

EVEKEO ODT- amphetamine sulfate tablet, orally disintegrating

Arbor Pharmaceuticals

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use EVEKEO ODT® safely and effectively. See full prescribing information for EVEKEO ODT.

EVEKEO ODT (amphetamine sulfate) orally disintegrating tablets, CII
Initial U.S. Approval: 1984

WARNING: ABUSE AND DEPENDENCE

See full prescribing information for complete boxed warning.

- **CNS stimulants, including EVEKEO ODT, other amphetamine-containing products, and methylphenidate, have a high potential for abuse and dependence. (5.1, 9.3)**
- **Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy. (9.2, 9.3)**

RECENT MAJOR CHANGES

Indications and Usage (1)	4/2021
Dosage and Administration (2.2)	4/2021

INDICATIONS AND USAGE

EVEKEO ODT is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 3 to 17 years of age. (1)

DOSAGE AND ADMINISTRATION

- Administer in the morning with or without food or liquid. (2.2)
- *Pediatric patients 3 to 5 years of age:* Recommended starting dosage is 2.5 mg daily. If necessary, administer an additional dose after 4 to 6 hours. Titrate the dosage in increments of 2.5 mg at weekly intervals. (2.2)
- *Pediatric patients 6 to 17 years of age:* Recommended starting dosage is 5 mg once or twice daily. If necessary, administer an additional dose after 4 to 6 hours. Titrate the dosage in increments of 2.5 mg or 5 mg at weekly intervals. (2.2)
- Only in rare cases will it be necessary to exceed a total of 40 mg daily. (2.2)
- Place the whole tablet on tongue and allow to disintegrate in saliva, so that it can be swallowed. (2.3)
- Do not substitute for other amphetamine products on a milligram-per-milligram basis because of different amphetamine salt compositions and differing pharmacokinetic profiles. (2.4)

DOSAGE FORMS AND STRENGTHS

Orally disintegrating tablets: 2.5 mg, 5 mg, 10 mg, 15 mg, and 20 mg. (3)

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

- *Serious Cardiovascular Reactions:* Sudden death has been reported in association with CNS stimulant treatment at recommended doses in pediatric patients with structural cardiac abnormalities or other serious heart problems. In adults, sudden death, stroke, and myocardial infarction have been reported. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, or coronary artery disease. (5.2)
- *Blood Pressure and Heart Rate Increases:* Monitor blood pressure and pulse. Consider benefits and risks before use in patients for whom blood pressure increases may be problematic. (5.3)
- *Psychiatric Adverse Reactions:* May cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to EVEKEO ODT use. (5.4)
- *Long-term Suppression of Growth:* Monitor height and weight in pediatric patients during treatment.

(5.5)

- *Seizures*: May lower the convulsive threshold. If a seizure occurs, discontinue EVEKEO ODT. (5.6)
- *Peripheral Vasculopathy, including Raynaud's Phenomenon*: Stimulants used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Careful observation for digital changes is necessary during treatment with ADHD stimulants. (5.7)
- *Serotonin Syndrome*: Increased risk when co-administered with serotonergic agents (e.g., SSRIs, SNRIs, triptans), but also during overdose situations. If it occurs, discontinue EVEKEO ODT and initiate supportive treatment. (5.8)

ADVERSE REACTIONS

Most common adverse reactions (incidence $\geq 4\%$ and at a rate at least twice placebo) in pediatric patients are: decreased appetite and insomnia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Arbor Pharmaceuticals, LLC at 1-866-516-4950 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Acidifying and Alkalinizing Agents: Agents that alter GI and urinary pH can alter blood levels of amphetamine. Acidifying agents (GI and urinary) can decrease amphetamine blood levels, while alkalinizing agents (GI and urinary) can increase amphetamine blood levels. Adjust EVEKEO ODT dosage accordingly. (2.5, 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: 2/2022

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FULL PRESCRIBING INFORMATION

WARNING: ABUSE AND DEPENDENCE

CNS stimulants, including EVEKEO ODT, other amphetamine-containing products, and methylphenidate, have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy [see Warnings and Precautions (5.1), and Drug Abuse and Dependence (9.2, 9.3)].

1 INDICATIONS AND USAGE

EVEKEO ODT is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 3 to 17 years of age.

2 DOSAGE AND ADMINISTRATION

2.1 Pre-treatment Screening

Prior to treating patients with EVEKEO 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)*].

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

2.2 Dosage Information

Administer EVEKEO ODT orally in the morning with or without food or liquid.

Pediatric Patients 3 to 5 years of age

The recommended starting dosage is 2.5 mg daily. If necessary, administer an additional dose after 4 to 6 hours. Titrate the dosage in increments of 2.5 mg at weekly intervals depending on response and tolerability.

Pediatric Patients 6 to 17 years of age

The recommended starting dosage is 5 mg once or twice daily. If necessary, administer an additional dose after 4 to 6 hours. Titrate the dosage in increments of 2.5 mg or 5 mg at weekly intervals depending on response and tolerability.

Only in rare cases will it be necessary to exceed a total of 40 mg daily.

Where possible, drug administration should be interrupted occasionally to determine if there is a recurrence of behavioral symptoms sufficient to require continued therapy.

Amphetamine should be administered at the lowest effective dosage and dosage should be individually adjusted.

2.3 Administration Instructions

Instruct the patient or caregiver on the following administration instructions:

- Do not remove the tablet from the blister pack until just prior to dosing. Do not store the tablet for future use.
- Use dry hands to open the blister.
- Remove the tablet by pushing it through the back of the foil-lined blister pack.
- As soon as the blister is opened, remove the tablet and place the tablet on the patient's tongue.
- Place the whole tablet on the tongue and allow it to disintegrate without chewing or crushing.
- The tablet will disintegrate in saliva so that it can be swallowed. No liquid is needed to take the tablet. The tablet can be actively moved around between the tongue and the roof of the mouth until it disintegrates.

2.4 Switching from Other Amphetamine Products

Switching from EVEKEO to EVEKEO ODT can be done on a milligram-per-milligram basis.

When switching from other amphetamine products, discontinue treatment and titrate with EVEKEO ODT using the titration schedule above. Do not substitute for other amphetamine products on a milligram-per-milligram basis because of different

amphetamine salt compositions and differing pharmacokinetic profiles [see *Description (11)*, *Clinical Pharmacology (12.3)*].

