and urinary disorders: hematuria

Reproductive system and breast disorders: gynecomastia

Respiratory, thoracic and mediastinal disorders: pharyngolaryngeal pain, dyspnea, cough

Skin and subcutaneous tissue disorders: scalp hair loss, hyperhidrosis, angioneurotic edema, erythema, exfoliative dermatitis, thrombocytopenic purpura, urticaria, erythema multiforme rash

Urogenital disorders: priapism

Vascular disorders: isolated cases of cerebral arteritis and/or occlusion

7 DRUG INTERACTIONS

Table 3 presents clinically important drug interactions with methylphenidate HCl extended-release capsules.

Table 3: Clinically Important Drug Interactions with Methylphenidate HCl Extended-Release Capsules

Monoamine Oxidase Inhibitors (MAOI)	
Clinical Impact:	Concomitant use of MAOIs and CNS stimulants, including methylphenidate HCl extended-release capsules, 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 methylphenidate HCl extended-release capsules with monoamine oxidase inhibitors (MAOIs) or within 14 days after discontinuing MAOI treatment is contraindicated.
Antihypertensive Drugs	
Clinical Impact:	Methylphenidate HCl extended-release capsules 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.
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

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ADHD medications, including methylphenidate HCl extended-release capsules, during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Psychostimulants at 1-866-961-2388.

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 53 times the MRHD given to adolescents. A decrease in pup body weight was observed in a pre- and postnatal 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 methylphenidate HCl extended-release capsules, 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.

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 adults 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 adults on a mg/m^2 basis), but no other effects on postnatal development were observed. The no effect level for pre- and postnatal development in rats was 15 mg/kg/day (~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 methylphenidate HCl extended-release capsules and any potential adverse effects on the breastfed infant from methylphenidate HCl extended-release capsules 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 methylphenidate HCl extended-release capsules for the treatment of ADHD have been established in pediatric patients 6 to 15 years of age. The safety and effectiveness of methylphenidate HCl extended-release capsules in pediatric patients younger than 6 years of age have not been established. Long-term efficacy of methylphenidate HCl extended-release capsules in pediatric patients have not been established.

Long-Term Suppression of Growth
Growth should be monitored during treatment with stimulants, including methylphenidate HCl extended-release capsules. Pediatric patients who are not growing or gaining weight as expected may need to have their treatment interrupted *[see Warnings and Precautions (5.6)]*.

Juvenile Animal Toxicity Data
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 6 times the MRHD 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 (12 times the MRHD on a mg/m^2 basis). The no effect level for juvenile neurobehavioral development in rats was 5 mg/kg/day (half the MRHD on a mg/m^2 basis). The clinical significance of the long-term behavioral effects observed in rats is unknown.

8.5 Geriatric Use

Methylphenidate HCl extended-release capsules have not been studied in patients over the age of 65 years.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Methylphenidate HCl extended-release capsules contain methylphenidate hydrochloride, a Schedule II controlled substance.

9.2 Abuse

CNS stimulants, including methylphenidate HCl extended-release capsules, other methylphenidate-containing products, and amphetamines have a high potential for abuse. Abuse is the intentional non-therapeutic use of a drug, even once, to achieve a desired psychological or physicological effect. Drug addiction is a cluster of behavioral, cognitive, and psychological 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. Both abuse and misuse may lead to addiction, and some individuals may develop addiction even when taking methylphenidate HCl extended-release capsules as prescribed.

Signs and symptoms of CNS stimulant abuse include increased heart rate, respiratory rate, blood pressure, and/or 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. Individual who abuser CNS stimulants may chew, snort, inject, or use other unapproved routes of administration which can result in overdose and death *[see Overdosage (10)]*.

To reduce the abuse of methylphenidate HCl extended-release capsules, assess the risk of abuse prior to prescribing. After prescribing, keep careful prescription records, educate patients and their families about abuse and on proper storage and disposal of CNS stimulants *[see How Supplied/Storage and Handling (16)]*, monitor for signs of abuse while on therapy, and re-evaluate the need for methylphenidate HCl extended-release capsules use.

9.3 Dependence

Physical Dependence
Methylphenidate HCl extended-release capsules may produce physical dependence from continued therapy. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by a withdrawal signs and symptoms after abrupt discontinuation or significant dose reduction of a drug. Withdrawal symptoms after abrupt cessation following prolonged high-dosage administration of CNS stimulants include dysphoric mood; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; and psychomotor retardation or agitation.

Tolerance
Methylphenidate HCl extended-release capsules may produce tolerance from continued therapy. 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

Human Experience
Signs and symptoms of acute methylphenidate overdosage, resulting principally from overstimulation of the CNS and from excessive sympathomimetic effects, may include the following: nausea, vomiting, diarrhea, restlessness, anxiety, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, hypotension, tachypnea,

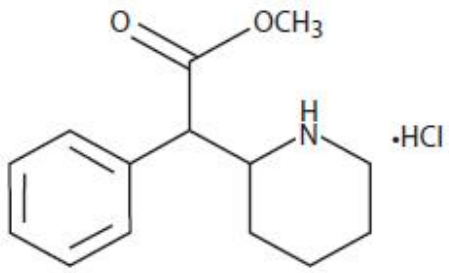
mydriasis, dryness of mucous membranes, and rhabdomyolysis.

Overdose Management
Consult with a Certified Poison Control Center (1-800-222-1222) for guidance and advice on the management of overdosage with methylphenidate. Provide supportive care, including close medication supervision and monitoring. Treatment should consist of those general measures employed in the management of overdosage with any drug. Consider the possibility of multiple drug overdosage.

