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

**WARNINGS AND PRECAUTIONS (5.1) 7/2019**

- **Children (ages 6-12):** Efficacy was established in one 3-week outpatient, controlled trial and one analogue classroom, controlled trial in children with ADHD. (14)
- **Adolescents (ages 13-17):** Efficacy was established in one 4-week controlled trial in adolescents with ADHD. (14)
- **Adults:** Efficacy was established in one 4-week controlled trial in adults with ADHD. (14)

**INDICATIONS AND USAGE**

ADDERALL XR, a CNS stimulant, is indicated for the treatment of attention deficit hyperactivity disorder (ADHD). (1)

**DOSAGE AND ADMINISTRATION**

- Pediatric patients (ages 6-17): 10 mg once daily in the morning. Maximum dose for children 6-12 years of age is 30 mg once daily. (2.2, 2.3, 2.4)
- Adults: 20 mg once daily in the morning. (2.5)
- Pediatric patients (ages 6-17) with severe renal impairment: 5 mg once daily in the morning. Maximum dose for children 6-12 years of age with severe renal impairment is 20 mg once daily. (2.6, 8.6)
- Adults with severe renal impairment: 15 mg once daily in the morning. (2.6, 8.6)
- Patients with ESRD: not recommended. (2.6, 8.6)

**ADVERSE REACTIONS**

- Children (ages 6 to 12): Most common adverse reactions (≥5% and with a higher incidence than on placebo) were loss of appetite, insomnia, abdominal pain, emotional lability, vomiting, nervousness, nausea, and fever. (6.1)
- Adolescents (ages 13 to 17): Most common adverse reactions (≥5% and with a higher incidence than on placebo) were loss of appetite, insomnia, abdominal pain, weight loss, and nervousness. (6.1)
- Adults: Most common adverse reactions (≥5% and with a higher incidence than on placebo) were dry mouth, loss of appetite, insomnia, headache, weight loss, and nervousness. (6.1)

**DRUG INTERACTIONS**

- MAOI antidepressants are contraindicated; MAOIs potentiate the effects of amphetamine. Do not administer ADDERALL XR during or within 14 days after use of MAOI. (4, 7.1)
- Alkalizing agents (GI antacids and urinary): These agents increase blood levels of amphetamine. (7.1)
- Acidifying agents (GI and urinary): These agents reduce blood levels of amphetamine. (7.1)
- Adrenergic blockers, antihistamines, antihypertensives, phenobarbital, phenytoin, veratrum alkaloids, and ethosuximide: Effects may be reduced by amphetamines. (7.1)
- Tricyclic antidepressants, norprenephrine, and meperidine: Effects may be potentiated by amphetamines. (7.1)

**USE IN SPECIFIC POPULATIONS**

- Pregnancy: May cause fetal harm. (8.1)
- Lactation: Breastfeeding not recommended. (8.2)

See 17 for **PATIENT COUNSELING INFORMATION** and Medication Guide.

Revised: 7/2019
WARNING: ABUSE AND DEPENDENCE

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ADDERALL, (for example, twice daily), may be switched to ADDERALL XR at the same total daily dose taken once daily. Titrate at weekly intervals to appropriate efficacy and tolerability as indicated.

Based on bioequivalence data, patients taking divided doses of immediate-release ADDERALL XR should not take anything less than one capsule per day. This is to ensure that the therapeutic effect is not compromised. The efficacy of ADDERALL XR in the treatment of ADHD was established on the basis of two controlled trials in children aged 6 to 12, one controlled trial in adolescents aged 13 to 17, and one controlled trial in adults who met DSM-IV® criteria for ADHD [see Clinical Studies (14)].

A diagnosis of 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., 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 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; blurt answers; can’t wait turn; intrusive. The Combined Type requires both inattentive and hyperactive-impulsive criteria to be met.

Special Diagnostic Considerations
Specific etiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of 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.

Need for Comprehensive Treatment Program
ADDERALL XR is indicated as an integral part of a total treatment program for ADHD with end stage renal disease (ESRD) (GFR <15 mL/min/1.73m²). In adult patients with severe renal impairment (GFR 15 to <30 mL/min/1.73m²), the recommended dose is 15 mg once daily in the morning. In pediatric patients (6 to 17 years of age) with severe renal impairment, the recommended dose is 5 mg once daily. The maximum dose for children 6 to 12 years of age with severe renal impairment is 20 mg once daily. ADDERALL XR is not recommended in patients with end stage renal disease (ESRD) (GFR <15 mL/min/1.73m²) [see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)].

ADDERALL XR may be taken with or without food. ADDERALL XR should be given upon awakening. Afternoon doses should be avoided because of the potential for insomnia. Where possible, ADDERALL XR therapy should be interrupted occasionally to determine if there is a recurrence of behavioral symptoms sufficient to require continued therapy.

Children In children with ADHD who are 6-12 years of age and are either starting treatment for the first time or switching from another medication, start with 10 mg once daily in the morning; daily dosage may be adjusted in increments of 5 mg or 10 mg at weekly intervals. When in the judgment of the clinician a lower initial dose is appropriate, patients may begin treatment with 5 mg once daily in the morning. The maximum recommended dose for children 6-12 years of age is 30 mg/day; doses greater than 30 mg/day have not been studied in children. ADDERALL XR has not been studied in children under 6 years of age.

Adolescents The recommended starting dose for adolescents with ADHD who are 13-17 years of age and are either starting treatment for the first time or switching from another medication is 10 mg/day. The dose may be increased to 20 mg/day after one week if ADHD symptoms are not adequately controlled.

Adults In adults with ADHD who are either starting treatment for the first time or switching from another medication, the recommended dose is 20 mg/day.

