DEXMETHYLPHENIDATE HYDROCHLORIDE - dexmethylphenidate hydrochloride tablet
Ascend Laboratories, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DEXMETHYLPHENIDATE HYDROCHLORIDE TABLETS safely and effectively. See full prescribing information for DEXMETHYLPHENIDATE HYDROCHLORIDE TABLETS.
Dexmethylphenidate hydrochloride tablets, for oral use, CII
Initial U.S. Approval: 2001

See full prescribing information for complete boxed warning.

- CNS stimulants, including Dexmethylphenidate hydrochloride, 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).

RECENT MAJOR CHANGES
Boxed Warning: 1/2019
Contraindications (4): 1/2019
Warnings and Precautions (5): 1/2019

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

DOSAGE AND ADMINISTRATION
- Administer orally twice daily, 4 hours apart with or without food (2)
- For patients new to methylphenidate: Recommend starting dose of 5 mg once daily (2.5 mg twice daily) (2.1)
- For patients currently taking methylphenidate: Initiate dexmethylphenidate hydrochloride therapy with half (1/2) the current total daily dose of methylphenidate (2.3)
- Titrate weekly in increments of 2.5 to 5 mg to a maximum of 20 mg/day (10 mg twice daily) (2.1)

DOSAGE FORMS AND STRENGTHS
Tablets: 2.5, 5, and 10 mg (3)

CONTRAINDICATIONS
- Known hypersensitivity to methylphenidate or other components of dexmethylphenidate hydrochloride tablet (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 usual doses in pediatric patients with structural cardiac abnormalities or other serious heart problems. In adults, sudden death, stroke, and myocardial infarction have been reported. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, arrhythmias, or coronary artery disease (5.2).
- Blood Pressure and Heart Rate Increases: Monitor blood pressure and pulse. Consider the benefits and risk in patients for whom an increase in blood pressure or heart rate would be problematic (5.3).
- Psychotic 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 preexisting psychotic or bipolar disorder prior to dexmethylphenidate hydrochloride 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 the pediatric population (5.7).

ADVERSE REACTIONS
The most common adverse reactions (greater than or equal to 5% and twice the rate of placebo) in pediatric patients 6 to 17 years were abdominal pain, fever, nausea, and anorexia (6.1).
To report SUSPECTED ADVERSE REACTIONS, contact Ascend Laboratories, LLC at 1-877-ASCRX01 (877-
DRUG INTERACTIONS

- Antihypertensive Drugs: Monitor blood pressure. Adjust dosage of antihypertensive drug as needed (7.1)
- Halogenated Anesthetics: Avoid use of dexmethylphenidate hydrochloride tablet on the day of surgery if halogenated anesthetics will be used (7.1)

See 17 for PATIENT COUNSELING INFORMATION.
17 PATIENT COUNSELING INFORMATION
* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

<table>
<thead>
<tr>
<th>WARNING: ABUSE AND DEPENDENCE</th>
</tr>
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</table>

WARNING: ABUSE AND DEPENDENCE

CNS stimulants, including Dexmethylphenidate hydrochloride, 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 & USAGE

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

2 DOSAGE & ADMINISTRATION

2.1 Pre-treatment Screening

Prior to treating pediatric patients and adults with central nervous system (CNS) stimulants, including dexmethylphenidate hydrochloride, 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 reevaluate the need for dexmethylphenidate hydrochloride tablet use [see Boxed Warning, Warnings and Precautions (5.1), Drug Abuse and Dependence (9)].

2.2 Pediatric Patients with ADHD

Patients New to Methylphenidate

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

Patients Currently on Methylphenidate

The recommended starting dose of dexmethylphenidate hydrochloride for pediatric patients currently using methylphenidate is half the total daily dose of racemic methylphenidate.

Titration Schedule

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

Maintenance/Extended Treatment

Pharmacological treatment of ADHD may be needed for extended periods. Periodically reevaluate the long-term use of dexmethylphenidate hydrochloride tablet and adjust dosage as needed.
2.3 Administration Instructions
Dexmethylphenidate hydrochloride tablet is administered orally twice daily, at least 4 hours apart.

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

3 DOSAGE FORMS & STRENGTHS
Dexmethylphenidate hydrochloride tablets are round uncoated tablet, debossed with “DM” on one side and dosage strength on other side in the following colors:
- 2.5 mg tablets – light blue to blue
- 5 mg tablets – light yellow to yellow
- 10 mg tablets – white to off white

2.5 mg and 5 mg tablets may have mottled appearance.