11 DESCRIPTION

Methylphenidate HCl extended-release capsules contain methylphenidate hydrochloride, a CNS stimulant. The extended-release capsules comprise both immediate-release (IR) and extended-release (ER) beads such that 30% of the dose is provided by the IR component and 70% of the dose is provided by the ER component. Methylphenidate HCl extended-release capsules are available in six capsule strengths containing 10 mg (3 mg IR; 7 mg ER), 20 mg (6 mg IR; 14 mg ER), 30 mg (9 mg IR; 21 mg ER), 40 mg (12 mg IR; 28 mg ER), 50 mg (15 mg IR; 35 mg ER), or 60 mg (18 mg IR; 42 mg ER) of methylphenidate hydrochloride for oral administration.

Chemically, methylphenidate HCl is *d*,*l* (racemic)-*threo*-methyl α-phenyl-2-piperidineacetate hydrochloride. Its empirical formula is $C_{14}H_{19}NO_2$•HCl. Its structural formula is:



$C_{14}H_{19}NO_2$•HCl MW = 269.77

Methylphenidate HCl USP is a white, odorless, crystalline powder. Its solutions are acid to litmus. It is freely soluble in water and in methanol, soluble in alcohol, and slightly soluble in chloroform and in acetone. Its molecular weight is 269.77.

Methylphenidate HCl extended-release capsules also contain the following inactive ingredients: Sugar Spheres, Ethylcellulose, Oleic Acid, Medium-Chain Triglycerides, Titanium Dioxide, Gelatin, Shellac, Propylene Glycol, Hypromellose, Polyethylene Glycol, and Black Iron Oxide.

The individual capsules contain the following color agents:

10 mg capsules: FD&C Blue No. 2, Yellow Iron Oxide, Sodium Hydroxide, Povidone

20 mg capsules: FD&C Blue No. 2, Sodium Hydroxide, Povidone

30 mg capsules: FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, Sodium Hydroxide, Povidone

40 mg capsules: Yellow Iron Oxide

50 mg capsules: FD&C Blue No. 2, Red Iron Oxide, Sodium Hydroxide, Povidone

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Methylphenidate hydrochloride is a central nervous system (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.

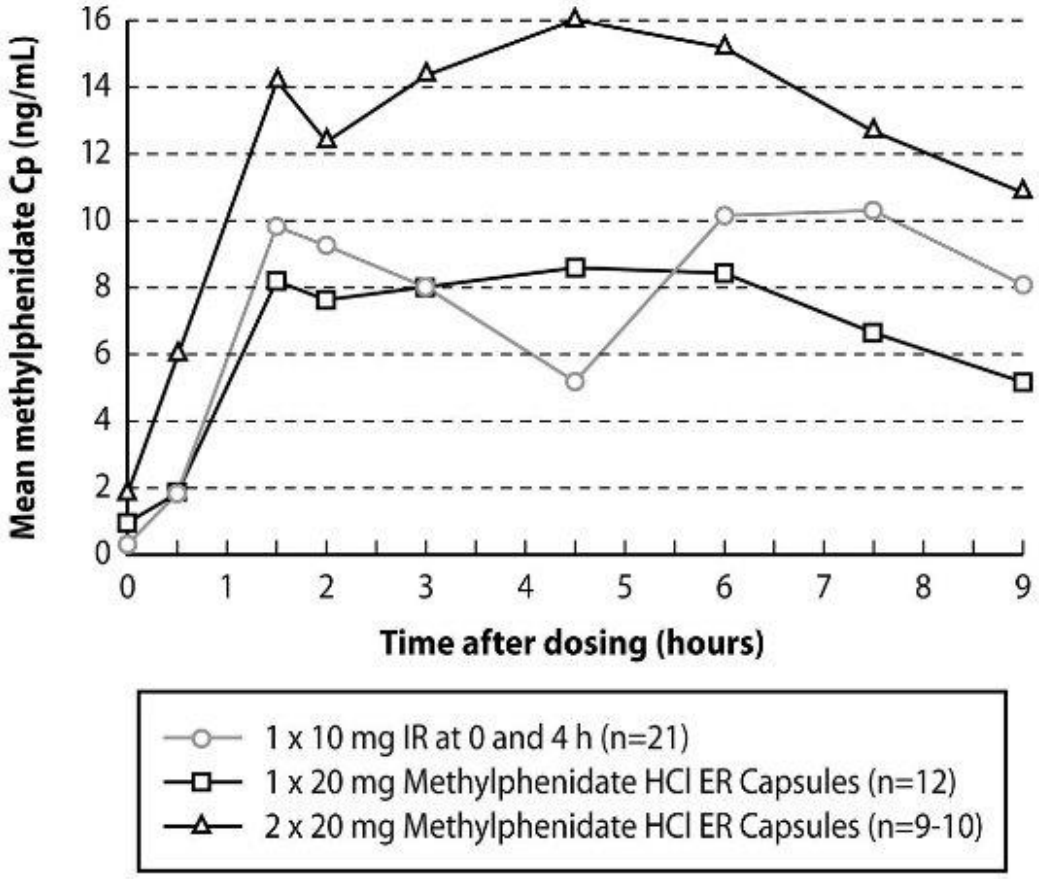
12.3 Pharmacokinetics

Following one week of once-daily doses of 20 mg or 40 mg methylphenidate HCl extended-release capsules to children aged 7 to 12 years old with ADHD, C_{max} and AUC of methylphenidate were approximately proportional to the administered doses.