Dosage in Patients with Renal Impairment
In adult patients with severe renal impairment (GFR 15 to <30 mL/min/1.73m²), the recommended dose is 15 mg once daily in the morning. In pediatric patients (6 to 17 years of age) with severe renal impairment, the recommended dose is 5 mg once daily. The maximum dose for children 6 to 12 years of age with severe renal impairment is 20 mg once daily. ADDERALL XR is not recommended in patients with end stage renal disease (ESRD) (GFR <15 mL/min/1.73m²) [see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)].

DOSAGE FORMS AND STRENGTHS
ADDERALL XR 5 mg extended release capsules: Clear/blue (imprinted ADDERALL XR 5 mg)
ADDERALL XR 10 mg extended release capsules: Blue/blue (imprinted ADDERALL XR 10 mg)
ADDERALL XR 15 mg extended release capsules: Blue/white (imprinted ADDERALL XR 15 mg)
ADDERALL XR 20 mg extended release capsules: Orange/orange (imprinted ADDERALL XR 20 mg)
ADDERALL XR 25 mg extended release capsules: Orange/white (imprinted ADDERALL XR 25 mg)
ADDERALL XR 30 mg extended release capsules: Natural/orange (imprinted ADDERALL XR 30 mg)

CONTRAINDICATIONS
ADDERALL XR administration is contraindicated in patients with the following conditions:
- Advanced arteriosclerosis
- Symptomatic cardiovascular disease
- Moderate to severe hypertension
- Hyperthyroidism
- In patients known to be hypersensitive to amphetamine, or other components of ADDERALL XR. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with other amphetamine products [see Adverse Reactions (6.2)]
- Glaucome
- Gastroesophageal reflux disease
- Agitated states
- History of drug abuse
- Patients taking monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOIs (including MAOIs such as lineozil and intravenous methylene blue), because of an increased risk of hypertensive crisis [see Warnings and Precautions (5.6) and Drug Interactions (7.1)]

WARNINGS AND PRECAUTIONS

5.1 Potential for Abuse and Dependence
CNS stimulants, including ADDERALL XR, other amphetamine-containing products, and methylphenidate, 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 and Pre-existing Structural Cardiac Abnormalities or Other Serious Heart Problems
Children and Adolescents
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 [see Contraindications (4)].

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 [see Contraindications (4)].

Hypertension and Other Cardiovascular Conditions
Stimulant medications cause a modest increase in average blood pressure (about 2-4 mmHg) and average heart rate (about 3-6 bpm), and individuals may have larger increases. While the mean changes alone would not be expected to have short-term consequences, all patients should be monitored for larger changes in heart rate and blood pressure. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., those with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular arrhythmia [see Contraindications (4) and Adverse Reactions (6)].

Assessing Cardiovascular Status in Patients being Treated with Stimulant Medications
Children, adolescents, or adults who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical exam to assess for a possible underlying cardiac disease, and should receive further cardiac evaluation if findings suggest such disease (e.g., electrocardiogram and echocardiogram). Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation.

5.3 Psychiatric Adverse Events

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

5.3.2 Bipolar Illness
Particular care should be taken in using stimulants to treat ADHD patients with comorbid bipolar disorder because of concern for possible induction of 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.

5.3.3 Emergence of New Psychotic or Manic Symptoms
Treatment-emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents without 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 in about 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.

5.3.4 Aggression
Aggressive behavior or hostility is often observed in children and adolescents 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.

5.4 Long-Term Suppression of Growth
Monitor growth in children during treatment with stimulants. Patients who are not growing or gaining weight as expected may need to have their treatment interrupted. Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this period of development. In a 22 month study of a single dose of methylphenidate, mean weight change from baseline within the initial 4 weeks of therapy was −1.1 lbs. and −2.8 lbs., respectively, for patients receiving 10 mg and 20 mg ADDERALL XR. Higher doses were associated with greater weight loss within the initial 4 weeks of treatment. Chronic use of amphetamines can be expected to cause a similar suppression of growth.

5.5 Seizures
There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities 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, ADDERALL XR should be discontinued.

5.6 Peripheral Vasculopathy, including Raynaud’s Phenomenon
Stimulants, including ADDERALL XR, 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 bruit in possible. 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 Serotonin Syndrome
Serotonin syndrome, a potentially life-threatening reaction, may occur when amphetamines are used in combination with other drugs that affect the serotonergic neurotransmitter systems such as MAOIs, selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John’s Wort [see Drug Interactions (7.1)]. Amphetamines and amphetamine derivatives are known to be metabolized, to some degree, by cytochrome P450 2D6 (CYP2D6) and display minor inhibition of CYP2D6 metabolism [see Clinical Pharmacology (12.3)]. The use of a pharmacologically active stimulation for a serotonin agonist can lead to stimulation of CYP2D6 inhibitors which may increase the risk with increased exposure to ADDERALL XR. In these situations, consider an alternative non-serotoninergic drug or an alternative drug that does not inhibit CYP2D6 [see Drug Interactions (7.1)]. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

Concomitant use of ADDERALL XR with MAOI drugs is contraindicated [see Contraindications (4)].

Discontinue treatment with ADDERALL XR and any concomitant serotonin agents immediately if symptoms of serotonin syndrome occur, and initiate supportive symptomatic treatment. Concomitant use of ADDERALL XR with other serotonergic drugs or CYP2D6 inhibitors should be used only if the potential benefit justifies the potential risk. If clinically warranted, consider initiating ADDERALL XR with lower doses, monitoring patients for the emergence of serotonin syndrome during drug initiation or titration, and informing patients of the increased risk for serotonin syndrome.

5.8 Visual Disturbance
Difficulties with accommodation and blurring of vision have been reported with stimulant treatment.