2.5 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 EVEKEO ODT dosage accordingly [see *Drug Interactions (7.1)*].

3 DOSAGE FORMS AND STRENGTHS

EVEKEO ODT (amphetamine sulfate) orally disintegrating tablets are supplied as follows:

- 2.5 mg: white to off-white, round, flat-faced radius-edged tablet with "2" on one side and "E" on the other.
- 5 mg: white to off-white, round, flat-faced radius-edged tablet with "5" on one side and "EVI" on the other.
- 10 mg: white to off-white, round, flat-faced radius-edged tablet with "10" on one side and "EVI" on the other.
- 15 mg: white to off-white, round, flat-faced radius-edged tablet with "15" on one side and "EVI" on the other.
- 20 mg: white to off-white, round, flat-faced radius-edged tablet with "20" on one side and "EVI" on the other.

4 CONTRAINDICATIONS

EVEKEO ODT is contraindicated in patients:

- With known hypersensitivity to amphetamine, or other components of EVEKEO ODT. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with other amphetamine products [see *Adverse Reactions (6.2)*].
- Receiving concomitant treatment with monoamine oxidase inhibitors (MAOIs), or within 14 days following discontinuation of treatment with an MAOI (including MAOIs such as linezolid or intravenous methylene blue), because of an increased risk of hypertensive crisis [see *Warnings and Precautions (5.8)*, *Drug Interactions (7.1)*].

5 WARNINGS AND PRECAUTIONS

5.1 Potential for Abuse and Dependence

CNS stimulants, including EVEKEO ODT, other amphetamine-containing products, and methylphenidate, have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy [see *Drug Abuse and Dependence (9.2, 9.3)*].

5.2 Serious Cardiovascular Reactions

Sudden death, stroke, and myocardial infarction have been reported in adults with CNS stimulant treatment at recommended doses. Sudden death has been reported in

pediatric patients with structural cardiac abnormalities and other serious heart problems taking CNS stimulants at recommended doses for ADHD. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease, and other serious heart problems. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during EVEKEO ODT treatment.

5.3 Blood Pressure and Heart Rate Increases

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

5.4 Psychiatric Adverse 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 Illness

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

New Psychotic or Manic Symptoms

CNS stimulants, at recommended doses, may cause psychotic or manic symptoms (e.g., hallucinations, delusional thinking, or mania) in patients without prior history of psychotic illness or mania. If such symptoms occur, consider discontinuing EVEKEO ODT. 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% in placebo-treated patients.

5.5 Long-Term Suppression of Growth

CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. Closely monitor growth (weight and height) in pediatric patients treated with CNS stimulants, including EVEKEO ODT.

Patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted [see *Use in Specific Populations (8.4)*].

5.6 Seizures

There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, discontinue EVEKEO ODT.

5.7 Peripheral Vasculopathy, including Raynaud's Phenomenon

Stimulants, including EVEKEO ODT, used to treat ADHD are associated with peripheral

vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; however, very rare sequelae include digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud's phenomenon, were observed in post-marketing reports at different times and at therapeutic doses in all age groups throughout the course of treatment. Signs and symptoms generally improve after reduction in dose or discontinuation of drug. Careful observation for digital changes is necessary during treatment with ADHD stimulants. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients.

5.8 Serotonin Syndrome

Serotonin syndrome, a potentially life-threatening reaction, may occur when amphetamines are used in combination with other drugs that affect the serotonergic neurotransmitter systems such as MAOIs, selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort [see *Drug Interactions (7.1)*]. The co-administration with cytochrome P450 2D6 (CYP2D6) inhibitors may also increase the risk with increased exposure to EVEKEO 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 EVEKEO ODT with MAOI drugs is contraindicated [see *Contraindications (4)*].

Discontinue treatment with EVEKEO ODT and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of EVEKEO ODT with other serotonergic drugs or CYP2D6 inhibitors is clinically warranted, initiate EVEKEO 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.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Abuse and Dependence [see *Boxed Warning, Warnings and Precautions (5.1)*, and *Drug Abuse and Dependence (9.2,9.3)*]
- Hypersensitivity to amphetamine, or other components of EVEKEO ODT [see *Contraindications (4)*]
- Hypertensive Crisis When Used Concomitantly with Monoamine Oxidase Inhibitors [see *Contraindications (4)* and *Drug Interactions (7.1)*]
- Serious Cardiovascular Reactions [see *Warnings and Precautions (5.2)*]
- Blood Pressure and Heart Rate Increases [see *Warnings and Precautions (5.3)*]
- Psychiatric Adverse Reactions [see *Warnings and Precautions (5.4)*]
- Seizures [see *Warnings and Precautions (5.6)*]

- Long-Term Suppression of Growth [see Warnings and Precautions (5.5)]
- Peripheral Vasculopathy, including Raynaud's Phenomenon [see Warnings and Precautions (5.7)]
- Serotonin 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.

Study 1 was conducted with EVEKEO tablets (i.e., not the ODT formulation) in children ages 6 to 12 years who met Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM-IV-TR) criteria for ADHD. This study began with an 8-week, open-label, dose-optimization phase followed by a 2-week double-blind, placebo-controlled, randomized, crossover phase. Adverse reactions reported in > 5% of patients (N=105; doses of 10 to 40 mg/day) during the open-label phase included: decreased appetite (28%), infections (22%), abdominal pain (15%), irritability (14%), headache (13%), nausea (6%), vomiting (6%), affect lability (includes mood swings; 9%), tachycardia (9%), insomnia (10%), fatigue (10%), and dry mouth (6%). During the open-label phase, six patients discontinued due to adverse reactions: irritability (n=3), affect lability (n=1), initial insomnia (n=1), and rash (n=1).

Table 1 lists the adverse reactions reported during the double-blind, cross-over phase. No patient discontinued the study for an adverse reaction during the double-blind crossover phase. Because of the trial design (an initial 8-week, open-label, active treatment phase), the adverse reaction rates described in the double-blind phase are lower than expected in clinical practice.

