Methylphenidate Hydrochloride Extended-Release Capsules CII

Rx only

40-9265
Rev. A 10/2019

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use METHYLPHENIDATE HYDROCHLORIDE EXTENDED-RELEASE CAPSULES safely and effectively. See full prescribing information for METHYLPHENIDATE HYDROCHLORIDE EXTENDED-RELEASE CAPSULES.

METHYLPHENIDATE HYDROCHLORIDE extended-release capsules, for oral use, CII

Initial U.S. Approval: 1955

WARNING: ABUSE AND DEPENDENCE
See full prescribing information for complete boxed warning.

- **CNS stimulants, including methylphenidate hydrochloride 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, 9.3)**

RECENT MAJOR CHANGES

Indications and Usage (1)	06/2019
Warnings and Precautions (5.7)	06/2019

INDICATIONS AND USAGE

Methylphenidate hydrochloride extended-release capsules are a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older. (1)

Limitations of Use:
Pediatric patients younger than 6 years of age experienced higher plasma exposure than patients 6 years and older at the same dose and high rates of adverse reactions, most notably weight loss. (8.4)

DOSAGE AND ADMINISTRATION

- Recommended starting dose for patients 6 years and older: 10 mg once daily with or without food in the morning. Dosage may be increased weekly in increments of 10 mg per day. Daily dosage above 60 mg is not recommended. (2.1)
- Capsules may be swallowed whole or opened and the entire contents sprinkled onto applesauce. (2.1)

DOSAGE FORMS AND STRENGTHS

- Extended-Release Capsules: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg of methylphenidate hydrochloride, which is equivalent to 8.6 mg, 13.0 mg, 17.3 mg, 25.9 mg, 34.6 mg, 43.2 mg, and 51.9 mg of methylphenidate free base, respectively, per capsule. (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

- *Serious Cardiovascular Events:* 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 arrhythmias, or coronary artery disease. (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 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 hydrochloride extended-release 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 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 in double-blind clinical trials (> 5% and twice the rate of placebo) in pediatric patients 6 to 17 years were abdominal pain, decreased appetite, headache and insomnia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Teva Pharmaceuticals USA, Inc. at 1-888-838-2872 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 10/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE AND DEPENDENCE

CNS stimulants, including methylphenidate hydrochloride 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 Warning and Precautions (5.1), Drug Abuse and Dependence (9.2, 9.3)]*.

1 INDICATIONS AND USAGE

Methylphenidate hydrochloride extended-release capsules are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older *[see Clinical Studies (14)]*.

Limitations of Use
Pediatric patients younger than 6 years of age experienced higher plasma exposure than patients 6 years and older at the same dose and high rates of adverse reactions, most notably weight loss *[see Use in Specific Populations (8.4)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Pretreatment Screening

Prior to treating pediatric patients and adults with CNS stimulants including methylphenidate hydrochloride extended-release capsules, 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]*.

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 hydrochloride extended-release capsule use *[see Boxed Warning, Warnings and Precautions (5.1), and Drug Abuse and Dependence (9)]*.

2.2 General Dosing Information

The recommended starting dose of methylphenidate hydrochloride extended-release capsules for patients 6 years and older is 10 mg once daily in the morning with or without food. Advise patients to establish a routine pattern with regard to meals. The dose should be individualized according to the needs and response of the patient.

The dose may be titrated weekly in increments of 10 mg. Daily doses above 60 mg have not been studied and are not recommended.

Methylphenidate hydrochloride extended-release capsules may be taken whole or the capsule may be opened and the entire contents sprinkled onto applesauce. If the patient is using the sprinkled administration method, the sprinkled applesauce should be consumed immediately; it should not be stored. Patients should take the applesauce with sprinkled beads in its entirety without chewing. The dose of a single capsule should not be divided. The contents of the entire capsule should be taken, and patients should not take anything less than one capsule per day.

Pharmacological treatment of ADHD may be needed for extended periods. Healthcare providers should periodically re-evaluate the long-term use of methylphenidate hydrochloride extended-release capsules, and adjust dosage as needed.

2.3 Dose Reduction and Discontinuation

If paradoxical aggravation of symptoms or other adverse reactions occur; the dosage should be reduced, or, if necessary, the drug should be discontinued.

If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.

3 DOSAGE FORMS AND STRENGTHS

Methylphenidate Hydrochloride Extended-Release Capsules are available as follows:

10 mg - Capsule with turquoise blue opaque cap and white opaque body printed with A854 on the cap and 10 mg on the body in black ink.

15 mg - Capsule with cream opaque cap and white opaque body printed with A862 on the cap and 15 mg on the body in black ink.

20 mg - Capsule with grey opaque cap and white opaque body printed with A869 on the cap and 20 mg on the body in black ink.

30 mg - Capsule with blue opaque cap and white opaque body printed with A873 on the cap and 30 mg on the body in black ink.

40 mg - Capsule with yellow opaque cap and white opaque body printed with A891 on the cap and 40 mg on the body in black ink.

50 mg - Capsule with green opaque cap and white opaque body printed with A895 on the cap and 50 mg on the body in black ink.

60 mg - Capsule with pink opaque cap and white opaque body printed with A902 on the cap and 60 mg on the body in black ink.

4 CONTRAINDICATIONS

- Hypersensitivity to methylphenidate or other components of the product. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with methylphenidate products *[see Adverse Reactions (6.1)]*.
- Concomitant treatment with monoamine oxidase inhibitors, and also within 14 days following discontinuation of treatment with a monoamine oxidase inhibitor, because of the risk of hypertensive crisis *[see Drug Interactions (7.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Potential for Abuse and Dependence

CNS stimulants, including methylphenidate hydrochloride 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 Boxed Warning and 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 arrhythmia, coronary artery disease, and other serious heart problems. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during methylphenidate hydrochloride extended-release capsule 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 hydrochloride 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 hydrochloride 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 post-marketing 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 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 pediatric patients over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated pediatric patients (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 hydrochloride 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 Boxed Warning, Warnings and Precautions (5.1), and Drug Abuse and Dependence (9.2, 9.3)]*
- Hypersensitivity to Methylphenidate *[see Contraindications (4)]*
- Hypertensive Crisis with Concomitant Use of Monoamine Oxidase Inhibitors *[see Contraindications (4) and Drug Interactions (7.1)]*
- 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 Trial Experience

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

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

Clinical Trials Experience with Methylphenidate Hydrochloride Extended-Release in Pediatric Patients with ADHD
The safety data in this section is based on data from two one-week controlled clinical studies of methylphenidate hydrochloride extended-release in pediatric patients with ADHD, one in children ages 6 to 12 years (RP-BP-EF001, hereafter "Study 1"), and one in children and adolescents ages 6 to 17 years (RP-BP-EF002, hereafter "Study 2").