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

5 WARNINGS AND PRECAUTIONS
5.1 Potential for Abuse and Dependence
CNS stimulants, including dexmethylphenidate hydrochloride, 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, 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 serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, and other serious heart problems. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during dexmethylphenidate hydrochloride 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 Preexisting Psychosis**

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

**Induction of a Manic Episode in Patients with Bipolar Disorder**

CNS stimulants may induce a manic or mixed mood episode in patients. Prior to initiating 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 dexmethylphenidate hydrochloride tablet. 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 dexmethylphenidate hydrochloride, 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 patients ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated patients over 36 months (to the ages of 10 to 13 years), suggests that 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 dexmethylphenidate hydrochloride, and 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), Drug Abuse and Dependence (9.2, 9.3)]
- Known hypersensitivity to methylphenidate or other ingredients of dexmethylphenidate hydrochloride tablet [see Contraindications (4)]
- Hypertensive crisis with Concomitant Use of Monoamine Oxidase Inhibitors [see Contraindications (4), Drug Interactions (7.1)]
- Serious Cardiovascular Events [see Warnings and Precautions (5.2)]
- Blood Pressure and Heart Rate Increases [see Warnings and Precautions (5.3)]
- Psychiatric Adverse Reactions [see Warnings and Precautions (5.4)]
- Priapism [see Warnings and Precautions (5.5)]
- Peripheral Vasculopathy, including Raynaud’s phenomenon [see Warnings and Precautions (5.6)]
- Long-term Suppression of Growth [see Warnings and Precautions (5.7)]

6.1 Clinical Trials Experience

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

Clinical Trials Experience with dexmethylphenidate hydrochloride in Pediatric Patients with ADHD

The safety data in this section is based on data related to dexmethylphenidate hydrochloride exposure during the premarketing development program in a total of 696 participants in clinical trials (684 patients, 12 healthy adult subjects). These participants received dexmethylphenidate hydrochloride tablets 5, 10, or 20 mg/day. The 684 ADHD patients (ages 6 to 17 years) were evaluated in 2 controlled clinical studies, 2 clinical pharmacology studies, and 2 open-label long-term safety studies.

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

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

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

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

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Reactions</th>
<th>Dexmethylphenidate hydrochloride (N = 79)</th>
<th>Placebo (N = 82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a Whole</td>
<td>Abdominal Pain</td>
<td>15%</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Digestive System</td>
<td>Anorexia</td>
<td>6%</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>9%</td>
<td>1%</td>
</tr>
</tbody>
</table>

6.2 Postmarketing Experience

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

**Adverse Reactions Reported with all Ritalin and dexmethylphenidate hydrochloride Formulations**

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

**Infections and Infestations:** nasopharyngitis

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

**Immune System Disorders:** hypersensitivity reactions, including angioedema and anaphylaxis

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

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

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

**Eye Disorders:** blurred vision, difficulties in visual accommodation

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

**Respiratory, Thoracic and Mediastinal Disorders:** cough

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

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

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

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

**Investigations:** weight loss (adult ADHD patients)

**Additional Adverse Reactions Reported with Other Methylphenidate-Containing Products**

The list below shows adverse reactions not listed with Ritalin and dexmethylphenidate hydrochloride formulations [see Adverse Reactions (6.2)] that have been reported with other methylphenidate products based on clinical trials data and postmarketing spontaneous reports.

**Blood and Lymphatic Disorders:** pancytopenia

**Immune System Disorders:** hypersensitivity reactions such as auricular swelling

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

**Nervous System Disorders:** migraine

**Eye Disorders:** diplopia, mydriasis

**Cardiac Disorders:** sudden cardiac death, myocardial infarction, bradycardia, extrasystole, supraventricular tachycardia, ventricular extrasystole
Vascular Disorders: peripheral coldness, Raynaud's phenomenon
Respiratory, Thoracic and Mediastinal Disorders: pharyngolaryngeal pain, dyspnea
Gastrointestinal Disorders: diarrhea, constipation
Skin and Subcutaneous Tissue Disorders: angioneurotic edema, erythema, fixed drug eruption
Musculoskeletal, Connective Tissue and Bone Disorders: myalgia, muscle twitching
Renal and Urinary Disorders: hematuria
Reproductive System and Breast Disorders: gynecomastia
General disorders: fatigue
Urogenital disorders: priapism

7 DRUG INTERACTIONS

7.1 Clinically Important Interactions with dexmethylphenidate hydrochloride
Table 2 presents clinically important drug interactions with dexmethylphenidate hydrochloride.