Table 1: Adverse Reactions Reported in \geq 2%, and > Placebo, of EVEKEO-Treated Pediatric Patients (6 to 12 Years) During the Double-Blind Cross-Over Weeks. *

System Organ Class Preferred Term	EVEKEO (n= 97)	Placebo (n= 97)
Subjects with at least one adverse event	22%	14%
Metabolism and Nutrition Disorders		
Decreased appetite	4%	0%
Gastrointestinal Disorders		
Abdominal pain	3%	0%
Psychiatric Disorders		
Affect Lability†	3%	0%
Insomnia	4%	0%
Injury, poisoning and procedural complications		
Injury	3%	2%

* Drug exposures and placebo exposures from cross-over were combined for analysis.

† Includes mood swings.

6.2 Postmarketing Experience

The following adverse reactions have been associated during post approval use of

amphetamines. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiovascular: Palpitations, tachycardia, elevation of blood pressure, sudden death, myocardial infarction. There have been isolated reports of cardiomyopathy associated with chronic amphetamine use.

Central Nervous System: Psychotic episodes at recommended doses, overstimulation, irritability, restlessness, dizziness, insomnia, euphoria, mood swings, aggression, anger, logorrhea, dermatillomania, dyskinesia, dysphoria, tremor, fatigue, headache, exacerbation of motor and phonic tics and Tourette's syndrome

Gastrointestinal: Dry mouth, unpleasant taste, constipation, nausea, intestinal ischemia, other gastrointestinal disturbances, anorexia, and weight loss.

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

Endocrine: Impotence, changes in libido, and frequent or prolonged erections.

Skin: Alopecia.

Vascular Disorders: Raynaud's phenomenon.

Musculoskeletal: Rhabdomyolysis.

7 DRUG INTERACTIONS

7.1 Drugs Having Clinically Important Interactions with Amphetamines

Table 2: 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 EVEKEO ODT during or within 14 days following the administration of MAOI [see <i>Contraindications (4)</i>].
Examples	selegiline, isocarboxazid, phenelzine, tranylcypromine, linezolid, methylene blue
Serotonergic Drugs	
Clinical Impact	The concomitant use of EVEKEO ODT and serotonergic drugs increases the risk of serotonin syndrome.
	Initiate with lower doses and monitor patients for signs

Intervention	and symptoms of serotonin syndrome, particularly during EVEKEO ODT initiation or dosage increase. If serotonin syndrome occurs, discontinue EVEKEO ODT and concomitant serotonergic drug(s) [see <i>Warnings and Precautions 5.8</i>].
Examples	Selective serotonin reuptake inhibitors (SSRI), serotonin norepinephrine reuptake inhibitors (SNRI), triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John's Wort
Alkalinizing Agents	
Clinical Impact	May increase exposure to amphetamine and exacerbate the action of amphetamine.
Intervention	Caution should be taken when co-administering EVEKEO ODT and gastrointestinal and urinary alkalinizing agents.
Examples	Gastrointestinal alkalinizing agents (e.g., sodium bicarbonate; proton pump inhibitors [e.g. omeprazole]) Urinary alkalinizing agents (e.g. acetazolamide, some thiazides)
Acidifying Agents	
Clinical Impact	Lower blood levels and efficacy of amphetamines.
Intervention	Increase dose of EVEKEO ODT based on clinical response.
Examples	Gastrointestinal acidifying agents (e.g., guanethidine, reserpine, glutamic acid HCl, ascorbic acid) Urinary acidifying agents (e.g., ammonium chloride, sodium acid phosphate, methenamine salts)
Tricyclic Antidepressants	
Clinical Impact	May enhance the activity of tricyclic or sympathomimetic agents causing sustained increases in the concentration of d- amphetamine in the brain; cardiovascular effects can be potentiated.
Intervention	Monitor frequently and adjust EVEKEO ODT dose or use alternative therapy based on clinical response.
Examples	desipramine, protriptyline
CYP2D6 Inhibitors	
Clinical Impact	The concomitant use of EVEKEO ODT and CYP2D6 inhibitors may increase the exposure of EVEKEO ODT compared to the use of the drug alone and increase the risk of serotonin syndrome.
Intervention	Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome particularly during EVEKEO ODT initiation and after a dosage increase. If serotonin syndrome occurs, discontinue EVEKEO ODT and the CYP2D6 inhibitor. Alternatively, consider using a drug that does not inhibit CYP2D6 [see <i>Warnings and Precautions (5.8) and Overdosage (10)</i>].
Examples	paroxetine and fluoxetine (also serotonergic drugs),

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 pregnancy outcomes in women exposed to ADHD medications, including EVEKEO ODT, during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Psychostimulants at 1-866-961-2388 or visiting online at <https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/othermedications/>.

Risk Summary

Available data from published epidemiologic studies and postmarketing reports on use of prescription amphetamine in pregnant women have not identified a drug-associated risk of major birth defects and miscarriage. 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*).

Dextroamphetamine sulfate has been shown to have embryotoxic effects when administered to A/Jax mice and C57BL mice in doses approximately 6 times the maximum human dose. Embryotoxic effects were not seen in New Zealand white rabbits.

The estimated 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 EVEKEO ODT, cause vasoconstriction and thereby 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.

8.2 Lactation

Risk Summary

Based on limited case reports in published literature, amphetamine (*d-* or *dl*) 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 breast feeding is not recommended during treatment with EVEKEO ODT.

8.4 Pediatric Use

The safety and effectiveness of EVEKEO ODT have been established in pediatric patients 3 years and older. Use of EVEKEO ODT is based on one adequate and well-controlled study with another immediate-release amphetamine sulfate product (EVEKEO) in pediatric patients 6 to 12 years [see *Clinical Studies (14)*], along with dosing and safety information for other amphetamine products.

Safety and efficacy in pediatric patients below the age of 3 years have not been established.

Long-Term Growth Suppression

Growth should be monitored during treatment with stimulants, including EVEKEO ODT. Pediatric patients aged 3 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)*, *Adverse Reactions (6.1)*].

8.5 Geriatric Use

EVEKEO ODT has not been studied in patients over the age of 65 years.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

EVEKEO ODT contains amphetamine, a Schedule II controlled substance.