Two methylphenidate hydrochloride extended-release clinical studies evaluated a total of 256 patients with ADHD. Two hundred and forty-three (243) patients participated in the double-blind phase of these two clinical studies.

Study 1 was a randomized, double-blind, single center, placebo-controlled, flexible-dose, cross-over study to evaluate the time of onset, duration of efficacy, tolerability and safety of methylphenidate hydrochloride extended-release 15 mg, 20 mg, 30 mg, or 40 mg administered for one week in 26 pediatric patients aged 6 to 12 years who met DSM-IV criteria for ADHD *[see Clinical Studies (14)]*.

Most Common Adverse Reactions (incidence of ≥ 5% and at a rate at least twice placebo): abdominal pain, pyrexia and headache.

Adverse Reactions Leading to Discontinuation: No subjects discontinued due to adverse reactions during the double-blind phase of this study.

Study 2 was a randomized, double-blind, multicenter, placebo-controlled, parallel group, fixed-dose study of 10 mg, 15 mg, 20 mg, and 40 mg of methylphenidate hydrochloride extended-release administered for one week in 221 pediatric patients (6 to 17 years of age) who met DSM-IV criteria for ADHD *[see Clinical Studies (14)]*.

Most Common Adverse Reactions (incidence of ≥ 5% and at a rate of at least twice placebo): abdominal pain, decreased appetite, headache and insomnia.

Adverse Reactions Leading to Discontinuation: Two patients (4.4%) in the methylphenidate hydrochloride extended-release 40 mg group discontinued due to insomnia, nausea and rapid heart rate, respectively during the double-blind phase of the study.

Table 1: Common Adverse Reactions Occurring in ≥ 2% of Pediatric Patients (6 to 17 years of age) with ADHD Taking Methylphenidate Hydrochloride Extended-Release and at a Rate Greater than Placebo (Study 2)

System Organ Class Adverse Reaction	Methylphenidate Hydrochloride Extended-Release (n=183)	Placebo (n=47)
Nervous System Disorders		
Headache	10.9%	8.5%
Insomnia	9.8%	2.1%
Dizziness	2.2%	2.1%
Gastrointestinal Disorders		
Abdominal pain upper	8.2%	0%
Nausea	3.8%	2.1%
Vomiting	3.8%	0%
Metabolism and Nutritional		
Decreased Appetite	4.9%	0%

6.2 Post-Marketing Experience

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

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

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

Eye Disorders: Diplopia, Mydriasis, Visual impairment

General Disorders: Chest pain, Chest discomfort, Hyperpyrexia

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

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

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

Nervous System: Convulsion, Grand mal convulsion, Dyskinesia, serotonin syndrome in combination with serotonergic drugs

Psychiatric Disorders: Disorientation, Libido changes

Skin and Subcutaneous Tissue Disorders: Alopecia, Erythema

7 DRUG INTERACTIONS

7.1 Clinically Important Interactions with Methylphenidate Hydrochloride Extended-Release Capsules

Monoamine Oxidase Inhibitors (MAOIs)
Do not administer methylphenidate hydrochloride extended-release capsules concomitantly or within 14 days after discontinuing MAOI treatment. Concomitant use of MAOIs and CNS stimulants can cause hypertensive crisis. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure *[see Contraindications (4)]*.

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 methylphenidate hydrochloride extended-release during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Psychostimulants at 1-866-961-2388.

Risk Summary
Limited published studies report on the use of methylphenidate in pregnant women; however, the data are insufficient to inform any drug-associated risks. 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 the highest dose of 60 mg/kg/day (6 times the MRHD given to adolescents) *[see Data]*. The background risk of major birth defects and miscarriage for the indicated population are unknown. However, the background risk in the U.S. general population of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

Clinical Considerations
Fetal/Neonatal adverse reactions
CNS stimulants, such as methylphenidate hydrochloride extended-release, 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 maximum recommended human dose (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 (2 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 postnatal development in rats was 15 mg/kg/day (1.5 times the MRHD given to adolescents on a mg/m^2 basis).

8.2 Lactation

Risk Summary
Limited published literature, based on breast milk sampling from five 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. However, 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 hydrochloride extended-release and any potential adverse effects on the breastfed infant from methylphenidate hydrochloride extended-release or from the underlying maternal condition.

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

8.4 Pediatric Use

The safety and effectiveness of methylphenidate hydrochloride extended-release in pediatric patients under 6 years have not been established.

Safety and efficacy of methylphenidate hydrochloride extended-release were evaluated in a multicenter, placebo-controlled, double-blind, parallel group study in 119 children 4 to <6 years of age with ADHD followed by a 12-month open-label extension in 44 of these children. In these studies, patients experienced high rates of adverse reactions, most notably weight loss. Comparing weights prior to initiation of methylphenidate hydrochloride extended-release (in the safety and efficacy study) to weights after 12 months of treatment (in the open-label extension), 20 of 39 patients with data (50%) had lost enough weight to decrease 10 or more percentiles on a Centers for Disease Control growth chart for weight. In addition, systemic drug exposures in patients 4 to <6 years of age were higher than those observed in older children and adolescents at the same dose (2 to 3 fold higher C_{max} and AUC). Therefore, the benefits of methylphenidate hydrochloride extended-release do not outweigh the risks in pediatric patients 4 to <6 years of age.

The safety and effectiveness of methylphenidate hydrochloride extended-release have been established in pediatric patients ages 6 to 17 years in two adequate and well-controlled clinical trials *[see Clinical Studies (14)]*. 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 methylphenidate hydrochloride extended-release. 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 6 times the maximum recommended human dose (MRHD) of 60 mg/day given to children on a mg/m^2 basis.

In the study conducted in young rats, methylphenidate was administered orally at doses of up to 100 mg/kg/day for 9 weeks, starting early in the postnatal period (postnatal day 7) and continuing through sexual maturity (postnatal week 10). When these animals were tested as adults (postnatal weeks 13 to 14), decreased spontaneous locomotor activity was observed in males and females previously treated with 50 mg/kg/day (approximately 6 times the 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 observed 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.

