1.25
21.125
1.25
15
040-T-00776
Rx Only
ADZENYS XR-ODT
040-T-00776
Rx Only
ADZENYS XR-ODT

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

ADZENYS XR-ODT (amphetamine) extended-release orally disintegrating tablets, CII
Initial U.S. Approval: 1960

WARNING: ABUSE, MISUSE AND ADDICTION
See full prescribing information for complete boxed warning.

ADZENYS XR-ODT has a high potential for abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Misuse and abuse of CNS stimulants, including ADZENYS XR-ODT, can result in overdose and death (5.1, 9.2, 10):
- **Before prescribing ADZENYS XR-ODT, assess each patient's risk for abuse, misuse, and addiction.**
- **Educate patients and their families about these risks, proper storage of the drug, and proper disposal of any unused drug.**
- **Throughout treatment, reassess each patient's risk and frequently monitor for signs and symptoms of abuse, misuse, and addiction.**

---------- RECENT MAJOR CHANGES ----------

Indications and Usage (1)	09/2025
Warnings and Precautions (5.5)	09/2025

---------- INDICATIONS AND USAGE ----------

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

Limitations of Use
The use of ADZENYS XR-ODT is not recommended in pediatric patients younger than 6 years of age because they had higher plasma exposure and a higher incidence of adverse reactions (e.g., weight loss) than patients 6 years and older at the same dosage. (5.5, 8.4)

---------- DOSAGE AND ADMINISTRATION ----------

- May be taken with or without food. Allow tablet to disintegrate in saliva then swallow. (2.2)
- Pediatric patients (ages 6 to 17 years): Starting dose is 6.3 mg once daily in the morning. Maximum dose is 18.8 mg once daily for patients 6 to 12 years, and 12.5 mg once daily for patients 13 to 17 years. (2.3)
- Adults: 12.5 mg 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 base compositions and differing pharmacokinetic profiles. (2.5, 5.7)

---------- DOSAGE FORMS AND STRENGTHS ----------

Extended-release orally disintegrating tablets: 3.1 mg, 6.3 mg, 9.4 mg, 12.5 mg, 15.7 mg, 18.8 mg (3)

---------- CONTRAINDICATIONS ----------

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

---------- WARNINGS AND PRECAUTIONS ----------

- *Risks to Patients with Serious Cardiac Disease:* Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease, or other serious cardiac disease. (5.2)
- *Increased Blood Pressure and Heart Rate:* Monitor blood pressure and pulse. (5.3)
- *Psychiatric Adverse Reactions:* Prior to initiating ADZENYS XR-ODT, screen patients for risk factors for developing a manic episode. If new psychotic or manic symptoms occur, consider discontinuing ADZENYS XR-ODT. (5.4)
- *Long-Term Suppression of Growth in Pediatric Patients:* Closely monitor growth (height and weight) in pediatric patients. Pediatric patients not growing or gaining height or weight as expected may need to have their treatment interrupted. (5.5)
- *Peripheral Vasculopathy, including Raynaud's phenomenon:* Careful observation for digital changes is necessary during ADZENYS XR-ODT treatment. Further clinical evaluation (e.g. rheumatology referral) may be appropriate for patients who develop signs or symptoms of peripheral vasculopathy. (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 XR-ODT and initiate supportive treatment. (5.7, 17)
- *Motor and Verbal Tics, and Worsening of Tourette's Syndrome:* Before initiating ADZENYS XR-ODT, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor patients for the emergence or worsening of tics or Tourette's syndrome. Discontinue treatment if clinically appropriate. (5.8)

---------- 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 1-888-319-1789 or http://www.adzenysxrodt.com 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 XR-ODT dosage accordingly. (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: 03/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: ABUSE, MISUSE, AND ADDICTION
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Pre-treatment Screening
2.2 General Administration Information
2.3 Dosage Recommendations in Pediatric Patients
2.4 Dosage Recommendations in Adults
2.5 Switching from Other Amphetamine Products
2.6 Dosage Modifications Due to Drug Interactions
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Abuse, Misuse, and Addiction
5.2 Risks to Patients with Serious Cardiac Disease
5.3 Increased Blood Pressure and Heart Rate
5.4 Psychiatric Adverse Reactions
5.5 Long-Term Suppression of Growth in Pediatric Patients
5.6 Peripheral Vasculopathy, including Raynaud's Phenomenon
5.7 Serotonin Syndrome
5.8 Motor and Verbal Tics, and Worsening of Tourette's Syndrome
5.9 Potential for Overdose Due to Medication Errors
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Adverse Reactions from Clinical Trials and Spontaneous Postmarketing Reports of Other Amphetamine Products
7 DRUG INTERACTIONS
7.1 Drugs Having Clinically Important Interactions with Amphetamines
7.2 Drug/Laboratory Test Interactions
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE, MISUSE, AND ADDICTION

ADZENYS XR-ODT has a high potential for abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Misuse and abuse of CNS stimulants, including ADZENYS XR-ODT, can result in overdose and death [*see Overdosage (10)*], and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.

Before prescribing ADZENYS XR-ODT, assess each patient's risk for abuse, misuse, and addiction. Educate patients and their families about these risks, proper storage of the drug, and proper disposal of any unused drug. Throughout ADZENYS XR-ODT treatment, reassess each patient's risk of abuse, misuse, and addiction and frequently monitor for signs and symptoms of abuse, misuse, and addiction *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9.2)]*.

1. INDICATIONS AND USAGE

ADZENYS XR-ODT is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older *[see Clinical Studies (14)]*.

Limitations of Use
The use of ADZENYS XR-ODT is not recommended in pediatric patients younger than 6 years of age because they had higher plasma exposure and a higher incidence of adverse reactions (e.g. weight loss) than patients 6 years and older at the same dosage *[see Warnings and Precautions (5.5), Use in Specific Populations (8.4)]*.

2. DOSAGE AND ADMINISTRATION

2.1 Pre-treatment Screening

Prior to treating patients with ADZENYS XR-ODT, 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)]*.
- the family history and clinically evaluate patients for motor or verbal tics or Tourette's syndrome before initiating ADZENYS XR-ODT *[see Warnings and Precautions (5.9)]*.

2.2 General Administration Information

ADZENYS XR-ODT may be taken orally with or without food. Individualize the dosage according to the therapeutic needs and response of the patient.

ADZENYS XR-ODT supplied in blister form should be taken as follows:
- The tablet should remain in the blister pack until the patient is ready to take it.
- The patient or caregiver should use dry hands to open the blister.
- Tear along the perforation, bend the blister where indicated and peel back the blister's labeled backing to take out the tablet. **The tablet should not be pushed through the foil.**

As soon as the blister is opened, the tablet should be removed and placed on the patient's tongue.
- The whole tablet should be placed on the tongue and allowed to disintegrate without chewing or crushing.
- The tablet will disintegrate in saliva so that it can be swallowed.

ADZENYS XR-ODT supplied in bottle form should be taken as follows:
- The tablet should remain in the bottle until the patient is ready to take it.
- The patient or caregiver should use dry hands to open the bottle.