<table>
<thead>
<tr>
<th>Monoamine Oxidase Inhibitors (MAOI)</th>
<th>Clinical Impact</th>
<th>Intervention</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Impact</td>
<td>Concomitant use of MAOIs and CNS stimulants, including dexmethylphenidate hydrochloride, can cause hypertensive crisis. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure [see Contraindications (4)].</td>
<td>Concomitant use of dexmethylphenidate hydrochloride with monoamine oxidase inhibitors (MAOIs) or within 14 days after discontinuing MAOI treatment is contraindicated.</td>
<td>selegiline, tranylcyromine, isocarboxazid, phenelzine, linezolid, methylene blue</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antihypertensive Drugs</th>
<th>Clinical Impact</th>
<th>Intervention</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Impact</td>
<td>Dexmethylphenidate hydrochloride may decrease the effectiveness of drugs used to treat hypertension [see Warnings and Precautions (5.3)].</td>
<td>Adjust the dosage of the antihypertensive drug as needed.</td>
<td>Potassium-sparing and thiazide diuretics, calcium channel blockers, angiotensin-converting-enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), beta blockers, centrally acting alpha-2 receptor agonists</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Halogenated Anesthetics</th>
<th>Clinical Impact</th>
<th>Intervention</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Impact</td>
<td>Concomitant use of halogenated anesthetics and dexmethylphenidate hydrochloride may increase the risk of sudden blood pressure and heart rate increase during surgery.</td>
<td>Monitor blood pressure and avoid use of dexmethylphenidate hydrochloride in patients being treated with anesthetics on the day of surgery.</td>
<td>halothane, isoflurane, enflurane, desflurane, sevoflurane</td>
</tr>
</tbody>
</table>

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
In studies conducted in rats and rabbits, dexmethylphenidate was administered orally at doses of up to 20 and 100 mg/kg/day, respectively, during the period of organogenesis. No evidence of teratogenic activity was found in either the rat or rabbit study; however, delayed fetal skeletal ossification was observed at the highest dose level in rats. When dexmethylphenidate was administered to rats
throughout pregnancy and lactation at doses of up to 20 mg/kg/day, postweaning body weight gain was
decreased in male offspring at the highest dose, but no other effects on postnatal development were
observed. At the highest doses tested, plasma levels (AUCs) of dexamphetamine in pregnant rats and
rabbits were approximately 5 and 1 times, respectively, those in adults dosed with the maximum
recommended human dose (MRHD) of 20 mg/day.

Racemic methylphenidate has been shown to have teratogenic effects in rabbits when given in doses of
200 mg/kg/day throughout organogenesis.

Adequate and well-controlled studies in pregnant women have not been conducted. Dexamphetamine
hydrochloride should be used during pregnancy only if the potential benefit justifies the potential risk to
the fetus.

8.3 Nursing Mothers

It is not known whether dexamphetamine is excreted in human milk. Because many drugs are excreted
in human milk, caution should be exercised if dexamphetamine hydrochloride is administered to a
nursing woman.

8.4 Pediatric Use

The safety and effectiveness of dexamphetamine hydrochloride tablet have been established in
pediatric patients ages 6 to 17 years in two adequate and well-controlled clinical trials [see Clinical
Studies (14)].

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

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

Long Term Suppression of Growth

Growth should be monitored during treatment with stimulants, including dexamphetamine
hydrochloride. 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

In a study conducted in young rats, racemic methylphenidate was administered orally at doses of up to
100 mg/kg/day for 9 weeks, starting early in the postnatal period (postnatal Day 7) and continuing
through sexual maturity (postnatal week 10). When these animals were tested as adults (postnatal Weeks
13 to 14), decreased spontaneous locomotor activity was observed in males and females previously
treated with 50 mg/kg/day (approximately 6 times the MRHD of 60 mg of racemic methylphenidate on a
mg/m² basis) or greater, and a deficit in the acquisition of a specific learning task was seen in females
exposed to the highest dose (12 times the MRHD of 60 mg of racemic methylphenidate on a mg/m² basis).
The no effect level for juvenile neurobehavioral development in rats was 5 mg/kg/day (half the
MRHD of 60 mg of racemic methylphenidate on a mg/m² basis). The clinical significance of the long-
term behavioral effects observed in rats is unknown.

8.5 Geriatric Use

Dexamphetamine hydrochloride has not been studied in the geriatric population.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Dexamphetamine hydrochloride tablet contains dexamphetamine hydrochloride, a Schedule II
controlled substance.

9.2 Abuse

CNS stimulants, including dexmethylphenidate hydrochloride, 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, and suicidal or homicidal ideation have also been observed. Abusers of CNS stimulants may chew, snort, inject, or use other unapproved routes of administration which may result in overdose and death [see Overdosage (10)].

To reduce the abuse of CNS stimulants including dexmethylphenidate hydrochloride, assess the risk of abuse prior to prescribing. After prescribing, keep careful prescription records, educate patients and their families about abuse and on proper storage and disposal of CNS stimulants [see How Supplied/Storage and Handling (16)], monitor for signs of abuse while on therapy, and reevaluate the need for dexmethylphenidate hydrochloride 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 dexmethylphenidate hydrochloride.

Dependence Physical dependence (which is 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 dexmethylphenidate hydrochloride. Withdrawal symptoms after abrupt cessation following prolonged high-dosage administration of CNS stimulants include dysphoric mood; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; and psychomotor retardation or agitation.