MEDICATION GUIDE
Methylphenidate Hydrochloride (meth" il fen' i date hye" droe klor' ide) CII Extended-Release Capsules

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

- **Abuse and dependence.** Methylphenidate hydrochloride 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 you or your child for signs of abuse and dependence before and during treatment with methylphenidate hydrochloride extended-release capsules.
  - Tell your healthcare provider if you or your child have 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, stroke, and heart attack in adults
  - sudden death in children who have heart problems or heart defects
  - increased blood pressure and heart rate

  Your healthcare provider should check you or your child carefully for heart problems before starting treatment with methylphenidate hydrochloride extended-release capsules. Tell your healthcare provider if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.

  Your doctor should check you or your child's blood pressure and heart rate regularly during treatment with methylphenidate hydrochloride extended-release capsules.

  Call your healthcare provider or go the nearest hospital emergency room right away if you or your child have any signs of heart problems such as chest pain, shortness of breath, or fainting during treatment with methylphenidate hydrochloride 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 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 during treatment with methylphenidate hydrochloride extended-release capsules, especially hearing voices, seeing or believing things that are not real, or new manic symptoms.

What are methylphenidate hydrochloride extended-release capsules?
Methylphenidate hydrochloride extended-release is a central nervous system (CNS) stimulant prescription medicine used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in people 6 years of age and older. Methylphenidate hydrochloride extended-release may help increase attention and decrease impulsiveness and hyperactivity in people with ADHD.

- **Methylphenidate hydrochloride extended-release is not for use in children under 6 years of age.**
- **Methylphenidate hydrochloride extended-release 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 methylphenidate hydrochloride extended-release capsules in a safe place to protect it from theft. Never give your methylphenidate hydrochloride extended-release capsules to anyone else, because it may cause death or harm them. Selling or giving away methylphenidate hydrochloride extended-release capsules may harm others and is against the law.

Do not take methylphenidate hydrochloride extended-release capsules if you or your child are:

- allergic to methylphenidate hydrochloride or any of the ingredients in methylphenidate hydrochloride extended-release capsules. See the end of this Medication Guide for a complete list of ingredients in methylphenidate hydrochloride extended-release capsules.
- taking or have stopped taking within the past 14 days a medicine used to treat depression called a monoamine oxidase inhibitor (MAOI).

Before taking methylphenidate hydrochloride extended-release capsules tell your healthcare provider about all medical conditions, including if you or your child:

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

Tell your healthcare provider about all the medicines that you or your child take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Methylphenidate hydrochloride 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 hydrochloride extended-release capsules. Your healthcare provider will decide whether methylphenidate hydrochloride extended-release capsules can be taken with other medicines.

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

Know the medicines that you or your child take. Keep a list of the medicines with you to show your healthcare provider and pharmacist. **Do not start any new medicine during treatment with methylphenidate hydrochloride extended-release capsules without talking to your healthcare provider first.**

MEDICATION GUIDE
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What is the most important information I should know about methylphenidate hydrochloride extended-release capsules?
Methylphenidate hydrochloride extended-release capsules can cause serious side effects, including:
- Abuse and dependence. Methylphenidate hydrochloride 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 you or your child for signs of abuse and dependence before and during treatment with methylphenidate hydrochloride extended-release capsules.
  - Tell your healthcare provider if you or your child have 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, stroke, and heart attack in adults
  - sudden death in children who have heart problems or heart defects
  - increased blood pressure and heart rate
  Your healthcare provider should check you or your child carefully for heart problems before starting treatment with methylphenidate hydrochloride extended-release capsules. Tell your healthcare provider if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.
  Your doctor should check you or your child's blood pressure and heart rate regularly during treatment with methylphenidate hydrochloride extended-release capsules.
  Call your healthcare provider or go the nearest hospital emergency room right away if you or your child have any signs of heart problems such as chest pain, shortness of breath, or fainting during treatment with methylphenidate hydrochloride 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 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 during treatment with methylphenidate hydrochloride extended-release capsules, especially hearing voices, seeing or believing things that are not real, or new manic symptoms.
What are methylphenidate hydrochloride extended-release capsules?
Methylphenidate hydrochloride extended-release is a central nervous system (CNS) stimulant prescription medicine used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in people 6 years of age and older. Methylphenidate hydrochloride extended-release may help increase attention and decrease impulsiveness and hyperactivity in people with ADHD.
- Methylphenidate hydrochloride extended-release is not for use in children under 6 years of age.
- Methylphenidate hydrochloride extended-release 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 methylphenidate hydrochloride extended-release capsules in a safe place to protect it from theft. Never give your methylphenidate hydrochloride extended-release capsules to anyone else, because it may cause death or harm them. Selling or giving away methylphenidate hydrochloride extended-release capsules may harm others and is against the law.
Do not take methylphenidate hydrochloride extended-release capsules if you or your child are:
- allergic to methylphenidate hydrochloride or any of the ingredients in methylphenidate hydrochloride extended-release capsules. See the end of this Medication Guide for a complete list of ingredients in methylphenidate hydrochloride extended-release capsules.
- taking or have stopped taking within the past 14 days a medicine used to treat depression called a monoamine oxidase inhibitor (MAOI).
Before taking methylphenidate hydrochloride extended-release capsules tell your healthcare provider about all medical conditions, including if you or your child:
- have heart problems, heart defects, high blood pressure
- have mental problems including psychosis, mania, bipolar illness, or depression, or have a family history of suicide, bipolar illness, or depression
- have circulation problems in fingers and toes
- are pregnant or plan to become pregnant. It is not known if methylphenidate hydrochloride extended-release capsules will harm your unborn baby.
  - There is a pregnancy registry for females who are exposed to methylphenidate hydrochloride extended-release capsules during pregnancy. The purpose of the registry is to collect information about the health of females exposed to methylphenidate hydrochloride extended-release capsules and their baby. If you or your child becomes pregnant during treatment with methylphenidate hydrochloride extended-release capsules, talk to your healthcare provider about registering with the National Pregnancy Registry for Psychostimulants at 1-866-961-2388.
- are breastfeeding or plan to breastfeed. Methylphenidate hydrochloride passes into breast milk. Talk to your healthcare provider about the best way to feed the baby during treatment with methylphenidate hydrochloride extended-release capsules.
Tell your healthcare provider about all the medicines that you or your child take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Methylphenidate hydrochloride 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 hydrochloride extended-release capsules. Your healthcare provider will decide whether methylphenidate hydrochloride extended-release capsules can be taken with other medicines.
Especially tell your healthcare provider if you or your child take a medicine used to treat depression called monoamine oxidase inhibitor (MAOI).
Know the medicines that you or your child take. Keep a list of the medicines with you to show your healthcare provider and pharmacist. Do not start any new medicine during treatment with methylphenidate hydrochloride extended-release capsules without talking to your healthcare provider first.