As soon as the bottle is opened, the tablet should be removed and placed on the patient's tongue.
- The whole tablet should be placed on the tongue and allowed to disintegrate without chewing or crushing.
- The tablet will disintegrate in saliva so that it can be swallowed.

2.3 Dosage Recommendations in Pediatric Patients

The recommended starting dosage is 6.3 mg once daily in the morning. Increase in increments of 3.1 mg or 6.3 mg at weekly intervals. The maximum recommended dose is 18.8 mg daily for patients 6 to 12 years, and 12.5 mg daily for patients 13 to 17 years *[see Use in Specific Populations (8.3), Clinical Studies (14)]*.

2.4 Dosage Recommendations in Adults

The recommended dose is ADZENYS XR-ODT 12.5 mg daily.

2.5 Switching from Other Amphetamine Products

Patients taking ADDERALL XR may be switched to ADZENYS XR-ODT at the equivalent dose taken once daily *[see Clinical Pharmacology (12.3)]*. Refer to Table 1 for equivalent doses of ADZENYS XR-ODT 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 XR-ODT and ADDERALL XR (Mixed Salts of a Single-Entity Amphetamine Product) Extended-Release Capsules

ADZENYS XR-ODT Amphetamine extended-release orally disintegrating tablets	3.1 mg	6.3 mg	9.4 mg	12.5 mg	15.7 mg	18.8 mg
ADDERALL XR	5 mg	10 mg	15 mg	20 mg	25 mg	30 mg
Mixed salts of a single-entity amphetamine product extended-release capsules (MAS ER)						

If switching from any other amphetamine products, discontinue that treatment, and titrate with ADZENYS XR-ODT 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 base compositions and differing pharmacokinetic profiles *[see Warnings and Precautions (5.9)]*.

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 XR-ODT dosage accordingly *[see Drug Interactions (7.1)]*.

3. DOSAGE FORMS AND STRENGTHS

ADZENYS XR-ODT 3.1 mg Amphetamine extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A1 on one side)
ADZENYS XR-ODT 6.3 mg Amphetamine extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A2 on one side)
ADZENYS XR-ODT 9.4 mg Amphetamine extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A3 on one side)
ADZENYS XR-ODT 12.5 mg Amphetamine extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A4 on one side)
ADZENYS XR-ODT 15.7 mg Amphetamine extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A5 on one side)
ADZENYS XR-ODT 18.8 mg Amphetamine extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A6 on one side)

4. CONTRAINDICATIONS

ADZENYS XR-ODT is contraindicated:
- In patients known to be hypersensitive to amphetamine, or other components of ADZENYS XR-ODT. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with other amphetamine products *[see Adverse Reactions (6.2)]*.
- 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 Abuse, Misuse, and Addiction

ADZENYS XR-ODT has a high potential for abuse and misuse. The use of ADZENYS XR-ODT exposes individuals to the risks of abuse and misuse, which can lead to the development of a substance use disorder, including addiction. ADZENYS XR-ODT can be diverted for non-medical use into illicit channels or distribution *[see Drug Abuse and Dependence (9.2)]*. Misuse and abuse of CNS stimulants, including ADZENYS XR-ODT, can result in overdose and death *[see Overdosage (10)]*, and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.

Before prescribing ADZENYS XR-ODT, assess each patient's risk for abuse, misuse, and addiction. Educate patients and their families about these risks and proper disposal of any unused drug. Advise patients to store ADZENYS XR-ODT in a safe place, preferably locked, and instruct patients to not give ADZENYS XR-ODT to anyone else. Throughout ADZENYS XR-ODT treatment, reassess each patient's risk of abuse, misuse, and addiction and frequently monitor for signs and symptoms of abuse, misuse, and addiction.

5.2 Risks to Patients with Serious Cardiac Disease

Sudden death has been reported in patients with structural cardiac abnormalities or other serious cardiac disease who were treated with CNS stimulants at the recommended ADHD dosage.
Avoid ADZENYS XR-ODT use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmia, coronary artery disease, or other serious cardiac disease.

5.3 Increased Blood Pressure and Heart Rate

CNS stimulants cause an increase in blood pressure (mean increase about 2 to 4 mm Hg) and heart rate (mean increase about 3 to 6 bpm). Some patients may have larger increases.
Monitor all ADZENYS XR-ODT-treated patients for potential tachycardia and hypertension.

5.4 Psychiatric Adverse Reactions

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 Disorder
CNS stimulants may induce a manic or mixed episode in patients. Prior to initiating ADZENYS XR-ODT 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
CNS stimulants, at the recommended dosage, may cause psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in patients without prior history of psychotic illness or mania. In a pooled analysis of multiple short-term, placebo-controlled studies of CNS stimulants, psychotic or manic symptoms occurred in 0.1% of CNS stimulant-treated patients compared to 0% of placebo-treated patients. If such symptoms occur, consider discontinuing ADZENYS XR-ODT.

5.5 Long-Term Suppression of Growth in Pediatric Patients

ADZENYS XR-ODT is not approved for use and is not recommended in pediatric patients below 6 years of age *[see Use in Specific Population (8.4)]*.
CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. Closely monitor growth (weight and height) in ADZENYS XR-ODT-treated pediatric patients treated with CNS stimulants.
Pediatric patients not growing or gaining height or weight as expected may need to have their treatment interrupted.

5.6 Peripheral Vasculopathy, including Raynaud's Phenomenon

CNS stimulants, including ADZENYS XR-ODT, used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; however, sequelae have included digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud's phenomenon, were observed in post-marketing reports and at the therapeutic dosage of CNS stimulants in all age groups throughout the course of treatment. Signs and symptoms generally improved after dosage reduction or discontinuation of the CNS stimulant.
Careful observation for digital changes is necessary during ADZENYS XR-ODT-treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for ADZENYS XR-ODT-treated patients who develop signs or symptoms of peripheral vasculopathy.

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 monoamine oxidase inhibitors (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)]*. The co-administration with cytochrome P450 2D6 (CYP2D6) inhibitors may also increase the risk with increased exposure to ADZENYS XR-ODT. In these situations, consider an alternative non-serotonergic 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 ADZENYS XR-ODT with MAOI drugs is contraindicated *[see Contraindications (4)]*.
Discontinue treatment with ADZENYS XR-ODT and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of ADZENYS XR-ODT with other serotonergic drugs or CYP2D6 inhibitors is clinically warranted, initiate ADZENYS XR-ODT with lower doses, monitor patients for the emergence of serotonin syndrome during drug initiation or titration, and inform patients of the increased risk for serotonin syndrome.

5.8 Motor and Verbal Tics, and Worsening of Tourette's Syndrome

CNS stimulants, including amphetamine, have been associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette's syndrome has also been reported *[see Adverse Reactions (6.2)]*.
Before initiating ADZENYS XR-ODT, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor ADZENYS XR-ODT-treated patients for the emergence or worsening of tics or Tourette's syndrome and discontinue treatment if clinically appropriate.

5.9 Potential for Overdose Due to Medication Errors

Medication errors, including substitution and dispensing errors, between ADZENYS XR-ODT and other amphetamine products could occur, leading to possible overdosage. To avoid substitution errors and overdosage, do not substitute for other amphetamine products on a milligram-per-milligram basis because of different amphetamine base compositions and differing pharmacokinetic profiles *[see Dosage and Administration (2.5)]*.

6. ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:
- Abuse, Misuse, and Addiction *[see Boxed Warning, Warnings and Precautions (5.1), and Drug Abuse and Dependence (9.2, 9.3)]*
- Hypersensitivity to amphetamine, or other components of ADZENYS XR-ODT *[see Contraindications (4)]*
- Hypertensive Crisis When Used Concomitantly with Monoamine Oxidase Inhibitors *[see Contraindications (4) and Drug Interactions (7.1)]*
- Risks to Patients with Serious Cardiac Disease *[see Warnings and Precautions (5.2)]*
- Increased Blood Pressure and Heart Rate *[see Warnings and Precautions (5.3)]*
- Psychiatric Adverse Reactions *[see Warnings and Precautions (5.4)]*
- Long-Term Suppression of Growth in Pediatric Patients *[see Warnings and Precautions (5.5)]*
- Peripheral Vasculopathy, including Raynaud's phenomenon *[see Warnings and Precautions (5.6)]*
- Serotonin Syndrome *[see Warnings and Precautions (5.7)]*
- Motor and Verbal Tics, and Worsening of Tourette's Syndrome *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.
The safety of ADZENYS XR-ODT has been established from adequate and well-controlled studies of single-entity amphetamine product extended-release (MAS ER) capsules The safety of ADZENYS XR-ODT has been established from adequate and well-controlled studies of single-entity amphetamine product extended-release (MAS ER) capsules *[see Clinical Studies (14)]*. The adverse reactions of MAS ER capsules in these adequate and well-controlled studies are described below.
The premarketing development program for MAS ER included exposures in a total of 1,315 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 years) were evaluated in two controlled clinical studies, one open-label clinical study, and two single-dose clinical pharmacology studies (N= 40).

Adverse Reactions Leading to Discontinuation of Treatment
The most frequent adverse reactions leading to discontinuation of MAS ER in controlled and uncontrolled, multiple-dose clinical trials of pediatric patients ages 6 to 12 years (N=595) were anorexia (loss of appetite) (2.9%), insomnia (1.5%), weight loss (1.2%), emotional lability (1%), and depression (0.7%).
In a separate placebo-controlled 4-week study in pediatric patients ages 13 to 17 years with ADHD, five patients (2.1%) discontinued treatment due to adverse events among MAS ER-treated patients (N=233) compared to 0% 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 MAS ER-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 MAS ER-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 MAS ER-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 Clinical Trials
Adverse reactions reported in a 3-week clinical trial of pediatric patients 6 to 12 years of age and a 4-week clinical trial in pediatric patients 13 to 17 years of age and adults, respectively, treated with MAS ER or placebo are presented in the tables below.

Table 2: Adverse Reactions Reported by 2% or More of Pediatric Patients (6-12 years old) Receiving MAS ER with Higher Incidence than on Placebo in a 584-Patient Clinical Study

Body System	Adverse Reaction	MAS ER (n=374)	Placebo (n=210)
General	Abdominal Pain (stomachache)	14%	10%
	Fever	5%	2%
	Infection	4%	2%
	Accidental Injury	3%	2%
	Asthenia (fatigue)	2%	0%
Digestive System	Loss of Appetite	22%	2%
	Vomiting	7%	4%
	Nausea	5%	3%
	Dyspepsia	2%	1%
Nervous System	Insomnia	17%	2%
	Emotional Lability	9%	2%
	Nervousness	6%	2%
	Dizziness	2%	0%
Metabolic/Nutritional	Weight Loss	4%	0%

Table 3: Adverse Reactions Reported by 5% or More of Pediatric Patients (13-17 Years Old) Weighing ≤ 75kg Receiving MAS ER with Higher Incidence than Placebo in a 287 Patient Clinical Forced Weekly-Dose Titration Study*

Body System	Adverse Reaction	MAS ER (n=233)	Placebo (n=54)
General	Abdominal Pain (stomachache)	11%	2%
Digestive System	Loss of Appetite [a]	36%	2%
Nervous System	Insomnia [a]	12%	4%
Metabolic/Nutritional	Weight Loss [a]	9%	0%

* Included doses up to 40 mg
[a] Dose-related adverse reactions

Note: The following reactions did not meet the criterion for inclusion in Table 3 but were reported by 2% to 4% of adolescent patients receiving MAS ER with a higher incidence than patients receiving placebo in this study:
accidental injury, asthenia (fatigue), dry mouth, dyspepsia, emotional lability, nausea, somnolence, and vomiting.

Table 4: Adverse Reactions Reported by 5% or More of Adults Receiving MAS ER with Higher Incidence Than Placebo in a 255 Patient Clinical Forced Weekly-Dose Titration Study*

Body System	Preferred Term	MAS ER (n=191)	Placebo (n=64)
General	Headache	26%	13%
	Asthenia	6%	5%
Digestive System	Dry Mouth	35%	5%
	Loss of Appetite	33%	3%
	Nausea	8%	3%
	Diarrhea	6%	0%
Nervous System	Insomnia	27%	13%
	Agitation	8%	5%
	Anxiety	8%	5%
	Dizziness	7%	0%
Cardiovascular System	Tachycardia	6%	3%
Metabolic/Nutritional	Weight Loss	10%	0%
Urogenital System	Urinary Tract Infection	5%	0%

* Included doses up to 60 mg.
Note: The following reactions did not meet the criterion for inclusion in Table 4 but were reported by 2% to 4% of adult patients receiving MAS ER with a higher incidence than patients receiving placebo in this study: 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.

6.2 Adverse Reactions from Clinical Trials and Spontaneous Postmarketing Reports of Other Amphetamine Products

The following adverse reactions are from clinical trials and spontaneous postmarketing reports of other amphetamine products in pediatric patients and adults with ADHD. Because some of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or to establish a causal relationship to drug exposure.
Cardiovascular: Palpitations, sudden death, myocardial infarction. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.
Central Nervous System: Restlessness, irritability, euphoria, dyskinesia, dysphoria, depression, tremor, aggression, anger, logorrhea, paresthesia (including formication), motor and verbal tics.
Eye Disorders: Vision blurred, mydriasis.
Gastrointestinal: Unpleasant taste, constipation, intestinal ischemia, and 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, change in libido, frequent or prolonged erections.
Skin: Alopecia.
Musculoskeletal, Connective Tissue, and Bone Disorders: rhabdomyolysis.
Psychiatric Disorders: dermatillomania, bruxism.
Vascular Disorders: Raynaud's phenomenon.

7. DRUG INTERACTIONS

7.1 Drugs Having Clinically Important Interactions with Amphetamines

Table 5: Drugs having clinically important interactions with amphetamines.