10 OVERDOSAGE

Human Experience

Signs and symptoms of acute methylphenidate overdosage, resulting principally from overstimulation of the CNS and from excessive sympathomimetic effects, may include the following: vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, mydriasis, and dryness of mucous membranes, and rhabdomyolysis.

Overdose Management

Consult with a Certified Poison Control Center (1-800-222-1222) for latest recommendations.

11 DESCRIPTION

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

Chemically, dexmethylphenidate hydrochloride is methyl α-phenyl-2-piperidineacetate hydrochloride,
(R,R’)-(+-). Its molecular formula is C$_{14}$H$_{19}$NO$_2$·HCl. Its structural formula is:

![Structural Formula](image)

Note: * = asymmetric carbon centers

Dexmethylphenidate hydrochloride is a white to off-white powder. Its solutions are acid to litmus. It is freely soluble in water and in methanol, soluble in alcohol, and slightly soluble in chloroform and in acetone. Its molecular weight is 269.77 g/mol.

Inactive Ingredients: anhydrous lactose, citric acid anhydrous, colloidal silicon dioxide, D & C Yellow # 10 (5 mg tablets), Lake Pigment HT 5516 FD&C Blue # 1 (2.5 mg tablets), magnesium stearate, microcrystalline cellulose, pregelatinized starch and sodium starch glycolate; the 10 mg tablet contains no dye.

12 CLINICAL PHARMACOLOGY

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

12.2 Pharmacodynamics

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

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

12.3 Pharmacokinetics

Absorption
Dexmethylphenidate hydrochloride is readily absorbed following oral administration of dexmethylphenidate hydrochloride. In patients with ADHD, plasma dexmethylphenidate concentrations increase rapidly, reaching a maximum in the fasted state at about 1 to 1.5 hours postdose. No differences in the pharmacokinetics of dexmethylphenidate hydrochloride tablets were noted following single and repeated twice daily dosing, thus indicating no significant drug accumulation in children with ADHD.

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

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

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

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

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

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

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

Studies in Special Populations
Male and Female Patients
Pharmacokinetic parameters were similar for boys and girls (mean age 10 years).

In a single dose study conducted in adults, the mean dexmethylphenidate AUC\text{0-inf} values (adjusted for body weight) following single two 10 mg doses of dexmethylphenidate hydrochloride tablet were 25% to 35% higher in adult female volunteers (n = 6) compared to male volunteers (n = 9). Both t\text{max} and t\text{1/2} were comparable for males and females.

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

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

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

**Patients with Hepatic Impairment**

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

**Drug Interaction Studies**

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

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis & Mutagenesis & Impairment Of Fertility

**Carcinogenesis**

Lifetime carcinogenicity studies have not been carried out with dexmethylphenidate. In a lifetime carcinogenicity study carried out in B6C3F1 mice, racemic methylphenidate caused an increase in hepatocellular adenomas, and in males only, an increase in hepatoblastomas was seen at a daily dose of approximately 60 mg/kg/day. This dose is approximately 2 times the MRHD of 60 mg of racemic methylphenidate in pediatric patients on a mg/m² basis. Hepatoblastoma is a relatively rare rodent malignant tumor type. There was no increase in total malignant hepatic tumors. The mouse strain used is sensitive to the development of hepatic tumors and the significance of these results to humans is unknown.

Racemic methylphenidate did not cause any increase in tumors in a lifetime carcinogenicity study carried out in F344 rats; the highest dose used was approximately 45 mg/kg/day, which is approximately 4 times the MRHD of 60 mg of racemic methylphenidate in pediatric patients on a mg/m² 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.

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

**Mutagenesis**

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

**Impairment of Fertility**

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

Fertility studies have not been conducted with dexmethylphenidate. Racemic methylphenidate did not impair fertility in male or female mice that were fed diets containing the drug in an 18-week continuous breeding study. The study was conducted at doses of up to 160 mg/kg/day, approximately 10-fold the maximum recommended dose of 60 mg of racemic methylphenidate in adolescents on a mg/m² basis.
14 CLINICAL STUDIES

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

In Study 1, patients were randomized to receive either dexmethylphenidate hydrochloride tablet (5, 10, or 20 mg/day total dose), racemic methylphenidate HCl (10, 20, or 40 mg/day total dose), or placebo in a multicenter, 4-week, parallel group study in 132 pediatric patients.

Patients received study medication twice daily separated by a 3.5 to 5.5 hours interval. Treatment was initiated with the lowest dose, and doses could be doubled at weekly intervals, depending on clinical response and tolerability, up to the maximum dose. The primary outcome was change from baseline to week 4 of the average score (an average of 2 ratings during the week) of the teacher’s version of the SNAP-ADHD Rating Scale. This 18 item scale measures ADHD symptoms of inattention and hyperactivity/impulsivity, rated on a scale of 0 (Not at All) to 3 (Very Much). Patients treated with dexmethylphenidate hydrochloride tablet showed a statistically significant improvement in symptom scores from baseline over patients who received placebo (Table 3).