Absorption
Following administration of methylphenidate HCl extended-release capsules in children aged 7 to 12 years old with ADHD, the plasma concentration time profile of methylphenidate showed two phases of drug release with a sharp, initial slope similar to a methylphenidate immediate-release tablet (median $T_{\mathbf{max1}}$ about 1.5 hours post dose), and a second rising portion approximately three hours later (median $T_{\mathbf{max2}}$ about 4.5 hours post dose)*, followed by a gradual decline (Figure 1). The means for C_{max} and area under the curve (AUC) following a dose of 20 mg were slightly lower than those seen with 10 mg of the immediate-release formulation, dosed at 0 and 4 hours.

*25-30% of the subjects had only one observed peak (C_{max}) concentration of methylphenidate.

Figure 1: Comparison of Immediate Release (IR) and Methylphenidate HCl Extended-Release Capsules Formulations After Repeated Doses of Methylphenidate HCl in Pediatric Patients 7 to 12 Years of Age with ADHD



Effect of Food

Ingestion of a high-fat meal with methylphenidate HCl extended-release capsules increased the mean C_{max} and AUC of methylphenidate by about 30% and 17%, respectively. The presence of food delayed the early peak by approximately 1 hour (range -2 to 5 hours delay) *[see Dosage and Administration (2.1)]*.

The bioavailability (C_{max} and AUC) of methylphenidate was unaffected by sprinkling the methylphenidate HCl extended-release capsule contents on applesauce as compared to the intact capsule.

Effect of Alcohol

At an alcohol concentration of 40%, there was an increase in the release rate of methylphenidate in the first hour, resulting in 84% of the methylphenidate being released. The results with the 60 mg capsule are considered to be representative of the other available capsule strengths *[see Drug Interactions (7)]*.

Distribution

Plasma protein binding is 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 mean terminal half-life (t½) of methylphenidate following administration of methylphenidate HCl extended-release capsules (t½=6.8 hours) is longer than the mean terminal t½ following administration of methylphenidate hydrochloride immediate-release tablets (t½=2.9 hours) and methylphenidate hydrochloride extended-release tablets (t½=3.4 hours) in healthy adult volunteers.

Metabolism
In vitro studies showed that methylphenidate was not metabolized by cytochrome P450 isoenzymes. Methylphenidate is metabolized primarily by deesterification to alpha-phenyl-piperidine acetic acid (ritalinic acid), which has little or no pharmacologic activity.

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

Specific Populations
Male and Female Patients

The pharmacokinetics of methylphenidate after a single dose of methylphenidate HCl extended-release capsules were similar between adult men and women.

Racial or Ethnic Groups
The influence of race on the pharmacokinetics of methylphenidate after methylphenidate HCl extended-release capsules administration has not been studied.

Pediatric Patients
The pharmacokinetics of methylphenidate after methylphenidate HCl extended-release capsules administration has not been studied in children less than 6 years of age.

Patients with Renal Impairment
Methylphenidate HCl extended-release capsules have not been studied in patients with renal insufficiency. Since renal clearance is not an important route of methylphenidate clearance, and the major metabolite (ritalinic acid), has little or no pharmacologic activity, renal insufficiency is expected to have minimal effect on the pharmacokinetics of methylphenidate HCl extended-release capsules.

Patients with Hepatic Impairment
Methylphenidate HCl extended-release capsules have not been studied in patients with hepatic insufficiency. 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.

Drug Interaction Studies
In vitro studies showed that methylphenidate did not inhibit cytochrome P450 isoenzymes at clinically observed plasma drug concentrations.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
In a lifetime carcinogenicity study carried out in B6C3F1 mice, methylphenidate caused an increase in hepatocellular adenomas and, in males only, an increase in hepatoblastomas, at a daily dose of approximately 60 mg/kg per day. This dose is approximately 2 times the maximum recommended human dose (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 increases in tumors in a lifetime carcinogenicity study carried out in F344 rats; the highest dose used was approximately 45 mg/kg/day, which

carried out in 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 per 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 per day, approximately 10 times the maximum recommended human dose of 60 mg/day given to adolescents on a mg/m^2 basis.

14 CLINICAL STUDIES

Methylphenidate HCl extended-release capsules were evaluated in a double-blind, parallel-group, placebo-controlled trial in which 321 untreated or previously treated pediatric patients with a DSM-IV diagnosis of Attention Deficit Hyperactivity Disorder (ADHD), 6 to 15 years of age, received a single morning dose for up to 3 weeks. Patients were required to have the combined or predominantly hyperactive-impulsive subtype of ADHD; patients with the predominantly inattentive subtype were excluded. Patients randomized to the methylphenidate HCl extended-release capsules group received 20 mg daily for the first week. Their dosage could be increased weekly to a maximum of 60 mg by the third week, depending on individual response to treatment.

The patient's regular school teacher completed the teachers' version of the Conners' Global Index Scale (TCGIS), a scale for assessing ADHD symptoms, in the morning and again in the afternoon on three alternate days of each treatment week. The primary efficacy endpoint was determined by the average of the total scores for the 10-item TCGIS completed by the classroom teacher in the morning and again in the afternoon on the three observation days during the last week of double-blind therapy. Patients treated with methylphenidate HCl extended-release capsules showed a statistically significant improvement in symptom scores from baseline over patients who received placebo (See Figure 2). Separate analyses of TCGIS scores in the morning and afternoon revealed superiority in improvement with methylphenidate HCl extended-release capsules over placebo during both time periods (See Figure 3).