5.9 Tics
Amphetamines have been reported to exacerbate motor and phonic tics and Tourette’s syndrome. Therefore, clinical evaluation for tics and Tourette’s syndrome in children and their families should precede use of stimulant medications.

5.10 Prescribing and Dispensing
The least amount of amphetamine feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. ADDERALL XR should be used with caution in patients who use other sympathomimetic drugs.

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

6.1 Clinical Trial Experience
The premarketing development program for ADDERALL XR included exposures in a total of 1315 participants in clinical trials (635 pediatric patients, 350 adolescent patients, 248 adult patients, and 82 healthy adult subjects). Of these, 635 patients (ages 6 to 12) were evaluated in two controlled clinical studies, one open-label clinical study, and two single-dose clinical pharmacology studies (N=40). Safety data on all patients are included in the discussion that follows. Adverse reactions were assessed by collecting adverse reactions, results of physical examinations, vital signs, weights, laboratory analyses, and ECGs. Adverse reactions during exposure were obtained primarily by general inquiry and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to compare these incidence rates to those observed in the clinical trials of a different drug product or observed in the clinical trials of a different indication for this drug product. It is not possible to estimate an incidence rate for a reaction, or to compare rates between studies and the incidence observed in clinical practice, since it is dependent on several factors, including the size of the treated population, duration of treatment, and the method of reporting adverse events.

The stated frequencies of adverse reactions represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed.
Adverse Reactions Leading to Discontinuation of Treatment

In two placebo-controlled studies of up to 5 weeks duration among children with ADHD, 2.4% (10/425) of ADDERALL XR-treated patients discontinued due to adverse reactions (including 3 patients with loss of appetite, one of whom also reported insomnia) compared to 2.7% (7/259) receiving placebo. The most frequent adverse reactions leading to discontinuation of ADDERALL XR in controlled and uncontrolled, multiple-dose clinical trials of children (N=595) were anorexia (loss of appetite) (2.9%), insomnia (1.5%), weight loss (1.2%), emotional lability (1%), and depression (0.7%). Over half of these patients were exposed to ADDERALL XR for 12 months or more.

In a separate placebo-controlled 4-week study in adolescents with ADHD, five patients (2.1%) discontinued treatment due to adverse events among ADDERALL XR-treated patients (N=233) compared to none who received placebo (N=54). The most frequent adverse event leading to discontinuation and considered to be drug-related (i.e. leading to discontinuation in at least 1% of ADDERALL XR-treated patients and at a rate at least twice that of placebo) was insomnia (1.3%, n=3).

In one placebo-controlled 4-week study among adults with ADHD with doses 20 mg to 60 mg, 23 patients (12.0%) discontinued treatment due to adverse events among ADDERALL XR-treated patients (N=191) compared to one patient (1.6%) who received placebo (N=64). The most frequent adverse events leading to discontinuation and considered to be drug-related (i.e. leading to discontinuation in at least 1% of ADDERALL XR-treated patients and at a rate at least twice that of placebo) were insomnia (5.2%, n=10), anxiety (2.1%, n=4), nervousness (1.6%, n=3), dry mouth (1.6%, n=3), anorexia (1.6%, n=3), tachycardia (1.6%, n=3), headache (1.6%, n=3), and asthenia (1.0%, n=2).

Adverse Reactions Occurring in Controlled Trials

Adverse reactions reported in a 3-week clinical trial of children and a 4-week clinical trial in adolescents and adults, respectively, treated with ADDERALL XR or placebo are presented in the tables below.

Table 1  Adverse Reactions Reported by 2% or More of Children (6-12 Years Old) Receiving ADDERALL XR with Higher Incidence Than on Placebo in a 584-Patient Clinical Study

<table>
<thead>
<tr>
<th>Body System</th>
<th>Preferred Term</th>
<th>ADDERALL XR (n=374)</th>
<th>Placebo (n=210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Abdominal Pain (stomachache)</td>
<td>14%</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Infection</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Accidental Injury</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Asthenia (fatigue)</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Digestive System</td>
<td>Loss of Appetite</td>
<td>22%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td>Dyspepsia</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Nervous System</td>
<td>Insomnia</td>
<td>17%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Emotional Lability</td>
<td>9%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Nervousness</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Metabolic/Nutritional</td>
<td>Weight Loss</td>
<td>4%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 2  Adverse Reactions Reported by 5% or More of Adolescents (13-17 Years Old) Weighing ≥75 kg/165 lbs Receiving ADDERALL XR with Higher Incidence Than Placebo in a 287 Patient Clinical Forced Weekly-Dose Titration Study*

<table>
<thead>
<tr>
<th>Body System</th>
<th>Preferred Term</th>
<th>ADDERALL XR (n=233)</th>
<th>Placebo (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Abdominal Pain (stomachache)</td>
<td>11%</td>
<td>2%</td>
</tr>
<tr>
<td>Digestive System</td>
<td>Loss of Appetite</td>
<td>36%</td>
<td>2%</td>
</tr>
<tr>
<td>Nervous System</td>
<td>Insomnia</td>
<td>12%</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>Nervousness</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Metabolic/Nutritional</td>
<td>Weight Loss</td>
<td>9%</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Includes doses up to 40 mg.

† Appears the same due to rounding.

‡ Dose-related adverse reactions.

Note: The following reactions did not meet the criterion for inclusion in Table 2 but were reported by 2% to 4% of adolescent patients receiving ADDERALL XR with a higher incidence than patients receiving placebo: infection, photosensitivity reaction, constipation, tooth disorder (e.g., teeth clenching, tooth infection), emotional lability, libido decreased, somnolence, speech disorder (e.g., stuttering, excessive speech), palpitation, twitching, dyspnea, sweating, dysmenorrhea, and impotence.

