

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

METHYLPHENIDATE HYDROCHLORIDE extended-release tablets, for oral use, **CI** Initial U.S. Approval: 2000

WARNING: DRUG DEPENDENCE
See full prescribing information for complete boxed warning.
Methylphenidate hydrochloride extended-release tablets should be given cautiously to patients with a history of drug dependence or alcoholism. Chronic abusive use can lead to marked tolerance and psychological dependence, with varying degrees of abnormal behavior.

INDICATIONS AND USAGE
Methylphenidate hydrochloride extended-release tablets, USP are a CNS stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children 6 years of age and older, adolescents, and adults up to the age of 65. (1)

- DOSSAGE AND ADMINISTRATION**
Methylphenidate hydrochloride extended-release tablets should be taken once daily in the morning and swallowed whole with the aid of liquids. Methylphenidate hydrochloride extended-release tablets should not be chewed or crushed. Methylphenidate hydrochloride extended-release tablets may be taken with or without food. (2.1)
- For children and adolescents new to methylphenidate, the recommended starting dosage is 18 mg once daily. Dosage may be increased by 18 mg/day at weekly intervals and should not exceed 54 mg/day in children and 72 mg/day in adolescents. (2.2)
 - For adult patients new to methylphenidate, the recommended starting dose is 18 or 36 mg/day. Dosage may be increased by 18 mg/day at weekly intervals and should not exceed 72 mg/day for adults. (2.2)
 - For patients currently using methylphenidate, dosing is based on current dose regimen and clinical judgment. (2.3)

DOSSAGE FORMS AND STRENGTHS
Tablets: 18 mg, 27 mg, 36 mg, and 54 mg (3)

- CONTRAINDICATIONS**
- Known hypersensitivity to the product (4.1)
 - Marked anxiety, tension, or agitation (4.2)
 - Glaucoma (4.3)
 - Tics or a family history or diagnosis of Tourette's syndrome (4.4)
 - Do not use methylphenidate hydrochloride extended-release tablets in patients currently using or within 2 weeks of using an MAO inhibitor (4.5)

- WARNINGS AND PRECAUTIONS**
- Serious Cardiovascular Events:** Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Sudden death, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Stimulant products generally should not be used in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm

- abnormalities, coronary artery disease, or other serious heart problems. (5.1)
- Increase in Blood Pressure:** Monitor patients for changes in heart rate and blood pressure and use with caution in patients for whom an increase in blood pressure or heart rate may be problematic. (5.1)
- Psychiatric Adverse Events:** Use of stimulants may cause treatment-emergent psychotic or manic symptoms in patients with no prior history, or exacerbation of preexisting psychotic or manic symptoms, psychiatric illness. Clinical evaluation for Bipolar Disorder is recommended prior to stimulant use. Monitor for aggressive behavior. (5.2)
- Seizures:** Stimulants may lower the convulsive threshold. Discontinue in the presence of seizures. (5.3)
- 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. (5.4)
- 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. (5.5)
- Visual Disturbance:** difficulties with accommodation and blurring of vision have been reported with stimulant treatment. (5.7)
- Long-Term Suppression of Growth:** monitor height and weight at appropriate intervals in pediatric patients. (5.6)
- Gastrointestinal obstruction** with preexisting GI narrowing. (5.8)
- Hematologic monitoring:** Periodic CBC, differential, and platelet counts are advised during prolonged therapy. (5.9)

ADVERSE REACTIONS
The most common adverse reaction in double-blind clinical trials (>5%) in children and adolescents was abdominal pain upper. The most common adverse reactions in double-blind clinical trials (>5%) in adult patients were decreased appetite, headache, dry mouth, nausea, insomnia, anxiety, dizziness, weight decreased, irritability, and hyperhidrosis. (6.1 and 6.2)
The most common adverse reactions associated with discontinuation ($\geq 1\%$) from either pediatric or adult clinical trials were anxiety, irritability, insomnia, and blood pressure increased. (6.3)

To report SUSPECTED ADVERSE REACTIONS, contact Impax Laboratories, Inc. at 1-800-594-6729 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