9.2 Abuse

CNS stimulants including EVEKEO ODT, other amphetamine-containing products, and methylphenidates have a high potential for abuse. Abuse is the intentional non-therapeutic use of a drug, even once, to achieve a desired psychological or physiological effect. Abuse is characterized by impaired control over drug use, compulsive use, continued use despite harm, and craving. 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. Both abuse and misuse may lead to addiction, and some individuals may develop addiction even when taking EVEKEO ODT as prescribed.

Signs and symptoms of amphetamine abuse may include increased heart rate, respiratory rate, blood pressure, and/or sweating, dilated pupils, hyperactivity, restlessness, insomnia, decreased appetite, loss of coordination, tremors, flushed skin, vomiting, and/or abdominal pain. Anxiety, psychosis, hostility, aggression, suicidal or homicidal ideation have also been seen. Abusers of amphetamine may use unapproved routes of administration which can result in overdose and death [see *Overdosage (10)*].

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

9.3 Dependence

Dependence

EVEKEO ODT may produce physical dependence from continued therapy. Physical dependence is a state of adaptation manifested by a withdrawal syndrome produced by abrupt cessation, rapid dose reduction, or administration of an antagonist. Withdrawal symptoms after abrupt cessation following prolonged high dosage administration of CNS stimulants include dysphoric mood; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; psychomotor retardation or agitation.

Tolerance

EVEKEO ODT may produce tolerance from continued therapy. Tolerance is a state of adaptation in which exposure to a specific dose of a drug results in a reduction of the drug's desired and/or undesired effects over time.

10 OVERDOSAGE

Consult with a Certified Poison Control Center (1-800-222-1222) for up-to-date guidance and advice for treatment of overdose. Individual patient response to amphetamines varies widely. Toxic symptoms may occur idiosyncratically at low doses.

Manifestations of amphetamine overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states, hyperpyrexia, and rhabdomyolysis. Fatigue and depression usually follow the central nervous system stimulation. Other reactions include arrhythmias, hypertension or hypotension, circulatory collapse, nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning is usually preceded by convulsions and coma.

D-amphetamine is not dialyzable.

11 DESCRIPTION

EVEKEO ODT orally disintegrating tablets contain amphetamine sulfate, a CNS stimulant, as a 1 to 1 ratio of dextroamphetamine sulfate and levoamphetamine sulfate (d- and l-amphetamine sulfate). Amphetamine sulfate is a white, odorless crystalline powder. It has a slightly bitter taste. Its solutions are acid to litmus, having a pH of 5.0 to 6.0. It is freely soluble in water and slightly soluble in alcohol.

Structural Formula:



MW 368.49

EVEKEO ODT tablets are intended for oral use. Each EVEKEO ODT tablet contains 2.5 mg, 5 mg, 10 mg, 15 mg, or 20 mg of racemic amphetamine sulfate. Each tablet also contains the following inactive ingredients: amino methacrylate copolymer, citric acid, crospovidone, ethylcellulose, dibutyl sebacate, magnesium stearate, malic acid, mannitol, microcrystalline cellulose, and sucralose.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Amphetamines are non-catecholamine sympathomimetic amines with central nervous system (CNS) stimulant activity. The mode of therapeutic action in ADHD is not known.

12.2 Pharmacodynamics

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

EVEKEO ODT is a 1:1 racemic mixture of *d*- and *l*-amphetamine. The *l*-isomer is more potent than the *d*-isomer in cardiovascular activity while the *d*-isomer is more potent than the *l*-isomer in causing CNS excitatory effects.

12.3 Pharmacokinetics

Amphetamine demonstrates linear pharmacokinetics over the dose range of 5 to 40 mg.

Absorption

Following a single-dose oral administration of Evekeo ODT 20 mg disintegrated/dissolved in the oral cavity in healthy subjects in a crossover study, exposures (C_{max} and AUC) to *d*- and *l*-amphetamine were comparable to that after administration of equal dose of immediate-release amphetamine sulfate tablets (Evekeo) tablets swallowed intact with water.

Median (range) T_{max} of *d*- and *l*-amphetamine was reached at approximately 3.5 (2-8) hours and 3.0 (1 -6) hours after administration without water and with water, respectively.

Effect of Food

Administration of food (a high fat meal) does not affect the observed AUC and C_{max} of *d*- and *l*-amphetamine after single-dose oral administration of EVEKEO ODT (20 mg) in

healthy adults who allowed the tablet to be disintegrated/dissolved in their oral cavity prior to swallowing without water. Median (range) T_{max} increased from 2.5 (1.5 - 6) hours to 4.5 (2.5 - 8.0) hours when administration without compared to with food.

Elimination

Amphetamine undergoes both hepatic and renal elimination. The plasma elimination half-life of *d*- and *l*-amphetamine averaged 10.0 and about 11.7 hours in healthy adult volunteers.

Metabolism

Amphetamine *d*- and *l*- enantiomers are highly metabolized largely by two primary oxidative pathways, one via CYP2D6 to produce active metabolite 4-hydroxyamphetamine, and the other by oxidative deamination. CYP2D6 is one of several enzymes involved in the biotransformation of amphetamine.

Excretion

Amphetamine is renally eliminated in a pH-dependent manner. The renal excretion rate of unchanged amphetamine at a urine pH of 6.6 averages 70% versus 17% - 43% at urine pH of >6.7.

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 4, 2, and 1 times, respectively, the maximum recommended human dose of 40 mg/day, on a mg/m² basis.

Mutagenesis

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.

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 effectiveness of EVEKEO ODT for the treatment of ADHD has been established based on an adequate and well-controlled study of immediate-release amphetamine sulfate (EVEKEO). Below is a description of this study and its results.

