PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

APO-DEXTROAMPHETAMINE

Dextroamphetamine Sulfate Tablets

Tablets, 5 mg, Oral

USP

Sympathomimetic

APOTEX INC.
150 Signet Drive
Toronto, Ontario
M9L 1T9

Date of Initial Authorization:
JUN 30, 2015

Date of Revision:
OCT 29, 2026

Submission Control Number: 502650

RECENT MAJOR LABEL CHANGES

2 CONTRAINDICATIONS	01/2025
4 DOSAGE AND ADMINISTRATION, 4.1 Dosing Considerations	01/2025
7 WARNING AND PRECAUTIONS	01/2025

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

APO-DEXTROAMPHETAMINE (dextroamphetamine sulfate) is indicated:

- in the adjunctive treatment of narcolepsy
- for the treatment of attention deficit hyperactivity disorder (ADHD)

Attention Deficit Hyperactivity Disorder (ADHD): A diagnosis of ADHD (DSM-IV) implies the presence of hyperactive-impulsive or inattentive symptoms that caused impairment and that were present before age 7 years. The symptoms must be persistent, must be more severe than is typically observed in individuals at a comparable level of development, must cause clinically significant impairment, e.g., in social, academic, or occupational functioning, and must be present in 2 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 6 of the following symptoms must have persisted for at least 6 months: lack of attention to details/careless mistakes, lack of sustained attention, poor listener, failure to follow through on tasks, poor organization, avoids tasks requiring sustained mental effort, loses things, easily distracted, forgetful. For the Hyperactive-Impulsive Type, at least 6 of the following symptoms must have persisted for at least 6 months: fidgeting/squirming, leaving seat, inappropriate running/climbing, difficulty with quiet activities, “on the go,” excessive talking, blurting answers, can’t wait turn, intrusive. For a Combined Type diagnosis, both inattentive and hyperactive-impulsive criteria must be met.

Special Diagnostic Considerations: The specific etiology of ADHD 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: APO-DEXTROAMPHETAMINE is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational and social) for patients with this syndrome. Drug treatment may not be indicated for all patients with this syndrome. Drug treatment is not intended for use in the patient who exhibits symptoms secondary to environmental factors and/or other primary psychiatric disorders, including psychosis. Appropriate educational placement is essential in children and adolescents with this diagnosis and psychosocial intervention is often helpful. When remedial measures alone are insufficient, the decision to prescribe drug treatment medication will depend upon the physician’s assessment of the chronicity and severity of the patient’s symptoms.

Long-term Use: The physician who elects to use APO-DEXTROAMPHETAMINE for extended

periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

1.1 Pediatrics

Pediatrics (< 6 years of age): Amphetamines are not recommended for use in Attention Deficit Hyperactivity Disorder in children under 6 years of age, since safety and efficacy in this age group have not been established. Long-term effects of amphetamines in children above 6 years of age have not been well established.

1.2 Geriatrics

Geriatrics (> 65 years of age): APO-DEXTROAMPHETAMINE should be used with caution in geriatric patients, taking into consideration the greater frequency of decreased hepatic or renal function, of cardiovascular disease, and of concomitant disease or other drug therapy in this patient population, which may necessitate dose adjustments and additional or more frequent monitoring.

2 CONTRAINDICATIONS

APO-DEXTROAMPHETAMINE (dextroamphetamine sulfate) is contraindicated in patients with:

- Hypersensitivity to APO-DEXTROAMPHETAMINE or to any ingredient in the formulation or component of the container. For complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- Hypersensitivity or idiosyncrasy to sympathomimetic amines
- Advanced arteriosclerosis
- Symptomatic cardiovascular disease
- Moderate to severe hypertension
- Hyperthyroidism
- Agitated state
- History of drug abuse
- Glaucoma
- Anxiety
- Tension
- Pheochromocytoma
- Motor tics or with a family history of diagnosis of Tourette's Syndrome (verbal tics).
- Concomitant treatment with monoamine oxidase inhibitors (MAOIs) or within 14 days following the withdrawal of MAOIs (see 9.4 Drug-Drug Interactions).

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions
Misuse and Serious Cardiovascular Adverse Events

Amphetamines have a potential for abuse, misuse, dependence, and diversion for non-therapeutic uses that physicians should consider when prescribing this product (see 7 WARNINGS AND PRECAUTIONS, Dependence/Tolerance).

The misuse of amphetamines may cause serious cardiovascular adverse events and sudden death.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- APO-DEXTROAMPHETAMINE should be administered starting at the lowest possible dose. Dosage should then be individually and slowly adjusted, to the lowest effective dosage, since individual patient response to dextroamphetamine sulfate varies widely.

- Prior to initiating treatment with APO-DEXTROAMPHETAMINE, a personal and family history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical examination should be obtained to assess for the presence of cardiac disease. In patients with relevant risk factors and based on the clinician's judgment, further cardiovascular evaluation may be considered (e.g., electrocardiogram and echocardiogram). APO-DEXTROAMPHETAMINE should not be used in patients with symptomatic cardiovascular disease and should generally not be used in patients with known structural cardiac abnormalities (see 2 CONTRAINDICATIONS and 7 WARNINGS AND PRECAUTIONS, Cardiovascular).

- Patients who are considered to need extended treatment with APO-DEXTROAMPHETAMINE should undergo periodic evaluation of their cardiovascular status (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular).

- APO-DEXTROAMPHETAMINE (tablet) contains lactose (see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING). It should not be used in patients with the following rare hereditary problems:
  - Galactose intolerance
  - Lactase deficiency

4.2 Recommended Dose and Dosage Adjustment

Amphetamines are not recommended for pediatric patients under 6 years of age. Therefore, APO-DEXTROAMPHETAMINE should not be used in this population.

Adjunctive treatment of Narcolepsy:

Daily dosage may range from 5 mg to 60 mg depending on individual patient response.