MEDICATION GUIDE
Methylphenidate Hydrochloride (meth" il fen' i date hye" droe klor' ide) CII Extended-Release Capsules

What is the most important information I should know about methylphenidate hydrochloride extended-release capsules?
Methylphenidate hydrochloride extended-release capsules can cause serious side effects, including:
- Abuse and dependence. Methylphenidate hydrochloride 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 you or your child for signs of abuse and dependence before and during treatment with methylphenidate hydrochloride extended-release capsules.
  - Tell your healthcare provider if you or your child have 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, stroke, and heart attack in adults
  - sudden death in children who have heart problems or heart defects
  - increased blood pressure and heart rate
  Your healthcare provider should check you or your child carefully for heart problems before starting treatment with methylphenidate hydrochloride extended-release capsules. Tell your healthcare provider if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.
  Your doctor should check you or your child's blood pressure and heart rate regularly during treatment with methylphenidate hydrochloride extended-release capsules.
  Call your healthcare provider or go the nearest hospital emergency room right away if you or your child have any signs of heart problems such as chest pain, shortness of breath, or fainting during treatment with methylphenidate hydrochloride 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 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 during treatment with methylphenidate hydrochloride extended-release capsules, especially hearing voices, seeing or believing things that are not real, or new manic symptoms.
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- Methylphenidate hydrochloride extended-release is not for use in children under 6 years of age.
- Methylphenidate hydrochloride extended-release 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 methylphenidate hydrochloride extended-release capsules in a safe place to protect it from theft. Never give your methylphenidate hydrochloride extended-release capsules to anyone else, because it may cause death or harm them. Selling or giving away methylphenidate hydrochloride extended-release capsules may harm others and is against the law.
Do not take methylphenidate hydrochloride extended-release capsules if you or your child are:
- allergic to methylphenidate hydrochloride or any of the ingredients in methylphenidate hydrochloride extended-release capsules. See the end of this Medication Guide for a complete list of ingredients in methylphenidate hydrochloride extended-release capsules.
- taking or have stopped taking within the past 14 days a medicine used to treat depression called a monoamine oxidase inhibitor (MAOI).
Before taking methylphenidate hydrochloride extended-release capsules tell your healthcare provider about all medical conditions, including if you or your child:
- have heart problems, heart defects, high blood pressure
- have mental problems including psychosis, mania, bipolar illness, or depression, or have a family history of suicide, bipolar illness, or depression
- have circulation problems in fingers and toes
- are pregnant or plan to become pregnant. It is not known if methylphenidate hydrochloride extended-release capsules will harm your unborn baby.
  - There is a pregnancy registry for females who are exposed to methylphenidate hydrochloride extended-release capsules during pregnancy. The purpose of the registry is to collect information about the health of females exposed to methylphenidate hydrochloride extended-release capsules and their baby. If you or your child becomes pregnant during treatment with methylphenidate hydrochloride extended-release capsules, talk to your healthcare provider about registering with the National Pregnancy Registry for Psychostimulants at 1-866-961-2388.
- are breastfeeding or plan to breastfeed. Methylphenidate hydrochloride passes into breast milk. Talk to your healthcare provider about the best way to feed the baby during treatment with methylphenidate hydrochloride extended-release capsules.
Tell your healthcare provider about all the medicines that you or your child take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Methylphenidate hydrochloride 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 hydrochloride extended-release capsules. Your healthcare provider will decide whether methylphenidate hydrochloride extended-release capsules can be taken with other medicines.
Especially tell your healthcare provider if you or your child take a medicine used to treat depression called monoamine oxidase inhibitor (MAOI).
Know the medicines that you or your child take. Keep a list of the medicines with you to show your healthcare provider and pharmacist. Do not start any new medicine during treatment with methylphenidate hydrochloride extended-release capsules without talking to your healthcare provider first.

How should methylphenidate hydrochloride extended-release capsules be taken?

- Take methylphenidate hydrochloride extended-release capsules exactly as prescribed by your healthcare provider.
- Your healthcare provider may change the dose if needed.
- Take methylphenidate hydrochloride extended-release capsules by mouth 1 time each day in the morning.
- Methylphenidate hydrochloride extended-release capsules can be taken with or without food but take it the same way each time.
- Swallow methylphenidate hydrochloride extended-release capsules whole, or if methylphenidate hydrochloride extended-release capsules cannot be swallowed whole, the capsules may be opened and sprinkled onto a tablespoonful of applesauce. Make sure to sprinkle all the medicine onto the applesauce. The methylphenidate hydrochloride extended-release capsules dose should not be divided.
  - swallow all the applesauce and medicine mixture without chewing right away or within 10 minutes
  - **do not** chew the applesauce and medicine mixture
  - **do not** store applesauce and medicine mixture
- Your healthcare provider may sometimes stop methylphenidate hydrochloride extended-release capsules treatment for a while to check ADHD symptoms.
- If a dose of methylphenidate hydrochloride extended-release capsules is missed, do not take the dose later in the day or take an extra dose to make up for the missed dose, wait until the next morning to take the next scheduled dose.
- **In case of poisoning call your poison control center at 1-800-222-1222 or go to the nearest hospital emergency room right away.**

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

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

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

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

See "What is the most important information I should know about methylphenidate hydrochloride extended-release capsules?"

- **Painful and prolonged erections (priapism).** Priapism has happened in males who take products that contain methylphenidate. **If you or your child develop 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 you have 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 have any signs of unexplained wounds appearing on fingers or toes during treatment with methylphenidate hydrochloride extended-release capsules.
- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with methylphenidate hydrochloride extended-release capsules. Methylphenidate hydrochloride extended-release capsules treatment may be stopped if your child is not growing or gaining weight.

The most common side effects of methylphenidate hydrochloride extended-release capsules in children 6 to 17 years of age include stomach pain, decreased appetite, headache, trouble sleeping.

These are not all the possible side effects of methylphenidate hydrochloride extended-release capsules.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Teva Pharmaceuticals at 1-888-838-2872.

How should I store methylphenidate hydrochloride extended-release capsules?

- Store methylphenidate hydrochloride extended-release capsules at room temperature between 68°F to 77°F (20°C to 25°C).
- Store methylphenidate hydrochloride extended-release capsules in a safe place, like a locked cabinet. Protect from moisture.
- Dispose of remaining, unused, or expired methylphenidate hydrochloride 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 hydrochloride 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 hydrochloride extended-release capsules in the household trash.
- **Keep methylphenidate hydrochloride extended-release capsules and all medicines out of the reach of children.**

General information about the safe and effective use of methylphenidate hydrochloride extended-release capsules.

