AMPHETAMINE EXTENDED-RELEASE- amphetamine extended-release tablet, orally disintegrating
Neos Therapeutics, LP

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use AMPHETAMINE EXTENDED-RELEASE ORALLY DISINTEGRATING TABLETS safely and effectively. See full prescribing information for AMPHETAMINE EXTENDED-RELEASE ORALLY DISINTEGRATING TABLETS.

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.

Amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets, can result in overdose and death (5.1,9.2,10**):**

- **Before prescribing amphetamine extended-release orally disintegrating tablets, 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.**

INDICATIONS AND USAGE

Amphetamine extended-release orally disintegrating tablets 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

- 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 amphetamine extended-release orally disintegrating tablets. (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 amphetamine extended-release orally disintegrating tablets, screen patients for risk factors for developing a manic episode. If new psychotic or manic symptoms occur, consider discontinuing amphetamine extended-release orally disintegrating tablets. (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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets and initiate supportive treatment. (5.7, 17)
- *Motor and Verbal Tics, and Worsening of Tourette's Syndrome:* Before initiating amphetamine extended-release orally disintegrating tablets, 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 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 amphetamine extended-release orally disintegrating tablets 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: 3/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE, MISUSE, AND ADDICTION

Amphetamine extended-release orally disintegrating tabletshas 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 amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets 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

Amphetamine extended-release orally disintegrating tablets 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)].*

2 DOSAGE AND ADMINISTRATION

2.1 Pre-treatment Screening

Prior to treating patients with amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets *[see Warnings and Precautions (5.9)]*.

2.2 General Administration Information

Amphetamine extended-release orally disintegrating tablets may be taken orally with or without food. Individualize the dosage according to the therapeutic needs and response of the patient.

Amphetamine extended-release orally disintegrating tablets 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.

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 amphetamine extended-release orally disintegrating tablets 12.5 mg daily.

2.5 Switching from Other Amphetamine Products

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

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 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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets dosage accordingly *[see Drug Interactions (7.1)]*.

3 DOSAGE FORMS AND STRENGTHS

Amphetamine extended-release orally disintegrating tablets 3.1 mg: round, orange to light orange mottled (debossed A1 on one side)

Amphetamine extended-release orally disintegrating tablets 6.3 mg: round, orange to light orange mottled (debossed A2 on one side)

Amphetamine extended-release orally disintegrating tablets 9.4 mg: round, orange to light orange mottled (debossed A3 on one side)

Amphetamine extended-release orally disintegrating tablets 12.5 mg: round, orange to light orange mottled (debossed A4 on one side)

Amphetamine extended-release orally disintegrating tablets 15.7 mg: round, orange to light orange mottled (debossed A5 on one side)

Amphetamine extended-release orally disintegrating tablets 18.8 mg: round, orange to light orange mottled (debossed A6 on one side)

4 CONTRAINDICATIONS

Amphetamine extended-release orally disintegrating tablets is contraindicated:

- In patients known to be hypersensitive to amphetamine, or other components of amphetamine extended-release orally disintegrating tablets. 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 Interactions7.1]*.

5 WARNINGS AND PRECAUTIONS

5.1 Abuse, Misuse, and Addiction

Amphetamine extended-release orally disintegrating tablets has a high potential for abuse and misuse. The use of amphetamine extended-release orally disintegrating tablets exposes individuals to the risks of abuse and misuse, which can lead to the development of a substance use disorder, including addiction. amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets in a safe place, preferably locked, and instruct patients to not give amphetamine extended-release orally disintegrating tablets to anyone else. Throughout amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets-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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets.

5.5 Long-Term Suppression of Growth in Pediatric Patients

CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. Closely monitor growth (weight and height) in amphetamine extended-release orally disintegrating tablets-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 amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets-treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for amphetamine extended-release orally disintegrating tablets-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 amphetamine extended-release orally disintegrating tablets. 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 amphetamine extended-release orally disintegrating tablets with MAOI drugs is contraindicated *[see Contraindications (4)].*

Discontinue treatment with amphetamine extended-release orally disintegrating tablets and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of amphetamine extended-release orally disintegrating tablets with other serotonergic drugs or CYP2D6 inhibitors is clinically warranted, initiate amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor amphetamine extended-release orally disintegrating tablets-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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets *[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 amphetamine extended-release orally disintegrating tablets 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	Preferred Term	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 amphetamine extended-release orally disintegrating tablets during or within 14 days following the administration of MAOI [see *Contraindications*(4)].
Serotonergic Drugs	
Clinical Impact	The concomitant use of amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets initiation or dosage increase. If serotonin syndrome occurs, discontinue amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets, 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 adverseoutcomes. 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 amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets, (d- to l- ratio of 3:1), had no apparent effects on embryofetal morphological development or survival when orally administered to 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 amphetamine extended-release orally disintegrating tablets) 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 amphetamine extended-release orally disintegrating tablets.