Figure 2: Least Squares Mean Change from Baseline in TCGIS Total Score in Pediatric Patients 6 to 15 years of Age with ADHD

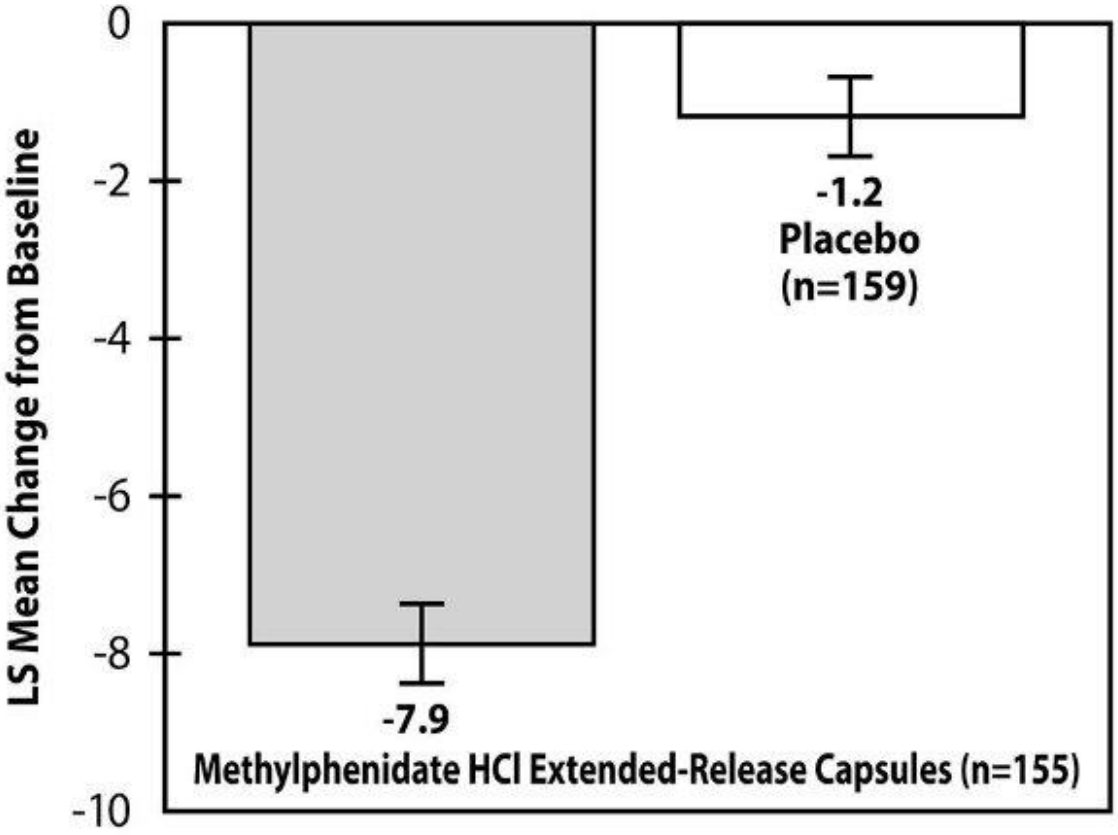
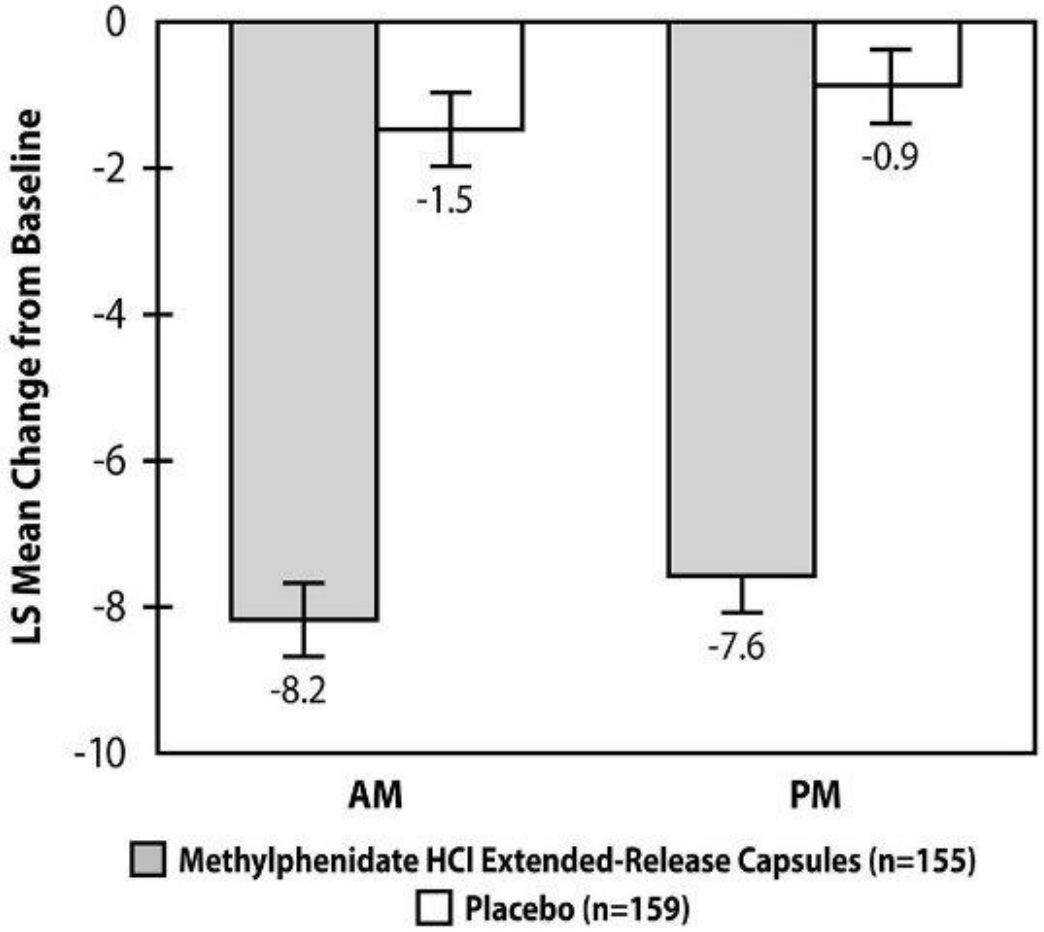


Figure 3: Least Squares Mean Change from Baseline in TCGIS Total Score in Pediatric Patients 6 to 15 years of Age with ADHD: Morning (AM) and Afternoon (PM)



* **FIGURES 2 & 3:** Last observation carried forward analysis at week 3.