Hypertension [see Warnings and Precautions (5.3)]

In a controlled 4-week outpatient clinical study of adolescents with ADHD, isolated systolic blood pressure elevations ≥15 mmHg were observed in 7/64 (11%) placebo-treated patients and 7/100 (7%) patients receiving ADDERALL XR 10 or 20 mg. Isolated elevations in diastolic blood pressure ≥5 mmHg were observed in 16/64 (25%) placebo-treated patients and 22/100 (22%) ADDERALL XR-treated patients. Similar results were observed at higher doses.

In a single-dose pharmacokinetic study in 23 adolescents with ADHD, isolated increases in systolic blood pressure (above the upper 95% CI for age, gender, and stature) were observed in 2/17 (12%) and 8/23 (35%), subjects administered 10 mg and 20 mg ADDERALL XR, respectively. Higher single doses were associated with a greater increase in systolic blood pressure. All increases were transient, appeared maximal at 2 to 4 hours post dose and not associated with symptoms.

6.2 Adverse Reactions Associated with the Use of Amphetamine, ADDERALL XR, or ADDERALL

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

Cardiovascular

Palpitations. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.

Central Nervous System

Psychotic episodes at recommended doses, overstimulation, restlessness, irritability, euphoria, dyskinesia, dysphoria, depression, tremor, tics, aggression, anger, logorrhea, dermatomyositis, paresthesia (including formication), and bruxism.

Eye Disorders

Vision blurred, mydriasis.

Gastrointestinal

Unpleasant taste, constipation, other gastrointestinal disturbances.

Allergic

Urticaria, rash, hypersensitivity reactions including angioedema and anaphylaxis. Serious skin rashes, including Stevens-Johnson Syndrome and toxic epidermal necrolysis have been reported.

Endocrine

Impotence, changes in libido, frequent or prolonged erections.

Skin

Alopecia.

Vascular Disorders

Raynaud’s phenomenon.

Musculoskeletal and Connective Tissue Disorders

Rhabdomyolysis
Drugs Having Clinically Important Interactions with Amphetamines

Table 4: Drugs Having Clinically Important Interactions with Amphetamines

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Clinical Impact</th>
<th>Time to maximum concentration (Tmax) of amphetamine is increased compared to the use of the drug alone.</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoamine Oxidase Inhibitors (MAOIs)</td>
<td>Concomitant use of MAOIs and CNS stimulants can cause hypertensive crisis. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure.</td>
<td></td>
<td>selegiline, tranylcypromine, isocarboxazid, phenelzine, linezolid, methylene blue</td>
</tr>
<tr>
<td>Proton Pump Inhibitors</td>
<td>Do not administer ADDERALL XR concomitantly or within 14 days after discontinuing MAOI [see Contraindications (4)].</td>
<td></td>
<td>desipramine, protriptyline</td>
</tr>
<tr>
<td>Serotonergic Drugs</td>
<td></td>
<td></td>
<td>selective serotonin reuptake inhibitors (SSRI), serotonin norepinephrine reuptake inhibitors (SNRI), triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John’s Wort</td>
</tr>
<tr>
<td>CYP2D6 Inhibitors</td>
<td>The concomitant use of ADDERALL XR and serotonergic drugs increases the risk of serotonin syndrome.</td>
<td></td>
<td>paroxetine and fluoxetine (also serotonergic drugs), quinidine, ritonavir</td>
</tr>
<tr>
<td>Alkalining Agents</td>
<td>Increase blood levels and potentate the action of amphetamine.</td>
<td></td>
<td>d-amphetamine doses of 50 mg/kg/day at doses similar to those used in clinical studies, with oral administration of amphetamine to rats and rabbits throughout the period of organogenesis at doses of up to 6 and 16 mg/kg/day, respectively. These doses are approximately 2 and 12 times, respectively, the maximum recommended human dose (MRHD) of 20 mg/day given to adolescents, on a mg/m² basis.</td>
</tr>
<tr>
<td>Tricyclic Antidepressants</td>
<td>May enhance the activity of tricyclic or sympathomimetic agents causing striking and sustained increases in the concentration of d-amphetamine in the brain; cardiovascular effects can be potentiated.</td>
<td></td>
<td>l-amphetamine, d,l-amphetamine doses of 50 mg/kg/day at doses similar to those used in clinical studies, with oral administration of amphetamine to rats and rabbits throughout the period of organogenesis at doses of up to 6 and 16 mg/kg/day, respectively. These doses are approximately 2 and 12 times, respectively, the maximum recommended human dose (MRHD) of 20 mg/day given to adolescents, on a mg/m² basis.</td>
</tr>
<tr>
<td>Proton Pump Inhibitors</td>
<td>Time to maximum concentration (Tmax) of amphetamine is decreased compared to when administered alone.</td>
<td></td>
<td>Omeprazole</td>
</tr>
</tbody>
</table>
whose lactation is not well established. Because of the potential for serious adverse reactions in nursing infants, advise patients that breastfeeding is not recommended during treatment with ADDERALL XR.

8.4 Pediatric Use
ADDERALL XR is indicated for use in children 6 years of age and older. The safety and efficacy of ADDERALL XR in children under 6 years of age have not been studied. Long-term effects of amphetamines in children have not been well established.

Long-Term Growth Suppression
Growth should be monitored during treatment with stimulants, including ADDERALL XR, and pediatric patients aged 6 to 17 years who are not growing or gaining weight as expected may need to have their treatment interrupted [see Warnings and Precautions (5.3)].

Juvenile Animal Toxicity Data
Juvenile rats treated with mixed amphetamine salts early in the postnatal period through sexual maturation demonstrated transient changes in motor activity. Learning and memory impairment was observed at approximately 6 times the maximum recommended human dose (MRHD) given to children on a mg/m² basis. No recovery was seen following a drug free period. A delay in the developmental milestones of vaginal opening and preputial separation was seen at 40 mg/kg but there was no effect on fertility.