- DRUG INTERACTIONS**
- Do not use methylphenidate hydrochloride extended-release tablets in patients currently using or within 2 weeks of using an MAO inhibitor (7.1)
 - MAO Inhibitors: Concurrent use of MAO inhibitors and methylphenidate may increase blood pressure; use cautiously with vasopressors (7.2)
 - Inhibition of metabolism of coumarin anticoagulants, anticonvulsants, and some antidepressants (7.3)

- USE IN SPECIFIC POPULATIONS**
- Caution should be exercised if administered to nursing mothers (8.3)
 - Safety and efficacy has not been established in children less than six years old or elderly patients greater than 65 years of age (8.4 and 8.5)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide. Revised: 5/2017

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FULL PRESCRIBING INFORMATION
WARNING: DRUG DEPENDENCE
Methylphenidate hydrochloride extended-release tablets should be given cautiously to patients with a history of drug dependence or alcoholism. Chronic abusive use can lead to marked tolerance and psychological dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parental abuse. Careful supervision is required during withdrawal from abusive use since severe depression may occur. Withdrawal following chronic therapeutic use may unmask symptoms of the underlying disorder that may require follow-up.

INDICATIONS AND USAGE
Methylphenidate hydrochloride extended-release tablets, USP are indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children 6 years of age and older, adolescents, and adults up to the age of 65 [see *Clinical Studies* (14)]. A diagnosis of Attention Deficit Hyperactivity Disorder (ADHD, DSM-IV) implies the presence of hyperactive-impulsive or inattentive symptoms that caused impairment and were present before age 7 years. The symptoms must cause clinically significant impairment, e.g., in social, academic, or occupational functioning, and be present in two or more settings (e.g., at school or work) and at home. The symptoms must not be better accounted for by another mental disorder. For the Inattentive Type, at least six of the following symptoms must have persisted for at least 6 months: lack of attention to details/caresless mistakes; lack of sustained attention; poor listener; failure to follow through on tasks; poor organization; avoids tasks requiring sustained mental effort; loses things, easily distracted; forgetful. For the Hyperactive-Impulsive Type, at least six of the following symptoms must have persisted for at least 6 months: fidgeting/squirming; leaving seat; inappropriate running/climbing; difficulty with quiet activities; "on the go," excessive talking; blurting answers; can't wait turn; intrusive. The Combined Type requires both inattentive and hyperactive-impulsive criteria to be met.

1.1 Special Diagnostic Considerations
Specific etiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use of medical and special psychological, educational, and social resources. Learning may or may not be impaired. The diagnosis must be based upon a complete history and evaluation of the patient and not solely on the presence of the required number of DSM-IV characteristics.

1.2 Need for Comprehensive Treatment Program
Methylphenidate hydrochloride extended-release tablets, USP are indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, social). Drug treatment may not be indicated for all patients with ADHD. Stimulants are not intended for use in patients who exhibit symptoms secondary to environmental factors and/or other primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and psychosocial intervention is often helpful. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the patient's symptoms.

2 DOSSAGE AND ADMINISTRATION
2.1 General Dosing Information
Methylphenidate hydrochloride extended-release tablets should be administered orally once daily in the morning with or without food. Methylphenidate hydrochloride extended-release tablets must be swallowed whole with the aid of liquids, and must not be chewed, divided, or crushed [see *Patient Counseling Information* (7.1)].

2.2 Patients New to Methylphenidate
The recommended starting dose of methylphenidate hydrochloride extended-release tablets for patients who are not currently taking methylphenidate or stimulants other than methylphenidate is 18 mg once daily for children and adolescents and 18 or 36 mg once daily for adults [see *Table 1*].