Study 1 (NCT01986062) was conducted with EVEKEO tablets in children ages 6 to 12 years who met DSM-IV-TR criteria for ADHD. Following 8 weeks of open-label dose optimization, patients were randomly assigned to continue their optimized dose of EVEKEO (10 to 40 mg/day in divided doses) or placebo for 1 week. After 1 week, patients crossed-over to receive the alternate treatment. At the end of each treatment week, efficacy assessments were conducted at 0.75, 2, 4, 6, 8, and 10 hours post-dose using the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale. SKAMP is a 13-item teacher-rated scale that assesses manifestations of ADHD in a classroom setting. The SKAMP-Combined score was obtained by summing items 1 through 13. The primary efficacy outcome assessed by the SKAMP-Combined score at 2 hours postdose was statistically significantly better in EVEKEO treatment compared to placebo (Table 3). Key secondary efficacy endpoints were the time-to-onset and duration-of-effect of EVEKEO using SKAMP-Combined scores. SKAMP-Combined scores were statistically significantly better for patients in the EVEKEO treatment group compared to patients in the placebo treatment group beginning at 0.75 hours post-dose and at each assessment through 10 hours post-dose. (Figure 1).

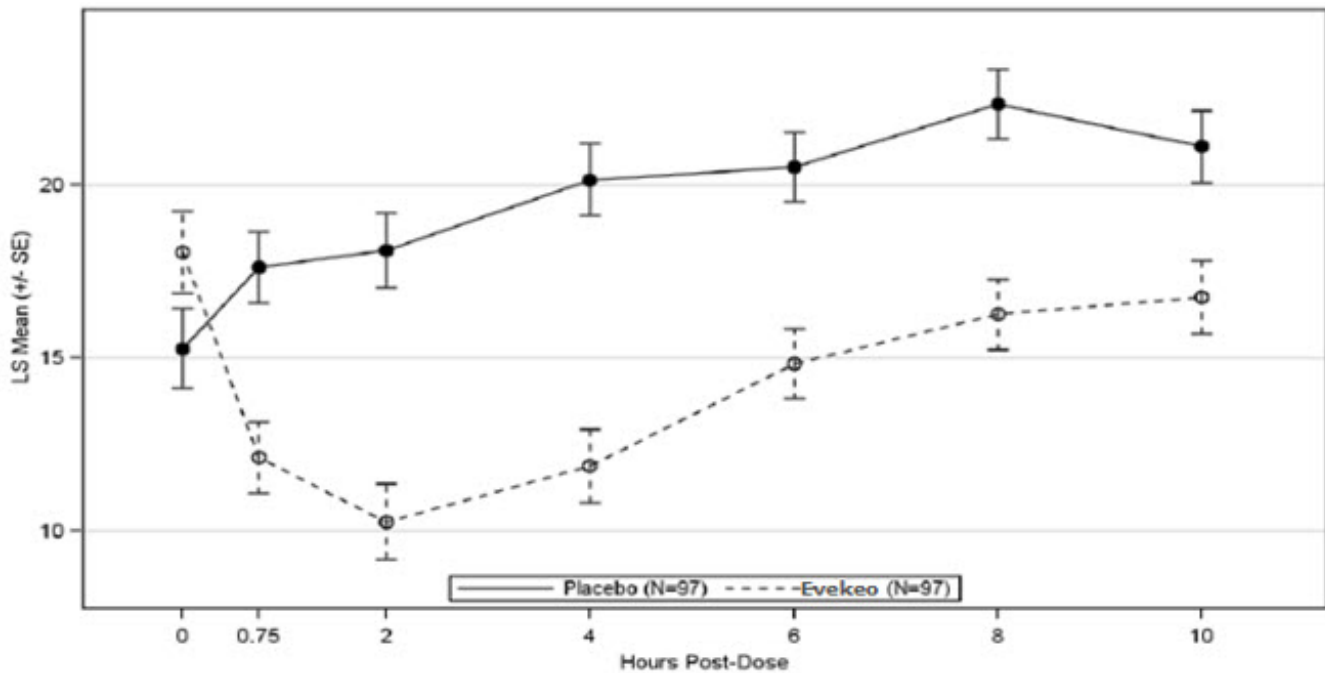
Table 3: Summary of Primary Efficacy Results in Pediatric Patients (6 to 12 years) with ADHD (Study 1)

Study Number	Treatment Group	Primary Efficacy Measure: SKAMP-Combined Score at 2 Hours Post-dose		
		Mean Pre-Dose Score (SD)	LS Mean (SE) at 2 Hours Post-dose	Placebo-subtracted Difference* (95% CI)
Study 1	Evekeo	18.1 (11.6)	10.3 (1.09)	-7.9 (-10.1, -5.6)
	Placebo	15.3 (11.4)	18.1 (1.09)	--

SD: standard deviation; SE: standard error; LS Mean: least-squares mean; CI: confidence interval.

* Difference (drug minus placebo) in least-squares mean.

Figure 1: LS Mean SKAMP-Combined Scores by Treatment and Timepoint for Pediatric Patients (6 to 12 years) with ADHD after 1 Week of Double Blind Treatment (Study 1)



The values at pre-dose hour (zero) are observed means.

16 HOW SUPPLIED/STORAGE AND HANDLING

EVEKEO ODT (amphetamine sulfate) orally disintegrating tablets are supplied as follows:

- 2.5 mg: white to off-white, round, flat-faced radius-edged tablet with "2" on one side and "E" on the other
 - NDC 24338-045-30: One blister card of 30-count 2.5 mg strength tablets within a plastic sleeve
 - NDC 24338-045-01: Carton containing one plastic sleeve.
- 5 mg: white to off-white, round, flat-faced radius-edged tablet with "5" on one side and "EVI" on the other
 - NDC 24338-031-30: One blister card of 30-count 5 mg strength tablets within a plastic sleeve
 - NDC 24338-031-01: Carton containing one plastic sleeve.
- 10 mg: white to off-white, round, flat-faced radius-edged tablet with "10" on one side and "EVI" on the other
 - NDC 24338-033-30: One blister card of 30-count 10 mg strength tablets within a plastic sleeve
 - NDC 24338-033-01: Carton containing one plastic sleeve
- 15 mg: white to off-white, round, flat-faced radius-edged tablet with "15" on one side and "EVI" on the other
 - NDC 24338-035-30: One blister card of 30-count 15 mg strength tablets within a plastic sleeve
 - NDC 24338-035-01: Carton containing one plastic sleeve
- 20 mg: white to off-white, round, flat-faced radius-edged tablet with "20" on one side and "EVI" on the other
 - NDC 24338-037-15: One blister card of 15-count 20 mg strength tablets within a plastic sleeve
 - NDC 24338-037-02: Carton containing two 15-count plastic sleeves

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

Store EVEKEO ODT blister packages in the provided plastic sleeve.

