HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ADZENYS ER safely and effectively. See full prescribing information for ADZENYS ER.

ADZENYS ER (amphetamine) extended-release oral suspension, CII
Initial U.S. Approval: 1960

WARNING: ABUSE AND DEPENDENCE
See full prescribing information for complete boxed warning.
- **CNS stimulants, including ADZENYS ER, other amphetamine-containing products, and methylphenidate, have a high potential for abuse and dependence. (5.1, 9.3)**
- **Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy (9.2, 9.3)**

INDICATIONS AND USAGE

ADZENYS ER is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older. (1)

DOSAGE AND ADMINISTRATION

- Shake bottle before administering the dose. (2.2)
- May be taken with or without food. (2.2)
- Do not mix with food or other liquids before consuming. (2.2)
- Pediatric patients (ages 6 to 17 years): Starting dose is 6.3 mg (5 mL) once daily in the morning. Maximum dose is 18.8 mg (15 mL) for patients 6 to 12 years, and 12.5 mg (10 mL) once daily for patients 13 to 17 years. (2.3)
- Adults: 12.5 mg (10 mL) once daily in the morning. (2.4)
- To avoid substitution errors and overdosage, do not substitute for other amphetamine products on a milligram-per-milligram basis because of different amphetamine salt compositions and differing pharmacokinetic profiles. (2.5, 5.8)

DOSAGE FORMS AND STRENGTHS

Extended-release oral suspension containing 1.25 mg amphetamine per mL. (3)

CONTRAINDICATIONS

- Known hypersensitivity to amphetamine products or other ingredients in ADZENYS ER. (4)
- Use of monoamine oxidase inhibitor (MAOI) or within 14 days of the last MAOI dose. (4)

WARNINGS AND PRECAUTIONS

- *Serious Cardiovascular Reactions:* Sudden death has been reported in association with CNS stimulant treatment at recommended doses in pediatric patients with structural cardiac abnormalities or other serious heart problems. In adults, sudden death, stroke, and myocardial infarction have been reported. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, or coronary artery disease. (5.2)
- *Blood Pressure and Heart Rate Increases:* Monitor blood pressure and pulse. Consider benefits and risks before use in patients for whom blood pressure increases may be problematic. (5.3)
- *Psychiatric Adverse Reactions:* May cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to stimulant use. (5.4)
- *Long-Term Suppression of Growth:* Monitor height and weight in pediatric patients during treatment. (5.5)
- *Peripheral Vasculopathy, including Raynaud's phenomenon*: Stimulants used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Careful observation for digital changes is necessary during treatment with ADHD stimulants. (5.6)
- *Serotonin Syndrome:* Increased risk when co-administered with serotonergic agents (e.g., SSRIs, SNRIs, triptans), but also during overdosage situations. If it occurs, discontinue ADZENYS ER and initiate supportive treatment. (5.7)

ADVERSE REACTIONS

- Pediatric patients ages 6 to 12 years: 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)
- Pediatric patients ages 13 to 17 years: 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, nausea, anxiety, agitation, dizziness, tachycardia, diarrhea, asthenia, and urinary tract infections. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Neos Therapeutics, Inc. at 1-888-219-1789 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Acidifying and Alkalinizing Agents: Agents that alter urinary pH can alter blood levels of amphetamine. Acidifying agents can decrease amphetamine blood levels, while alkalinizing agents can increase amphetamine blood levels. Adjust ADZENYS ER dosage accordingly. (7.1)

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm. (8.1)
- Lactation: Breastfeeding not recommended. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 9/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE AND DEPENDENCE

CNS stimulants, including ADZENYS ER, 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 Warnings and Precautions (5.1) and Drug Abuse and Dependence (9.2, 9.3)]*.

1 INDICATIONS AND USAGE

ADZENYS ER is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older *[see Clinical Studies (14)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Pre-Treatment Screening

Prior to treating patients with ADZENYS ER, assess for the presence of cardiac disease (i.e., perform a careful history, family history of sudden death or ventricular arrhythmia, and physical exam) *[see Warnings and Precautions (5.2)]*.

Assess the risk of abuse prior to prescribing, and monitor for signs of abuse and dependence while on therapy. Maintain careful prescription records, educate patients about abuse, monitor for signs of abuse and overdose, and periodically re-evaluate the need for ADZENYS ER use *[see Warnings and Precautions (5.1), and Drug Abuse and Dependence (9)]*.