Error bars represent the standard error of the mean.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Methylphenidate HCl extended-release capsules are available in six strengths (see Table 4):

Table 4: Strengths, Identifying Characteristics, and Packaging Configurations of Methylphenidate HCl Extended-Release Capsules

Strength	Capsule Color (cap/body)	Imprinting on Capsule Cap	Imprinting on Capsule Body	Capsules per Bottle	NDC Number
10 mg	dark green/white	“M” in a box over “1810” in white letters	“10 mg” in black letters	100	NDC 0406-1810-01
	medium	“M” in a box over	“20 mg” in		NDC

20 mg	medium blue/white	“1820” in white letters	black letters	100	0406-1820-01
30 mg	maroon/white	“M” in a box over “1830” in white letters	“30 mg” in black letters	100	NDC 0406-1830-01
40 mg	yellow ivory/white	“M” in a box over “1840” in black letters	“40 mg” in black letters	100	NDC 0406-1840-01
50 mg	purple/white	“M” in a box over “1850” in white letters	“50 mg” in black letters	100	NDC 0406-1850-01
60 mg	white/white	“M” in a box over “1860” in black letters	“60 mg” in black letters	100	NDC 0406-1860-01

Storage and Handling
Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

Disposal
Comply with local laws and regulations on drug disposal of CNS stimulants. Dispose of remaining, unused, or expired methylphenidate HCl extended-release capsules by a medicine take-back program or by an authorized collector registered with the Drug Enforcement Administration. If no take-back program or authorized collector is available, mix methylphenidate HCl extended-release capsules with an undesirable, nontoxic substance to make it less appealing to children and pets. Place the mixture in a container such as a sealed plastic bag and discard methylphenidate HCl extended-release capsules in the household trash.

17 PATIENT COUNSELING INFORMATION

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

Controlled Substance Status/Potential for Abuse and Dependence
Advise patients and their caregivers that methylphenidate HCl extended-release capsules are a federally controlled substance, and it can be abused and lead to dependence *[see Drug Abuse and Dependence (9.1, 9.2, and 9.3)]*. Instruct patients that they should not give methylphenidate HCl extended-release capsules to anyone else. Advise patients to store methylphenidate HCl extended-release capsules in a safe place, preferably locked, to prevent abuse. Advise patients to comply with laws and regulations on drug disposal. Advise patients to dispose of remaining, unused, or expired methylphenidate HCl extended-release capsules by a medicine take-back program if available *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9), How Supplied/Storage and*

Handling (16)].

Administration Instructions
Instruct patients and their caregivers that the methylphenidate HCl extended-release capsules and the capsule contents must not be crushed or chewed. Instruct patients that the capsule may be swallowed whole, or alternatively, the capsule may be opened and the capsule contents sprinkled onto a small amount (tablespoon) of applesauce and given immediately, and not stored for future use *[see Dosage and Administration (2.3)]*.

Serious Cardiovascular Risks
Advise patients and their caregivers that there is a potential for serious cardiovascular risks including sudden death, myocardial infarction, stroke, and hypertension with methylphenidate HCl extended-release capsules 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)]*.

Blood Pressure and Heart Rate Increases
Instruct patients and their caregivers that methylphenidate HCl extended-release capsules can cause elevations of their blood pressure and pulse rate *[see Warnings and Precautions (5.3)]*.

Psychiatric Risks
Advise patients and their caregivers that methylphenidate HCl extended-release capsules, at recommended doses, can cause psychotic or manic symptoms, even in patients without a prior history of psychotic symptoms or mania *[see Warnings and Precautions (5.4)]*.

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

Circulation Problems in Fingers and Toes (peripheral vasculopathy, including Raynaud's phenomenon)
- Instruct patients 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. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients *[see Warnings and Precautions (5.6)]*.

Suppression of Growth
Advise patients and their caregivers that methylphenidate HCl extended-release capsules can cause slowing of growth and weight loss *[see Warnings and Precautions (5.7)]*.

Pregnancy Registry
Inform patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to methylphenidate HCl extended-release capsules during pregnancy *[see Use in Specific Populations (8.1)]*.

Alcohol Use
Advise patients to avoid alcohol while taking methylphenidate HCl extended-release capsules. Consumption of alcohol while taking methylphenidate HCl extended-release

capsules may result in a more rapid release of the dose of methylphenidate *[see Drug Interactions (7)]*.

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Manufactured by:
SpecGx LLC
Webster Groves, MO 63119 USA

Mallinckrodt™
Pharmaceuticals

An electronic copy of this medication guide can be obtained from www.mallinckrodt.com/Medguide/L20M54.pdf or by calling 1-800-778-7898 for alternate delivery options.