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

What are the ingredients in methylphenidate hydrochloride extended-release capsules?

Active Ingredient: methylphenidate hydrochloride

Inactive Ingredients: ammonio methacrylate copolymer type B, fumaric acid, gelatin, hypromellose 2910, methacrylic acid copolymer type A, polyethylene glycol 400, polyethylene glycol 8000, sugar spheres (which contains sucrose and corn starch), talc, titanium dioxide and triethyl citrate. The 10 mg capsules also contain FD&C Blue #1. The 15 mg capsules also contain FD&C Yellow #6. The 20 mg capsules also contain black iron oxide. The 30 mg capsules also contain FD&C Blue#1 and FD&C Red #3. The 40 mg capsules also contain yellow iron oxide. The 50 mg capsules also contain FD&C Blue #1 and yellow iron oxide. The 60 mg capsules also contain FD&C Blue #1 and FD&C Red #40. Black printing ink SW-9008/SW-9009 contains black iron oxide, potassium hydroxide, propylene glycol, shellac, and strong ammonia solution.

Teva Pharmaceuticals USA, Inc., North Wales, PA 19454

For more information, you may also contact Teva Pharmaceuticals USA, Inc. (the distributor for methylphenidate hydrochloride extended-release capsules) at 1-888-838-2872.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Rev. A 10/2019

How should methylphenidate hydrochloride extended-release capsules be taken?

- Take methylphenidate hydrochloride extended-release capsules exactly as prescribed by your healthcare provider.
- Your healthcare provider may change the dose if needed.
- Take methylphenidate hydrochloride extended-release capsules by mouth 1 time each day in the morning.
- Methylphenidate hydrochloride extended-release capsules can be taken with or without food but take it the same way each time.
- Swallow methylphenidate hydrochloride extended-release capsules whole, or if methylphenidate hydrochloride extended-release capsules cannot be swallowed whole, the capsules may be opened and sprinkled onto a tablespoonful of applesauce. Make sure to sprinkle all the medicine onto the applesauce. The methylphenidate hydrochloride extended-release capsules dose should not be divided.
  - swallow all the applesauce and medicine mixture without chewing right away or within 10 minutes
  - **do not** chew the applesauce and medicine mixture
  - **do not** store applesauce and medicine mixture
- Your healthcare provider may sometimes stop methylphenidate hydrochloride extended-release capsules treatment for a while to check ADHD symptoms.
- If a dose of methylphenidate hydrochloride extended-release capsules is missed, do not take the dose later in the day or take an extra dose to make up for the missed dose, wait until the next morning to take the next scheduled dose.
- **In case of poisoning call your poison control center at 1-800-222-1222 or go to the nearest hospital emergency room right away.**

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

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

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

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

See "What is the most important information I should know about methylphenidate hydrochloride extended-release capsules?"

- **Painful and prolonged erections (priapism).** Priapism has happened in males who take products that contain methylphenidate. **If you or your child develop 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 you have 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 have any signs of unexplained wounds appearing on fingers or toes during treatment with methylphenidate hydrochloride extended-release capsules.
- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with methylphenidate hydrochloride extended-release capsules. Methylphenidate hydrochloride extended-release capsules treatment may be stopped if your child is not growing or gaining weight.

The most common side effects of methylphenidate hydrochloride extended-release capsules in children 6 to 17 years of age include stomach pain, decreased appetite, headache, trouble sleeping.

These are not all the possible side effects of methylphenidate hydrochloride extended-release capsules.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Teva Pharmaceuticals at 1-888-838-2872.

How should I store methylphenidate hydrochloride extended-release capsules?

- Store methylphenidate hydrochloride extended-release capsules at room temperature between 68°F to 77°F (20°C to 25°C).
- Store methylphenidate hydrochloride extended-release capsules in a safe place, like a locked cabinet. Protect from moisture.
- Dispose of remaining, unused, or expired methylphenidate hydrochloride 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 hydrochloride 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 hydrochloride extended-release capsules in the household trash.
- **Keep methylphenidate hydrochloride extended-release capsules and all medicines out of the reach of children.**

General information about the safe and effective use of methylphenidate hydrochloride extended-release capsules.

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

What are the ingredients in methylphenidate hydrochloride extended-release capsules?

Active Ingredient: methylphenidate hydrochloride

Inactive Ingredients: ammonio methacrylate copolymer type B, fumaric acid, gelatin, hypromellose 2910, methacrylic acid copolymer type A, polyethylene glycol 400, polyethylene glycol 8000, sugar spheres (which contains sucrose and corn starch), talc, titanium dioxide and triethyl citrate. The 10 mg capsules also contain FD&C Blue #1. The 15 mg capsules also contain FD&C Yellow #6. The 20 mg capsules also contain black iron oxide. The 30 mg capsules also contain FD&C Blue#1 and FD&C Red #3. The 40 mg capsules also contain yellow iron oxide. The 50 mg capsules also contain FD&C Blue #1 and yellow iron oxide. The 60 mg capsules also contain FD&C Blue #1 and FD&C Red #40. Black printing ink SW-9008/SW-9009 contains black iron oxide, potassium hydroxide, propylene glycol, shellac, and strong ammonia solution.

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- Take methylphenidate hydrochloride extended-release capsules by mouth 1 time each day in the morning.
- Methylphenidate hydrochloride extended-release capsules can be taken with or without food but take it the same way each time.
- Swallow methylphenidate hydrochloride extended-release capsules whole, or if methylphenidate hydrochloride extended-release capsules cannot be swallowed whole, the capsules may be opened and sprinkled onto a tablespoonful of applesauce. Make sure to sprinkle all the medicine onto the applesauce. The methylphenidate hydrochloride extended-release capsules dose should not be divided.
  - swallow all the applesauce and medicine mixture without chewing right away or within 10 minutes
  - **do not** chew the applesauce and medicine mixture
  - **do not** store applesauce and medicine mixture
- Your healthcare provider may sometimes stop methylphenidate hydrochloride extended-release capsules treatment for a while to check ADHD symptoms.
- If a dose of methylphenidate hydrochloride extended-release capsules is missed, do not take the dose later in the day or take an extra dose to make up for the missed dose, wait until the next morning to take the next scheduled dose.
- **In case of poisoning call your poison control center at 1-800-222-1222 or go to the nearest hospital emergency room right away.**

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

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

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

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

See "What is the most important information I should know about methylphenidate hydrochloride extended-release capsules?"