2.2 Dosing Considerations for All Patients

Administer ADZENYS ER orally once daily in the morning with or without food. The dose should be individualized according to the therapeutic needs and response of the patient.

Shake the bottle of ADZENYS ER before administering the dose. Do not add ADZENYS ER to food or mix ADZENYS ER with other liquids before consuming.

2.3 Pediatric Patients

The recommended starting dose for patients 6 to 17 years of age is 6.3 mg (5 mL) once daily in the morning. Increase in increments of 3.1 mg (2.5 mL) or 6.3 mg (5 mL) at weekly intervals. The maximum dose is 18.8 mg (15 mL) daily for patients 6 to 12 years, and 12.5 mg (10 mL) daily for patients 13 to 17 years.

2.4 Adults

The recommended dose of ADZENYS ER for adults is 12.5 mg (10 mL) daily.

2.5 Switching from Other Amphetamine Products

Patients taking ADDERALL XR may be switched to ADZENYS ER at the equivalent dose taken once daily *[see Clinical Pharmacology (12)]*. Refer to Table 1 for equivalent doses of ADZENYS ER and ADDERALL XR. ADDERALL XR (dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine aspartate monohydrate, and amphetamine sulfate extended-release capsules) is also referred to as mixed salts of a single-entity amphetamine product extended-release capsules (MAS ER).

Table 1: Equivalent Doses of ADZENYS ER and ADDERALL XR (Mixed Salts of a Single-Entity Amphetamine Product) Extended-Release Capsules

ADZENYS ER Amphetamine extended-release oral suspension	3.1 mg (2.5 mL)	6.3 mg (5 mL)	9.4 mg (7.5 mL)	12.5 mg (10 mL)	15.7 mg (12.5 mL)	18.8 mg (15 mL)
ADDERALL XR Mixed salts of a single-entity amphetamine product extended-release capsules (MAS ER)	5 mg	10 mg	15 mg	20 mg	25 mg	30 mg

If switching from any other amphetamine products, discontinue that treatment, and titrate with ADZENYS ER using the titration schedule *[see Dosage and Administration (2.3, 2.4)]*.

Do not substitute for other amphetamine products on a milligram-per-milligram basis because of different amphetamine salt compositions and differing pharmacokinetic profiles *[see Warnings and Precautions (5.8)]*.

2.6 Dosage Modifications Due to Drug Interactions

Agents that alter urinary pH can impact urinary excretion and alter blood levels of amphetamine. Acidifying agents (e.g., ascorbic acid) decrease blood levels, while alkalinizing agents (e.g., sodium bicarbonate) increase blood levels. Adjust ADZENYS ER dosage accordingly *[see Drug Interactions (7.1)]*.

3 DOSAGE FORMS AND STRENGTHS

Extended-release oral suspension contains 1.25 mg amphetamine per mL.

4 CONTRAINDICATIONS

ADZENYS ER is contraindicated:

- In patients known to be hypersensitive to amphetamine, or other components of ADZENYS ER. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with other amphetamine products *[see Adverse Reactions (6.2)]*.
- In patients taking monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOIs (including MAOIs such as linezolid or intravenous methylene blue), because of an increased risk of hypertensive crisis *[see Warnings and Precautions (5.7) Drug Interactions (7.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Potential for Abuse or Dependence

CNS stimulants, including ADZENYS ER, 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, stroke, and myocardial infarction have been reported in adults with CNS stimulant treatment at recommended doses. Sudden death has been reported in children and adolescents with structural cardiac abnormalities and other serious heart problems taking CNS stimulants at recommended doses for ADHD. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease, and other serious heart problems. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during ADZENYS ER treatment.

5.3 Blood Pressure and Heart Rate Increases

CNS stimulants cause an increase in blood pressure (mean increase about 2-4 mm Hg) and heart rate (mean increase about 3-6 bpm). Monitor all patients for potential tachycardia and hypertension.

5.4 Psychiatric Adverse Events

Exacerbation of Pre-Existing Psychosis

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

Induction of a Manic Episode in Patients with Bipolar Illness

CNS stimulants may induce a mixed or manic episode in patients with bipolar disorder. Prior to initiating treatment, screen patients for risk factors for developing a manic episode (e.g., comorbid or has a history of depressive symptoms or a family history of suicide, bipolar disorder, and depression).

New Psychotic or Manic Symptoms

DOCKET ALARM

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