- Suggested initial dosage for pediatric patients aged 6 to 12: start with 5 mg daily. Daily dosage may be raised in increments of 5 mg at weekly intervals until optimal response

is obtained.
- In adults and pediatric patients 12 years of age and older: start with 10 mg daily. Daily dosage may be raised in increments of 10 mg at weekly intervals until optimal response is obtained.

If bothersome adverse reactions appear (e.g., insomnia or anorexia), dosage should be reduced. The first dose is to be taken upon awakening in the morning and additional doses (1 or 2) can be taken at intervals of 4 to 6 hours.

Attention Deficit Hyperactivity Disorder in adults and pediatric patients 6 years of age and older:

Daily dosage may range from 2.5 mg to 40 mg, although some patients may require more than 40 mg daily for optimal response.

- In adults and pediatric patients 6 years of age or older, start with 5 mg once or twice daily. Daily dosage may be raised in increments of 5 mg at weekly intervals until optimal response is obtained. Only in rare cases will it be necessary to exceed a total of 40 mg per day.

If bothersome adverse reactions appear (e.g., insomnia or anorexia), dosage should be reduced. The first dose is to be taken upon awakening in the morning and additional doses (1 or 2) can be taken at intervals of 4 to 6 hours.

Most patients suffering from ADHD require medication for several years, although once symptoms have been controlled, it may be possible to reduce dosage or to interrupt drug therapy during the summer months and at other times when the patient is under less stress. During periods of interrupted drug therapy, behavioral symptoms should be assessed to determine whether their recurrence is sufficient to justify the resumption of treatment.

Patients with severe renal impairment or undergoing dialysis:

Due to reduced clearance in patients with severe renal impairment (GFR 15 to < 30 mL/min/ 1.73 m^2), dosage reduction should be considered in these patients.

As d-amphetamines are not dialyzable, dosage reduction may be considered in patients undergoing dialysis.

4.4 Administration

Time of administration should receive special attention because of possible insomnia. Late evening medication should be avoided.

4.5 Missed Dose

If forgotten, the medicine should be taken as soon as remembered and administration should continue as usual. A double dose should not be taken to make up for forgotten individual doses. Late evening medication should be avoided.

5 OVERDOSAGE

The toxic dose of amphetamine varies widely according to the degree of tolerance present. Blood levels are, therefore, of little value in assessing the severity of the overdose; this assessment must depend almost entirely on clinical signs.

Signs and Symptoms: Manifestations of acute overdosage include dilated and reactive pupils, shallow rapid respiration, rhabdomyolysis, hyperpyrexia, fever, chills, sweating and hyperactive tendon reflexes.

Other manifestations:

Central effects may include restlessness, tremor, aggressiveness, anxiety, confusion, delirium, hallucinations, panic attacks and even suicidal or homicidal tendencies. The stimulant effect is usually followed by depression, lethargy and exhaustion.

Cardiovascular effects may include anginal pain, extrasystoles and other arrhythmias, flushing, headache, hypertension or hypotension, pallor, palpitations and tachycardia. Circulatory collapse and syncope may occur.

Gastrointestinal effects include nausea, vomiting, diarrhea and abdominal cramps.

Posterior reversible encephalopathy syndrome (PRES) has been reported in association with amphetamine overdose. Symptoms indicating PRES include headache, altered mental status, seizures and visual disturbances. Diagnosis should be confirmed by radiological procedure (e.g., MRI). If PRES is suspected or diagnosed, appropriate measures should be taken. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. Delay in diagnosis and treatment may lead to permanent neurological sequelae.

Fatal poisoning is usually preceded by convulsions and coma.

Treatment: Consult with a Certified Poison Control Center for up to date guidance and advice. Treatment is essentially symptomatic and supportive. In addition to the usual measures, including administration of activated charcoal (use of activated charcoal should be avoided in patients with significant risk of aspiration in whom the airway is not protected) and catharsis, sedatives should be given when indicated.

Benzodiazepines are first-line agents in amphetamine overdose for agitation, movement disorders, seizures, tachycardia, and hypertension.

Second-line therapies may include antipsychotics such as chlorpromazine, ziprasidone or haloperidol. These drugs antagonize the central stimulant effects of amphetamines and can be used to treat amphetamine intoxication. However, caution should be exercised when administering these products, as they may worsen clinical outcomes related to the toxicity of co-ingestants, including other stimulants (e.g., cocaine) and ethanol withdrawal. Central alpha-2 adrenergic agonists, such as dexmedetomidine, are sometimes used for refractory amphetamine-induced agitation as they may have an additional advantage in that they can mitigate the tachycardia and hypertension often seen in these situations.

If acute severe hypertension complicates amphetamine overdosage, administration of intravenous phentolamine has been suggested. However, a gradual drop in blood pressure will usually result when sufficient sedation has been achieved. In the presence of severe hypotension, the usual procedures employed for shock should be instituted.

Seizures resistant to benzodiazepines may respond to barbiturates, or require escalation of care, including endotracheal intubation and initiation of propofol infusion.

Although previously advocated, enhancing amphetamine excretion via urine acidification is no longer recommended due to lack of effects on amphetamine toxicity and potential compromises in overall patient management (systemic acidosis, renal effects from rhabdomyolysis).

The d-amphetamines are not dialyzable. No data is available to support the recommendation of forced diuresis, hemodialysis, peritoneal dialysis or charcoal hemoperfusion in this regard.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Oral	Tablet 5 mg dextroamphetamine sulfate	Anhydrous lactose, colloidal silicon dioxide, crospovidone, D&C yellow #10 aluminum lake 14-18%, magnesium stearate, microcrystalline cellulose and sunset yellow aluminum lake 40%.

APO-DEXTROAMPHETAMINE (dextroamphetamine sulfate) 5 mg Tablets:

Each orange, round, flat face bevelled edge tablet is engraved “D” over score on one side, the other side plain.

Available in bottles of 100 and 500 tablets.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

Cardiovascular

Sudden Death and Pre-existing Structural Cardiac Abnormalities:

Children and Adolescents: Sudden death has been reported in association with stimulant drugs used for ADHD treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems.