- **Painful and prolonged erections (priapism).** Priapism has happened in males who take products that contain methylphenidate. **If you or your child develop priapism, get medical help right away.**
- **Circulation problems in fingers and toes (peripheral vasculopathy, including Raynaud's Phenomenon).** Signs and symptoms may include:
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  Tell your healthcare provider if you have or your child have numbness, pain, skin color change, or sensitivity to temperature in the fingers or toes.

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

The most common side effects of methylphenidate hydrochloride extended-release capsules in children 6 to 17 years of age include stomach pain, decreased appetite, headache, trouble sleeping.

These are not all the possible side effects of methylphenidate hydrochloride extended-release capsules.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Teva Pharmaceuticals at 1-888-838-2872.

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- Store methylphenidate hydrochloride extended-release capsules at room temperature between 68°F to 77°F (20°C to 25°C).
- Store methylphenidate hydrochloride extended-release capsules in a safe place, like a locked cabinet. Protect from moisture.
- Dispose of remaining, unused, or expired methylphenidate hydrochloride 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 hydrochloride 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 hydrochloride extended-release capsules in the household trash.
- **Keep methylphenidate hydrochloride extended-release capsules and all medicines out of the reach of children.**

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8.5 Geriatric Use

Clinical trials of methylphenidate hydrochloride extended-release did not include any patients aged 65 years and over. In general, dose selection for an elderly patient start at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

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

9.2 Abuse

CNS stimulants including methylphenidate hydrochloride extended-release capsules, other methylphenidate-containing products, and amphetamines have a high potential for abuse. Abuse is characterized by impaired control over drug use despite harm, and craving.

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, suicidal or homicidal ideation have also been observed. Abusers of 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 CNS stimulants including methylphenidate hydrochloride 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, monitor for signs of abuse while on therapy, and re-evaluate the need for methylphenidate hydrochloride extended-release capsule use.

9.3 Dependence

Tolerance

Tolerance (a state of adaptation in which exposure to a drug results in a reduction of the drug's desired and/or undesired effects over time) can occur during chronic therapy with CNS stimulants including methylphenidate hydrochloride extended-release capsules.

Dependence

Physical dependence (a state of adaptation manifested by a withdrawal syndrome produced by abrupt cessation, rapid dose reduction, or administration of an antagonist) can occur in patients treated with CNS stimulants including methylphenidate hydrochloride extended-release capsules. Withdrawal symptoms after abrupt cessation following prolonged high-dosage administration of CNS stimulants include extreme fatigue and depression.

10 OVERDOSAGE

10.1 Signs and Symptoms

Signs and symptoms of acute methylphenidate overdose, 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.

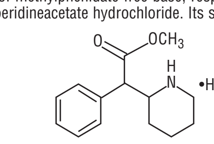
10.2 Management of Overdose

Consult with a Certified Poison Control Center (1-800-222-1222) for up-to-date guidance and advice on the management of overdosage with methylphenidate. Provide supportive care, including close medical 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 overdosages. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. Use supportive and symptomatic measures.

Gastric contents may be evacuated by gastric lavage as indicated. Before performing gastric lavage, control agitation and seizures if present and protect the airway. Other measures to detoxify the gut include administration of activated charcoal and a cathartic. Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for pyrexia.

11 DESCRIPTION

Methylphenidate Hydrochloride Extended-Release Capsules contain methylphenidate hydrochloride, USP a central nervous system (CNS) stimulant. Methylphenidate Hydrochloride Extended-Release Capsules contain multi layered beads, which are composed of an immediate-release layer which contains approximately 40% of the methylphenidate dose, and a controlled release layer which contains approximately 60% of the methylphenidate dose. Methylphenidate Hydrochloride Extended-Release Capsules are available in seven capsule strengths. Each extended-release capsule for once-a-day oral administration contains 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, or 60 mg of methylphenidate hydrochloride USP, which is equivalent to 8.6 mg, 13.0 mg, 17.3 mg, 25.9 mg, 34.6 mg, 43.2 mg, or 51.9 mg of methylphenidate free base, respectively. Chemically, methylphenidate hydrochloride, USP is *d,l* (racemic) methyl α-phenyl-2piperidineacetate hydrochloride. Its structural formula is:



$C_{14}H_{19}NO_2$•HCl M.W. 269.77

Methylphenidate hydrochloride, USP is a white to off-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.

Inactive Ingredients: ammonio methacrylate copolymer type B, fumaric acid, gelatin, hypromellose 2910, methacrylic acid copolymer type A, polyethylene glycol 400, polyethylene glycol 8000, sugar spheres (which contains sucrose and corn starch), talc, titanium dioxide and triethyl citrate. The 10 mg capsules also contain FD&C Blue #1. The 15 mg capsules also contain FD&C Yellow #6. The 20 mg capsules also contain black iron oxide. The 30 mg capsules also contain FD&C Blue#1 and FD&C Red #3. The 40 mg capsules also contain yellow iron oxide. The 50 mg capsules also contain FD&C Blue #1 and yellow iron oxide. The 60 mg capsules also contain FD&C Blue #1 and FD&C Red #40. Black printing ink SW-9008/SW-9009 contains black iron oxide, potassium hydroxide, propylene glycol, shellac, and strong ammonia solution.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Methylphenidate HCl 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*-isomers. The *d*-isomer is more pharmacologically active than the *l*-isomer. Methylphenidate blocks the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

12.3 Pharmacokinetics

Absorption

Following oral administration of methylphenidate hydrochloride extended-release in adults, plasma methylphenidate concentrations increase rapidly, reaching an initial maximum at about 2 hours, followed by gradual descending concentrations over the next 4 to 6 hours, after which a gradual increase begins, reaching a second peak at approximately 8 hours (Figure 1). The relative bioavailability of methylphenidate hydrochloride extended-release given once daily as compared to a methylphenidate immediate-release oral product given three times daily in adults is comparable. The relative bioavailability is 102%.

The pharmacokinetic profiles and parameters of methylphenidate are similar when methylphenidate hydrochloride extended-release is administered either as a whole capsule or sprinkled onto applesauce in subjects under fasting conditions (see Table 2 and Figure 1).