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 *[seeAdverse Reactions (6.1), Clinical Pharmacology (12), Clinical Studies (14)]*. The safety and efficacy of amphetamine extended-release orally disintegrating tablets in pediatric patients less than 6 years have not been established.

Long-Term Growth Suppression

Growth should be monitored during treatment with stimulants, including amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets) 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

Amphetamine extended-release orally disintegrating tablets has not been studied in the geriatric population.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Amphetamine extended-release orally disintegrating tablets contains amphetamine, a Schedule II controlled substance.

9.2 Abuse

Amphetamine extended-release orally disintegrating tablets 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)]*. Amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets, 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

Amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets include dysphoric mood; depression; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; and psychomotor retardation or agitation.

Tolerance

Amphetamine extended-release orally disintegrating tablets 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 104ºF) and rhabdomyolysis may develop.

Overdose Management

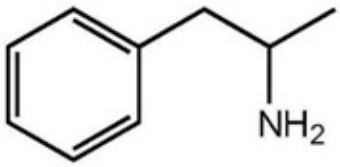
Consider the possibility of multiple drug ingestion. The pharmacokinetic profile of amphetamine extended-release orally disintegrating tablets should be considered when treating patients with overdose. D-amphetamine is not dialyzable. Consider contacting the Poison Help line (1-800-222-1222) or a medical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

11 DESCRIPTION

Amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets 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

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

Amphetamine extended-release orally disintegrating tablets 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

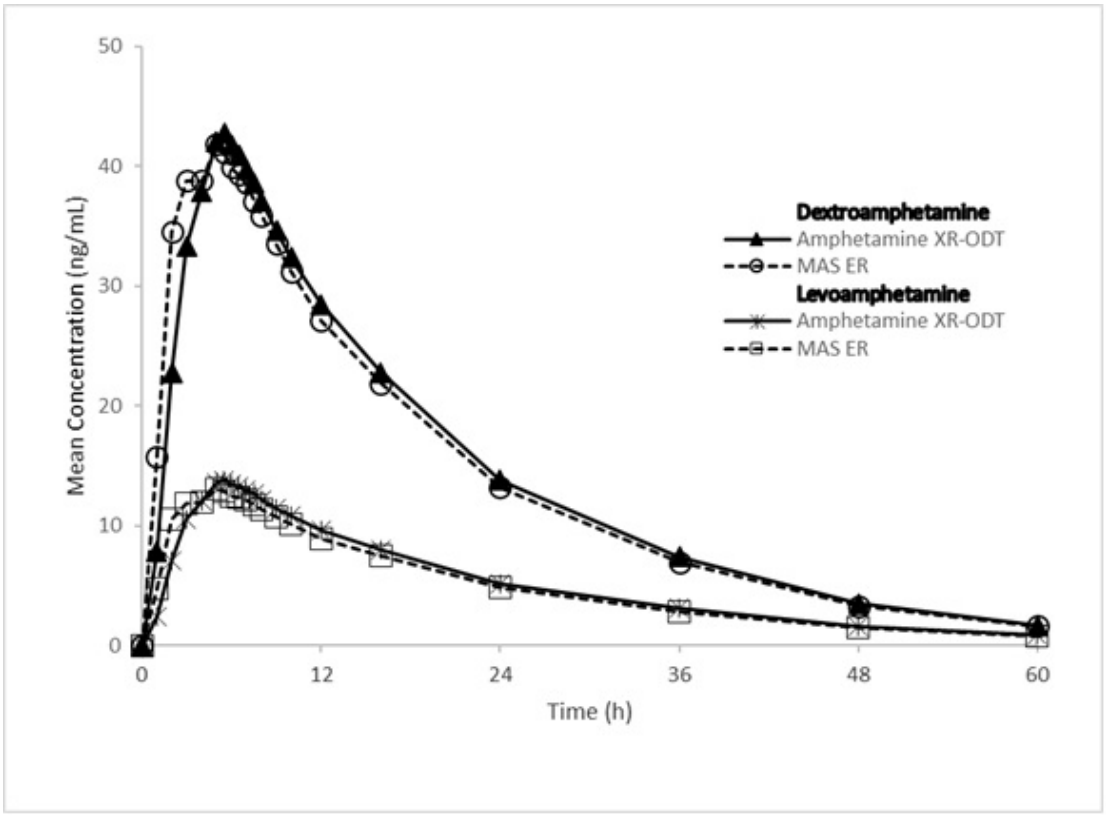
12.1 Mechanism of Action

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 amphetamine extended-release orally disintegrating tablets 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).



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 amphetamine extended-release orally disintegrating tablets.

Table 6: d-Amphetamine PK Parameters (mean + SD) after amphetamine extended-release orally disintegrating tablets 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 $\pm$2.0	11.33 $\pm$2.0
C_{max}(ng/ml)	44.9 $\pm$8.9	36.3 $\pm$6.9
AUC_{inf}(hr*ng/mL)	876.9 $\pm$182.4	856.3 $\pm$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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets. 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_{∞}) and maximum plasma concentration (C_{max}) decreased with increases in body weight, while oral volume of distribution (V_Z/F), oral clearance (CL/F), and elimination half-life ($t_{1/2}$) increased with increases in body weight.