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

Adults: Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs (see 2 CONTRAINDICATIONS).

Hypertension and other Cardiovascular Conditions: Stimulant medications cause a modest increase in average blood pressure (about 2 to 4 mmHg) and average heart rate (about 3 to 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 2 CONTRAINDICATIONS).

Assessing Cardiovascular Status in Patients being Treated with Stimulant Medications:

Theoretically, there exists a pharmacological potential for all ADHD drugs to increase the risk of sudden/cardiac death. Although confirmation of an incremental risk for adverse

cardiac events arising from treatment with ADHD medications is lacking, prescribers should consider this potential risk.

All drugs with sympathomimetic effects should be used with caution in patients who: a) are involved in strenuous exercise or activities, b) use other stimulants or c) have a family history of sudden/cardiac death. Patients 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 the presence of 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.

Dependence/Tolerance

Amphetamines have been extensively abused (see 3 SERIOUS WARNINGS AND PRECAUTION BOX). Tolerance, extreme psychological dependence, and severe social disability can occur. There are reports of patients who have increased the dosage to levels many times higher than recommended. The smallest possible amount of the drug should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

The possibility of tolerance and psychological dependence, particularly with excessive use, should be kept in mind. Therefore, care should be used in the selection of candidates for APO-DEXTROAMPHETAMINE therapy, in particular if patients have a previous history of drug or alcohol abuse/dependence. Should psychological dependence occur, discontinue medication. Abrupt cessation following prolonged high dosage administration may result in extreme fatigue and mental depression. Changes have also been noted on the sleep EEG. Careful supervision is therefore recommended during drug withdrawal.

Manifestations of chronic intoxication with amphetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

Driving and Operating Machinery

Amphetamines may mask extreme fatigue, which can impair the ability to perform potentially hazardous activities such as operating machinery or driving motor vehicles; patients should be cautioned accordingly.

Endocrine and Metabolism

Lactose intolerance: APO-DEXTROAMPHETAMINE (tablet) contains lactose (see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING). It should not be used in patients with the following rare hereditary problems:

- Galactose intolerance
- Lactase deficiency

Long-Term Suppression of Growth: Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or 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. Published data are inadequate to determine whether chronic use of amphetamines may cause a similar suppression of growth, however, it is anticipated that they likely have this effect as well. Therefore, growth should be monitored during treatment with stimulants, and pediatric patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

Neurologic

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 absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

Tics: Amphetamines have been reported to exacerbate motor and phonic tics in Tourette's syndrome. Therefore, careful clinical evaluation for tics in Tourette's syndrome in patients and their families should precede use of stimulant medications (see 2 CONTRAINDICATIONS).

Serotonin toxicity/Serotonin syndrome: Serotonin toxicity, also known as serotonin syndrome, is a potentially life-threatening condition and has been rarely reported with amphetamines, particularly during combined use with other serotonergic drugs. It has also been reported in association with an overdose of amphetamines (see 5 OVERDOSAGE).

Serotonin toxicity is characterized by neuromuscular excitation, autonomic stimulation (e.g., tachycardia, flushing) and altered mental state (e.g., anxiety, agitation hypomania). In accordance with the Hunter Criteria, serotonin toxicity diagnosis is likely when, in the presence of at least one serotonergic agent, one of the following is observed:

- Spontaneous clonus
- Inducible clonus or ocular clonus with agitation or diaphoresis
- Tremor and hyperreflexia
- Hypotonia and body temperature ≥38°C and ocular clonus or inducible clonus

Concomitant use with monoamine oxidase inhibitors is contraindicated (see 2 CONTRAINDICATIONS). If concomitant treatment with APO-DEXTROAMPHETAMINE and other serotonergic agents is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases (see 9.4 Drug-Drug Interactions). If serotonin toxicity is suspected, discontinuation of the serotonergic agent should be considered.

Ophthalmologic

Difficulties with accommodation and blurring of vision have been reported with stimulant treatment (see 2 CONTRAINDICATIONS).

Psychiatric

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

Bipolar Illness: Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression.

Emergence of New Psychotic or Manic Symptoms: Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents without a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant, and discontinuation of treatment may be appropriate. In a pooled analysis of multiple short- term, placebo-controlled studies, such symptoms occurred 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.

Aggression: Aggressive behavior (or hostility) is often observed in children and adolescents with ADHD. This behavior has been reported in clinical trials and the post-marketing 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.

Suicidal Behavior and Ideation: There have been post-marketing reports of suicide-related events in patients treated with ADHD drugs, including cases of ideation, attempts, and very rarely, completed suicide. The mechanism of this risk is not known. ADHD and its related co-morbidities may be associated with increased risk of suicidal ideation and/or behavior.

It is recommended for patients treated with ADHD drugs that caregivers and physicians monitor for signs of suicide-related behavior, including at dose initiation/optimization and drug discontinuation. Patients should be encouraged to report any distressing thoughts or feelings at any time to their healthcare professional. Patients with emergent suicidal ideation and behavior should be evaluated immediately. The physician should initiate appropriate treatment of the underlying psychiatric condition and consider a possible change in the ADHD treatment regimen (see 8.5 Post-Market Adverse Reactions).

Renal

Due to reduced clearance in patients with severe renal impairment (GFR 15 to < 30 mL/min/1.73 m^2), dosage reduction should be considered in these patients.

As d-amphetamines are not dialyzable, dosage reduction may be considered in patients undergoing dialysis.

Vascular

Peripheral Vasculopathy, Including Raynaud's Phenomenon: Stimulants used to treat ADHD, such as APO-DEXTROAMPHETAMINE, 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.

7.1 Special Populations

7.1.1 Pregnant Women

Safe use in pregnancy has not been established. Infants born to mothers dependent on amphetamines have an increased risk of premature delivery and low birth weight. Also, these infants may experience symptoms of withdrawal as manifested by dysphoria, agitation and significant lassitude. Reproductive studies in mammals at high multiples of the human dose

have suggested an embryotoxic and a teratogenic potential. Use of amphetamines by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child.