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

<table>
<thead>
<tr>
<th>Study Number</th>
<th>Treatment Group</th>
<th>Primary Efficacy Measure: Teacher SNAP-ADHD Total Score&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Mean Baseline Score (SD)</th>
<th>Mean Change from Baseline Week 4 Score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>Dexmethylphenidate hydrochloride 5-20 mg/day&lt;sup&gt;b&lt;/sup&gt; (n = 44)</td>
<td>1.4 (0.7) (n = 42)</td>
<td>- 0.7 (0.7) (n = 42)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 42)</td>
<td>1.6 (0.7) (n = 41)</td>
<td>- 0.2 (0.7) (n = 39)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: SD: standard deviation; n = number of patients available at the assessment time point.

<sup>a</sup>Average of two ratings.

<sup>b</sup>Statistically significantly different from placebo.

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

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

<table>
<thead>
<tr>
<th>Study Number</th>
<th>Treatment Group</th>
<th>Primary Efficacy Measure: Proportion of Treatment Failure&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Number of Treatment Failures /Number of Randomized Patients</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Study 2</td>
<td>Dexmethylphenidate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hydrochloride</td>
<td>6/35</td>
<td>17.1%</td>
<td></td>
<td></td>
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<tr>
<td>---------------</td>
<td>------</td>
<td>-------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-20 mg/day(^b)</td>
<td>25/40</td>
<td>62.5%</td>
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</table>

\(^a\)One patient did not have the value at Visit 10 and hence not included in this analysis.

\(^b\)Statistically significantly different from placebo.

16 HOW SUPPLIED/STORAGE AND HANDLING

2.5 mg Tablets: Round, light blue to blue uncoated tablet, debossed with “DM” on one side and “2.5” on other side, may have mottled appearance.

Bottle of 30………………………………………………….NDC 67877-655-30
Bottle of 100………………………………………………….NDC 67877-655-01
Bottle of 500………………………………………………….NDC 67877-655-05

5 mg Tablets: Round, light yellow to yellow uncoated tablet, debossed with “DM” on one side and “5” on other side, may have mottled appearance.

Bottle of 30………………………………………………….NDC 67877-656-30
Bottle of 100………………………………………………….NDC 67877-656-01
Bottle of 500………………………………………………….NDC 67877-656-05

10 mg Tablets: Round, white to off white uncoated tablet, debossed with “DM” on one side and “10” on other side.

Bottle of 30………………………………………………….NDC 67877-657-30
Bottle of 100………………………………………………….NDC 67877-657-01
Bottle of 500………………………………………………….NDC 67877-657-05

Store at 20°C to 25°C (68°F to 77°F), with excursions permitted between 15°C and 30°C (59°F to 86°F) [See USP Controlled Room Temperature].

Dispense in tight, light-resistant container (USP).

Disposal

Comply with local laws and regulations on drug disposal of CNS stimulants. Dispose of remaining, unused, or expired dexamphetamine hydrochloride tablet 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 dexamphetamine hydrochloride tablet 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 dexamphetamine hydrochloride tablet in the household trash.

17 PATIENT COUNSELING INFORMATION

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

Controlled Substance Status/High Potential for Abuse and Dependence

Advise patients that dexamphetamine hydrochloride is a controlled substance, and it can be abused and lead to dependence. Instruct patients that they should not give dexamphetamine hydrochloride tablet to anyone else. Advise patients to store dexamphetamine hydrochloride tablet 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 dexamphetamine hydrochloride tablet by a medicine take-back program if available [see Boxed Warning, Warnings and
Serious Cardiovascular Risks

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

Psychiatric Risks

Advise patients that dexmethylphenidate hydrochloride tablet, at recommended doses, can cause psychotic or manic symptoms, even in patients without prior history of psychotic symptoms or mania [see Warnings and Precautions (5.4)].

Priapism

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

Circulation Problems in Fingers and Toes [Peripheral vasculopathy, including Raynaud’s Phenomenon]

Instruct patients beginning treatment with dexmethylphenidate hydrochloride tablet about the risk of peripheral vasculopathy, including Raynaud’s phenomenon, and associated signs and symptoms: fingers or toes may feel numb, cool, painful, and/or may change color from pale, to blue, to red. Instruct patients to report to their physician any new numbness, pain, skin color change, or sensitivity to temperature in fingers or toes.

Instruct patients to call their physician immediately with any signs of unexplained wounds appearing on fingers or toes while taking dexmethylphenidate hydrochloride tablets. 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 dexmethylphenidate hydrochloride tablets may cause slowing of growth and weight loss [see Warnings and Precautions (5.7)].