Pediatric Patients

The pharmacokinetics of amphetamine extended-release orally disintegrating tablets 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 (t1/2) 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 (Cmax 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 amphetamine extended-release orally disintegrating tablets (d- tol- 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 amphetamine extended-release orally disintegrating tablets (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 amphetamine extended-release orally disintegrating tablets 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

How Supplied

Amphetamine extended-release orally disintegrating tablets 3.1 mg: 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 62542-005-30

Amphetamine extended-release orally disintegrating tablets 6.3 mg: 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 62542-010-30

Amphetamine extended-release orally disintegrating tablets 9.4 mg: 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 62542-015-30

Amphetamine extended-release orally disintegrating tablets 12.5 mg: 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 62542-020-30

Amphetamine extended-release orally disintegrating tablets 15.7 mg: 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 62542-025-30

Amphetamine extended-release orally disintegrating tablets 18.8 mg: 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 62542-030-30

Storage

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

Store amphetamine extended-release orally disintegrating tabletsblister packagesin 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 amphetamine extended-release orally disintegrating tablets, 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

amphetamine extended-release orally disintegrating tablets in a safe place, preferably locked, and instruct patients to not give amphetamine extended-release orally disintegrating tablets to anyone else.

Dosage and Administration Instructions

Provide the following instructions on administration to the patient:

- 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.

Risks to Patients with Serious Cardiac Disease

Advise patients that there are potential risks to patients with serious cardiac disease, including sudden death, with amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets can cause elevations of their blood pressure and pulse rate *[see Warnings and Precautions (5.3)]*.

PsychiatricAdverse Reactions

Advise patients that amphetamine extended-release orally disintegrating tablets, at recommended doses, may cause psychotic symptoms or mania *[see Warnings and Precautions (5.4)]*.

Long-Term Suppression of Growth

Advise patients that amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets.

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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets. 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 amphetamine extended-release orally disintegrating tablets during pregnancy. Advise patients to notify their healthcare provider if they become pregnant or intend to become pregnant during treatment with amphetamine extended-release orally disintegrating tablets. Advise patients of the potential fetal effects from the use of amphetamine extended-release orally disintegrating tablets during pregnancy *[see Use in Specific Populations (8.1)]*.

Lactation

Advise patients not to breastfeed if they are taking amphetamine extended-release orally disintegrating tablets *[see Use in Specific Populations (8.2)]*.

Alcohol

Advise patients to avoid alcohol while taking amphetamine extended-release orally disintegrating tablets. Consumption of alcohol while taking amphetamine extended-release orally disintegrating tablets may result in a more rapid release of the dose of amphetamine *[see Clinical Pharmacology (12)]*.

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

For more informationcall 1-888-319-1789.

Patent Number 8,709,491 B2

MEDICATION GUIDE **AMPHETAMINE EXTENDED-RELEASE ORALLY DISINTEGRATING TABLETS** **(am-fet'-a-meen), CII**
What is the most important information I should know about

amphetamine extended-release orally disintegrating tablets?
Amphetamine extended-release orally disintegrating tablets may cause serious side effects, including:

- **Abuse, misuse, and addiction.**Amphetamine extended-release orally disintegrating tablets has a high chance for abuse and misuse and may lead to substance use problems, including addiction. Misuse and abuse of amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets and will monitor you or your child during treatment.
  - Amphetamine extended-release orally disintegrating tablets may lead to physical dependence after prolonged use, even if taken as directed by your healthcare provider.
  - Do not give amphetamine extended-release orally disintegrating tablets to anyone else. See " **What is amphetamine extended-release orally disintegrating tablets?**" for more information.
  - Keep amphetamine extended-release orally disintegrating tablets in a safe place and properly dispose of any unused medicine. See " **How should I store amphetamine extended-release orally disintegrating tablets?**" 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 amphetamine extended-release orally disintegrating tablets. 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 amphetamine extended-release orally disintegrating tablets.**
- **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 amphetamine extended-release orally disintegrating tablets.
- **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 amphetamine extended-release orally disintegrating tablets, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

What is amphetamine extended-release orally disintegrating tablets?

Amphetamine extended-release orally disintegrating tablets is a central nervous system (CNS) stimulant prescription medicine. **It is used for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD)**. Amphetamine extended-release orally disintegrating tablets may help increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.

It is not known if amphetamine extended-release orally disintegrating tablets is safe and effective in children under 6 years of age.

Amphetamine extended-release orally disintegrating tablets is a federally controlled substance (CII) because it contains amphetamine that can be a target for people who abuse prescription medicines or street drugs. Keep amphetamine extended-release orally disintegrating tablets in a safe place to prevent it from theft. Never give your amphetamine extended-release orally disintegrating tablets to anyone else, because it may harm them. Selling or giving away amphetamine extended-release orally disintegrating tablets may harm others and is against the law.