7.1.2 Breast-feeding

Amphetamines are excreted in human milk. Mothers taking APO-DEXTROAMPHETAMINE should be advised to refrain from nursing. Long-term neurodevelopmental effects on infants from amphetamine exposure are unknown. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

7.1.3 Pediatrics

Pediatrics (< 6 years of age): Amphetamines are not recommended for use in ADHD in children under 6 years of age, since safety and efficacy in this age group have not been established.

Long-term effects of amphetamines in children above 6 years of age have not been well established.

Chronic administration of amphetamines may be associated with growth inhibition; growth should be monitored during treatment (see 7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism).

Clinical experience suggests that in psychotic children, administration of amphetamines may exacerbate symptoms of behavior disturbance and thought disorder (see 7 WARNINGS AND PRECAUTIONS, Psychiatric).

The presence of tics or Tourette's syndrome should be ruled out before administering amphetamines to children (see 2 CONTRAINDICATIONS and 7 WARNINGS AND PRECAUTIONS, Neurologic).

7.1.4 Geriatrics

Geriatrics (> 65 years of age): APO-DEXTROAMPHETAMINE should be used with caution in geriatric patients, taking into consideration the greater frequency of decreased hepatic or renal function, of cardiovascular disease, and of concomitant disease or other drug therapy, which may necessitate dose adjustments and additional or more frequent monitoring.

8 ADVERSE REACTIONS

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction

information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Cardiac Disorders: palpitations, tachycardia, elevation of blood pressure. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.

Gastrointestinal Disorders: dryness of the mouth, unpleasant taste, loss of appetite, diarrhea, constipation, other gastrointestinal disturbances, anorexia and weight loss

Nervous System Disorders: overstimulation, restlessness, dizziness, euphoria or dysphoria, dyskinesia, headache, insomnia, exacerbation of motor and phonic tics, Tourette's syndrome, tremor; rarely, psychotic episodes at recommended doses

Psychiatric Disorders: changes in libido

Reproductive System and Breast Disorders: impotence

Skin and Subcutaneous Tissue Disorders: urticaria

8.5 Post-Market Adverse Reactions

The following unexpected serious adverse events have been reported in users of APO-DEXTROAMPHETAMINE in the post-marketing period. These adverse events are compiled from spontaneous reports and are listed regardless of frequency and whether or not causal relationship with APO-DEXTROAMPHETAMINE has been established.

Cardiac Disorders: atrial fibrillation, blood pressure abnormal, heart rate irregular, hypotension, myocardial infarction, sudden/cardiac death, thrombosis

Endocrine Disorders: blood sugar fluctuation, blood glucose increased, hypoglycemia

Gastrointestinal Disorders: tooth disorder, intestinal ischemia

General Disorders and Administration Site Conditions: condition aggravated, chest pain, drug ineffective, feeling abnormal, general physical health deterioration

Immune System Disorders: anaphylactic reaction

Investigations: prostatic specific antigen increased, sperm concentration zero

Musculoskeletal and Connective Tissue Disorders: muscle spasm

Neoplasms Benign, Malignant and Unspecified (incl cysts and polyps): pancreatic neoplasm, prostate cancer

Nervous System Disorders: cerebrovascular accident, fall, hemorrhagic stroke, subdural hematoma

Psychiatric Disorders: screaming

Suicidal Behavior and Ideation: There have been post-marketing reports of suicide-related events, including completed suicide, suicide attempt, and suicidal ideation in patients treated with ADHD drugs. In some of these reports, comorbid conditions may have contributed to the event (see 7 WARNINGS AND PRECAUTIONS, Psychiatric, Suicidal Behavior and Ideation).

Renal and Urinary Disorders: bladder disorder, incontinence, urinary incontinence

Skin and Subcutaneous Tissue Disorders: livedo reticularis, skin discoloration

Vascular Disorders: epistaxis, contusion

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions

Serious Drug Interactions
• Concomitant use with monoamine oxidase inhibitors (MAOIs) (see 2 CONTRAINDICATIONS and 9.4 Drug-Drug Interactions)

9.2 Drug Interactions Overview

Caution should be exercised when co-prescribing amphetamines and other drugs since clinically significant interactions with a number of drugs have been reported. In some instances, potentiation of CNS and cardiac effects could be life-threatening. Dosages should be closely monitored.

Amphetamines and amphetamine derivatives are known to be metabolized, to some degree, by cytochrome P450 2D6 (CYP2D6) and display minor inhibition of CYP2D6 metabolism. The potential for a pharmacokinetic interaction exists with the co-administration of CYP2D6 inhibitors (e.g., terbinafine, cimetidine, quinidine, bupropion, paroxetine and fluoxetine) which may result in an increased exposure to APO-DEXTROAMPHETAMINE (see also 9.4 Drug-Drug Interactions, Serotonergic Drugs below).

9.4 Drug-Drug Interactions

The drugs listed below are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Monoamine Oxidase Inhibitors (MAOIs): APO-DEXTROAMPHETAMINE is contraindicated during or within 14 days following the administration of MAOIs. MAOIs and amphetamines, when co-administered, can increase the release of norepinephrine and other monoamines. This can cause headaches and other signs of hypertensive crisis. A variety of neurological toxic effects and malignant hyperpyrexia can occur, sometimes with fatal results (see 2 CONTRAINDICATIONS).

Serotonergic drugs: Due to the risk of serotonin toxicity, APO-DEXTROAMPHETAMINE should be used with caution in combination with serotonergic and/or neuroleptic drugs, e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors (SNRIs), triptans, lithium, St. John's Wort, tryptophan (see 7 WARNINGS AND PRECAUTIONS, Neurologic, Serotonin toxicity/Serotonin syndrome; see also Tricyclic antidepressants and Opioid analgesics below).

Tricyclic antidepressants: Cardiovascular effects of amphetamines can be potentiated by tricyclic antidepressants.