Disposal

Comply with local laws and regulations on drug disposal of CNS stimulants. Dispose of remaining, unused, or expired EVEKEO ODT at authorized collection sites such as retail pharmacies, hospital or clinic pharmacies, and law enforcement locations. If no take-back program or authorized collector is available, mix EVEKEO ODT with an undesirable, nontoxic substance to make it less appealing to children and pets. Place the mixture in a container such as a sealed plastic bag and discard EVEKEO ODT in the household trash.

17 PATIENT COUNSELING INFORMATION

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

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

Advise patients and their caregivers that EVEKEO ODT is a federally controlled substance because it can be abused or lead to dependence. Advise patients to store EVEKEO ODT in a safe place, preferably locked, to prevent abuse. Advise patients to comply with laws and regulations on drug disposal. Advise patients to dispose of remaining, unused, or expired EVEKEO ODT by a medicine take-back program if available [see *Warnings and Precautions (5.1) and Drug Abuse and Dependence (9.2)*].

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.
- Remove the tablet by pushing it through the back of the foil-lined blister packaging.
- As soon as the blister is opened, place the tablet 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.

Serious Cardiovascular Risks

Advise patients, caregivers, and family members that there is a potential serious cardiovascular risk (including sudden death, myocardial infarction, stroke, and hypertension) with EVEKEO ODT. 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)*].

Blood Pressure and Heart Rate Increases

Instruct patients and their caregivers that EVEKEO ODT can cause elevations of their blood pressure and pulse rate and that patients should be monitored for such effects [see *Warnings and Precautions (5.3)*].

Psychiatric Risks

Advise patients and their caregivers that EVEKEO ODT, at recommended doses, may cause psychotic symptoms or mania even in patients without prior history of psychotic symptoms or mania [see *Warnings and Precautions (5.4)*].

Long-Term Suppression of Growth

Advise patients, family members, and caregivers that EVEKEO ODT may cause slowing of growth including weight loss [see *Warnings and Precautions (5.5)*].

Circulation Problems in Fingers and Toes [Peripheral Vasculopathy, including Raynaud's Phenomenon]

Instruct patients and their caregivers beginning treatment with EVEKEO 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 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 EVEKEO ODT. Further clinical evaluation (e.g. rheumatology referral) may be appropriate for certain patients [see *Warnings and Precautions (5.7)*].

Serotonin Syndrome

Caution patients and their caregivers about the risk of serotonin syndrome with concomitant use of EVEKEO 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 (5.8)* and *Drug Interactions (7.1)*]. Advise patients to contact their healthcare provider or report to the emergency room if they experience signs or symptoms of serotonin syndrome.

Concomitant Medications

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

Pregnancy Registry

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

Pregnancy

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

Lactation

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

Evekeo ODT® manufactured for Arbor Pharmaceuticals, LLC Atlanta, GA 30328 by

MEDICATION GUIDE
EVEKEO ODT® (ee-VEEK-ee-o)
(amphetamine sulfate)
orally disintegrating tablets, CII

What is the most important information I should know about EVEKEO ODT?

EVEKEO ODT can cause serious side effects, including:

- **Abuse and dependence.** EVEKEO ODT, other amphetamine-containing medicines, and methylphenidate have a high chance for abuse and can cause physical and psychological dependence. Your healthcare provider should check you or your child for signs of abuse and dependence before and during treatment with EVEKEO ODT.
 - Tell your healthcare provider if you or your child have ever abused or been dependent on alcohol, prescription medicines, or street drugs.
 - Your healthcare provider can tell you more about the differences between physical and psychological dependence and drug addiction.
- **Heart-related problems, including:**
 - sudden death in children and adolescents who have heart problems or heart defects
 - increased blood pressure and heart rate

Your healthcare provider should check you or your child carefully for heart problems before starting treatment with EVEKEO ODT. Tell your healthcare provider if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.

Your healthcare provider should check you or your child's blood pressure and heart rate regularly during treatment with EVEKEO ODT.

Call your healthcare provider or go to the nearest hospital emergency room right away if you or your child have any signs of heart problems such as chest pain, shortness of breath, or fainting during treatment with EVEKEO ODT.

- **Mental (psychiatric) problems, including:**
 - new or worse behavior and thought problems
 - new or worse bipolar illness
 - new psychotic symptoms (such as hearing voices, or seeing or believing things that are not real) 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 during treatment with EVEKEO ODT, especially hearing voices, seeing or believing things that are not real, or new manic symptoms.

What is EVEKEO ODT?

EVEKEO ODT is a central nervous system (CNS) stimulant prescription medicine used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children 3 to 17

years of age. EVEKEO ODT may help increase attention and decrease impulsiveness and hyperactivity in people with ADHD.

It is not known if EVEKEO ODT is safe and effective in children under 3 years of age.

EVEKEO ODT 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 EVEKEO ODT in a safe place to protect it from theft. Never give your EVEKEO ODT to anyone else, because it may cause death or harm them. Selling or giving away EVEKEO ODT may harm others and is against the law.

Do not take EVEKEO ODT if you or your child are:

- allergic to amphetamine or any of the ingredients in EVEKEO ODT. See the end of this Medication Guide for a complete list of ingredients in EVEKEO ODT.
- taking, or have stopped taking in the last 14 days, a medicine called a monoamine oxidase inhibitor (MAOI), including the antibiotic linezolid and the intravenous medicine methylene blue. Ask your healthcare provider or pharmacist if you are not sure if you or your child take one of these medicines.

Before taking EVEKEO ODT, tell your healthcare provider about all medical conditions, including if you or your child:

- have heart problems, heart defects, or high blood pressure
- have mental problems including psychosis, mania, bipolar illness, or depression, or have a family history of suicide, bipolar illness, or depression
- have or have had seizures (convulsions) or have had an abnormal brain wave test (EEG)
- have circulation problems in fingers and toes
- are pregnant or plan to become pregnant. It is not known if EVEKEO ODT will harm the unborn baby.
 - There is a pregnancy registry for females who are exposed to EVEKEO ODT during pregnancy. The purpose of the registry is to collect information about the health of females exposed to EVEKEO ODT and their baby. If you or your child becomes pregnant during treatment with EVEKEO ODT, talk to your healthcare provider about registering with the National Pregnancy Registry for Psychostimulants at 1-866-961-2388 or visit online at <https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/othermedications/>.
- are breastfeeding or plan to breastfeed. EVEKEO ODT passes into breast milk. You should not breastfeed during treatment with EVEKEO ODT. Talk to your healthcare provider about the best way to feed the baby during treatment with EVEKEO ODT.