Table 1. Methylphenidate Hydrochloride Extended-Release Tablets Recommended Starting Doses and Dose Ranges			
Patient Age	Recommended Starting Dose	Dose Range	
Children 6–12 years of age	18 mg/day	18 mg – 54 mg/day	
Adolescents 13–17 years of age	18 mg/day	18 mg – 72 mg/day not to exceed 72 mg/day	
Adults 18–65 years of age	18 or 36 mg/day	2 mg/kg/day 18 mg – 72 mg/day	

2.3 Patients Currently Using Methylphenidate
The recommended dose of methylphenidate hydrochloride extended-release tablets for patients who are currently taking methylphenidate twice daily or three times daily at doses of 10 to 60 mg/day is provided in Table 2. Dosing recommendations are based on current dose regimen and clinical judgment. Conversion dosage should not exceed 72 mg daily.

Table 2. Recommended Dose Conversion from Methylphenidate Regimens to Methylphenidate Hydrochloride Extended-Release Tablets	
Previous Methylphenidate Daily Dose	Recommended Methylphenidate Hydrochloride Extended-Release Tablets Starting Dose
5 mg Methylphenidate twice daily or three times daily	18 mg every morning
10 mg Methylphenidate twice daily or three times daily	36 mg every morning
15 mg Methylphenidate twice daily or three times daily	54 mg every morning
20 mg Methylphenidate twice daily or three times daily	72 mg every morning

Other methylphenidate regimens: Clinical judgment should be used when selecting the appropriate dose.

2.4 Dose Titration
Doses may be increased in 18 mg increments at weekly intervals for patients who have not achieved an optimal response at a lower dose. Daily dosages above 54 mg in children and 72 mg in adolescents have not been studied and are not recommended. Daily dosages above 72 mg in adults are not recommended. A 27 mg dosage strength is available for physicians who wish to prescribe between the 18 mg and 36 mg dosages.

2.5 Maintenance/Extended Treatment
There is no body of evidence available from controlled trials to indicate how long the patient with ADHD should be treated with methylphenidate hydrochloride extended-release tablets. It is generally agreed, however, that pharmacological treatment of ADHD may be needed for extended periods.

The effectiveness of methylphenidate hydrochloride extended-release tablets for long-term use, i.e., for more than 7 weeks, has not been systematically evaluated in controlled trials. The physician who elects to use methylphenidate hydrochloride extended-release tablets for extended periods in patients with ADHD should periodically re-evaluate the long-term usefulness of the drug for the individual patient with trials off medication to assess the patient's functioning without pharmacotherapy. Improvement may be sustained when the drug is either temporarily or permanently discontinued.

2.6 Dose Reduction and Discontinuation
If paradoxical aggravation of symptoms or other adverse events 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 DOSSAGE FORMS AND STRENGTHS
Methylphenidate hydrochloride extended-release tablets, USP are available in the following dosage strengths: 18 mg tablets are yellow and printed with CP 342, 27 mg tablets are gray and printed with CP 340, 36 mg tablets are white and printed with CP 339, and 54 mg tablets are brownish-red and printed with CP 341.

4 CONTRAINDICATIONS
4.1 Hypersensitivity to Methylphenidate
Hypersensitivity reactions, such as angioedema and anaphylactic reactions, have been observed in patients treated with methylphenidate hydrochloride extended-release tablets. Therefore, methylphenidate hydrochloride extended-release tablets are contraindicated in patients known to be hypersensitive to methylphenidate or other components of the product [see *Adverse Reactions* (6.6)].

4.2 Agitation
Methylphenidate hydrochloride extended-release tablets are contraindicated in patients with marked anxiety, tension, and agitation, since the drug may aggravate these symptoms.

4.3 Glaucoma
Methylphenidate hydrochloride extended-release tablets are contraindicated in patients with glaucoma.

4.4 Tics
Methylphenidate hydrochloride extended-release tablets are contraindicated in patients with motor tics or with a family history or diagnosis of Tourette's syndrome [see *Adverse Reactions* (4.4)].

4.5 Monoamine Oxidase Inhibitors
Methylphenidate hydrochloride extended-release tablets are contraindicated during treatment with monoamine oxidase (MAO) inhibitors, and also within a minimum of 14 days following discontinuation of a MAO inhibitor (hypertensive crisis may result) [see *Drug Interactions* (7.1)].