MEDICATION GUIDE
Methylphenidate HCl Extended-Release Capsules, CII
(METH il FEN i date)

What is the most important information I should know about methylphenidate HCl extended-release capsules?
Methylphenidate HCl extended-release capsules can cause serious side effects, including:

- **Abuse and dependence.** Methylphenidate HCl extended-release capsules, other methylphenidate containing medicines, and amphetamines have a high chance for abuse and can cause physical and psychological dependence. Your healthcare provider should check your child for signs of abuse and dependence before and during treatment with methylphenidate HCl extended-release capsules.
  - Tell your healthcare provider if your child has ever abused or been dependent on alcohol, prescription medicines, or street drugs.
  - Your healthcare provider can tell you more about the differences between physical and psychological dependence and drug addiction.
- **Heart-related problems, including:**
  - sudden death in children who have heart problems or heart defects
  - increased blood pressure and heart rate

  Your healthcare provider should check your child carefully for heart problems before starting treatment with methylphenidate HCl extended-release capsules. Tell your healthcare provider if your child has any heart problems, heart defects, high blood pressure, or has a family history of these problems.
  Your healthcare provider should check your child’s blood pressure and heart rate regularly during treatment with methylphenidate HCl extended-release capsules.
  Call your healthcare provider or go to the nearest hospital emergency room right away if your child has any signs of heart problems such as chest pain, shortness of breath, or fainting during treatment with methylphenidate HCl extended-release capsules.
- **Mental (psychiatric) problems, including:**
  - new or worse behavior and thought problems
  - new or worse bipolar illness
  - new psychotic symptoms (such as hearing voices, or seeing or believing things that are not real) or new manic symptoms

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

Call your healthcare provider right away if your child has any new or worsening mental symptoms or problems during treatment with methylphenidate HCl extended-release capsules, especially hearing voices, seeing or believing things that are not real, or new manic symptoms.

What are methylphenidate HCl extended-release capsules?

Methylphenidate HCl extended-release capsules are a prescription medicine used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children 6 to 15 years of age. Methylphenidate HCl extended-release capsules may help increase attention and decrease impulsiveness and hyperactivity in people with ADHD.

It is not known if methylphenidate HCl extended-release capsules are safe and effective for use in children younger than 6 years of age or older than 15 years of age.

Methylphenidate HCl extended-release capsules are a federally controlled substance (CII) because it contains methylphenidate that can be a target for people who abuse prescription medicines or street drugs.

Keep methylphenidate HCl extended-release capsules in a safe place to protect it from theft. Never give your methylphenidate HCl extended-release capsules to anyone else, because it may cause death or harm them. Selling or giving away methylphenidate HCl extended-release capsules may harm others and is against the law.

Who should not take methylphenidate HCl extended-release capsules?

Your child should not take methylphenidate HCl extended-release capsules if your child:

- is allergic to methylphenidate hydrochloride or any of the ingredients in methylphenidate HCl extended-release capsules. See the end of this Medication Guide for a complete list of ingredients in methylphenidate HCl extended-release capsules.
- has a rare inherited problem with the breaking down, absorbing, and processing of certain types of sugar in the body. Methylphenidate HCl extended-release capsules contain a type of sugar called sucrose.
- is taking, or has stopped taking within the past 14 days, a medicine called a monoamine oxidase inhibitor (MAOI).

Before starting methylphenidate HCl extended-release capsules tell your healthcare provider about all your child's medical conditions, including:

if your child:

- has heart problems, heart defects, or high blood pressure
- has mental problems including psychosis, mania, bipolar illness, or depression or has a family history of suicide, bipolar illness, or depression
- has circulation problems in fingers and toes
- is pregnant or plan to become pregnant. It is not known if methylphenidate HCl extended-release capsules will harm the unborn baby.
  - There is a pregnancy registry for females who are exposed to methylphenidate HCl extended-release capsules during pregnancy. The purpose of the registry is to collect information about the health of females exposed to methylphenidate HCl extended-release capsules and their baby. If you or your child becomes pregnant during treatment with methylphenidate HCl extended-release capsules, talk to your healthcare provider about registering with the National Pregnancy Registry for Psychostimulants at 1-866-961-2388.
- is breastfeeding or plan to breastfeed. Methylphenidate HCl passes into breast milk. Talk to your healthcare provider about the best way to feed the baby during treatment with methylphenidate HCl extended-release capsules.

Tell your healthcare provider about all the medicines that your child takes, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Methylphenidate HCl extended-release capsules and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be changed during treatment with methylphenidate HCl extended-release capsules. Your healthcare provider will decide whether methylphenidate HCl extended-release capsules can be taken with other medicines.

Especially tell your healthcare provider if your child takes a medicine used to treat depression called a monoamine oxidase inhibitor (MAOI).

Know the medicines that your child takes. Keep a list of the medicines with you to show your healthcare provider and pharmacist. **Your child should not start taking any new medicines during treatment with methylphenidate HCl extended-release capsules without talking to your healthcare provider first.**

How should methylphenidate HCl extended-release capsules be taken?

- Take methylphenidate HCl extended-release capsules exactly as prescribed by your healthcare provider.
- Your healthcare provider may change the dose if needed.
- Take methylphenidate HCl extended-release capsules 1 time each day in the morning before breakfast.
- Swallow methylphenidate HCl extended-release capsules whole with water or other liquids. If methylphenidate HCl extended-release capsules cannot be swallowed whole, the capsule may be opened and the contents sprinkled onto a tablespoonful of applesauce.
  - Follow with a drink of water or other liquid.
  - **Do not** chew the applesauce and medicine mixture.
  - Swallow all the applesauce and medicine mixture right away. **Do not** store the applesauce and medicine mixture.
- Your healthcare provider may sometimes stop methylphenidate HCl extended-release capsules treatment for a while to check ADHD symptoms.
- **If your child takes too much methylphenidate HCl extended-release capsules, call your poison control center at 1-800-222-1222 or go to your nearest hospital emergency room right away.**

What should be avoided during treatment with methylphenidate HCl extended-release capsules?