Tell your healthcare provider about all the medicines that you or your child take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

EVEKEO ODT and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be changed while taking EVEKEO ODT.

Especially tell your healthcare provider if you or your child take medicines used to treat depression including MAOIs.

Know the medicines that you or your child takes. Keep a list of all medicines with you to show your healthcare provider and pharmacist when you get a new medicine.

Your healthcare provider will decide whether EVEKEO ODT can be taken with other

medicines. **Do not start any new medicine during treatment with EVEKEO ODT without talking to your healthcare provider first.**

How should EVEKEO ODT be taken?

- Take EVEKEO ODT exactly as prescribed by your healthcare provider.
- Your healthcare provider may change the dose if needed.
- The first dose of EVEKEO ODT should be taken in the morning.
- EVEKEO ODT can be taken with or without food or liquid.
- Your healthcare provider may sometimes stop EVEKEO ODT treatment for a while to check ADHD symptoms.

Use the following instructions when taking EVEKEO ODT:

- The tablet should remain in the blister pack until you are ready to take or give it. Do not store the tablet for future use.
- Use dry hands to open the blister.
- Remove the tablet by pushing it through the back of the foil-lined blister pack.
- Place the whole tablet on the tongue and allow to dissolve in saliva without chewing or crushing. The tablet can be moved around between the tongue and roof of the mouth until it fully dissolves.

If you or your child take too much EVEKEO ODT, call your healthcare provider or poison control center, or go to the nearest hospital emergency room right away. In case of poisoning call your poison control center at 1-800-222-1222.

What are possible side effects of EVEKEO ODT?

EVEKEO ODT may cause serious side effects, including:

- See "**What is the most important information I should know about EVEKEO ODT?**"
- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with EVEKEO ODT. EVEKEO ODT treatment may be stopped if your child is not growing or gaining weight.
- **Seizures (convulsions).** Your healthcare provider may stop treatment with EVEKEO ODT if you have a seizure.
- **Circulation problems in fingers and toes (peripheral vasculopathy, including Raynaud's phenomenon).** Signs and symptoms may include:
 - fingers or toes may feel numb, cool, painful
 - fingers or toes may change color from pale, to blue, to red

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

Call your healthcare provider right away if you or your child has any signs of unexplained wounds appearing on fingers or toes during treatment with EVEKEO ODT.

- **Serotonin Syndrome.** A potentially life-threatening problem called serotonin syndrome may happen when EVEKEO ODT is taken with certain other medicines. Stop taking EVEKEO ODT and call your healthcare provider or go to the nearest hospital emergency room right away if you or your child develop any of the following signs and symptoms of serotonin syndrome:
 - agitation
 - confusion
 - dizziness

- fast heart beat
- flushing
- seizures
- coma
- sweating
- loss of coordination
- tremors, stiff muscles, or muscle twitching
- seeing or hearing things that are not real (hallucination)
- changes in blood pressure
- high body temperature (hyperthermia)
- nausea, vomiting, diarrhea

The most common side effects of EVEKEO ODT include decreased appetite and trouble sleeping.

These are not all the possible side effects of EVEKEO ODT.

Call your doctor for medical advice about side effects. You may report side effects to Arbor Pharmaceuticals, LLC at 1-866-516-4950 or FDA at 1-800-FDA-1088.

How should I store EVEKEO ODT?

- Store EVEKEO ODT at room temperature between 68°F to 77°F (20°C to 25°C).
- Store EVEKEO ODT blister packages in the provided plastic sleeve.
- Store EVEKEO ODT in a safe place, like a locked cabinet.
- Dispose of remaining, unused, or expired EVEKEO ODT by a medicine take-back program at authorized collection sites such as retail pharmacies, hospital or clinic pharmacies, and law enforcement locations. If no take-back program or authorized collector is available, mix EVEKEO 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 EVEKEO ODT in the household trash.

Keep EVEKEO ODT and all medicines out of the reach of children.

General information about the safe and effective use of EVEKEO ODT.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use EVEKEO ODT for a condition for which it was not prescribed. Do not give EVEKEO ODT to other people, even if they have the same symptoms. It may harm them and it is against the law. You can ask your healthcare provider or pharmacist for information about EVEKEO ODT that was written for healthcare professionals.

What are the ingredients in EVEKEO ODT?

Active ingredient: amphetamine sulfate

Inactive ingredients: mannitol, silicified microcrystalline cellulose, crospovidone, ethylcellulose, amino methacrylate copolymer, anhydrous citric acid, magnesium stearate, dibutyl sebacate, malic acid and sucralose

Distributed by: Arbor® Pharmaceuticals, LLC, Atlanta, GA 30328

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For more information about EVEKEO ODT, please contact Arbor Pharmaceuticals, LLC at 1-866-516-4950.

This Medication Guide has been approved by the U.S. Food and Drug Administration.
EVK-MG-02

Revised: 4/2021

PRINCIPAL DISPLAY PANEL - 2.5 mg Tablet Blister Pack Case Label

NDC 24338-045-30

Rx Only

EVEKEO ODT® CII

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

2.5 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets

arbor®

PHARMACEUTICALS, LLC

Press here to open
↓
1. Press and hold tab with thumb.
2. Pull tablet card to the right.