MAO Inhibitors (MAOI)	
Clinical Impact	MAOI antidepressants slow amphetamine metabolism, increasing amphetamines effect on the release of norepinephrine and other monoamines from adrenergic nerve endings causing headaches and other signs of hypertensive crisis. Toxic neurological effects and malignant hyperpyrexia can occur, sometimes with fatal results.
Intervention	Do not administer ADZENYS XR-ODT during or within 14 days following the administration of MAOI [see *Contraindications* (4)].
Serotonergic Drugs	
Clinical Impact	The concomitant use of ADZENYS XR-ODT and serotonergic drugs increases the risk of serotonin syndrome.
Intervention	Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome, particularly during ADZENYS XR-ODT initiation or dosage increase. If serotonin syndrome occurs, discontinue ADZENYS XR-ODT and the concomitant serotonergic drug(s) [see *Warnings and Precautions (5.7)*].
Alkalinizing Agents	
Clinical Impact	Increase blood levels and potentiate the action of amphetamine.
Intervention	Co-administration of ADZENYS XR-ODT and gastrointestinal alkalinizing agents should be avoided.
Acidifying Agents	
Clinical Impact	Lower blood levels and efficacy of amphetamines.
Intervention	Increase dose based on clinical response.
Tricyclic Antidepressants	
Clinical Impact	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.
Intervention	Monitor frequently and adjust or use alternative therapy based on clinical response.

7.2 Drug/Laboratory Test Interactions

Amphetamines can cause a significant elevation in plasma corticosteroid levels. This increase is greatest in the evening. Amphetamines may interfere with urinary steroid determinations.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry
There is a pregnancy exposure registry that monitors outcomes in women exposed to ADHD medications, including ADZENYS XR-ODT, during pregnancy. Healthcare providers are encouraged to advise patients to register by contacting the National Pregnancy Registry for ADHD Medication at 1-866-961-2388 or online at www.womensmentalhealth.org/pregnancyregistry.

Risk Summary
Available data from epidemiologic studies and postmarketing reports on the use of amphetamine in pregnant women over decades of use have not identified a drug-associated risk of major birth defects or miscarriage. Neonates exposed to amphetamine in utero are at risk for withdrawal symptoms following delivery. Adverse pregnancy outcomes including premature delivery and low birth weight have been seen in infants born to mothers taking amphetamines during pregnancy *(see Clinical Considerations)*.
No apparent effects on morphological development were observed in embryo-fetal development studies, with oral administration of amphetamine to rats and rabbits during organogenesis. However, in a pre- and post-natal development study, amphetamine (d- to l- ratio of 3:1) administered orally to pregnant rats during gestation and lactation caused a decrease in pup survival and a decrease in pup body weight that correlated with a delay in developmental landmarks at clinically relevant doses of amphetamine. In addition, adverse effects on reproductive performance were observed in pups whose mothers were treated with amphetamine. Long-term neurochemical and behavioral effects have also been reported in animal developmental studies using clinically relevant doses of amphetamine *(see Data)*.
The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations
Fetal/Neonatal Adverse Reactions
Amphetamines, such as ADZENYS XR-ODT, cause vasoconstriction and thereby may decrease placental perfusion. In addition, amphetamines can stimulate uterine contractions, increasing the risk of premature delivery. Infants born to mothers taking amphetamines during pregnancy have an increased risk of premature delivery and low birth weight.
Monitor infants born to mothers taking amphetamines for symptoms of withdrawal such as feeding difficulties, irritability, agitation, and excessive drowsiness.

Data
Animal Data
Amphetamine, in the enantiomer ratio present in ADZENYS XR-ODT, (d- to l- ratio of 3:1), had no apparent effects on embryofetal morphological development or survival when orally administered to

---

MEDICATION GUIDE
ADZENYS XR-ODT (add-ZEN-iss)
(amphetamine)
extended-release orally disintegrating tablets, CII

What is the most important information I should know about ADZENYS XR-ODT?
ADZENYS XR-ODT may cause serious side effects, including:
- **Abuse, misuse, and addiction.** ADZENYS XR-ODT has a high chance for abuse and misuse and may lead to substance use problems, including addiction. Misuse and abuse of ADZENYS XR-ODT, other amphetamine containing medicines, and methylphenidate containing medicines, can lead to overdose and death. The risk of overdose and death is increased with higher doses of ADZENYS XR-ODT or when it is used in ways that are not approved, such as snorting or injection.
  - Your healthcare provider should check you or your child's risk for abuse, misuse, and addiction before starting treatment with ADZENYS XR-ODT and will monitor you or your child during treatment.
  - ADZENYS XR-ODT may lead to physical dependence after prolonged use, even if taken as directed by your healthcare provider.
  - Do not give ADZENYS XR-ODT to anyone else. See **"What is ADZENYS XR-ODT?"** for more information.
  - Keep ADZENYS XR-ODT in a safe place and properly dispose of any unused medicine. See **"How should I store ADZENYS XR-ODT?"** for more information.
  - Tell your healthcare provider if you or your child have ever abused or been dependent on alcohol, prescription medicines, or street drugs.
- **Risks for people with serious heart disease.** Sudden death has happened in people who have heart defects or other serious heart disease.
  Your healthcare provider should check you or your child carefully for heart problems before starting ADZENYS XR-ODT. Tell your healthcare provider if you or your child has any heart problems, heart disease, or heart defects.
  Call your healthcare provider or go to the nearest hospital emergency room right away if you or your child has any signs of heart problems such as chest pain, shortness of breath, or fainting while taking ADZENYS XR-ODT.
- **Increased blood pressure and heart rate.**
  Your healthcare provider should check you or your child's blood pressure and heart rate regularly during treatment with ADZENYS XR-ODT.
- **Mental (Psychiatric) problems:**
  All Patients
  - new or worse behavior and thought problems
  - new or worse bipolar illness
  - new psychotic symptoms (such as hearing voices, believing things that are not true, are suspicious) or new manic symptoms.
  Tell your healthcare provider about any mental problems you or your child have, or about a family history of suicide, bipolar illness, or depression.
  **Call your healthcare provider right away if you or your child have any new or worsening mental symptoms or problems while taking ADZENYS XR-ODT, especially seeing or hearing things that are not real, believ

- Take ADZENYS XR-ODT as soon as you open the blister pack. The tablet will dissolve in your mouth (saliva) so that it can be swallowed.
- Do not crush or chew.

○ ADZENYS XR-ODT supplied in bottle form:
- Leave the tablet in the bottle until you are ready to take or give it.
- Place the tablet on the tongue.
- Take ADZENYS XR-ODT as soon as you open the bottle. The tablet will dissolve in your mouth (saliva) so that it can be swallowed.
- Do not crush or chew.

- ADZENYS XR-ODT can be taken with or without food.
- Your healthcare provider may do regular checks of your or your child's blood, heart, and blood pressure while taking ADZENYS XR-ODT.
- Children should have their height and weight checked often while taking ADZENYS XR-ODT. ADZENYS XR-ODT treatment may be stopped if a problem is found during these check-ups.

If you or your child take too much ADZENYS XR-ODT, call your healthcare provider or Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away.

What should I avoid while taking ADZENYS XR-ODT?
- drinking alcohol

What are possible side effects of ADZENYS XR-ODT?
ADZENYS XR-ODT can cause serious side effects, including
- See **"What is the most important information I should know about ADZENYS XR-ODT?"** for information on reported heart and mental problems.
- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with ADZENYS XR-ODT. Your healthcare provider may stop your child's ADZENYS XR-ODT treatment if they are not growing or gaining weight as expected.
- **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 healthcare provider if you have or your child has numbness, pain, skin color change, or sensitivity to temperature in your fingers or toes.
  Call your healthcare provider right away if you have or your child has any unexplained wounds appearing on fingers or toes while taking ADZENYS XR-ODT.
- **New or worsening tics or worsening Tourette's syndrome.** Tell your healthcare provider if you or your child get any new or worsening tics or worsening Tourette's syndrome during treatment with ADZENYS XR-ODT.