Tricyclic antidepressants may enhance the serotonergic effects of amphetamines. This may, on rare occasions, result in serotonergic toxicity. Therefore, the combination of amphetamines with tricyclic antidepressants should be used with caution (see 7 WARNINGS AND PRECAUTIONS, Neurologic, Serotonin toxicity/Serotonin syndrome).

Opioid analgesics: Amphetamines may enhance the analgesic effect of opioid analgesics such as morphine and meperidine. The analgesic response to opioid analgesics should be monitored in patients treated with amphetamines. A lower opioid dose may be required to provide appropriate analgesia.

Opioid analgesics may enhance the serotonergic effects of amphetamines. This may, on rare occasions, result in serotonergic toxicity. Therefore, the combination of amphetamines with opioid analgesics should be used with caution (see 7 WARNINGS AND PRECAUTIONS, Neurologic, Serotonin toxicity/Serotonin syndrome).

Agents that alter gastrointestinal pH and impact the absorption of amphetamine

- Gastrointestinal acidifying agents (e.g., glutamic acid hydrochloride and ascorbic acid) may lower the absorption of amphetamines.
- Gastrointestinal alkalinizing agents (e.g., proton pump inhibitors and other antiacids) may increase the absorption of amphetamines.

Agents that alter urinary pH and impact the urinary excretion and half-life of amphetamine

- Agents (e.g., ammonium chloride and sodium acid phosphate) that acidify urine increase urinary excretion and decrease the half-life of amphetamine.
- Agents (e.g., sodium bicarbonate, acetazolamide and thiazides) that alkalinize urine decrease urinary excretion and extend the half-life of amphetamine.

Agents whose effects may be reduced by amphetamines

- **Antihypertensives:** Amphetamines may decrease the effectiveness of guanethidine, clonidine, adrenergic blockers or other antihypertensives.

Agents whose effects may be potentiated by amphetamines

- **Sympathomimetic drugs:** Because of possible additive cardiovascular effects, APO-DEXTROAMPHETAMINE should be used with caution in patients being treated with drugs with similar pharmacological actions (e.g., other sympathomimetic drugs such as central nervous system stimulants, decongestants, and norepinephrine) (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular).

Agents that may reduce the effects of amphetamines

- **Chlorpromazine:** Chlorpromazine blocks dopamine and norepinephrine receptors, thus inhibiting the central stimulant effects of amphetamines, and can be used to treat amphetamine poisoning.
- **Haloperidol:** Haloperidol blocks dopamine receptors, thus inhibiting the central stimulant effects of amphetamines.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

APO-DEXTROAMPHETAMINE should be used with caution in combination with St. John's Wort (see 9.4 Drug-Drug Interactions).

9.7 Drug-Laboratory Test Interactions

Amphetamines can cause a significant elevation in plasma corticosteroid levels particularly in the evening, and thus may affect urinary steroid determinations.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Dextroamphetamine (dexamphetamine, d-amphetamine) sulfate is a sympathomimetic agent. Like other amphetamines, dextroamphetamine substantially blocks the reuptake of norepinephrine and dopamine into the presynaptic neuron and increases the release of these monoamines into the extraneuronal space. It has actions qualitatively similar to those of amphetamine sulfate but is approximately twice as potent. It has a marked stimulant effect on the central nervous system, particularly the cerebral cortex and the respiratory and vasomotor centers.

Dextroamphetamine sulfate causes a lessening of fatigue, an increase in mental activity, an elevation of mood, and a general feeling of well-being. However, its indiscriminate use in attempts to increase capacity for work or to overcome fatigue is undesirable. At high doses, it produces a euphoria, which upon abrupt withdrawal of the drug reverts to severe depression and lethargy.

The mechanism by which amphetamines produce mental and behavioral effects in children is not conclusively established.

10.3 Pharmacokinetics

Metabolism: Amphetamines and amphetamine derivatives are known to be metabolized, to some degree, by cytochrome P450 2D6 (CYP2D6) and display minor inhibition of CYP2D6 metabolism. As CYP2D6 is genetically polymorphic, population variations in amphetamine metabolism are a possibility.

11 STORAGE, STABILITY AND DISPOSAL

Keep out of the reach and sight of children. APO-DEXTROAMPHETAMINE tablets should be stored at room temperature 15°C - 30°C in a well closed container.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

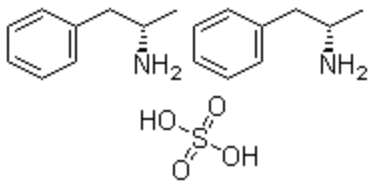
Drug Substance

Proper name: dextroamphetamine sulfate

Chemical name: (+)-α-Methylphenethylamine hemisulfate salt

Molecular formula and molecular mass: $2(C_9H_{13}N)\cdot H_2SO_4$; 368.49 g/mol

Structural formula:



14 CLINICAL TRIALS

14.2 Comparative Bioavailability Studies

A randomized, two-way, single dose, crossover comparative oral bioavailability study of APO-DEXTROAMPHETAMINE 5 mg tablet (Apotex Inc.) and DEXEDRINE® 5 mg tablet (Paladin Labs Inc.). was conducted in healthy, adult, male and female subjects under fasting conditions. Comparative bioavailability data from the 24 subjects that were included in the statistical analysis are presented in the following table.

SUMMARY TABLE OF THE COMPARATIVE BIOAVAILABILITY DATA

Dextroamphetamine (1 x 5 mg) Geometric Mean Arithmetic Mean (CV%)				
Parameter	**Test[1]**	**Reference[2]**	**% Ratio of Geometric Means**	**90% Confidence Interval**
AUC_T (pg·h/mL)	222150.70 226712.23 (20.93)	217572.78 221149.30 (18.05)	102.1	98.2 - 106.2
AUC_I	229194.10	224203.31	102.2	98.3 - 106.4

Dextroamphetamine (1 x 5 mg) Geometric Mean Arithmetic Mean (CV%)				
Parameter	**Test[1]**	**Reference[2]**	**% Ratio of Geometric Means**	**90% Confidence Interval**
(pg·h/mL)	234386.98 (22.09)	228222.14 (18.94)		
C_{MAX} (pg/mL)	13081.05 13259.09 (16.91)	13133.22 13338.64 (18.09)	99.60	95.7 - 103.7
T_{MAX}[3] (h)	2.00 (0.75-3.02)	2.50 (1.00-5.00)		
$T_{1/2}$[4] (h)	11.36 (22.44)	11.21 (18.25)		

[1] APO-DEXTROAMPHETAMINE (dextroamphetamine as dextroamphetamine sulfate) tablets, 5 mg (Apotex Inc.)