Table 2: The Single Dose Pharmacokinetics of *d,l*-Methylphenidate[1] ER Capsule and Sprinkle following an Oral Dose of 80 mg Methylphenidate Hydrochloride Extended-Release Capsules under Fast Conditions in Healthy Adults

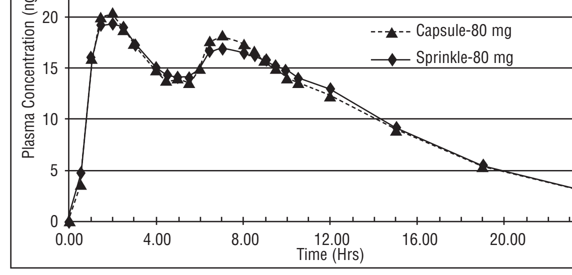
Pharmacokinetic Parameters	Capsule	Sprinkle
C_{max}[2] (ng/mL)	23.47 ± 11.4	21.78 ± 9.5
$AUC_{(0-t)}$[2] (ng.hr/mL)	262.7 ± 135	262.9 ± 128
$AUC_{(0-inf)}$[2] (ng.hr/mL)	258.1 ± 94.2	258.0 ± 84.4
T_{max} (hr) ‡	2.0	2.0
Half-life (hr)	5.09	5.43
Relative bioavailability	102%	101%

[1] *d,l* (racemic) methylphenidate HCl

[2] C_{max}, $AUC_{(0-t)}$ $AUC_{(0-inf)}$ presented as mean ± SD

‡ data presented as median (range)

Figure 1: Mean *d,l*-Methylphenidate Plasma Concentration-Time Profiles following 80 mg Administered as Capsule and Sprinkle Dose in Healthy Adults



Metabolism and Excretion

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

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

Food Effects

Administration of methylphenidate hydrochloride extended-release with high fat meal showed a decreased or diminished second peak. A high-fat meal also increased the average C_{max} of methylphenidate by about 28% and the AUC by about 19%. In the clinical trials of methylphenidate hydrochloride extended-release, it was administered without regard to meals.

Alcohol Effect

At an alcohol concentration up to 40%, there was 96% release of methylphenidate from methylphenidate hydrochloride extended-release 80 mg capsule within two hours. The results with the 80 mg capsule are considered to be representative of the other available capsules strengths.

Studies in Specific Populations

Gender

There is insufficient experience with the use of methylphenidate hydrochloride extended-release to detect gender variations in pharmacokinetics.

Race

There is insufficient experience with the use of methylphenidate hydrochloride extended-release to detect ethnic variations in pharmacokinetics.

Age

The pharmacokinetics of methylphenidate after methylphenidate hydrochloride extended-release administration was studied in pediatric patients with ADHD between 6 and 12 years of age. Following administration of methylphenidate hydrochloride extended-release, the bi-phasic plasma methylphenidate concentration profile was qualitatively similar in healthy adult volunteers and pediatric patients with ADHD. The bi-phasic profile in both groups is characterized by an early peak due to rapid absorption of the immediate-release component followed by a delayed, secondary peak due to the controlled-release component of methylphenidate hydrochloride extended-release.

Renal Insufficiency

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

Hepatic Insufficiency

There is no experience with the use of methylphenidate hydrochloride extended-release in patients with hepatic insufficiency.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

In a lifetime carcinogenicity study carried out in B6C3F1 mice, methylphenidate caused an increase in hepatocellular adenomas and, in males only, an increase in hepatoblastomas, at a daily dose of approximately 60 mg/kg/day. This dose is approximately 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 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.

Mutagenesis

Methylphenidate was not mutagenic in the *in vitro* Ames reverse mutation assay or in the *in vitro* mouse lymphoma cell forward mutation assay. Sister chromatid exchanges and chromosome aberrations were increased, indicative of a weak clastogenic response, in an *in vitro* assay in cultured Chinese Hamster Ovary (CHO) cells. Methylphenidate was negative *in 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 of up to 160 mg/kg/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

The efficacy of methylphenidate hydrochloride extended-release for the treatment of ADHD was established in a randomized, double-blind, single center, placebo-controlled, flexible-dose, cross-over trial in pediatric patients aged 6 to 12 years and a second randomized, double-blind, multicenter, placebo-controlled, fixed-dose trial in pediatric patients 6 to 17 years.

Pediatric Patients

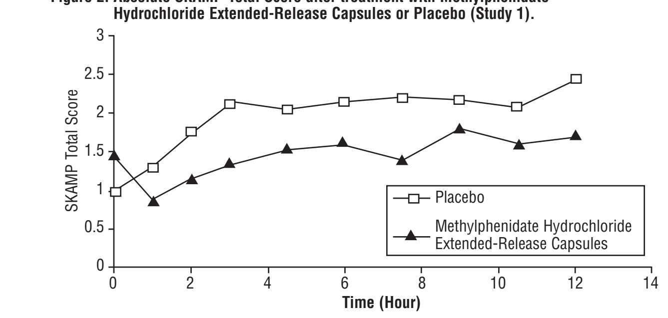
A randomized, double-blind, placebo-controlled, flexible-dose, cross-over, analog classroom study (Study 1) was conducted in pediatric patients ages 6 to 12 years (N=26) who met DSM-IV-TR criteria for ADHD inattentive, hyperactive-impulsive or combined inattentive/hyperactive-impulsive subtypes.

Following a 2 to 4 week open-label dose optimization phase in which patients received flexible-dose methylphenidate hydrochloride extended-release capsules 15 mg, 20 mg, 30 mg, or 40 mg administered once daily in the morning, patients were randomly assigned to methylphenidate hydrochloride extended-release capsules (dose from open-label phase) or placebo. After 1-week of treatment, patients were evaluated over a period of 12 hours. Subsequently, patients were given the opposite treatment for 1-week and returned for the second evaluation. Patients could then enter an open-label extension phase for up to 21 months.

Efficacy assessments were conducted at 1, 2, 3, 4.5, 6, 7.5, 9, 10.5 and 12 hours post-dose using the Swanson, Kotkin, Agler, M. Flynn, and Pelham Total score (SKAMP). The primary efficacy endpoint was the average SKAMP Total Score, comparing methylphenidate hydrochloride extended-release capsules to placebo. SKAMP is a validated 13-item teacher-rated scale that assesses manifestations of ADHD in a classroom setting.

The SKAMP Total Scores were statistically significantly better (lower) for methylphenidate hydrochloride extended-release capsules than for placebo at the test day average and at all time points (1, 2, 3, 4.5, 6, 7.5, 9, 10.5 and 12 hours) post-dosing (see Figure 2).

Figure 2: Absolute SKAMP-Total Score after treatment with Methylphenidate Hydrochloride Extended-Release Capsules or Placebo (Study 1).



A randomized, double-blind, multicenter, placebo-controlled, parallel-group, fixed-dose study (Study 2) was conducted in pediatric patients age 6 to 17 years (N=230) who met DSM-IV-TR criteria for ADHD inattentive, hyperactive-impulsive or combined inattentive/hyperactive-impulsive subtypes.

The ADHD-RS-IV is an 18-item questionnaire with a score range of 0 to 54 points that measures the core symptoms of ADHD and includes both hyperactive/impulsive and inattentive subscales.