Common side effects of ADZENYS XR-ODT include decreased appetite and problems sleeping.
Common side effects of ADZENYS XR-ODT in children 6 to 12 years of age also include:
• stomach pain • extreme mood change • vomiting • nervousness • nausea • fever
Common side effects of ADZENYS XR-ODT in children 13 to 17 years of age also include:
• stomach pain • weight loss
Common side effects of ADZENYS XR-ODT in adults also include:
• dry mouth • headache • weight loss • nausea • anxiety • restlessness • dizziness
• fast heart beat • diarrhea • weakness • urinary tract infections
Talk to your healthcare provider if you or your child have side effects that are bothersome or do not go away.
These are not all the possible side effects ADZENYS XR-ODT.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1800-FDA-1088.

How should I store ADZENYS XR-ODT?
- Store ADZENYS XR-ODT blister or bottle packaging in a cool, dry place at room temperature between 68° F to 77° F (20° C to 25° C).
- Store ADZENYS XR-ODT in a safe place, like a locked cabinet.
- Store ADZENYS XR-ODT in the blister or bottle packaging until you are ready to take or give it.
- Store ADZENYS XR-ODT blister packages in the hard plastic travel case provided after removal from the carton.
- Dispose of remaining, unused, or expired ADZENYS XR-ODT by a medicine take-back program at a U.S. Drug Enforcement Administration (DEA) authorized collection site. If no take-back program or DEA authorized collector is available, mix ADZENYS XR-ODT with an undesirable, nontoxic substance such as dirt, cat litter, or used coffee grounds to make it less appealing to children and pets. Place the mixture in a container such as a sealed plastic bag and throw away ADZENYS XR-ODT in the household trash. Visit www.fda.gov/drugdisposal for additional information on disposal of unused medicines.

Keep ADZENYS XR-ODT and all medicines out of the reach of children.

General information about the safe and effective use of ADZENYS XR-ODT
Medicines are sometimes prescribed for purposes other than those listed in the Medication Guide. Do not use ADZENYS XR-ODT for a condition for which it has not been prescribed. Do not give ADZENYS XR-ODT 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 ADZENYS XR-ODT. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about ADZENYS XR-ODT that is written for healthcare professionals.

For more information about ADZENYS XR-ODT or to get a plastic travel case contact Neos Therapeutics, Inc. at 1-888-236-6816 or go to www.adzenysxrodt.com.

What are the ingredients in ADZENYS XR-ODT?
Active Ingredients: Amphetamine
Inactive Ingredients: Mannitol, Crospovidone, Microcrystalline Cellulose, Methacrylic Acid, Sodium Polystyrene Sulfonate, Citric Acid, Fructose, Orange Flavor, Colloidal Silicon Dioxide, Triethyl Citrate, Sucralose, Lake Blend Orange, Magnesium Stearate, and Polyethylene Glycol 3350.

Manufactured for Neos Therapeutics Brands, LLC, Denver, CO 80237.
ADZENYS XR-ODT is registered in the US Patent and Trademark Office© 2017 Neos Therapeutics, Inc.

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Revised: 03/2026

pregnant 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) for adolescents of 12.5 mg/day (as base), on a mg/m^2 body surface area basis. Fetal malformations and death have been reported in mice following parenteral administration of d-amphetamine doses of 50 mg/kg/day (approximately 10 times the MRHD for adolescents on a mg/m^2 basis) or greater to pregnant animals. Administration of these doses was also associated with severe maternal toxicity.

A study was conducted in which pregnant rats received daily oral doses of amphetamine (d- to l-enantiomer ratio of 3:1, the same as in ADZENYS XR-ODT) of 2, 6, and 10 mg/kg from gestation day 6 to lactation day 20. These doses are approximately 0.8, 2, and 4 times the MRHD for adolescents of 12.5 mg/day (as base), on a mg/m^2 basis. All doses caused hyperactivity and decreased weight gain in the dams. A decrease in pup survival was seen at all doses. A decrease in pup bodyweight was seen at 6 and 10 mg/kg which correlated with delays in developmental landmarks. Increased pup locomotor activity was seen at 10 mg/kg on day 22 postpartum but not at 5 weeks post-weaning. When pups were tested for reproductive performance at maturation, gestational weight gain, number of implantations, and number of delivered pups were decreased in the group whose mothers had been given 10 mg/kg.

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.

8.2 Lactation

Risk Summary
Based on limited case reports in published literature, amphetamine (d- or d, l-) is present in human milk at relative infant doses of 2% to 13.8% of the maternal weight-adjusted dosage and a milk/plasma ratio ranging between 1.9 and 7.5. There are no reports of adverse effects on the breastfed infant. Long-term neurodevelopmental effects on infants from amphetamine exposure are unknown. It is possible that large dosages of amphetamine might interfere with milk production, especially in women 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 ADZENYS XR-ODT.

8.4 Pediatric Use

The safety and effectiveness have been established in pediatric patients with ADHD ages 6 to 17 years of age in three adequate and well-controlled clinical trials of up to 4 weeks in duration *[see Adverse Reactions (6.1), Clinical Pharmacology (12), Clinical Studies (14)]*.

The safety and effectiveness of ADZENYS XR-ODT have not been established in pediatric patients below the age of 6 years.

In studies evaluating extended-release amphetamine products, patients 4 to <6 years of age had higher systemic amphetamine exposures than those observed in older pediatric patients at the same dosage. Pediatric patients 4 to <6 years of age also had a higher incidence of adverse reactions, including weight loss.

Long-Term Growth Suppression
Growth should be monitored during treatment with stimulants, including ADZENYS XR-ODT, in 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 (5.5)]*.

Juvenile Animal Data
In a juvenile developmental study, rats received daily oral doses of amphetamine (d to l enantiomer ratio of 3:1, the same as in ADZENYS XR-ODT) of 2, 6, or 20 mg/kg on days 7 to 13 of age; from day 14 to approximately day 60 of age these doses were given twice daily for total daily doses of 4, 12, or 40 mg/kg. The latter doses are approximately 0.6, 2, and 6 times the maximum recommended human dose for children of 18.8 mg/day (as base), on a mg/m^2 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

ADZENYS XR-ODT has not been studied in the geriatric population.

9. DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

ADZENYS XR-ODT contains amphetamine, a Schedule II controlled substance.

9.2 Abuse

ADZENYS XR-ODT has a high potential for abuse and misuse which can lead to the development of a substance use disorder, including addiction *[see Warnings and Precautions (5.1)]*. ADZENYS XR-ODT can be diverted for non-medical use into illicit channels or distribution.

Abuse is the intentional non-therapeutic use of a drug, even once, to achieve a desired psychological or physiological effect. Misuse is the intentional use, for therapeutic purposes, of a drug by an individual in a way other than prescribed by a health care provider or for whom it was not prescribed. Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use (e.g., continuing drug use despite harmful consequences, giving a higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence.