Who should not take amphetamine extended-release orally disintegrating tablets?

Amphetamine extended-release orally disintegrating tablets should not be taken if you or your child:

- are allergic to amphetamine, or any of the ingredients in amphetamine extended-release orally disintegrating tablets. See the end of this Medication Guide for a complete list of ingredients in amphetamine extended-release orally disintegrating tablets.
- are taking or have taken within the past 14 days an anti-depression medicine called monoamine oxidase inhibitor or MAOI.

What should I tell my healthcare provider before taking amphetamine extended-release orally disintegrating tablets?

Amphetamine extended-release orally disintegrating tablets may not be right for you or your child. Before starting amphetamine extended-release orally disintegrating tablets, tell your or your child's healthcare provider about all health conditions (or a family history of) including:

- heart problems, heart disease, heart defects, or high blood pressure
- mental problems including psychosis, mania, bipolar illness, or depression
- circulation problems in fingers and toes

Tell your healthcare provider:

- if you or your child have kidney problems. Your healthcare provider may lower the dose.
- have or had repeated movements or sounds (tics) or Tourette's syndrome, or have a family history of tics or Tourette's syndrome.
- if you or your child are pregnant, or plan to become pregnant. It is not known if amphetamine extended-release orally disintegrating tablets will harm your unborn baby.
    - There is a pregnancy registry for women who are exposed to Amphetamine extended-release orally disintegrating tablets during pregnancy. The purpose of the registry is to collect information about the health of females exposed to amphetamine extended-release orally disintegrating tablets and their babies. If you or your child becomes pregnant during treatment with amphetamine extended-release orally disintegrating tablets, talk to your healthcare provider about registering with the National Pregnancy Registry for Psychostimulants. You can register by calling 1-866-961-2388 or by visiting online at https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/othermedications/.
- if you or your child is breastfeeding or plan to breastfeed. Amphetamine extended-release orally disintegrating tablets passes into breast milk. You should not breastfeed while you are taking amphetamine extended-release orally disintegrating tablets. Talk to your healthcare provider about the best way to feed the baby during treatment with amphetamine extended-release orally disintegrating tablets.

Tell your healthcare provider about all of the medicines that you or your child takesincluding prescription and over-the-counter medicines, vitamins, and herbal supplements. Amphetamine extended-release orally disintegrating tablets and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be adjusted while taking amphetamine extended-release orally disintegrating tablets.
Your healthcare provider will decide whether amphetamine extended-release orally disintegrating tablets can be taken with other medicines.
Especially tell your healthcare provider if you or your child takes:

- anti-depression medicines including MAOIs

Know the medicines that you or your child take. Keep a list of your medicines with you to show your healthcare provider and pharmacist.
Do not start any new medicine while taking amphetamine extended-release orally disintegrating tablets without talking to your healthcare provider first.

How should amphetamine extended-release orally disintegrating tablets be taken?

- Take amphetamine extended-release orally disintegrating tablets exactly as prescribed. Your healthcare provider may adjust the dose until it is right for you or your child.
- Take amphetamine extended-release orally disintegrating tablets 1 time each day in the morning.
    - Leave the tablet in the blister pack until you are ready to take or

give it.
    - Use dry hands to open the blister pack.
    - Tear along the perforation, bend the blister where indicated and peel back the blister's labeled backing to take out the tablet. **Do not push the tablet through the foil.**
    - Place the tablet on the tongue.
    - Take amphetamine extended-release orally disintegrating tablets 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.
- Amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets.
- Children should have their height and weight checked often while taking amphetamine extended-release orally disintegrating tablets. Amphetamine extended-release orally disintegrating tablets treatment may be stopped if a problem is found during these check-ups.

If you or your child take too much amphetamine extended-release orally disintegrating tablets, 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 amphetamine extended-release orally disintegrating tablets?

- drinking alcohol

What are possible side effects of amphetamine extended-release orally disintegrating tablets?
amphetamine extended-release orally disintegrating tabletscan cause serious side effects, including:

- See **"What is the most important information I should know about amphetamine extended-release orally disintegrating tablets?"**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 amphetamine extended-release orally disintegrating tablets. Your healthcare provider may stop your child's amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally

disintegrating tablets.

- **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 amphetamine extended-release orally disintegrating tablets.

Common side effects of amphetamine extended-release orally disintegrating tablets includedecreased appetite and problems sleeping **.**

Common side effects of amphetamine extended-release orally disintegrating tablets in children 6 to 12 years of age also include:

- stomach pain
- nervousness
- extreme mood change
- nausea
- vomiting
- fever

Common side effects of amphetamine extended-release orally disintegrating tablets in children 13 to 17 years of age also include:

- stomach pain
- weight loss

Common side effects of amphetamine extended-release orally disintegrating tablets in adults also include:

- dry mouth
- nausea
- dizziness
- weakness
- headache
- anxiety
- fast heart beat
- urinary tract infections
- weight loss
- restlessness
- diarrhea

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 amphetamine extended-release orally disintegrating tablets.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1800-FDA-1088.