Avoid drinking alcohol during treatment with methylphenidate HCl extended-release capsules. This may cause a faster release of the methylphenidate HCl extended-release capsules medicine.

What are the possible side effects of methylphenidate HCl extended-release capsules?

Methylphenidate HCl extended-release capsules can cause serious side effects, including:

- See "**What is the most important information I should know about methylphenidate HCl extended-release capsules?**"
- **Painful and prolonged erections (priapism).** Priapism has happened in males who take products that contain methylphenidate. **If your child develops priapism, get medical help right away.**
- **Circulation problems in fingers and toes (peripheral vasculopathy, including Raynaud's phenomenon).**
  Signs and symptoms may include:
  - fingers or toes may feel numb, cool, painful
  - fingers or toes may change color from pale, to blue, to red

Tell your healthcare provider if your child has numbness, pain, skin color change, or sensitivity to temperature in the fingers or toes.
Call your healthcare provider right away if your child has any signs of unexplained wounds appearing on the fingers or toes during treatment with methylphenidate HCl extended-release capsules.

- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with methylphenidate HCl extended-release capsules. Methylphenidate HCl extended-release capsules treatment may be stopped if your child is not growing or gaining weight.

The most common side effects of methylphenidate HCl extended-release capsules include anorexia and trouble sleeping.
These are not all the possible side effects of methylphenidate HCl extended-release capsules. 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 methylphenidate HCl extended-release capsules?

- Store methylphenidate HCl extended-release capsules at room temperature between 68°F to 77°F (20°C to 25°C).
- Store methylphenidate HCl extended-release capsules in a safe place, like a locked cabinet. Protect from light and moisture.
- Dispose of remaining, unused, or expired methylphenidate HCl extended-release capsules by a medication take-back program at authorized collection sites such as retail pharmacies, hospital or clinic pharmacies, and law enforcement locations. If no take-back program or authorized collector is available, mix methylphenidate HCl extended-release capsules 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 methylphenidate HCl extended-release capsules in the household trash.

Keep methylphenidate HCl extended-release capsules and all medicines out of the reach of children.

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

What are the ingredients in methylphenidate HCl extended-release capsules?
Active Ingredient: methylphenidate hydrochloride
Inactive Ingredients: Sugar Spheres, Ethylcellulose, Oleic Acid, Medium-Chain Triglycerides, Titanium Dioxide, Gelatin, Shellac, Propylene Glycol, Hypromellose, Polyethylene Glycol, and Black Iron Oxide.
The individual capsules contain the following coloring agents:
10 mg capsules: FD&C Blue No. 2, Yellow Iron Oxide, Sodium Hydroxide, Povidone
20 mg capsules: FD&C Blue No. 2, Sodium Hydroxide, Povidone
30 mg capsules: FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, Sodium Hydroxide, Povidone
40 mg capsules: Yellow Iron Oxide
50 mg capsules: FD&C Blue No. 2, Red Iron Oxide, Sodium Hydroxide, Povidone
Manufactured by:
SpecGx LLC
Webster Groves, MO 63119 USA

Mallinckrodt™

For more information about methylphenidate HCl extended-release capsules call 1-800-778-7898.

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Revised: 05/2022

L20M54

PRINCIPAL DISPLAY PANEL 10 mg Label

NDC 0406-1810-01

100 CAPSULES

Once Daily
Methylphenidate HCl
Extended-Release Capsules

10 mg

CII

Rx only

PHARMACIST: Dispense the Medication Guide provided separately to each patient.

Mallinckrodt™

L0M135 Rev 09/2017

PRINCIPAL DISPLAY PANEL 20 mg Label

NDC 0406-1820-01

100 CAPSULES

Once Daily
Methylphenidate HCl
Extended-Release Capsules

20 mg

CII

Rx only

PHARMACIST: Dispense the Medication Guide provided separately to each patient.

Mallinckrodt™

L0M136 Rev 09/2017

PRINCIPAL DISPLAY PANEL 30 mg Label

NDC 0406-1830-01

100 CAPSULES

Once Daily
Methylphenidate HCl
Extended-Release Capsules

30 mg

CII

Rx only

PHARMACIST: Dispense the Medication Guide provided separately to each patient.

Mallinckrodt™

L0M137 Rev 09/2017

PRINCIPAL DISPLAY PANEL 40 mg Label

NDC 0406-1840-01

100 CAPSULES

Once Daily
Methylphenidate HCl
Extended-Release Capsules

40 mg

CII

Rx only

PHARMACIST: Dispense the Medication Guide provided separately to each patient.

Mallinckrodt™

L0M138 Rev 09/2017

PRINCIPAL DISPLAY PANEL 50 mg Label

NDC 0406-1850-01

100 CAPSULES

Once Daily
Methylphenidate HCl
Extended-Release Capsules

50 mg

CII

Rx only

PHARMACIST: Dispense the Medication Guide provided separately to each patient.

Mallinckrodt™

L0M139 Rev 09/2017

PRINCIPAL DISPLAY PANEL 60 mg Label

NDC 0406-1850-01

100 CAPSULES

Once Daily
Methylphenidate HCl
Extended-Release Capsules

60 mg

CII

Rx only

PHARMACIST: Dispense the Medication Guide provided separately to each patient.