In a juvenile developmental study, rats received daily oral doses of amphetamine (d to l amphetamine ratio of 3:1) of 2, 6, or 20 mg/kg on days 7-13 of age; from day 14 to approximately day 60 of age these doses were given b.i.d. for total daily doses of 4, 12, or 40 mg/kg. The latter doses are approximately 0.6, 2, and 6 times the MRHD of 30 mg/day, given to children on a mg/m² basis. Post dosing hyperactivity was seen at all doses; motor activity measured prior to the daily dose was decreased during the dosing period but the decreased motor activity was largely absent after an 18 day drug-free recovery period. Performance in the Morris water maze test for learning and memory was impaired at the 40 mg/kg dose, and sporadically at the lower doses, when measured prior to the daily dose during the treatment period; no recovery was seen after a 19 day drug-free period. A delay in the developmental milestones of vaginal opening and preputial separation was seen at 40 mg/kg but there was no effect on fertility.

8.5 Geriatric Use
ADDERALL XR has not been studied in the geriatric population.

8.6 Renal Impairment
Due to reduced clearance of amphetamines in patients with severe renal impairment (GFR 15 to <30 mL/min/1.73 m²), the recommended dose should be reduced. ADDERALL XR is not recommended in patients with ESRD (GFR <15 mL/min/1.73 m²) [see Dosage and Administration (2.5), Clinical Pharmacology (12.3)]. d-Amphetamine is not dialyzable.

9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
ADDERALL XR contains amphetamine, a Schedule II controlled substance.

9.2 Abuse
ADDERALL XR is a CNS stimulant that contains amphetamine, which has a high potential for abuse. Abuse is characterized by impaired control of drug use, compulsive use despite harm, and craving. Signs and symptoms of amphetamine abuse may include increased heart rate, respiratory rate, blood pressure, and/or sweating, dilated pupils, hyperactivity, restlessness, insomnia, decreased appetite, loss of coordination, tremors, flushed skin, vomiting, and/or abdominal pain. Anxiety, psychosis, hostility, aggression, suicidal or homicidal ideation have also been observed. Abusers of amphetamines may use other unapproved routes of administration which can result in overdose and death [see Overdosage (10)].

To reduce the abuse of CNS stimulants, including ADDERALL XR, assess the risk of abuse prior to prescribing. After prescribing, keep careful prescription records, educate patients and their families about abuse and proper storage and disposal of CNS stimulants. Monitor for signs of abuse while on therapy and re-evaluate the need for ADDERALL XR use.

9.3 Dependence
Tolerance (a state of adaptation in which exposure to a specific dose of a drug results in a reduction of the drug's desired and/or undesired effects over time) and cross-tolerance to other CNS stimulants and abused drugs is common. Physical Dependence (which is manifested by a withdrawal syndrome produced by abrupt cessation, rapid dose reduction, or administration of an antagonist) may occur in patients treated with CNS stimulants including ADDERALL XR. Withdrawal symptoms after abrupt cessation of CNS stimulants include dysphoric mood; fatigue; vivid, unpleasant dreams; insomnia or hyperinsomnia; increased appetite; and psychomotor retardation or agitation.

10 OVERDOSAGE
Manufactures of amphetamine overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, hallucinations, hallucinations, panic states, hyperpyrexia and rhabdomyolysis. Fatigue and depression usually follow the central nervous system stimulation. Serotoner syndrom has been reported with amphetamine use, including ADDERALL XR. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea and abdominal cramps. Fatal poisoning is usually preceded by convulsions and coma.

Treatment
Consult with a Certified Poison Control Center for up to date guidance and advice. The prolonged release of mixed amphetamine salts from ADDERALL XR should be considered when treating patients with overdose.

d-Amphetamine is not dialyzable.

11 DESCRIPTION
ADDERALL XR extended-release capsules contain mixed salts of a single-entity amphetamine, a CNS stimulant. ADDERALL XR contains equal amounts (by weight) of four salts: dextroamphetamine sulfate, amphetamine sulfate, dextroamphetamine saccharate and amphetamine (D,L)-aspartate monohydrate. This results in a 3:1 mixture of dextro- to levo-amphetamine base equivalent.

The 5 mg, 10 mg, 15 mg, 20 mg, 25 mg and 30 mg strength extended release capsules are for oral administration. ADDERALL XR contains two types of drug-containing beads (immediate-release and delayed release) which prolong the release of amphetamine compared to the ADDERALL (immediate-release) tablet formulation.

Each capsule contains:

<table>
<thead>
<tr>
<th>Capsule Strength</th>
<th>5 mg</th>
<th>10 mg</th>
<th>15 mg</th>
<th>20 mg</th>
<th>25 mg</th>
<th>30 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextroamphetamine</td>
<td>1.25 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>6.25 mg</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Saccharate</td>
<td>1.25 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>6.25 mg</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Amphetamine (D,L)-Aspartate Monohydrate</td>
<td>1.25 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>6.25 mg</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>1.25 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>6.25 mg</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Sulfate</td>
<td>1.25 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>6.25 mg</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Amphetamine Sulfate</td>
<td>1.25 mg</td>
<td>2.5 mg</td>
<td>3.75 mg</td>
<td>5.0 mg</td>
<td>6.25 mg</td>
<td>7.5 mg</td>
</tr>
</tbody>
</table>

| Total amphetamine | 3.1 mg | 6.3 mg | 9.4 mg | 12.5 mg | 15.6 mg | 18.8 mg |
| d-amphetamine base equivalence | 2.4 mg | 4.7 mg | 7.1 mg | 9.5 mg | 11.9 mg | 14.2 mg |
| l-amphetamine base equivalence | 0.75 mg | 1.5 mg | 2.3 mg | 3.0 mg | 3.8 mg | 4.5 mg |