Patients were randomized to a daily morning dose of methylphenidate hydrochloride extended-release capsules 10 mg, 15 mg, 20 mg, or 40 mg, or placebo for 1 week. An 11-week open label phase followed the double-blind phase. Patients could then enter another open-label phase for up to 21 months.

The primary efficacy endpoint was the mean decrease from baseline to the end of Week 1 in the ADHD-RS-IV Total Score. Each of the four methylphenidate hydrochloride extended-release capsule doses (10 mg, 15 mg, 20 mg, and 40 mg/day) was compared to placebo at the end of week 1. For both the 20 mg/day and the 40 mg/day doses, methylphenidate hydrochloride extended-release was superior to placebo in reduction of the ADHD-RS-IV Total Score, but not for the 10 mg/day or the 15 mg/day doses.

A total of 221 patients completed the 1-week double-blind phase. Among those, 200 (90.5%) completed the 11-week open label phase and 173 (86.5%) patients continued into the 21-month open-label extension phase.

Table 3: Summary of Parallel-Group Study

Study Number	Treatment Group	Primary Efficacy Measure: ADHD-RS-IV Total Score		
		Mean Baseline Score (SD)	LS Mean Reduction from Baseline (SE)	Placebo-subtracted Difference[a] (95% CI)
Study 2 (Pediatric)	Methylphenidate Hydrochloride Extended-Release Capsules 10 mg/day	37.6 (8.32)	9.1 (1.40)	3.7 (-0.31, 7.66)
	Methylphenidate Hydrochloride Extended-Release Capsules15 mg/day	38.0 (8.64)	10.3 (1.59)	4.9 (0.63, 9.07)
	Methylphenidate Hydrochloride Extended-Release Capsules 20 mg/day*	36.2 (8.46)	11.4 (1.49)	6.0 (1.92, 10.02)
	Methylphenidate Hydrochloride Extended-Release Capsules 40 mg/day*	35.6 (9.16)	12.8 (1.49)	7.4 (3.38, 11.45)
	Placebo	33.4 (11.01)	5.4 (1.48)	--

Note: SD: standard deviation; SE: standard error; LS Mean: least-squares mean;

CI: confidence interval, not adjusted for multiple comparisons.

[a]Difference (placebo minus drug) in least-squares mean change from baseline. Positive numbers indicate reduction (improvement).

*Doses that are demonstrated to be effective.

16 HOW SUPPLIED/STORAGE AND HANDLING

Methylphenidate Hydrochloride Extended-Release Capsules are available as follows:

10 mg - Capsule with turquoise blue opaque cap and white opaque body printed with A854 on the cap and 10 mg on the body in black ink. Capsules are supplied in bottles of 90, NDC 0591-3854-19.

15 mg - Capsule with cream opaque cap and white opaque body printed with A862 on the cap and 15 mg on the body in black ink. Capsules are supplied in bottles of 90, NDC 0591-3862-19.

20 mg - Capsule with grey opaque cap and white opaque body printed with A869 on the cap and 20 mg on the body in black ink. Capsules are supplied in bottles of 90, NDC 0591-3869-19.

30 mg - Capsule with blue opaque cap and white opaque body printed with A873 on the cap and 30 mg on the body in black ink. Capsules are supplied in bottles of 90, NDC 0591-3873-19.

40 mg - Capsule with yellow opaque cap and white opaque body printed with A891 on the cap and 40 mg on the body in black ink. Capsules are supplied in bottles of 90, NDC 0591-3891-19.

50 mg - Capsule with green opaque cap and white opaque body printed with A895 on the cap and 50 mg on the body in black ink. Capsules are supplied in bottles of 90, NDC 0591-3895-19.

60 mg - Capsule with pink opaque cap and white opaque body printed with A902 on the cap and 60 mg on the body in black ink. Capsules are supplied in bottles of 90, NDC 0591-3902-19.

Storage and Handling

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Protect from moisture.

Dispense in a tight, light-resistant container with a child-resistant closure.

Keep this and all drugs out of the reach of children.

Disposal

Comply with local laws and regulations on drug disposal of CNS stimulants. Dispose of remaining, unused, or expired Methylphenidate Hydrochloride Extended-Release Capsules by a medicine takeback program or by an authorized collector registered with the Drug Enforcement Administration. If no take-back program or authorized collector is available, mix Methylphenidate Hydrochloride 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 Hydrochloride Extended-Release Capsules in the household trash.

17 PATIENT COUNSELING INFORMATION

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

Controlled Substance Status/High Potential for Abuse and Dependence

Advise patients that methylphenidate hydrochloride extended-release capsules are a controlled substance, and it can be abused and lead to dependence. Instruct patients that they should not give methylphenidate hydrochloride extended-release capsules to anyone else. Advise patients to store methylphenidate hydrochloride 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 hydrochloride extended-release capsules by a medicine take-back program if available *[see Boxed Warning, Warnings and Precautions (5.1), Drug Abuse and Dependence (9.1, 9.2, and 9.3)]*.

Dosage and Administration Instructions

Advise patients that methylphenidate hydrochloride extended-release capsules can be taken with or without food and that they should establish a routine pattern of taking methylphenidate hydrochloride extended-release capsules with regard to meals. For patients who take methylphenidate hydrochloride extended-release capsules sprinkled over applesauce, the contents of the entire capsule should be consumed immediately; it should not be stored. Patients should take the applesauce with sprinkled beads in its entirety without chewing. When initiating treatment with methylphenidate hydrochloride extended-release capsules, provide dosage escalation and administration instructions *[see Dosage and Administration (2.2)]*.

Serious Cardiovascular Risks

Advise patients that there is a potential serious cardiovascular risk including sudden death, myocardial infarction, stroke, and hypertension with methylphenidate hydrochloride extended-release capsule 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 that methylphenidate hydrochloride extended-release capsules can cause elevations of their blood pressure and pulse rate *[see Warnings and Precautions (5.3)]*.

Psychiatric Risks

Advise patients that methylphenidate hydrochloride extended-release capsules, 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 methylphenidate hydrochloride extended-release capsules 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 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 methylphenidate hydrochloride extended-release capsules. Further clinical evaluation (e.g. rheumatology referral) may be appropriate for certain patients *[see Warnings and Precautions (5.6)]*.

Suppression of Growth

Advise patients that methylphenidate hydrochloride extended-release capsules may cause slowing of growth and weight loss *[see Warnings and Precautions (5.7)]*.

Alcohol

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

Teva Pharmaceuticals USA, Inc.
North Wales, PA 19454

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