Misuse and abuse of amphetamine may cause increased heart rate, respiratory rate, or blood pressure; sweating; dilated pupils; hyperactivity; restlessness; insomnia; decreased appetite; loss of coordination; tremors; flushed skin; vomiting; and/or abdominal pain. Anxiety, psychosis, hostility, aggression, and suicidal or homicidal ideation have also been observed with CNS stimulants abuse and/or misuse. Misuse and abuse of CNS stimulants, including ADZENYS XR-ODT, can result in overdose and death *[see Overdosage (10)]*, and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.

9.3 Dependence

Physical Dependence
ADZENYS XR-ODT may produce physical dependence. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug.

Withdrawal signs and symptoms after abrupt discontinuation or dose reduction following prolonged use of CNS stimulants including ADZENYS XR-ODT include dysphoric mood; depression; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; and psychomotor retardation or agitation.

Tolerance
ADZENYS XR-ODT may produce tolerance. Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose).

10. OVERDOSAGE

Clinical Effects of Overdose

Overdose of CNS stimulants is characterized by the following sympathomimetic effects:
- Cardiovascular effects including tachyarrhythmias, and hypertension or hypotension. Vasospasm, myocardial infarction, or aortic dissection may precipitate sudden cardiac death. Takotsubo cardiomyopathy may develop.
- CNS effects including psychomotor agitation, confusion, and hallucination. Serotonin syndrome, seizures, cerebral vascular accidents, and coma may occur.
- Life-threatening hyperthermia (temperatures greater than 104°F) and rhabdomyolysis may develop.

Overdose Management

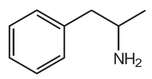
Consider the possibility of multiple drug ingestion. The pharmacokinetic profile of ADZENYS XR-ODT should be considered when treating patients with overdose. D-amphetamine is not dialyzable. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

11. DESCRIPTION

ADZENYS XR-ODT (amphetamine) extended-release orally disintegrating tablet contains a 3 to 1 ratio of d- to l-amphetamine, a central nervous system stimulant.

The labeled strengths reflect the amount of amphetamine base in ADZENYS XR-ODT whereas the strengths of the (mixed salts of a single-entity amphetamine) products are in terms of the amount of amphetamine salts. Table 1 in Section 2.5 details the equivalent amounts of active ingredient in these products.

Structural Formula:



$C_9H_{13}N$ MW 135.21

ADZENYS XR-ODT is an extended-release orally disintegrating tablet containing 50% immediate-release and 50% delayed-release amphetamine for once daily dosing.

ADZENYS XR-ODT also contains the following inactive ingredients: Mannitol, Crospovidone, Microcrystalline Cellulose, Methacrylic Acid, Sodium Polystyrene Sulfonate, Citric Acid, Fructose, Orange Flavor, Colloidal Silicon Dioxide, Triethyl Citrate, Sucralose, Lake Blend Orange, Magnesium Stearate, and Polyethylene Glycol 3350.

12. CLINICAL PHARMACOLOGY

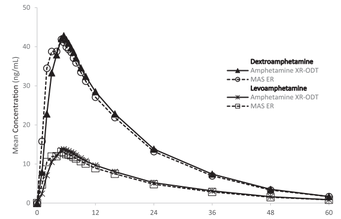
12.1 Mechanism of Action

Amphetamines are non-catecholamine sympathomimetic amines with CNS stimulant activity. The mode of therapeutic action in ADHD is not known. Amphetamines are thought to 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

Absorption
Following a single, 18.8 mg oral dose of ADZENYS XR-ODT in 40 healthy adult subjects in a crossover study under fasting conditions, d-amphetamine mean (+SD) peak plasma concentrations of 44.9 (+8.9) ng/mL occurred at a median time of 5.0 hours after dosing, and l-amphetamine mean (+SD) peak plasma concentrations of 14.5 (+ 3.0 ng/mL occurred at a median time of 5.25 hours after dosing (Figure 1).

Figure 1: Mean Concentration of D-Amphetamine and L-Amphetamine vs Time for ADZENYS XR-ODT (18.8 mg) and Mixed Salts of a Single-Entity Amphetamine Product Extended-Release Capsules (MAS ER 30 mg) in the Fasted State



The single dose pharmacokinetics of d-amphetamine under fed conditions are summarized (Table 6) from studies in healthy adults following an oral dose of 18.8 mg ADZENYS XR-ODT.

Table 6: d-Amphetamine PK Parameters (mean + SD) after ADZENYS XR-ODT 18.8 mg

PK parameter	Adults Fasted	Adults Fed[a]
T_{max} (hr)[b]	5.00 (3.00-12.00)	7.00 (3.00-16.00)
$T_{1/2}$ (hr)	11.25±2.0	11.33±2.0
C_{max} (ng/ml)	44.9±8.9	36.3±6.9
AUC_{inf} (hr*ng/mL)	876.9±182.4	856.3±166.1

[a] A high-fat meal was consumed 30 minutes prior to drug administration
[b] Data presented as median (range)

A single dose of ADZENYS XR-ODT 18.8 mg provided comparable plasma concentration profiles of both d-amphetamine and l-amphetamine to mixed salts of a single-entity amphetamine product extended-release capsules (MAS ER) 30 mg.

The mean elimination half-life for d-amphetamine is 11 hours in adults and 9-10 hours in pediatric patients aged 6 to 12 years. For l-amphetamine, the mean elimination half-life in adults is 14 hours and 10-11 hours in pediatric patients aged 6 to 12 years. Mean weight-normalized clearance values for d-amphetamine and l-amphetamine decreased slightly with an increase in age.

Food Effect
Food does not affect the extent of absorption of d-amphetamine and l-amphetamine but caused a 19% reduction in C_{max}. Food also prolonged the median t_{max} by approximately 2.0 hours for d-amphetamine and by 2.5 hours for l-amphetamine after administration of ADZENYS XR-ODT. These changes are not considered clinically significant.

Alcohol Effect
In an *in vitro* alcohol-induced dose dumping study, a substantial increase in amphetamine release occurred in the presence of 40% alcohol but not with 5%, 10% and 20% alcohol.

Elimination
Metabolism and Excretion
Amphetamine is reported to be oxidized at the 4 position of the benzene ring to form 4-hydroxyamphetamine, or on the side chain α or β carbons to form alpha-hydroxy-amphetamine or norephedrine, respectively. Norephedrine and 4-hydroxy-amphetamine are both active and each is subsequently oxidized to form 4-hydroxy-norephedrine. Alpha-hydroxy-amphetamine undergoes deamination to form phenylacetone, which ultimately forms benzoic acid and its glucuronide and the glycine conjugate hippuric acid. Although the enzymes involved in amphetamine metabolism have not been clearly defined, CYP2D6 is known to be involved with formation of 4-hydroxy-amphetamine. Since CYP2D6 is genetically polymorphic, population variations in amphetamine metabolism are a possibility.