Manufactured in India by:

Alkem Laboratories Limited
H.O.: ALKEM HOUSE,
Senapati Bapat Marg, Lower Parel,
Mumbai – 400 013, INDIA

Distributed by:
Ascend Laboratories, LLC
Parsippany, NJ 07054
Revised: February 2019

MEDICATION GUIDE

Dexmethylphenidate hydrochloride (dex” meth il fen’ i date hye” droe klor’ ide) Tablets CII
What is the most important information I should know about Dexmethylphenidate hydrochloride tablets?

Dexmethylphenidate hydrochloride tablet is a federal controlled substance (CII) because it can be abused or lead to dependence. Keep dexmethylphenidate hydrochloride tablet in a safe place to prevent misuse and abuse. Selling or giving away dexmethylphenidate hydrochloride tablet may harm others, and is against the law.

Tell your doctor if you or your child have abused or been dependent on alcohol, prescription medicines or street drugs.

The following have been reported with use of methylphenidate hydrochloride and other stimulant medicines.

1. Heart-related problems:
   • sudden death in patients who have heart problems or heart defects
   • stroke and heart attack in adults
   • increased blood pressure and heart rate

Tell your doctor 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 carefully for heart problems before starting dexmethylphenidate hydrochloride tablets.

Your doctor should check your or your child’s blood pressure and heart rate regularly during treatment with dexmethylphenidate hydrochloride tablets.

Call your doctor right away if you or your child has any signs of heart problems such as chest pain, shortness of breath, or fainting while taking dexmethylphenidate hydrochloride tablets.

2. Mental (Psychiatric) problems:
   All Patients
   • new or worse behavior and thought problems
   • new or worse bipolar illness
   • new or worse aggressive behavior or hostility
   • new psychotic symptoms (such as hearing voices, believing things that are not true, are suspicious) or new manic symptoms

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

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

What is dexmethylphenidate hydrochloride tablet?

• Dexmethylphenidate hydrochloride tablet is a central nervous system stimulant (CNS) prescription medicine. It is used for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD).

Dexmethylphenidate hydrochloride tablet may help increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.

• Dexmethylphenidate hydrochloride tablet should be used as a part of a total treatment program for ADHD that may include counseling or other therapies.

Who should not take Dexmethylphenidate hydrochloride tablet:

Dexmethylphenidate hydrochloride tablet should not be taken if you or your child:

• are allergic to methylphenidate hydrochloride, or any of the ingredients in dexmethylphenidate hydrochloride tablet. See the end of this Medication Guide for a complete list of ingredients in dexmethylphenidate hydrochloride tablet.

• are taking or have taken within the past 14 days an anti-depression medicine called a monoamine oxidase inhibitor or MAOI.

Dexmethylphenidate hydrochloride tablet may not be right for you or your child. Before starting dexmethylphenidate hydrochloride tablet tell your or your child’s doctor about all health conditions (or a family history of) including:

• heart problems, heart defects, high blood pressure
• mental problems including psychosis, mania, bipolar illness, or depression
• circulation problems in fingers or toes
• if you are pregnant or plan to become pregnant. It is not known if dexmethylphenidate hydrochloride tablet will harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant.
• if you are breastfeeding or plan to breastfeed. Dexmethylphenidate hydrochloride passes into your breast milk. You and your doctor should decide if you will take dexmethylphenidate hydrochloride tablet or breastfeed.

Tell your doctor about all of the medicines that you or your child takes including prescription and over-the-counter medicines, vitamins, and herbal supplements. Dexmethylphenidate hydrochloride tablet and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be adjusted while taking dexmethylphenidate hydrochloride tablet.
Your doctor will decide whether dexmethylphenidate hydrochloride tablet can be taken with other medicines.

Especially tell your doctor if you or your child takes:
• anti-depression medicines including MAOIs
• blood pressure medicines (anti-hypertensive)

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

Do not start any new medicine while taking dexmethylphenidate hydrochloride tablet without talking to your doctor first.

How should dexmethylphenidate hydrochloride tablet be taken?
• Take dexmethylphenidate hydrochloride tablet exactly as prescribed. Your doctor may adjust the dose until it is right for you or your child.
• Take dexmethylphenidate hydrochloride tablet twice daily, at least 4 hours apart.
• Dexmethylphenidate hydrochloride tablet may be taken with or without food.
• From time to time, your doctor may stop dexmethylphenidate hydrochloride tablet treatment for a while to check ADHD symptoms.
• Your doctor may do regular checks of the blood, heart, and blood pressure while taking dexmethylphenidate hydrochloride tablet.
• Children should have their height and weight checked often while taking dexmethylphenidate hydrochloride tablet. Dexmethylphenidate hydrochloride tablet treatment may be stopped if a problem is found during these check-ups.
• In case of poisoning call your poison control center at 1-800-222-1222 right away, or go to the nearest hospital emergency room.