How should I store amphetamine extended-release orally disintegrating tablets?

- Store amphetamine extended-release orally disintegrating tablets at room temperature between 68° F to 77° F (20° C to 25° C).
- Store amphetamine extended-release orally disintegrating tablets in a safe place, like a locked cabinet.
- Store amphetamine extended-release orally disintegrating tablets in the blister packaging until you are ready to take or give it.
- Store amphetamine extended-release orally disintegrating tablets blister packages in the hard plastic travel case provided after removal from the carton.
- Dispose of remaining, unused, or expired amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets in the household trash. Visit www.fda.gov/drugdisposal for additional information on disposal of unused medicines.

Keep amphetamine extended-release orally disintegrating tablets and all medicines out of the reach of children.

General information about the safe and effective use of amphetamine extended-release orally disintegrating tablets

Medicines are sometimes prescribed for purposes other than those listed in the Medication Guide. Do not use amphetamine extended-release orally disintegrating tablets for a condition for which it has not been prescribed. Do not give amphetamine extended-release orally disintegrating tablets 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 amphetamine extended-release orally disintegrating tablets. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about amphetamine extended-release orally disintegrating tablets that is written for healthcare professionals.

For more information about amphetamine extended-release orally disintegrating tablets or to get a plastic travel case contact Neos Therapeutics, Inc. at 1-888-236-6816.

What are the ingredients in amphetamine extended-release orally disintegrating tablets?

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 LP, Denver, CO 80237.

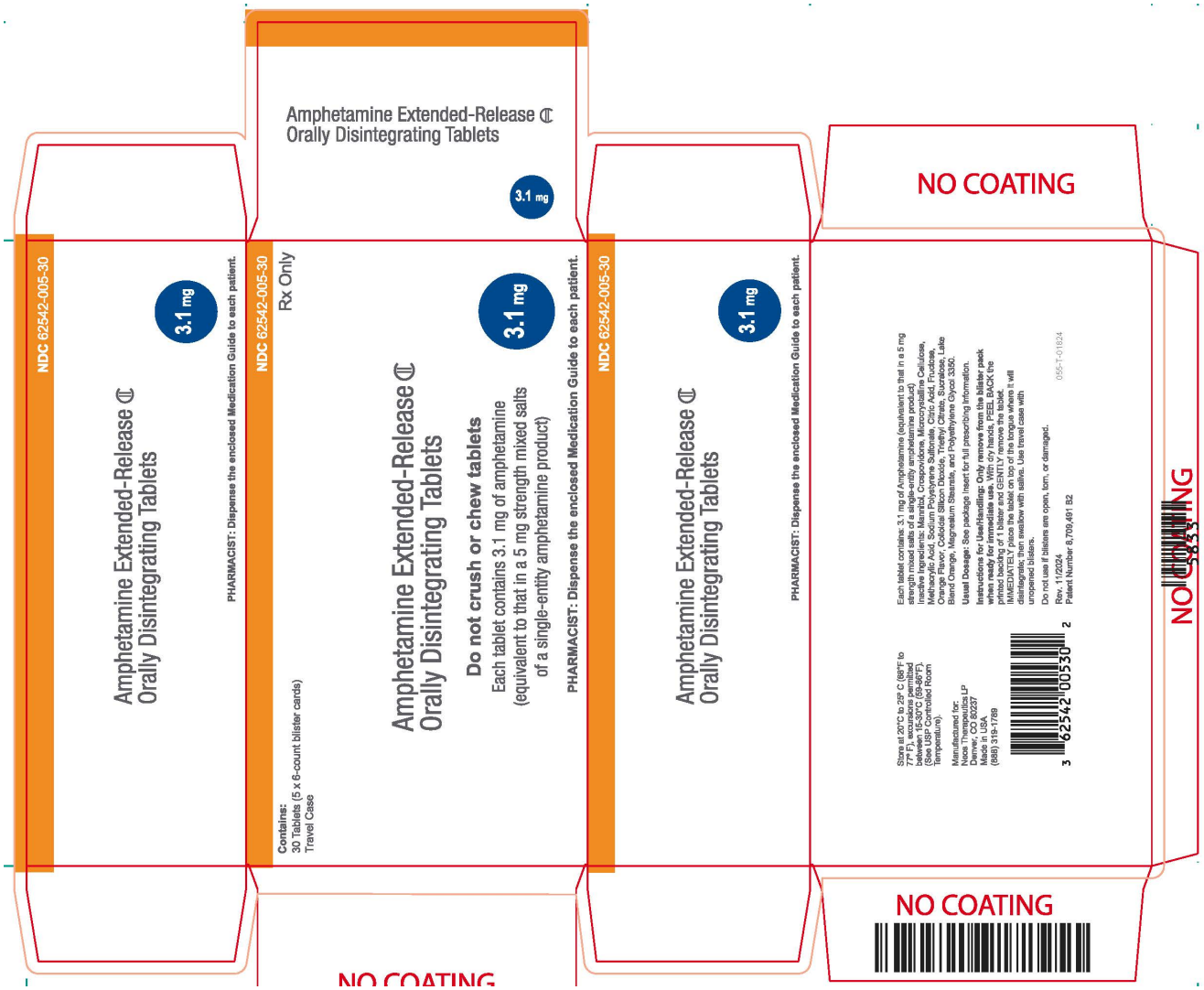
This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 3/2025