Amphetamine is known to inhibit monoamine oxidase, whereas the ability of amphetamine and its metabolites to inhibit various P450 isozymes and other enzymes has not been adequately elucidated. *In vitro* experiments with human microsomes indicate minor inhibition of CYP2D6 by amphetamine and minor inhibition of CYP1A2, 2D6, and 3A4 by one or more metabolites. However, due to the probability of auto-inhibition and the lack of information on the concentration of these metabolites relative to *in vivo* concentrations, no predications regarding the potential for amphetamine or its metabolites to inhibit the metabolism of other drugs by CYP isozymes *in vivo* can be made.

With normal urine pHs, approximately half of an administered dose of amphetamine is recoverable in urine as derivatives of alpha-hydroxy-amphetamine and approximately another 30-40% of the dose is recoverable in urine as amphetamine itself. Since amphetamine has a pKa of 9 .9, urinary recovery of amphetamine is highly dependent on pH and urine flow rates. Alkaline urine pHs result in less ionization and reduced renal elimination, and acidic pHs and high flow rates result in increased renal elimination with clearances greater than glomerular filtration rates, indicating the involvement of active secretion. Urinary recovery of amphetamine has been reported to range from 1% to 75%, depending on urinary pH, with the remaining fraction of the dose hepatically metabolized. Consequently, both hepatic and renal dysfunction have the potential to inhibit the elimination of amphetamine and result in prolonged exposures.

In addition, drugs that effect urinary pH are known to alter the elimination of amphetamine, and any decrease in amphetamine's metabolism that might occur due to drug interactions or genetic polymorphisms is more likely to be clinically significant when renal elimination is decreased *[see Drug Interactions (7)]*.

Specific Populations
Comparison of the pharmacokinetics of d- and l-amphetamine after oral administration of MAS ER in pediatric patients (6-12 years) and adolescent (13-17 years) ADHD patients and healthy adult volunteers indicates that body weight is the primary determinant of apparent differences in the pharmacokinetics of d-and l-amphetamine across the age range. Systemic exposure measured by area under the curve to infinity (AUC_{inf}) and maximum plasma concentration (C_{max}) decreased with increases in body weight, while oral volume of distribution (V/F), oral clearance (CL/F), and elimination half-life ($t_{1/2}$) increased with increases in body weight.

Pediatric Patients
The pharmacokinetics of ADZENYS XR-ODT in pediatric patients has been established based on the pharmacokinetics of MAS ER in pediatric patients. On a mg/kg weight basis, pediatric patients eliminate amphetamine faster than adults. The elimination half-life ($t_{1/2}$) is approximately 1 hour shorter for d-amphetamine and 2 hours shorter for l-amphetamine in pediatric patients than in adults. However, for a given dose of MAS ER, pediatric patients had higher systemic exposure to amphetamine (C_{max} and AUC) than adults which was attributed to the higher dose administered to pediatric patients on a mg/kg body weight basis compared to adults. Upon dose normalization on a mg/kg basis, pediatric patients showed 30% less systemic exposure compared to adults.

Gender
Systemic exposure to amphetamine was 20-30% higher in women (N=20) than in men (N=20) due to the higher dose administered to women on a mg/kg body weight basis. When the exposure parameters (C_{max} and AUC) were normalized by dose (mg/kg), these differences diminished. Age and gender had no direct effect on the pharmacokinetics of d- and l-amphetamine.

Race
Formal pharmacokinetic studies for race have not been conducted. However, amphetamine pharmacokinetics appeared to be comparable among Caucasians (N=33), Blacks (N=8) and Hispanics (N=10).

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
No evidence of carcinogenicity was found in studies in which d,l-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 for children of 18.8 mg/day (as base), on a mg/m^2 body surface area basis.

Mutagenesis
Amphetamine, in the enantiomer ratio present in ADZENYS XR-ODT (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,l-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.

Amphetamine, in the enantiomer ratio present in ADZENYS XR-ODT (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 for adolescents of 12.5 mg/day (as base), on a mg/m^2 body surface area 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

The safety and efficacy of ADZENYS XR-ODT has been established based on adequate and well-controlled studies of mixed salts of a single-entity amphetamine product extended-release capsules in the treatment of ADHD. Below is a description of the results of the adequate and well-controlled studies of mixed salts of a single-entity amphetamine product extended-release capsules (MAS ER) in the treatment of ADHD.

Pediatric Patients
A double-blind, randomized, placebo-controlled, parallel-group study was conducted in pediatric patients 6 to 12 years of age (N=584) who met DSM-IV criteria for ADHD (either the combined type or the hyperactive-impulsive type). Patients were randomized to fixed-dose treatment groups receiving final doses of 10, 20 or 30 mg of mixed salts of a single-entity amphetamine product extended-release capsules or placebo once daily in the morning for three 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. Significant improvements on the ADHD-RS-IV, based upon teacher ratings of attention and hyperactivity, were observed for all doses compared to patients who received placebo, for all three weeks, including the first week of treatment, when all subjects were receiving a dose of 10 mg/day. Patients who received MAS ER showed improvements on the ADHD-RS-IV total score in both morning and afternoon assessments compared to patients on placebo.

In a classroom analogue study, patients (N=51) receiving fixed doses of 10 mg, 20 mg or 30 mg MAS ER demonstrated statistically significant improvements on teacher-rated Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) scale Attention and Deportment variables and Permanent Product Measure of Performance (PERMP) scales compared to patients treated with placebo. SKAMP is a validated 13-item teacher-rated scale that assesses manifestations of ADHD in a classroom setting. PERMP is a skill-adjusted math test that measure attention in ADHD.

A double-blind, randomized, multi-center, parallel-group, placebo-controlled study was conducted in pediatric patients 13 to 17 years of age (N=327) who met DSM-IV criteria for ADHD. The primary cohort of patients (n=287, weighing ≤ 75kg) was 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 MAS ER 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. Improvements in the primary cohort were statistically significantly greater in all four primary cohort active treatment groups (MAS ER 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 MAS ER or placebo once daily in the morning for four weeks. Improvements, measured with the Attention Deficit Hyperactivity Disorder-Rating Scale (ADHD-RS) were observed at endpoint for MAS ER 20, 40 and 60 mg, compared to patients who received placebo for all four weeks. However, there was not adequate evidence that doses greater than 20 mg/day conferred additional benefit.

16. HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

ADZENYS XR-ODT 3.1 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A1 on one side), carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets, NDC 70165-005-30

ADZENYS XR-ODT 3.1 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A1 on one side), bottle containing 30 tablets each, for a total of 30 tablets, NDC 70165-005-31

ADZENYS XR-ODT 6.3 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A2 on one side), carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets, NDC 70165-010-30

ADZENYS XR-ODT 6.3 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A2 on one side), bottle containing 30 tablets each, for a total of 30 tablets, NDC 70165-010-31

ADZENYS XR-ODT 9.4 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A3 on one side), carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets, NDC 70165-015-30

ADZENYS XR-ODT 9.4 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A3 on one side), bottle containing 30 tablets each, for a total of 30 tablets, NDC 70165-015-31

ADZENYS XR-ODT 12.5 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A4 on one side), carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets, NDC 70165-020-30

ADZENYS XR-ODT 12.5 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A4 on one side), bottle containing 30 tablets each, for a total of 30 tablets, NDC 70165-020-31

ADZENYS XR-ODT 15.7 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A5 on one side), carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets, NDC 70165-025-30