What are the possible side effects of dexmethylphenidate hydrochloride tablet?
Dexmethylphenidate hydrochloride tablet may cause serious side effects, including:
What are possible side effects of dexmethylphenidate hydrochloride tablet?
• See "What is the most important information I should know about dexmethylphenidate hydrochloride tablet?" for information on reported heart and mental problems.
• painful and prolonged erections (priapism) have occurred with methylphenidate. If you or your child develops priapism, seek medical help right away. Because of the potential for lasting damage, priapism should be evaluated by a doctor immediately.
• circulation problems in fingers and toes (Peripheral vasculopathy, including Raynaud’s phenomenon):
  • fingers or toes may feel numb, cool, painful
  • fingers or toes may change color from pale, to blue, to red
Tell your doctor if you or your child have, numbness, pain, skin color change, or sensitivity to temperature in the fingers or toes.
Call your doctor right away if you have or your child has any signs of unexplained wounds appearing on fingers or toes while taking dexmethylphenidate hydrochloride tablet.

- **slowing of growth (height and weight) in children**

Common side effects include:

- abdominal pain
- fever
- anorexia
- nausea

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

**How should I store dexmethylphenidate hydrochloride tablet?**

- Store dexmethylphenidate hydrochloride tablet in a safe place and in a tightly closed container at room temperature between 68°F to 77°F (20°C to 25°C).
- Protect from light.
- Dispose of remaining, unused, or expired dexmethylphenidate hydrochloride tablet by a medicine take-back program at 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 dexmethylphenidate hydrochloride tablet with an undesirable, nontoxic substance such as dirt, cat litter, or used coffee grounds to make it less appealing to children and pets. Place the mixture in a container such as a sealed plastic bag and throw away (discard) dexmethylphenidate hydrochloride tablet in the household trash.

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

**General information about the safe and effective use of dexmethylphenidate hydrochloride tablet.**

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

**What are the ingredients in dexmethylphenidate hydrochloride tablet?**

**Active ingredient:** Dexmethylphenidate hydrochloride

**Inactive ingredients:** anhydrous lactose, citric acid anhydrous, colloidal silicon dioxide, D & C Yellow # 10 (5 mg tablets), Lake Pigment HT 5516 FD&C Blue # 1 (2.5 mg tablets), magnesium stearate, microcrystalline cellulose, pregelatinized starch and sodium starch glycolate; the 10 mg tablet contains no dye.

**Distributed by:**
Ascend Laboratories, LLC
Parsippany, NJ 07054

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

Revised: February 2019
Dispense medication Guide attached or provided separately.

Each tablet contains dexmethylphenidate hydrochloride 2.5 mg

Usual Dosage: See package insert.

Store at 25°C (77°F), excursions permitted to 15°C to 30°C (59°F to 86°F).

[see USP Controlled Room Temperature]

Protect from light and moisture.

Dispense in a tight container, USP.

STORE THIS AND ALL DRUGS OUT OF THE
REACH OF CHILDREN.

Manufactured by: Allara Laboratories Ltd.,
Mumbai - 400 013, INDIA.

Distributed by: Ascend Laboratories, LLC
Pune-30, M.L. No. 000004

Rx Only

NDC 67877-655-01
Dexmethylphenidate Hydrochloride 5 mg
100 Tablets

Dispense medication Guide attached or provided separately.
Each tablet contains dexmethylphenidate hydrochloride 5 mg.

**Usual Dosage:** See package insert.

Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F).
(see USP Controlled Room Temperature).
Protect from light and moisture.
Dispense in a tight container, USP.

STORE THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

**Manufactured by:** Alkan Laboratories Ltd.,
Mumbai- 400 013, INDIA.

**Distributed by:** Ascend Laboratories, LLC
 Parsippany, NJ 07054

Rx Only
NDC 67877-657-01
Dexmethylphenidate Hydrochloride 10 mg
100 Tablets
Dispense medication Guide attached or provided separately.
# DEXMETHYLPHENIDATE HYDROCHLORIDE

dexamethylphenidate hydrochloride tablet

## Product Information

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<th>Product Type</th>
<th>HUMAN PRESCRIPTION DRUG</th>
<th>Item Code (Source)</th>
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<td>Route of Administration</td>
<td>ORAL</td>
<td>DEA Schedule</td>
<td>CII</td>
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## Active Ingredient/Active Moiety

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<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
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<tr>
<td>DEXMETHYLPHENIDATE HYDROCHLORIDE (UNII: 16780K0E08) (DEXMETHYLPHENIDATE - UNII:M32RH9MFGP)</td>
<td>DEXMETHYLPHENIDATE HYDROCHLORIDE</td>
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## Inactive Ingredients

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<th>Strength</th>
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<td>ANHYDROUS LACTOSE (UNII: 3SY5LH0PMK)</td>
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<td>MICROCRYSTALLINE CELLULOSE (UNII: OPIR32D61U)</td>
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<td>FD&amp;C BLUE NO. 1 (UNII: HBR47K3TBD)</td>
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<td>ANHYDROUS CITRIC ACID (UNII: XFR417D3PSL)</td>
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<td>SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)</td>
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**MAGNESIUM STEARATE** (UNII: 70097M6I30)