Inactive Ingredients and Colors
The inactive ingredients in ADDERALL XR extended release capsules include: gelatin capsules, hydroxypropyl methylcellulose, methacrylic acid copolymer, opadry beige, sugar spheres, talc, and triethyl citrate. Gelatin capsules contain edible inks, kosher gelatin, and titanium dioxide. The 5 mg, 10 mg, and 15 mg capsules also contain FD&C Blue #2. The 20 mg, 25 mg, and 30 mg capsules also contain red iron oxide and yellow iron oxide.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Amphetamines are non-catecholamine sympathomimetic amines with CNS stimulant activity. The mode of therapeutic action in ADHD is not known.

12.2 Pharmacodynamics
Amphetamines block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

12.3 Pharmacokinetics
Pharmacokinetic studies of ADDERALL XR have been conducted in healthy adult and pediatric (children aged 6-12 yrs) subjects, and adolescent (13-17 yrs) and children with ADHD. Both ADDERALL (immediate-release) tablets and ADDERALL XR extended release capsules contain d-amphetamine and l-amphetamine salts in the ratio of 3:1. Following administration of ADDERALL (immediate-release), the peak plasma concentrations occurred in about 3 hours for both d-amphetamine and l-amphetamine. The time to reach maximum plasma concentration (Tmax) for ADDERALL XR is about 7 hours, which is about 4 hours longer compared to ADDERALL (immediate-release). This is consistent with the extended-release nature of the product.
clearances greater than glomerular filtration rates, indicating the involvement of active by CYP isozymes on pH and urine flow rates. Alkaline urine pHs result in less ionization and reduced renal With normal urine pHs, approximately half of an administered dose of amphetamine is these metabolites relative to 4-hydroxyamphetamine, or on the side chain Metabolism and Excretion Amphetamine is reported to be oxidized at the 4 position of the benzene ring to form 4-hydroxyamphetamine. Although the enzymes involved in amphetamine Carcinogenesis 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility Carcinogenesis No evidence of carcinogenicity was found in studies in which d-amphetamine (enantiomer ratio of 1:1) was administered to mice and rats in the diet for 2 years at doses of up to 30 mg/kg/day in male mice, 19 mg/kg/day in female mice, and 5 mg/kg/day in male and female rats. These doses are approximately 2.4, 1.5, and 0.8 times, respectively, the maximum recommended human dose of 30 mg/day given to children, on a mg/m² basis. Mutagenesis Amphetamine, in the enantiomer ratio d- to l- ratio of 3:1, was not clastogenic in the mouse bone marrow micronucleus test in vivo and was negative when tested in the E. coli component of the Ames test in vitro. d,Amphetamine (1:1 enantiomer ratio) has been reported to produce a positive response in the mouse bone marrow micronucleus test, an equivocal response in the Ames test, and negative responses in the in vitro sister chromatid exchange and chromosomal aberration assays. Impairment of Fertility Amphetamine, in the enantiomer ratio d- to l- ratio of 3:1, did not adversely affect fertility or early embryonic development in the rat at doses of up to 20 mg/kg/day (approximately 8 times the maximum recommended human dose of 20 mg/day given to adolescents, on a mg/m² basis). 13.2 Animal Toxicology and/or Pharmacology Acute administration of high doses of amphetamine (d- or d,l-) has been shown to produce long-lasting neurotoxic effects, including irreversible nerve fiber damage, in rodents. The significance of these findings to humans is unknown. 14 CLINICAL STUDIES Pediatric Patients A double-blind, randomized, placebo-controlled, parallel-group study was conducted in children aged 6-12 (N=584) who met DSM-IV criteria for ADHD (either the combined type or the hyperactive-impulsive type). Patients were randomized to two treatment groups receiving doses of 10, 20, or 30 mg of ADDERALL XR or placebo once daily in the morning for three weeks. Significant improvements in patient behavior, based upon teacher ratings of attention and hyperactivity, were
observed for all ADDERALL XR doses compared to patients who received placebo, for all three weeks, including the first week of treatment, when all ADDERALL XR subjects were receiving a dose of 10 mg/day. Patients who received ADDERALL XR showed behavioral improvements in both morning and afternoon assessments compared to patients treated with placebo.

In a classroom analogue study, patients (N=51) receiving fixed doses of 10 mg, 20 mg or 30 mg ADDERALL XR demonstrated statistically significant improvements in teacher-rated behavior and performance measures, compared to patients treated with placebo.

A double-blind, randomized, multi-center, parallel-group, placebo-controlled study was conducted in adults aged 13-17 (N=327) who met DSM-IV criteria for ADHD. The primary cohort of patients (n=287, weighing ≥75kg/165lbs) who were randomized to fixed-dose treatment groups and received four weeks of treatment. Patients were randomized to receive final doses of 10 mg, 20 mg, 30 mg, and 40 mg ADDERALL XR or placebo once daily in the morning. Patients randomized to doses greater than 10 mg were titrated to their final doses by 10 mg each week. The secondary cohort consisted of 40 subjects weighing >75kg/165lbs who were randomized to fixed-dose treatment groups receiving final doses of 50 mg and 60 mg ADDERALL XR or placebo once daily in the morning for 4 weeks. The primary efficacy variable was the Attention Deficit Hyperactivity Disorder-Rating Scale IV (ADHD-RS-IV) total score for the primary cohort. The ADHD-RS-IV is an 18-item scale that measures the core symptoms of ADHD. Improvements in the primary cohort were statistically significantly greater in all four primary cohort active treatment groups (ADDERALL XR 10 mg, 20 mg, 30 mg, and 40 mg) compared with the placebo group. There was not adequate evidence that doses greater than 20 mg/day conferred additional benefit.