5 WARNINGS AND PRECAUTIONS
5.1 Serious Cardiovascular Events
Sudden Death and Preexisting Structural Cardiac Abnormalities or Other Serious Heart Problems

Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone carry an increased risk of sudden death, stimulant products generally should not be used in children or adolescents with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems, that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug.

Adults
Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs. In double-blind clinical trials (>5%) in adult patients, there were decreased appetite, headache, dry mouth, nausea, insomnia, anxiety, dizziness, weight decreased, irritability, and hyperhidrosis. (6.1 and 6.2)
The most common adverse reactions associated with discontinuation ($\geq 1\%$) from either pediatric or adult clinical trials were anxiety, irritability, insomnia, and blood pressure increased. (6.3)

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DRUG INTERACTIONS

- Do not use methylphenidate hydrochloride extended-release tablets in patients currently using or within 2 weeks of using an MAO inhibitor (7.1)
- MAO Inhibitors: Concurrent use of MAO inhibitors and methylphenidate may increase blood pressure; use cautiously with vasopressors (7.2)
- Inhibition of metabolism of coumarin anticoagulants, anticonvulsants, and some antidepressants (7.3)

USE IN SPECIFIC POPULATIONS

- Caution should be exercised if administered to nursing mothers (8.3)
- Safety and efficacy has not been established in children less than six years old or elderly patients greater than 65 years of age (8.4 and 8.5)

5.2 Psychiatric Adverse Events
Preexisting Psychosis
Administration of stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a preexisting psychotic disorder.
Bipolar Illness
Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression.
Emergence of New Psychotic or Manic Symptoms
Treatment-emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in the absence of a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant, and discontinuation of treatment may be appropriate. In a pooled analysis of multiple short-term, placebo-controlled studies, such symptoms occurred with 0.1% (4 patients with events out of 3482 exposed to methylphenidate or amphetamine for several weeks at usual doses) of stimulant-treated patients compared to 0 in placebo-treated patients.
Aggression
Aggressive behavior or hostility is often observed in patients with ADHD, and has been reported in clinical trials and the postmarketing experience of some medications indicated for the treatment of ADHD. Although there is no systematic evidence that stimulants cause aggressive behavior or hostility, patients beginning treatment for ADHD should be monitored for the appearance of or worsening of aggressive behavior or hostility.

5.3 Seizures
There is some clinical evidence that stimulants may lower the convulsive threshold in patients with epilepsy; however, the risk of seizure induction in patients with epilepsy in the absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

5.4 Priapism
Prolonged and painful erections, sometimes requiring surgical intervention, have been reported with methylphenidate products, including methylphenidate hydrochloride extended-release tablets, in both pediatric and adult patients [see *Adverse Reactions* (6.6)]. Priapism was not reported with drug initiation but may have 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 abnormal sustained or frequent and painful erections should seek immediate medical attention.

5.5 Peripheral Vasculopathy, including Raynaud's Phenomenon
Stimulants, including methylphenidate hydrochloride extended-release tablets, 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., hematology related) may be appropriate for certain patients.

5.6 Long-Term Suppression of Growth
Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or nonmedication treatment groups over 14 months, as well as in naturalistic subgroups (nearly 7 years phenidate-treated and nonmedication-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 loss of 1 cm in height and 2.7 kg less growth in weight over 5 years), without evidence of growth rebound during this period of development. Published data are inadequate to determine whether chronic use of amphetamines may cause similar suppression of growth; however, it is anticipated that they likely have a similar effect as well. The monitored during treatment with methylphenidate stimulants, and patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

5.7 Visual Disturbance
Difficulty with accommodation and blurring of vision have been reported with stimulant treatment.

5.8 Potential for Gastrointestinal Obstruction
Because the methylphenidate hydrochloride extended-release tablet is nondeformable and does not alter appreciable change in shape in the GI tract, methylphenidate hydrochloride extended-release tablets should not ordinarily be administered to patients with preexisting severe gastrointestinal narrowing (pathologic or iatrogenic, for example: esophageal motility disorders, small bowel inflammatory disease, "short gut" syndrome due to adhesions or decreased transit time, past history of peritonitis, cystic fibrosis, chronic intestinal pseudo-obstruction, or Meckel's diverticulum). There have been rare reports of obstructive symptoms in patients with known strictures in association with the ingestion of drugs in nondeformable controlled-release formulations. Due to the controlled-release design of the tablet, methylphenidate hydrochloride extended-release tablets should be used only in patients who are able to swallow the tablet whole [see *Patient Counseling Information* (7.7)].