[2] DEXEDRINE® (dextroamphetamine as dextroamphetamine sulfate) tablets, 5 mg (Paladin Labs Inc.), purchased in Canada.

[3] Expressed as the median (range) only.

[4] Expressed as the arithmetic mean (CV %) only.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

Reproductive and Developmental Toxicology: A number of studies in rodents indicate that prenatal or early postnatal exposure to amphetamine (*d*- or *d,l*-) at doses similar to those used clinically can result in long-term neurochemical and behavioral alterations. Reported behavioral effects include learning and memory deficits, altered locomotor activity, and changes in sexual function.

17 SUPPORTING PRODUCT MONOGRAPHS

1. DEXEDRINE® (Dextroamphetamine sulfate tablets, 5 mg) and DEXEDRINE® SPANSULE® (Dextroamphetamine sulfate sustained-release capsules, 10 mg and 15 mg), submission control 289181, Product Monograph, Endo Operations Ltd., (NOV 06, 2024)

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

APO-DEXTROAMPHETAMINE

Dextroamphetamine Sulfate Tablets

Read this carefully before you start taking **APO-DEXTROAMPHETAMINE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **APO-DEXTROAMPHETAMINE**.

Serious Warnings and Precautions

Drug dependence: Like other stimulants, APO-DEXTROAMPHETAMINE have the potential to be abused. This can lead to you becoming dependent on APO-DEXTROAMPHETAMINE or feeling like you need to take more of it over time.

Misusing APO-DEXTROAMPHETAMINE may cause serious heart problems and even sudden death.

What is APO-DEXTROAMPHETAMINE used for?

APO-DEXTROAMPHETAMINE is used, along with other therapies, in children 6 years of age or older, adolescents and adults to treat:

- narcolepsy (a type of sleep disorder). This disorder causes excessive sleepiness during the day and frequent and uncontrollable episodes of falling asleep.
- Attention Deficit Hyperactivity Disorder (ADHD). Treatment with APO-DEXTROAMPHETAMINE should be combined with other measures such as psychological counselling, educational and social measures, as part of a total treatment program.

APO-DEXTROAMPHETAMINE is not recommended for use in children under 6 years of age.

How does APO-DEXTROAMPHETAMINE work?

APO-DEXTROAMPHETAMINE belong to a group of medicines called sympathomimetics. APO-DEXTROAMPHETAMINE work by raising the levels of chemicals in the brain called dopamine and norepinephrine. This helps to:

- increase alertness and wakefulness in patients with narcolepsy.
- increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.

What are the ingredients in APO-DEXTROAMPHETAMINE?

Medicinal ingredients: Dextroamphetamine sulfate

Non-medicinal ingredients: Anhydrous lactose, colloidal silicon dioxide, crospovidone, D&C yellow # 10 aluminum lake 14-18%, magnesium stearate, microcrystalline cellulose and sunset yellow aluminum lake 40%

APO-DEXTROAMPHETAMINE comes in the following dosage forms:

APO-DEXTROAMPHETAMINE (tablets): 5 mg

Do not use APO-DEXTROAMPHETAMINE if you/your child:

- are allergic to dextroamphetamine sulfate or any of the other ingredients in APO-DEXTROAMPHETAMINE.
- are sensitive to, allergic to, or had a reaction to other stimulant medicines.
- have symptoms of heart disease.
- have moderate to severe high blood pressure.
- have advanced arteriosclerosis (hardened arteries).
- have hyperthyroidism (an overactive thyroid gland).
- have glaucoma (an eye disease with increased pressure in the eye).
- have a condition that causes you to feel anxious, tense, or agitated.
- have, or have a family history of, motor tics (hard to control, repeat twitching of any parts of the body), verbal tics (hard to control, repeating of sounds or words) or Tourette's syndrome.
- are taking or have recently taken (in the past 14 days) any medications from the group of medicines called monoamine oxidase inhibitors (MAOIs).
- have a history of drug abuse.
- have a condition called pheochromocytoma (a rare tumour that usually grows in the adrenal glands, above your kidneys).

To help avoid side effects and ensure proper use, talk to your or your child's healthcare professional before APO-DEXTROAMPHETAMINE is taken. Talk about any health conditions or problems, including if you/your child:

- take other stimulant medications.
- have structural heart abnormalities, cardiomyopathy, serious heart rhythm abnormalities or other serious heart problems.
- have mild high blood pressure.
- have a family history of sudden death or death related to heart problems.
- have a family history of an irregular heartbeat.
- have or have a family history of mental health problems, including:

- psychosis
- mania
- bipolar illness
- aggression
- depression
- suicide

- have a history of seizures (convulsions, epilepsy) or have had abnormal brain wave tests (electroencephalogram; EEGs).
- do strenuous exercise or activities.
- have severe kidney problems, including if you are undergoing dialysis.
- have the following rare hereditary conditions:
  − Galactose intolerance
  − Lactase deficiency
  APO-DEXTROAMPHETAMINE contains lactose.
- have a history of drug dependence or alcoholism.
- are pregnant, think you might be pregnant or planning to become pregnant.
- are breast feeding or planning to breastfeed.

Other warnings you should know about:

Dependence and tolerance: Like other stimulants, APO-DEXTROAMPHETAMINE has the potential to be abused. This can lead to dependence, tolerance and severe social disorders. If you have a history of drug or alcohol abuse, talk to your healthcare professional.