**Adult Patients**

A double-blind, randomized, placebo-controlled, parallel-group study was conducted in adults (N=255) who met DSM-IV criteria for ADHD. Patients were randomized to fixed-dose treatment groups receiving final doses of 20, 40, or 60 mg of ADDERALL XR or placebo once daily in the morning for four weeks. Significant improvements, measured with the Attention Deficit Hyperactivity Disorder-Rating Scale (ADHD-RS), an 18-item scale that measures the core symptoms of ADHD, were observed at endpoint for all ADDERALL XR doses compared to patients who received placebo for all four weeks. There was not adequate evidence that doses greater than 20 mg/day conferred additional benefit.

**16 HOW SUPPLIED/STORAGE AND HANDLING**

ADDERALL XR 5 mg extended release capsules: Clear/blue (imprinted ADDERALL XR 5 mg), bottles of 100, NDC 54092-381-01

ADDERALL XR 10 mg extended release capsules: Blue/blue (imprinted ADDERALL XR 10 mg), bottles of 100, NDC 54092-383-01

ADDERALL XR 15 mg extended release capsules: Blue/white (imprinted ADDERALL XR 15 mg), bottles of 100, NDC 54092-385-01

ADDERALL XR 20 mg extended release capsules: Orange/orange (imprinted ADDERALL XR 20 mg), bottles of 100, NDC 54092-387-01

ADDERALL XR 25 mg extended release capsules: Orange/white (imprinted ADDERALL XR 25 mg), bottles of 100, NDC 54092-389-01

ADDERALL XR 30 mg extended release capsules: Natural/orange (imprinted ADDERALL XR 30 mg), bottles of 100, NDC 54092-391-01

Dispense in a tight, light-resistant container as defined in the USP. Store at room temperature, 20° C to 25° C (68° F to 77° F). Excursions permitted to 15-30° C (59-86° F) [see USP CONTROLLED ROOM TEMPERATURE]

**Disposal**

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

**17 PATIENT COUNSELING INFORMATION**

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

**Controlled Substance Status/Potential for Abuse, Misuse, and Dependence**

Advise patients that ADDERALL XR is a federally controlled substance because it can be abused or lead to dependence. Additionally, emphasize that ADDERALL XR should be stored in a safe place to prevent misuse and/or abuse. Evaluate patient history (including family history) of abuse or dependence on alcohol, prescription medicines, or illicit drugs [see Warnings and Precautions (5.1), Drug Abuse and Dependence (9)].

**Serious Cardiovascular Risks**

Advise patients of serious cardiovascular risk (including sudden death, myocardial infarction, stroke, and hypertension) with ADDERALL XR. Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during treatment should undergo a prompt cardiac evaluation [see Warnings and Precautions (5.1)].

**Psychiatric Risks**

Prior to initiating treatment with ADDERALL XR, adequately screen patients with comorbid depressive symptoms 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/or depression. Additionally, ADDERALL XR therapy at usual doses may cause treatment-emergent psychotic or manic symptoms in patients without prior history of psychotic symptoms or mania [see Warnings and Precautions (5.2)]

**Circulation problems in fingers and toes [Peripheral vasculopathy, including Raynaud’s phenomenon]**

Instruct patients beginning treatment with ADDERALL XR about the risk of peripheral vasculopathy, including Raynaud’s Phenomenon, and in 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 ADDERALL XR. Further clinical evaluation (e.g., rheumatologic referral) may be appropriate for certain patients [see Warnings and Precautions (5.5)].

**Serotonin Syndrome**

Caution patients about the risk of serotonin syndrome with concomitant use of ADDERALL XR and other serotonergic drugs including SSRIs, SNRIs, triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John’s Wort, and with drugs that impair metabolism of serotonin (in particular MAOIs, both those intended to treat psychiatric disorders and also others such as linezolid [see Contraindications (4), Warnings and Precautions (5.6) and Drug Interactions (7.1)]. Advise patients to contact their healthcare provider or report to the emergency room if they experience signs or symptoms of serotonin syndrome.

**Concomitant Medications**

Advise patients to notify their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs because there is a potential for interactions [see Drug Interactions (7.1)].

**Pregnancy Registry**

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

**Pregnancy**

Advise patients to notify their healthcare provider if they become pregnant or intend to become pregnant during treatment with ADDERALL XR. Advise patients of the potential fetal effects from the use of ADDERALL XR during pregnancy [see Use in Specific Populations (8.1)].

**Lactation**

Advise women not to breastfeed if they are taking ADDERALL XR [see Use in Specific Populations (8.2)].

**Impairment in Ability to Operate Machinery or Vehicles**

ADDERALL XR may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or vehicles; the patient should therefore be cautioned accordingly.

Manufactured for Shire US Inc., 300 Shire Way, Lexington, MA 02421. Made in USA. For more information call 1-800-828-2088

ADDERALL XR® is a registered trademark of Shire LLC, a Takeda company

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SS1519 08/19
What is the most important information I should know about ADDERALL XR?

ADDERALL XR is a stimulant medicine. The following have been reported with use of 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 ADDERALL XR.

Your doctor should check you or your child’s blood pressure and heart rate regularly during treatment with ADDERALL XR.

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 ADDERALL XR.

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

Children and Teenagers
   - 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 ADDERALL XR, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

3. 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 from pale, to blue, to red

Tell your doctor if you have or your child has numbness, pain, skin color change, or sensitivity to temperature in your fingers or toes.

Call your doctor right away if you have or your child has any unexplained wounds appearing on fingers or toes while taking ADDERALL XR.