PRINCIPAL DISPLAY PANEL - 3.1 mg

Amphetamine extended-release orally disintegrating tablets 3.1 mg

Carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets

NDC 62542-005-30



PRINCIPAL DISPLAY PANEL - 6.3 mg

Amphetamine extended-release orally disintegrating tablets 6.3 mg

Carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets

NDC 62542-010-30

PRINCIPAL DISPLAY PANEL - 9.4 mg

Amphetamine extended-release orally disintegrating tablets 9.4 mg

Carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets

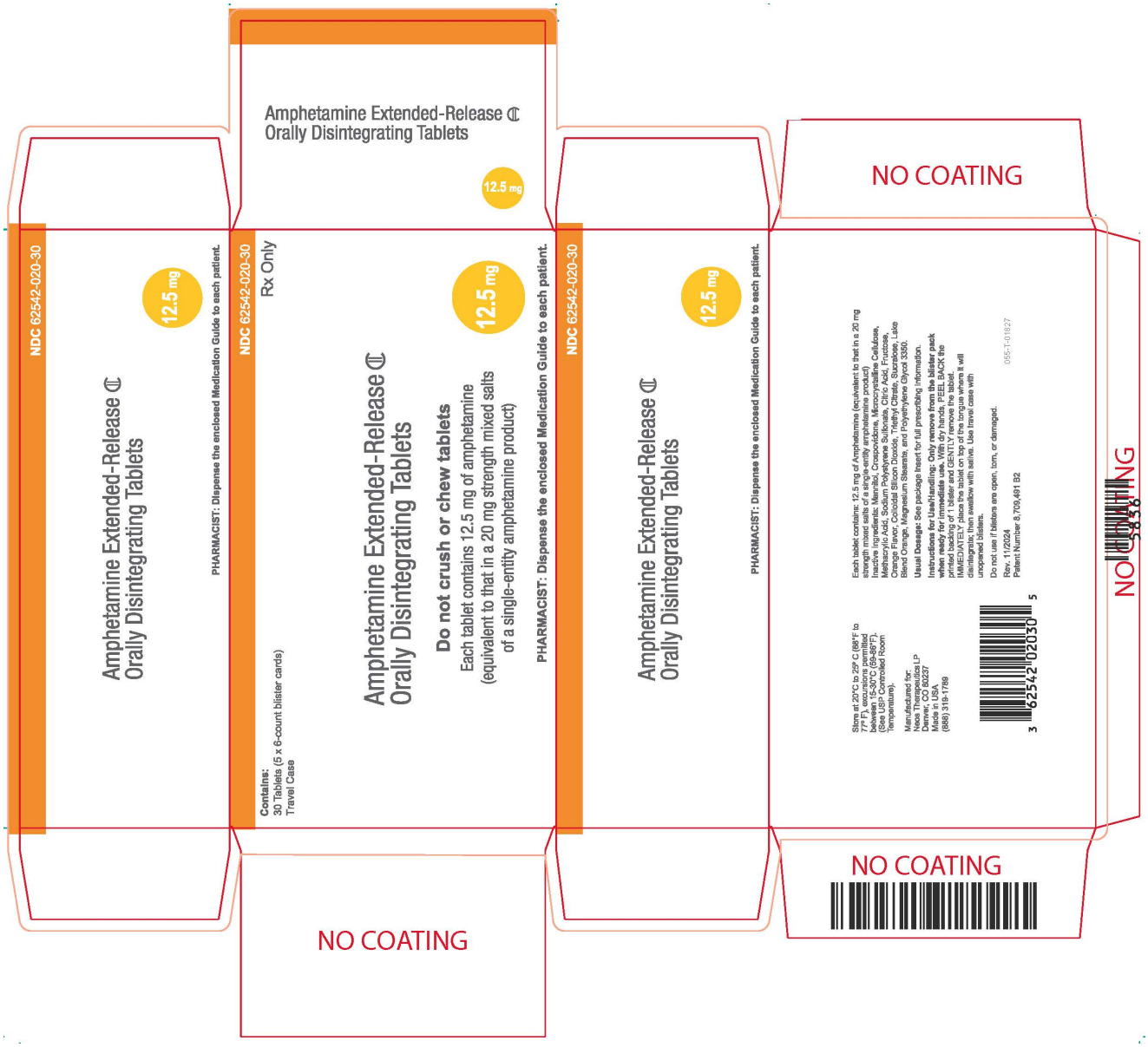
NDC 62542-015-30

PRINCIPAL DISPLAY PANEL - 12.5 mg

Amphetamine extended-release orally disintegrating tablets 12.5 mg

Carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets

NDC 62542-020-30

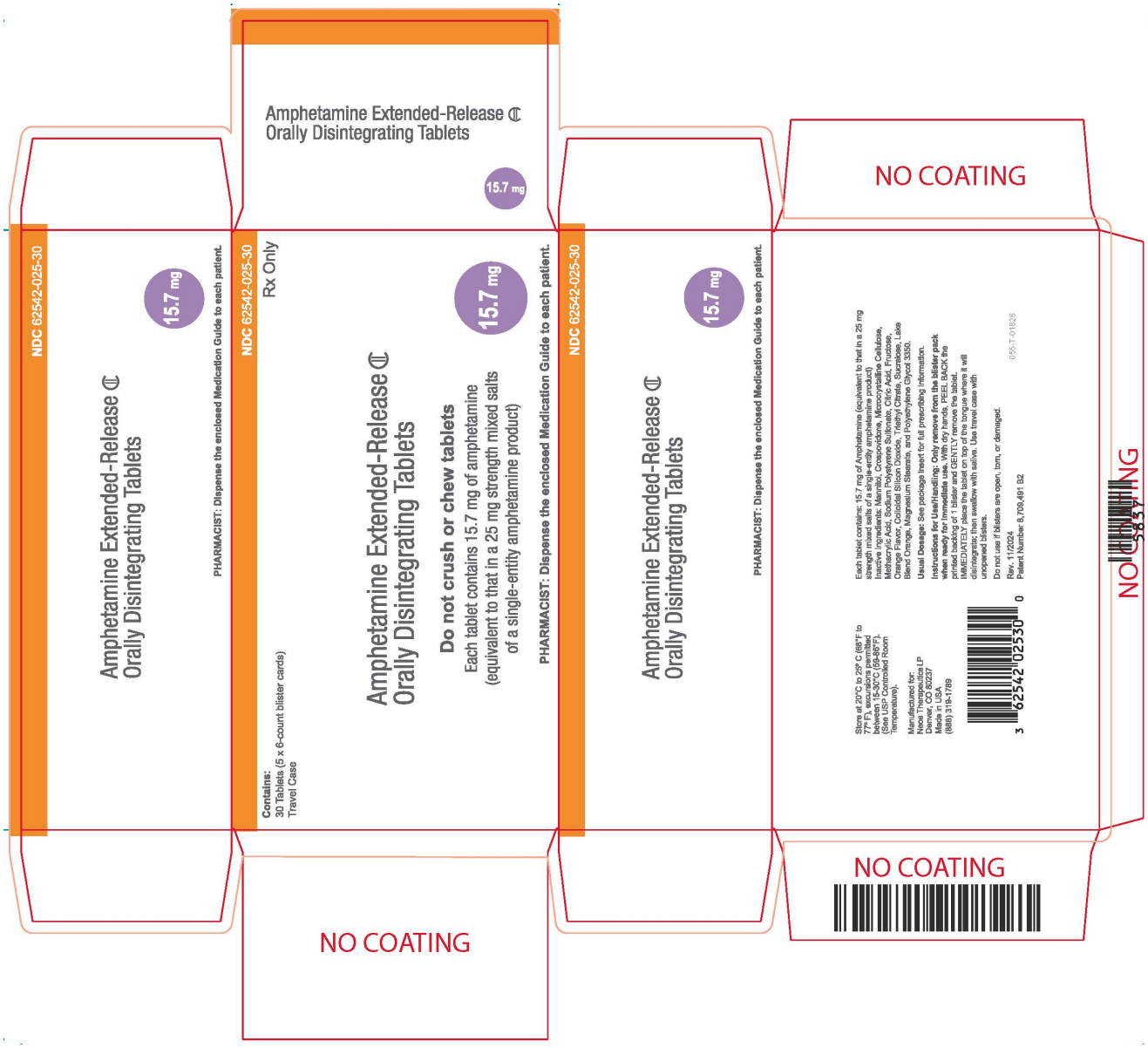


PRINCIPAL DISPLAY PANEL - 15.7 mg

Amphetamine extended-release orally disintegrating tablets 15.7 mg

Carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets

NDC 62542-025-30



PRINCIPAL DISPLAY PANEL - 18.8 mg

Amphetamine extended-release orally disintegrating tablets 18.8 mg

Carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets

NDC 62542-030-30

AMPHETAMINE EXTENDED-RELEASE

amphetamine extended-release tablet, orally disintegrating

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:62542-005
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
AMPHETAMINE (UNII: CK833KGX7E) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE	3.1 mg

Inactive Ingredients	
Ingredient Name	**Strength**
MANNITOL (UNII: 3OWL53L36A)	
CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 68401960MK)	

MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
METHACRYLIC ACID (UNII: 1CS02G8656)	
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
FRUCTOSE (UNII: 6YSS42VSEV)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
TRIETHYL CITRATE (UNII: 8Z96QXD6UM)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	

Product Characteristics

Color	orange (orange;to;light;orange;mottled)	**Score**	no score
Shape	ROUND	**Size**	3mm
Flavor		**Imprint Code**	A1
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:62542-005-30	30 in 1 CARTON	09/01/2025	
1		6 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA204326	09/01/2025	

AMPHETAMINE EXTENDED-RELEASE

amphetamine extended-release tablet, orally disintegrating

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:62542-010
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMPHETAMINE (UNII: CK833KGX7E) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE	6.3 mg

Inactive Ingredients

Ingredient Name	Strength
MANNITOL (UNII: 3OWL53L36A)	
CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 68401960MK)	

MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
METHACRYLIC ACID (UNII: 1CS02G8656)	
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
FRUCTOSE (UNII: 6YSS42VSEV)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
TRIETHYL CITRATE (UNII: 8Z96QXD6UM)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	

Product Characteristics

Color	orange (orange;to;light;orange;mottled)	**Score**	no score
Shape	ROUND	**Size**	4mm
Flavor		**Imprint Code**	A2
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:62542-010-30	30 in 1 CARTON	09/01/2025	
1		6 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA204326	09/01/2025	

AMPHETAMINE EXTENDED-RELEASE

amphetamine extended-release tablet, orally disintegrating

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:62542-015
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMPHETAMINE (UNII: CK833KGX7E) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE	9.4 mg

Inactive Ingredients

Ingredient Name	Strength
MANNITOL (UNII: 3OWL53L36A)	
CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 68401960MK)	

MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
METHACRYLIC ACID (UNII: 1CS02G8656)	
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
FRUCTOSE (UNII: 6YSS42VSEV)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
TRIETHYL CITRATE (UNII: 8Z96QXD6UM)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	

Product Characteristics

Color	orange (orange;to;light;orange;mottled)	**Score**	no score
Shape	ROUND	**Size**	5mm
Flavor		**Imprint Code**	A3
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:62542-015-30	30 in 1 CARTON	09/01/2025	
1		6 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA204326	09/01/2025	

AMPHETAMINE EXTENDED-RELEASE

amphetamine extended-release tablet, orally disintegrating

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:62542-020
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMPHETAMINE (UNII: CK833KGX7E) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE	12.5 mg

Inactive Ingredients

Ingredient Name	Strength
MANNITOL (UNII: 3OWL53L36A)	

CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 68401960MK)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
METHACRYLIC ACID (UNII: 1CS02G8656)	
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
FRUCTOSE (UNII: 6YSS42VSEV)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
TRIETHYL CITRATE (UNII: 8Z96QXD6UM)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	

Product Characteristics

Color	orange (orange;to;light;orange;mottled)	**Score**	no score
Shape	ROUND	**Size**	5mm
Flavor		**Imprint Code**	A4
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:62542-020-30	30 in 1 CARTON	09/01/2025	
1		6 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA204326	09/01/2025	

AMPHETAMINE EXTENDED-RELEASE

amphetamine extended-release tablet, orally disintegrating

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:62542-025
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMPHETAMINE (UNII: CK833KGX7E) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE	15.7 mg

Inactive Ingredients

Ingredient Name	Strength
MANNITOL (UNII: 3OWL53L36A)	

CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 68401960MK)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
METHACRYLIC ACID (UNII: 1CS02G8656)	
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
FRUCTOSE (UNII: 6YSS42VSEV)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
TRIETHYL CITRATE (UNII: 8Z96QXD6UM)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	

Product Characteristics

Color	orange (orange;to;light;orange;mottled)	**Score**	no score
Shape	ROUND	**Size**	6mm
Flavor		**Imprint Code**	A5
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:62542-025-30	30 in 1 CARTON	09/01/2025	
1		6 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA204326	09/01/2025	

AMPHETAMINE EXTENDED-RELEASE

amphetamine extended-release tablet, orally disintegrating

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:62542-030
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMPHETAMINE (UNII: CK833KGX7E) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE	18.8 mg

Inactive Ingredients

Ingredient Name	Strength
MANNITOL (UNII: 3OWL53L36A)	

CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 68401960MK)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
METHACRYLIC ACID (UNII: 1CS02G8656)	
SODIUM POLYSTYRENE SULFONATE (UNII: 1699G8679Z)	
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
FRUCTOSE (UNII: 6YSS42VSEV)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
TRIETHYL CITRATE (UNII: 8Z96QXD6UM)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	

Product Characteristics

Color	orange (orange;to;light;orange;mottled)	**Score**	no score
Shape	ROUND	**Size**	6mm
Flavor		**Imprint Code**	A6
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:62542-030-30	30 in 1 CARTON	09/01/2025	
1		6 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA204326	09/01/2025	

Labeler - Neos Therapeutics, LP (836126052)

Revised: 8/2025 Neos Therapeutics, LP