During treatment, do not change your dose or stop taking APO-DEXTROAMPHETAMINE without first talking to your healthcare professional. If you find that you are craving more APO-DEXTROAMPHETAMINE than you are supposed to take, tell your healthcare professional **right away**.

Careful supervision from your healthcare professional is needed when you stop taking APO-DEXTROAMPHETAMINE. If you suddenly stop your treatment, especially if you have been taking high doses of APO-DEXTROAMPHETAMINE for a long time, you may experience:

- extreme fatigue.
- depression.
- changes in sleep patterns.

Driving and using machines: APO-DEXTROAMPHETAMINE may hide extreme fatigue and can affect your ability to drive and use tools or machinery. You should not drive or use tools or machinery until you know how you respond to APO-DEXTROAMPHETAMINE.

Pregnancy and breastfeeding:

- Taking APO-DEXTROAMPHETAMINE during pregnancy may cause harm to your unborn baby. If APO-DEXTROAMPHETAMINE is required during pregnancy, the risks to the unborn baby will be weighed against the benefits to the mother. Your healthcare professional will discuss these risks with you. If you discover that you are pregnant while taking APO-DEXTROAMPHETAMINE, tell your healthcare professional **right away**.
- APO-DEXTROAMPHETAMINE can pass through your breast milk and may harm your baby. You should not breastfeed while you are taking APO-DEXTROAMPHETAMINE. You should consult with your healthcare professional to determine if you should stop breastfeeding or discontinue APO-DEXTROAMPHETAMINE.

The following have been reported with use of APO-DEXTROAMPHETAMINE and other medicines used to treat ADHD:

Growth in children: Slower growth (weight and/or height) has been reported with long-term use of stimulant medicines in children. Your child's healthcare professional will carefully monitor their height and weight. If your child is not growing or gaining weight as expected, your child's healthcare professional may stop their treatment.

Heart-related problems: The following heart related problems have been reported in people taking stimulant medicines, like APO-DEXTROAMPHETAMINE:

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

Sudden death has been reported in association with stimulant medicines for ADHD treatment in children with structural heart abnormalities. APO-DEXTROAMPHETAMINE generally should not be used in children, adolescents or adults with known structural heart abnormalities.

Tell your healthcare professional if you/your child have any heart problems, heart defects, high blood pressure, or a family history of these problems. Your healthcare professional will check:

- you/your child for heart problems before starting APO-DEXTROAMPHETAMINE.
- your/your child blood pressure and heart rate regularly during treatment with APO-DEXTROAMPHETAMINE.

Seek immediate medical help if you/your child have any signs of heart problems such as chest pain, shortness of breath, or fainting while taking APO-DEXTROAMPHETAMINE.

Mental health problems: The following mental health problems have been reported in people taking stimulant medicines, like APO-DEXTROAMPHETAMINE:

- new or worse thoughts or feelings related to suicide (thinking about or feeling like killing

yourself) and suicide actions (suicide attempt, suicidal ideation and completed suicide).
- new or worse symptoms of bipolar disorder (extreme mood swings, with periods of impulsiveness or unusual excitement, switching between periods of sadness).
- new or worse aggressive behaviour or hostility.
- new psychotic symptoms (such as hearing voices, believing things that are not true, being suspicious).

These new or worse mental health symptoms may be more likely to occur if you/your child have mental health conditions that you may or may not know about. Tell your healthcare professional about any mental health problems you or your child have, or about any personal or family history of suicide, bipolar illness, or depression.

A small number of patients taking stimulant medicines may experience unusual feelings of agitation, hostility or anxiety, or have impulsive or disturbing thoughts such as thoughts of suicide, self-harm or harm to others. Those suicidal thoughts or behaviors may occur at any time during treatment, particularly at the start or during dose changes, and also after stopping APO-DEXTROAMPHETAMINE.

Should this happen to you, or to those in your care if you are a caregiver or guardian, consult your healthcare professional immediately. Close observation by a healthcare professional is necessary in this situation.

Raynaud's phenomenon: Stimulant medicines, such as APO-DEXTROAMPHETAMINE, are associated with Raynaud's phenomenon. During treatment with APO-DEXTROAMPHETAMINE, your healthcare professional may check for problems with the circulation in your fingers and toes, including numbness, feeling cold or pain.

Serotonin toxicity (also known as Serotonin Syndrome): Serotonin toxicity is a rare but potentially life-threatening condition. It can cause serious changes in how your brain, muscles and digestive system work. You may develop serotonin toxicity if you take APO-DEXTROAMPHETAMINE with certain anti-depressants or migraine medications. Serotonin toxicity symptoms include:

- fever, sweating, shivering, diarrhea, nausea, vomiting;
- muscle shakes, jerks, twitches or stiffness, overactive reflexes, loss of coordination;
- fast heartbeat, changes in blood pressure;
- confusion, agitation, restlessness, hallucinations, mood changes, unconsciousness, and coma.

Tell your healthcare professional about all the medicines you/your child take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Serious Drug Interactions

Do not take APO-DEXTROAMPHETAMINE if you:

- are taking or have recently taken (in the last 14 days) any MAOIs such as phenelzine, tranylcypromine, or moclobemide as you may have serious side effects.

The following may also interact with APO-DEXTROAMPHETAMINE:

- medicines that make your urine or digestive contents more acidic (e.g., glutamic acid hydrochloride, ascorbic acid (vitamin C), ammonium chloride, sodium acid phosphate).
- medicines that make your urine or digestive contents more alkaline (e.g., sodium bicarbonate, antacids, acetazolamide, thiazides, proton pump inhibitors, cimetidine).
- medicines used to treat high blood pressure (e.g., guanethidine, clonidine, beta blockers) or other medicines that can affect blood pressure (e.g., norepinephrine).
- other stimulant medications.
- medicines used to treat depression, such as bupropion, tricyclic antidepressants (e.g., desipramine), selective serotonin reuptake inhibitors (SSRIs) (e.g., paroxetine, fluoxetine), serotonin and noradrenaline reuptake inhibitors (SNRIs), and tryptophan (an essential amino acid).
- medicines used to treat migraines (e.g., sumatriptan, rizatriptan, zolmitriptan).
- medicines used to treat psychiatric disorders, such as schizophrenia (e.g., chlorpromazine, haloperidol) and bipolar disorder (e.g., lithium carbonate).
- opioid medicines, used to relieve pain (e.g., fentanyl, tramadol, tapentadol, meperidine and methadone).
- terbinafine, used to treat fungal infections.
- quinidine, used to treat an irregular heartbeat.
- cold and allergy medicines.
- St. John's Wort, a herbal remedy.