**Product Characteristics**

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<tr>
<th>Characteristic</th>
<th>Value</th>
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<tr>
<td>Shape</td>
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<tr>
<td>Size</td>
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<td>Imprint Code</td>
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**DEXMETHYLPHENIDATE HYDROCHLORIDE**
dexmethylphenidate hydrochloride tablet

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<tr>
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<td>DEXMETHYLPHENIDATE HYDROCHLORIDE</td>
<td>5 mg</td>
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<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)</td>
<td></td>
</tr>
<tr>
<td>MICROCRYSTALLINE CELLULOSE (UNII: OPIR32D61U)</td>
<td></td>
</tr>
<tr>
<td>D&amp;C YELLOW NO. 10 (UNII: 35SW5USQ3G)</td>
<td></td>
</tr>
<tr>
<td>ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)</td>
<td></td>
</tr>
<tr>
<td>STARCH, CORN (UNII: 08232NY3S1)</td>
<td></td>
</tr>
<tr>
<td>SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)</td>
<td></td>
</tr>
<tr>
<td>SILICON DIOXIDE (UNII: ETJ7Z6XBU4)</td>
<td></td>
</tr>
<tr>
<td>MAGNESIUM STEARATE (UNII: 70097M6I30)</td>
<td></td>
</tr>
</tbody>
</table>
### Product Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>YELLOW (Light yellow to yellow)</td>
</tr>
<tr>
<td>Shape</td>
<td>ROUND</td>
</tr>
<tr>
<td>Flavor</td>
<td>ROUND</td>
</tr>
<tr>
<td>Size</td>
<td>7mm</td>
</tr>
<tr>
<td>Imprint Code</td>
<td>DM;5</td>
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</tbody>
</table>

### Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:67877-656-30</td>
<td>30 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>07/21/2019</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>NDC:67877-656-01</td>
<td>100 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>07/21/2019</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>NDC:67877-656-05</td>
<td>500 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>07/21/2019</td>
<td></td>
</tr>
</tbody>
</table>

### Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANDA</td>
<td>ANDA212631</td>
<td>07/21/2019</td>
<td></td>
</tr>
</tbody>
</table>

### DEXMETHYLPHENIDATE HYDROCHLORIDE
dexamethasone hydrochloride tablet

### Product Information

<table>
<thead>
<tr>
<th>Product Type</th>
<th>HUMAN PRESCRIPTION DRUG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route of Administration</td>
<td>ORAL</td>
</tr>
<tr>
<td>Item Code (Source)</td>
<td>NDC:67877-657</td>
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<tr>
<td>DEA Schedule</td>
<td>CII</td>
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### Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEXMETHYLPHENIDATE HYDROCHLORIDE (UNII: 1678OK0E08)</td>
<td>DEXMETHYLPHENIDATE HYDROCHLORIDE</td>
<td>10 mg</td>
</tr>
<tr>
<td>(DEXMETHYLPHENIDATE - UNII:M32RH9MFGP)</td>
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</table>

### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
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</thead>
<tbody>
<tr>
<td>ANHYDROUS LACTOSE (UNII: 3S5LHBPBK)</td>
<td></td>
</tr>
<tr>
<td>MICROCRYSTALLINE CELLULOSE (UNII: OPR32616U)</td>
<td></td>
</tr>
<tr>
<td>ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)</td>
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</tr>
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<td>STARCH, CORN (UNII: O8232NY3SJ)</td>
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</tr>
<tr>
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</tr>
<tr>
<td>SILICON DIOXIDE (UNII: ETJ7Z6XBU4)</td>
<td></td>
</tr>
<tr>
<td>MAGNESIUM STEARATE (UNII: 709097M6B0)</td>
<td></td>
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</table>

### Product Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>WHITE (White to off white)</td>
</tr>
<tr>
<td>Score</td>
<td>no score</td>
</tr>
<tr>
<td>Shape</td>
<td>ROUND</td>
</tr>
<tr>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>Flavor</td>
<td>Imprint Code</td>
</tr>
<tr>
<td>Contains</td>
<td></td>
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<td>07/21/2019</td>
<td></td>
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</tbody>
</table>

**Labeler** - Ascend Laboratories, LLC (141250469)

<p>| Establishment | | | |</p>
<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
<th>ID/FEI</th>
<th>Business Operations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkem Laboratories Limited</td>
<td></td>
<td>915628612</td>
<td>ANALYSIS(67877-657) , REPACK(67877-657) , MANUFACTURE(67877-655, 67877-656, 67877-657) , PACK(67877-657)</td>
</tr>
</tbody>
</table>

Revised: 7/2019

Ascend Laboratories, LLC