Mallinckrodt™

METHYLPHENIDATE HYDROCHLORIDE EXTENDED-RELEASE

methylphenidate hydrochloride capsule, extended release

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0406-1810
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	10 mg

Inactive Ingredients

Ingredient Name	Strength
SUCROSE (UNII: C151H8M554)	
STARCH, CORN (UNII: O8232NY3SJ)	
ETHYLCELLULOSE, UNSPECIFIED (UNII: 7Z8S9VYZ4B)	
OLEIC ACID (UNII: 2UMI9U37CP)	
MEDIUM-CHAIN TRIGLYCERIDES (UNII: C9H2L21V7U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
SHELLAC (UNII: 46N107B71O)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	

FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics			
Color	white, green (dark green)	**Score**	no score
Shape	CAPSULE	**Size**	14mm
Flavor		**Imprint Code**	10;MG;M;1810
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0406-1810-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	09/29/2015	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA203583	09/29/2015	

METHYLPHENIDATE HYDROCHLORIDE EXTENDED-RELEASE

methylphenidate hydrochloride capsule, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0406-1820
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	20 mg

Inactive Ingredients

Ingredient Name	Strength
SUCROSE (UNII: C151H8M554)	
STARCH, CORN (UNII: O8232NY3SJ)	
ETHYLCELLULOSE, UNSPECIFIED (UNII: 7Z8S9VYZ4B)	
OLEIC ACID (UNII: 2UMI9U37CP)	
MEDIUM-CHAIN TRIGLYCERIDES (UNII: C9H2L21V7U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
SHELLAC (UNII: 46N107B71O)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	

HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	white, blue (medium blue)	**Score**	no score
Shape	CAPSULE	**Size**	16mm
Flavor		**Imprint Code**	20;MG;M;1820
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0406-1820-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	09/29/2015	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA203583	09/29/2015	

METHYLPHENIDATE HYDROCHLORIDE EXTENDED-RELEASE

methylphenidate hydrochloride capsule, extended release

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0406-1830
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	30 mg

Inactive Ingredients

Ingredient Name	Strength
SUCROSE (UNII: C151H8M554)	
STARCH, CORN (UNII: O8232NY3SJ)	
ETHYLCELLULOSE, UNSPECIFIED (UNII: 7Z8S9VYZ4B)	
OLEIC ACID (UNII: 2UMI9U37CP)	
MEDIUM-CHAIN TRIGLYCERIDES (UNII: C9H2L21V7U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
SHELLAC (UNII: 46N107B71O)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	

Product Characteristics

Color	white, red (maroon)	**Score**	no score
Shape	CAPSULE	**Size**	18mm
Flavor		**Imprint Code**	30;MG;M;1830
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0406-1830-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	09/29/2015	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA203583	09/29/2015	

METHYLPHENIDATE HYDROCHLORIDE EXTENDED-RELEASE

methylphenidate hydrochloride capsule, extended release

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0406-1840
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	40 mg

Inactive Ingredients

Ingredient Name	Strength
SUCROSE (UNII: C151H8M554)	

STARCH, CORN (UNII: O8232NY3SJ)	
ETHYLCELLULOSE, UNSPECIFIED (UNII: 7Z8S9VYZ4B)	
OLEIC ACID (UNII: 2UMI9U37CP)	
MEDIUM-CHAIN TRIGLYCERIDES (UNII: C9H2L21V7U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
SHELLAC (UNII: 46N107B71O)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	

Product Characteristics

Color	white, yellow (yellow ivory)	**Score**	no score
Shape	CAPSULE	**Size**	19mm
Flavor		**Imprint Code**	40;MG;M;1840
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0406-1840-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	09/29/2015	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA203583	09/29/2015	

METHYLPHENIDATE HYDROCHLORIDE EXTENDED-RELEASE

methylphenidate hydrochloride capsule, extended release

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0406-1850
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	50 mg

Inactive Ingredients

Ingredient Name	Strength

SUCROSE (UNII: C151H8M554)	
STARCH, CORN (UNII: O8232NY3SJ)	
ETHYLCELLULOSE, UNSPECIFIED (UNII: 7Z8S9VYZ4B)	
OLEIC ACID (UNII: 2UMI9U37CP)	
MEDIUM-CHAIN TRIGLYCERIDES (UNII: C9H2L21V7U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
SHELLAC (UNII: 46N107B71O)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
FERRIC OXIDE RED (UNII: 1K09F3G675)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

Product Characteristics

Color	white, purple	**Score**	no score
Shape	CAPSULE	**Size**	22mm
Flavor		**Imprint Code**	50;MG;M;1850
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0406-1850-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	09/29/2015	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA203583	09/29/2015	

METHYLPHENIDATE HYDROCHLORIDE EXTENDED-RELEASE

methylphenidate hydrochloride capsule, extended release

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0406-1860
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHYLPHENIDATE HYDROCHLORIDE (UNII: 4B3SC438HI) (METHYLPHENIDATE - UNII:207ZZ9QZ49)	METHYLPHENIDATE HYDROCHLORIDE	60 mg

Inactive Ingredients

Ingredient Name	Strength
SUCROSE (UNII: C151H8M554)	
STARCH, CORN (UNII: O8232NY3SJ)	
ETHYLCELLULOSE, UNSPECIFIED (UNII: 7Z8S9VYZ4B)	
OLEIC ACID (UNII: 2UMI9U37CP)	
MEDIUM-CHAIN TRIGLYCERIDES (UNII: C9H2L21V7U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
SHELLAC (UNII: 46N107B71O)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	

Product Characteristics

Color	white, white	**Score**	no score
Shape	CAPSULE	**Size**	22mm
Flavor		**Imprint Code**	60;MG;M;1860
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0406-1860-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	09/29/2015	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA203583	09/29/2015	

Labeler - SpecGx LLC (080679498)

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