While on APO-DEXTROAMPHETAMINE, do not start taking a new medicine or herbal remedy before checking with your healthcare professional.

How to take APO-DEXTROAMPHETAMINE:

- **If you are taking APO-DEXTROAMPHETAMINE** (tablets), take your first dose when you wake up in the morning. If more doses are prescribed during the day, take them as directed by your healthcare professional, usually 4 to 6 hours apart.
- Avoid taking APO-DEXTROAMPHETAMINE late in the evening as they can cause insomnia.

Usual dose:

Take APO-DEXTROAMPHETAMINE exactly as prescribed by your/your child's healthcare professional. Do NOT change your dose or stop taking APO-DEXTROAMPHETAMINE without first discussing with your/your child's healthcare professional.

Your/your child's healthcare professional may gradually adjust the dose until it is right for you/your child. Follow their instructions carefully.

- **To treat narcolepsy**

  - Children (6 to 12 years of age): the usual starting dose is 5 mg per day.
  - Adolescents (12 to 17 years of age) and adults: the usual starting dose is 10 mg per day.

- **To treat ADHD**

  - Children 6 years of age or older, adolescents and adults: The usual starting dose is 5 mg once a day or twice a day.

From time to time, your/your child's healthcare professional may interrupt your/your child's treatment to check your/your child's ADHD symptoms while you/your child are not taking the medicine.

Overdose:

If you think you, or a person you are caring for, have taken too much APO-DEXTROAMPHETAMINE, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you missed a dose, take it as soon as you remember. Then continue with your next scheduled dose as usual. Do not take a late evening dose. Do not take a double dose to make up for a forgotten dose.

What are possible side effects from using APO-DEXTROAMPHETAMINE?

These are not all the possible side effects you may have when taking APO-DEXTROAMPHETAMINE. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- dry mouth, unpleasant taste
- loss of appetite, weight loss
- diarrhea, constipation
- itchy skin, lace-like pattern of darkened skin, skin discolouration
- dizziness
- headache
- difficulty falling or staying asleep
- problems with your teeth
- bladder problems
- muscle spasm, shaking (tremors), uncontrolled and involuntary movements (dyskinesia)
- screaming
- feeling irritable, restless, uneasy or overexcited
- changes in sex drive, inability to get or keep an erection
- nosebleeds
- bruising

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Anxiety	✓		
New tics: hard to control motion tics (repeat twitching of any parts of the body) or verbal tics (repeating of sounds or words)		✓	
Palpitations (fast-beating, fluttering or pounding heart)		✓	
Slowing of growth (height and weight) in children		✓	
UNCOMMON			
Allergic Reaction: difficulty swallowing or breathing, wheezing, feeling sick to your stomach and throwing up, swelling of the face, lips, tongue or throat, hives or rash			✓
Aggressive Behaviour or Hostility		✓	

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Depression (sad mood that won't go away): difficulty sleeping or sleeping too much, changes in appetite or weight, feelings of worthlessness, guilt, regret, helplessness or hopelessness, withdrawal from social situations, family, gatherings and activities with friends, reduced libido (sex drive). If you have a history of depression, your depression may become worse.		✓	
New or worsening mental health problems: paranoia, delusions, hallucinations (seeing, feeling or hearing things that are not there), mania (feeling unusually excited, over-active, or inhibited)		✓	
Vision problems: changes in vision or blurry vision		✓	
RARE			
Serotonin Toxicity (also known as Serotonin Syndrome): feeling of agitation or restlessness, flushing, muscle twitching, involuntary eye movements, heavy sweating, high body temperature (above 38°C), rigid muscles			✓
UNKNOWN FREQUENCY			
Cardiomyopathy (signs of heart muscle disease): breathlessness or swelling of the legs		✓	
Cerebrovascular disorders (problems with the blood vessels in the brain, stroke): severe headaches, weakness or paralysis of any body part, or problems with coordination, vision, speaking, finding words or with your memory			✓
Hypertension (high blood pressure): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or fast or uneven heartbeat		✓	
Intestinal ischemia (blood flow to your intestines decreases due to a narrowed or blocked blood vessel): sudden or worsening abdominal pain (usually severe), urgent need to have a bowel movement, frequent, forceful bowel movements, nausea, vomiting, diarrhea, blood in your stool, confusion in older adults			✓

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Myocardial infarction (heart attack): pressure or squeezing pain in the chest, jaw, left arm, between the shoulder blades or upper abdomen, shortness of breath, dizziness, fatigue, light-headedness, clammy skin, sweating, indigestion, anxiety, feeling faint and possible irregular heartbeat			✓
Raynaud's Phenomenon (episodes of reduced blood flow): cold feeling in fingers and toes (and sometimes nose, lips and ears), prickly or stinging feeling, change in skin colour to white then blue		✓	
Seizures (fits): uncontrollable shaking with or without loss of consciousness			✓
Suicidal Behaviour: thoughts or actions about hurting or killing yourself			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or

- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- APO-DEXTROAMPHETAMINE tablets should be stored at room temperature 15°C - 30°C in a well closed container.
- Do not take your medicine after the expiry date shown on the bottle.
- Keep this medicine out of the reach and sight of children.

If you want more information about APO-DEXTROAMPHETAMINE:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (http://www.apotex.ca/products), or by calling 1-800-667-4708.

This leaflet was prepared by Apotex Inc., Toronto, Ontario, M9L 1T9.

Last Revised: OCT 29, 2026