ADZENYS XR-ODT 15.7 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A5 on one side), bottle containing 30 tablets each, for a total of 30 tablets, NDC 70165-025-31

ADZENYS XR-ODT 18.8 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A6 on one side), carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets, NDC 70165-030-30

ADZENYS XR-ODT 18.8 mg extended-release orally disintegrating tablet: round, orange to light orange mottled (debossed A6 on one side), bottle containing 30 tablets each, for a total of 30 tablets, NDC 70165-030-31

Storage

Store at 20°C to 25° C (68°F to 77° F). Excursions permitted to 15-30° C (59-86° F) [see USP Controlled Room Temperature]

Store ADZENYS XR-ODT bottle packaging in a cool, dry place at 20°C to 25° C (68°F to 77° F). Excursions permitted to 15-30° C (59-86° F) [see USP Controlled Room Temperature]

Store ADZENYS XR-ODT blister packages in the rigid, plastic travel case provided after removal from the carton. To obtain additional travel cases, patients and health care professionals can call Neos Therapeutics, Inc., at 1-888-236-6816.

17. PATIENT COUNSELING INFORMATION

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

Abuse, Misuse, and Addiction
Educate patients and their families about the risks of abuse, misuse, and addiction of ADZENYS XR-ODT, which can lead to overdose and death, and proper disposal of any unused drug *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9.2), Overdosage (10)]*. Advise patients to store ADZENYS XR-ODT in a safe place, preferably locked, and instruct patients to not give ADZENYS XR-ODT to anyone else.

Dosage and Administration Instructions
Provide the following instructions on administration to the patient in the blister packaging form:
- The tablet should remain in the blister pack until the patient is ready to take it.
- The patient or caregiver should use dry hands to open the blister.
- Tear along the perforation, bend the blister where indicated and peel back the blister's labeled backing to take out the tablet. **The tablet should not be pushed through the foil.**
- As soon as the blister is opened, the tablet should be removed and placed on the patient's tongue.
- The whole tablet should be placed on the tongue and allowed to disintegrate without chewing or crushing.
- The tablet will disintegrate in saliva so that it can be swallowed.

Provide the following instructions on administration to the patient in the bottle packaging form:
- The tablet should remain in the bottle until the patient is ready to take it.
- The tablet should be taken immediately after removing it from bottle. It should not be stored for future use.
- The patient or caregiver should use dry hands to open the bottle.
- As soon as the tablet is removed from the bottle, the tablet should be removed and placed on the patient's tongue.
- The whole tablet should be placed on the tongue and allowed to disintegrate without chewing or crushing.
- The tablet will disintegrate in saliva so that it can be swallowed.

Risks to Patients with Serious Cardiac Disease
Advise patients that there are potential risks to patients with serious cardiac disease, including sudden death, with ADZENYS XR-ODT use. Instruct patients to contact a healthcare provider immediately if they develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease *[see Warnings and Precautions (5.2)]*.

Increased Blood Pressure and Heart Rate
Instruct patients that ADZENYS XR-ODT can cause elevations of their blood pressure and pulse rate *[see Warnings and Precautions (5.3)]*.

Psychiatric Adverse Reactions
Advise patients that ADZENYS XR-ODT, at recommended doses, may cause psychotic symptoms or mania *[see Warnings and Precautions (5.4)]*.

Long-Term Suppression of Growth
Advise patients that ADZENYS XR-ODT may cause slowing of growth and weight loss *[see Warnings and Precautions (5.5)]*.

Circulation problems in Fingers and Toes [Peripheral vasculopathy, including Raynaud's phenomenon]
Instruct patients beginning treatment with ADZENYS XR-ODT about the risk of peripheral vasculopathy, including Raynaud's phenomenon, and associated signs and symptoms: fingers or toes may feel numb, cool, painful, and/or may change color from pale, to blue, to red.

Instruct patients to report to their physician any new numbness, pain, skin color change, or sensitivity to temperature in fingers or toes.

Instruct patients to call their physician immediately with any signs of unexplained wounds appearing on fingers or toes while taking ADZENYS XR-ODT.

Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients *[see Warnings and Precautions (5.6)]*.

Serotonin Syndrome
Caution patients about the risk of serotonin syndrome with concomitant use of ADZENYS XR-ODT 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 (5.7) 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.

Motor and Verbal Tics, and Worsening of Tourette's Syndrome
Advise patients that motor and verbal tics and worsening of Tourette's syndrome may occur during treatment with ADZENYS XR-ODT. Instruct patients to notify their healthcare provider if emergence of new tics or worsening of tics or Tourette's syndrome occurs *[see Warnings and Precautions (5.8)]*.

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
Advise patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ADZENYS XR-ODT during pregnancy. Advise patients to notify their healthcare provider if they become pregnant or intend to become pregnant during treatment with ADZENYS XR-ODT. Advise patients of the potential fetal effects from the use of ADZENYS XR-ODT during pregnancy *[see Use in Specific Populations (8.1)]*.

Lactation
Advise patients not to breastfeed if they are taking ADZENYS XR-ODT *[see Use in Specific Populations (8.2)]*.

Alcohol
Advise patients to avoid alcohol while taking ADZENYS XR-ODT. Consumption of alcohol while taking ADZENYS XR-ODT may result in a more rapid release of the dose of amphetamine *[see Clinical Pharmacology (12)]*.

Manufactured for Neos Therapeutics Brands, LLC, Denver, CO 80237. Made in USA.

For more information call 1-888-319-1789.

ADZENYS XR-ODT is a registered trademark of Neos Therapeutics, Inc.

Copyright© 2017, Neos Therapeutics, Inc.

Patent Number 8,709,491 B2

DRAWING #39535R1
21.125 X 15.00

Proof (A) B C D E F G

PLEASE SIGN AND RETURN

☑ OK to Print

☐ Send Another Proof

Signature *Lilly Vasquez* Date 08/05/2026

040-T-00776

Job No. P429801-2 **Item No.** 8/2026

Date Sent 8-05-26 Date Returned _____

☐ Art Sent ☐ Art Returned

This proof is printed on proof paper and is not intended to show the paper or the ink used on the finished job.

PLEASE READ PROOF CAREFULLY FOR ERRORS

If proof is correct, check "OK to Print" box, sign and date it. If changes are needed, show such changes clearly in the margin of the proof, check "Send Another Proof" box, sign and date it. We cannot assume responsibility for corrections other than those indicated on proof.

If the copy as originally submitted is changed when the proof is returned, the changes in the copy are considered alterations. Alterations will be an additional charge.

PLEASE RETURN COPY WITH PROOF

COLBERT PACKAGING

CORPORATE HEADQUARTERS

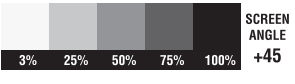
9949 58th Place, Kenosha, Wisconsin 53144
Tel: (262) 925-4740 Fax: (262) 925-4749

1511 West Lusher, Elkhart, Indiana 46517
Tel: (574) 295-6605 Fax: (574) 522-0910

Form 131R4

Operator	Init.	Date
Proofer 1	Init.	Date
Proofer 2	Init.	Date

JOB HISTORY:

PROOF A

BLACK