5.9 Hematologic Monitoring
Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

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

- Drug Dependence [see *Box Warning*]
- Hypersensitivity to Methylphenidate [see *Contraindications* (4.1)]
- Agitation [see *Warnings and Precautions* (5.2)]
- Glaucoma [see *Contraindications* (4.3)]
- Tics [see *Contraindications* (4.4)]
- Monoamine Oxidase Inhibitors [see *Contraindications* (4.5) and *Drug Interactions* (7.1)]
- Serious Cardiovascular Events [see *Warnings and Precautions* (5.1)]
- Psychiatric Adverse Events [see *Warnings and Precautions* (5.2)]
- Seizures [see *Warnings and Precautions* (5.3)]
- Priapism [see *Warnings and Precautions* (5.4)]
- Long-Term Suppression of Growth [see *Warnings and Precautions* (5.6)]
- Visual Disturbance [see *Warnings and Precautions* (5.7)]
- Potential for Gastrointestinal Obstruction [see *Warnings and Precautions* (5.8)]
- Hematologic Monitoring [see *Warnings and Precautions* (5.9)]

The most common adverse reaction in double-blind clinical trials (>5%) in pediatric patients (children and adolescents) was abdominal pain upper. The most common adverse reactions in double-blind clinical trials (>5%) in adult patients were decreased appetite, headache, dry mouth, nausea, insomnia, anxiety, dizziness, weight decreased, irritability, and hyperhidrosis [see *Adverse Reactions* (6.1)]. The most common adverse reactions associated with discontinuation ($\geq 1\%$) from

either pediatric or adult clinical trials were anxiety, irritability, insomnia, and blood pressure increased [see *Adverse Reactions* (6.3)].

The development program for methylphenidate hydrochloride extended-release tablets included exposures in a total of 3906 participants in clinical trials. Children, adolescents, and adults with ADHD were evaluated in 6 controlled clinical studies and 11 open-label clinical studies [see *Table 3*]. Safety was assessed by collecting adverse events, vital signs, weights, and ECGs, and by performing physical examinations and laboratory analyses.

Table 3. Methylphenidate Hydrochloride Extended-Release Tablets Exposure in Double-Blind and Open-Label Clinical Studies

Patient Population	N	Dose Range
Children	2216	18 to 54 mg once daily
Adolescents	502	18 to 72 mg once daily
Adults	1188	18 to 108 mg once daily

Adverse events during exposure were obtained primarily by general inquiry and recorded by clinical investigators using their own terminology. Consequently, to provide a meaningful estimate of the proportion of individuals experiencing adverse events, events were grouped in standardized categories using MedDRA terminology. The stated frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation.

Throughout this section, adverse reactions are reported. Adverse reactions are adverse events that were considered to be reasonably associated with the use of methylphenidate hydrochloride extended-release tablets based on the comprehensive assessment of the available adverse event information. A causal association for methylphenidate hydrochloride extended-release tablets often cannot be reliably established in individual cases. Further, 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 clinical trials of another drug and may not reflect the rates observed in clinical practice. The majority of adverse reactions were mild to moderate in severity.

6.1 Commonly Observed Adverse Reactions in Double-Blind, Placebo-Controlled Clinical Trials
Adverse reactions in either the pediatric or adult double-blind adverse reactions may be relevant for both patient populations.

Children and Adolescents
Table 4 lists the adverse reactions reported in 1% or more of methylphenidate hydrochloride extended-release tablets-treated children and adolescent subjects in 4 placebo-controlled, double-blind clinical trials.