What Is ADDERALL XR?

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

Who should not take ADDERALL XR?

ADDERALL XR should not be taken if you or your child:
   - have heart disease or hardening of the arteries
   - have moderate to severe high blood pressure
   - have hyperthyroidism
   - have an eye problem called glaucoma
   - are very anxious, tense, or agitated
   - have a history of drug abuse
   - are taking or have taken within the past 14 days an anti-depression medicine called a monoamine oxidase inhibitor or MAOI.
   - is sensitive to, allergic to, or had a reaction to other stimulant medicines

ADDERALL XR has not been studied in children less than 6 years old.

ADDERALL XR may not be right for you or your child. Before starting ADDERALL XR tell you or your child’s doctor about all health conditions (or a family history of) including if you or your child:
   - have heart problems, heart defects, or high blood pressure
   - have mental problems including psychosis, mania, bipolar illness, or depression
   - have tics or Tourette’s syndrome
   - have liver problems
   - have kidney problems
   - have end stage renal disease (ESRD)
   - have thyroid problems
   - have seizures or have had an abnormal brain wave test (EEG)
   - have circulation problems in fingers and toes
   - are pregnant or plan to become pregnant. It is not known if ADDERALL XR will harm your unborn baby.

- There is a pregnancy registry for females who are exposed to ADDERALL XR during pregnancy. The purpose of the registry is to collect information about the health of females exposed to ADDERALL XR and their baby. If you or your child becomes pregnant during treatment with ADDERALL XR, talk to your healthcare provider about registering with the National Pregnancy Registry of Psychostimulants at 1-866-961-2388 or visit online at https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/othermedications/.

- are breastfeeding or plan to breastfeed. ADDERALL XR passes into breast milk. You or your child should not breastfeed during treatment with ADDERALL XR.
Can ADDERALL XR be taken with other medicines?
Tell your doctor about all of the medicines that you or your child takes including prescription and non-prescription medicines, vitamins, and herbal supplements. ADDERALL XR 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 ADDERALL XR.

Your doctor will decide whether ADDERALL XR can be taken with other medicines.

Especially tell your doctor if you or your child takes:
• anti-depression medicines including MAOIs
• anti-psychotic medicines
• lithium
• narcotic pain medicines
• seizure medicines
• blood thinner medicines
• blood pressure medicines
• stomach acid medicines
• cold or allergy medicines that contain decongestants

Know the medicines that you or your child takes. Keep a list of your medicines with you to show your doctor and pharmacist.

Do not start any new medicine while taking ADDERALL XR without talking to your doctor first.

How should ADDERALL XR be taken?
• Take ADDERALL XR exactly as prescribed. Your doctor may adjust the dose until it is right for you or your child.
• Take ADDERALL XR once a day in the morning when you first wake up. ADDERALL XR is an extended release capsule. It releases medicine into your body throughout the day.
• Swallow ADDERALL XR extended release capsules whole with water or other liquids. If you or your child cannot swallow the capsule, open it and sprinkle the medicine over a spoonful of applesauce. Swallow all of the applesauce and medicine mixture without chewing immediately. Follow with a drink of water or other liquid. Never chew or crush the capsule or the medicine inside the capsule.
• ADDERALL XR can be taken with or without food.
• From time to time, your doctor may stop ADDERALL XR treatment for a while to check ADHD symptoms.
• Your doctor may do regular checks of the heart, and blood pressure while taking ADDERALL XR. Children should have their height and weight checked often while taking ADDERALL XR. ADDERALL XR treatment may be stopped if a problem is found during these check-ups.
• If you or your child takes too much ADDERALL XR or overdoses, call your doctor or poison control center right away, or get emergency treatment.

What are possible side effects of ADDERALL XR?
See “What is the most important information I should know about ADDERALL XR?” for information on reported heart and mental problems.

Other serious side effects include:
• slowing of growth (height and weight) in children
• seizures, mainly in patients with a history of seizures
• eyesight changes or blurred vision

Common side effects include:
• headache
• stomach ache
• trouble sleeping
• weight loss
• dry mouth
• decreased appetite
• nervousness
• mood swings
• dizziness
• fast heart beat

ADDERALL XR may affect you or your child’s ability to drive or do other dangerous activities.

Talk to your doctor if you or your child has side effects that are bothersome or do not go away.

This is not a complete list of possible side effects. Ask your doctor or pharmacist for more information.

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 ADDERALL XR?
• Store ADDERALL XR in a safe place at room temperature, 59 to 86° F (15 to 30° C).
• Keep ADDERALL XR and all medicines out of the reach of children.

General information about ADDERALL XR
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ADDERALL XR for a condition for which it was not prescribed. Do not give ADDERALL XR to other people, even if they have the same condition. It may harm them and it is against the law.

This Medication Guide summarizes the most important information about ADDERALL XR. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about ADDERALL XR that was written for healthcare professionals. For more information, you may also contact Shire Pharmaceuticals (the maker of ADDERALL XR) at 1-800-828-2088 or visit the website at http://www.adderallxr.com.

What are the ingredients in ADDERALL XR?
Active Ingredients: dextroamphetamine saccharate, amphetamine aspartate monohydrate, dextroamphetamine sulfate, amphetamine sulfate

Inactive Ingredients: gelatin capsules, hydroxypropyl methylcellulose, methacrylic acid copolymer, opadry beige, sugar spheres, talc, and triethyl citrate. Gelatin capsules contain edible inks, kosher gelatin, and titanium dioxide. The 5 mg, 10 mg, and 15 mg capsules also contain FD&C Blue #2. The 20 mg, 25 mg, and 30 mg capsules also contain red iron oxide and yellow iron oxide

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Rev. 7/2019 S51519

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