Table 4. Adverse Reactions Reported by $\geq 1\%$ of Methylphenidate Hydrochloride Extended-Release Tablets-Treated Children and Adolescent Subjects in 4 Placebo-Controlled, Double-Blind Clinical Trials of Methylphenidate Hydrochloride Extended-Release Tablets

System/Organ Class Adverse Reaction	Methylphenidate Hydrochloride Extended-Release Tablets (n=321)	Placebo (n=318)
Gastrointestinal Disorders		
Abdominal pain upper	6.2	3.8
Vomiting	2.8	1.6
General Disorders and Administration Site Conditions		
Pyrrexia	2.2	0.9
Infections and Infestations		
Nasopharyngitis	2.8	2.2
Nervous System Disorders		
Dizziness	1.9	0
Psychiatric Disorders		
Insomnia	2.8	0.3
Respiratory, Thoracic and Mediastinal Disorders		
Cough	1.9	0.9
Oropharyngeal pain	1.2	0.9

*Terms of Initial Insomnia (methylphenidate hydrochloride extended-release tablets-0.6%) and Insomnia (methylphenidate hydrochloride extended-release tablets-2.2%) are combined into Insomnia.

The majority of adverse reactions were mild to moderate in severity.

Adults
Table 5 lists the adverse reactions reported in 1% or more of methylphenidate hydrochloride extended-release tablets-treated adults in 2 placebo-controlled, double-blind clinical trials.

Table 5. Adverse Reactions Reported by $\geq 1\%$ of Methylphenidate Hydrochloride Extended-Release Tablets-Treated Adult Subjects in 2 Placebo-Controlled, Double-Blind Clinical Trials*

System/Organ Class Adverse Reaction	Methylphenidate Hydrochloride Extended-Release Tablets (n=415) %	Placebo (n=212) %
Cardiac Disorders		
Tachycardia	4.8	0
Palpitations	3.1	0.9
Ear and Labyrinth Disorders		
Vertigo	1.7	0
Eye Disorders		
Vision blurred	1.7	0.5
Gastrointestinal Disorders		
Dry mouth	14.0	3.8
Nausea	12.8	3.3
Dyspepsia	2.2	0.9
Vomiting	1.7	0.5
Constipation	1.4	0.9
General Disorders and Administration Site Conditions		
Irritability	5.8	1.4
Infections and Infestations		
Upper respiratory tract infection	2.2	0.9
Investigations		
Weight decreased	6.5	3.3
Metabolism and Nutrition Disorders		
Decreased appetite	25.3	6.6
Anorexia	1.7	0
Musculoskeletal and Connective Tissue Disorders		
Muscle tightness	1.9	0
Nervous System Disorders		
Headache	22.2	15.6
Dizziness	2.7	0.5
Tremor	2.7	0.5
Paresthesia	1.2	0
Sedation	1.2	0
Tension headache	1.2	0.5
Psychiatric Disorders		
Insomnia	12.3	6.1
Anxiety	8.2	2.4
Initial insomnia	4.3	1.8
Depressed mood	3.9	1.4
Nervousness	3.1	0.5
Restlessness	3.1	0.5
Agitation	2.2	0.5
Aggression	2.2	0.5
Bruxism	1.7	0.5
Depression	1.7	0.9
Libido decreased	1.7	0.5
Affect lability	1.4	0.9
Confusional state	1.2	0.5
Tension	1.2	0.5
Respiratory, Thoracic and Mediastinal Disorders		
Oropharyngeal pain	1.7	1.4
Skin and Subcutaneous Tissue Disorders		
Pruritus	1.7	0.5
Rash	1.7	0.5
Urticaria	1.7	0.5
Special Sensory Disorders		
Altered taste	1.7	0.5
Urogenital Disorders		
Urinary frequency	1.7	0.5
Urinary urgency	1.7	0.5
Urinary incontinence	1.7	0.5
Visual Disorders		
Double vision	1.7	0.5
Blurred vision	1.7	0.5
Other Disorders		
Weight increased	1.7	0.5
Weight decreased	1.7	0.5
Weight stable	1.7	0.5