EVK-SH25-00 Rev. 6/2020

Usual dosage: See package insert for full prescribing information.
Active ingredient: Each tablet contains 2.5 mg of amphetamine sulfate.
Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

NDC 24338-045-30 Rx Only

EVEKEO ODT® CII
amphetamine sulfate
ORALLY DISINTEGRATING TABLET

2.5 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets

arbor
PHARMACEUTICALS, LLC

Evekeo ODT® an ADVATAB® and MICROCAPS® drug delivery product manufactured for Arbor Pharmaceuticals, LLC Atlanta, GA 30328 by Adare Pharmaceuticals, Inc. Vandalia, OH 45377

FPO
N 24338 04530 5

PRINCIPAL DISPLAY PANEL - 5 mg Tablet Blister Pack Case Label

NDC 24338-031-30

Rx Only

EVEKEO ODT™ CII

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

5 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets

arbor®
PHARMACEUTICALS, LLC

Press here to open

1. Press and hold tab with thumb.
2. Pull tablet card to the right.

EVK-SH05-00 Rev. 01/2019

Usual dosage: See package insert for full prescribing information.

Active ingredient: Each tablet contains 5 mg of amphetamine sulfate.

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

NDC 24338-031-30 **Rx Only**

EVEKEO ODT™ CII
amphetamine sulfate
ORALLY DISINTEGRATING TABLET

5 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets

arbor®
PHARMACEUTICALS, LLC

Manufactured for:
Arbor Pharmaceuticals, LLC
Atlanta, GA 30328

Lot: XXXXXXX
Exp: MM YYYY

PRINCIPAL DISPLAY PANEL - 10 mg Tablet Blister Pack Case Label

NDC 24338-033-30

Rx Only

EVEKEO ODT™ CII

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

10 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets

arbor®
PHARMACEUTICALS, LLC

Press here to open



1. Press and hold tab with thumb.
2. Pull tablet card to the right.

EVK-SH10-00 Rev. 01/2019

Usual dosage: See package insert for full prescribing information.

Active ingredient: Each tablet contains 10 mg of amphetamine sulfate.

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



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Manufactured for:
Arbor Pharmaceuticals, LLC
Atlanta, GA 30328

Lot: XXXXXX

Exp: MM YYYY

NDC 24338-033-30

Rx Only



EVEKEO ODT™ CII

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

10 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets

arbor
PHARMACEUTICALS, LLC

PRINCIPAL DISPLAY PANEL - 15 mg Tablet Blister Pack Case Label

NDC 24338-035-30

Rx Only

EVEKEO ODT™ CII

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

15 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets

arbor®
PHARMACEUTICALS, LLC

Press here to open



1. Press and hold tab with thumb.
2. Pull tablet card to the right.

EVK-SH15-00 Rev. 01/2019

Usual dosage: See package insert for full prescribing information.

Active ingredient: Each tablet contains 15 mg of amphetamine sulfate.

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



Manufactured for:
Arbor Pharmaceuticals, LLC
Atlanta, GA 30328

Lot: XXXXXX

Exp: MM YYYY

NDC 24338-035-30

Rx Only



EVEKEO ODT™ CII

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

15 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets

arbor®
PHARMACEUTICALS, LLC

PRINCIPAL DISPLAY PANEL - 20 mg Tablet Blister Pack Case Label

NDC 24338-037-15

Rx Only

EVEKEO ODT™ CII

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

20 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 15 Tablets

arbor®
PHARMACEUTICALS, LLC

Press here to open



1. Press and hold tab with thumb.
2. Pull tablet card to the right.

EVK-SH20-00 Rev. 01/2019

Usual dosage: See package insert for full prescribing information.

Active ingredient: Each tablet contains 20 mg of amphetamine sulfate.

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



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Manufactured for:
Arbor Pharmaceuticals, LLC
Atlanta, GA 30328

Lot: XXXXXXX

Exp: MM YYYY

NDC 24338-037-15

Rx Only



EVEKEO ODT[®] CII

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

20 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 15 Tablets

arbor[®]
PHARMACEUTICALS, LLC

PRINCIPAL DISPLAY PANEL - 2.5 mg Tablet Blister Pack Case Carton

NDC 24338-045-01

Rx Only

EVEKEO ODT[®] CII

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

2.5 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets (One plastic sleeve)

arbor[®]

PHARMACEUTICALS, LLC

Glue Area

ARBOR
PHARMACEUTICALS, LLC



Evekeo ODT[®] manufactured for Arbor
Pharmaceuticals, LLC Atlanta, GA 30328 by
Adare Pharmaceuticals, Inc. Vandalia, OH 45377
Rev. 6/2020 BK-TC-25-00

- Instructions for Use**
- The tablet should remain in the blister pack until you are ready to take or give it. Do not store the tablet for future use.
 - Use dry hands to open the blister.
 - Remove the tablet by pushing it through the back of the foil-lined blister pack.
 - Place the whole tablet on the tongue and allow to dissolve in saliva without chewing or crushing. The tablet can be moved around between the tongue and the roof of the mouth until it fully dissolves.

Usual Dosage: See package insert for full prescribing information.
Active ingredient: Each tablet contains 2.5 mg of amphetamine sulfate.
Inactive ingredients: mannitol, silicified microcrystalline cellulose, croscopolldone, ethylcellulose, amino methacrylate copolymer, anhydrous citric acid, magnesium stearate, dibutyl sebacate, malic acid and sucralose.
Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].
Store EVEKEO ODT blister packs in the provided plastic sleeve.

ARBOR
PHARMACEUTICALS, LLC

Contains 30 Tablets (One plastic sleeve)

2.5 mg tablets

ORALLY DISINTEGRATING TABLET

amphetamine sulfate

EVEKEO ODT[®]

NDC 24338-045-01

Rx Only

EVEKEO ODT[®]

amphetamine sulfate

ORALLY DISINTEGRATING TABLET

2.5 mg tablets

Do not crush or chew tablets.

Dispenser: Please provide the accompanying Medication Guide to each patient.

Contains 30 Tablets (One plastic sleeve)

ARBOR
PHARMACEUTICALS, LLC

EVEKEO ODT[®]

amphetamine sulfate
ORALLY DISINTEGRATING TABLET

2.5 mg tablets

Contains 30 Tablets (One plastic sleeve)

ARBOR
PHARMACEUTICALS, LLC

EVEKEO ODT

amphetamine sulfate tablet, orally disintegrating

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:24338-031
Route of Administration	ORAL	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMPHETAMINE SULFATE (UNII: 6DPV8NK46S) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE SULFATE	5 mg

Inactive Ingredients

Ingredient Name	Strength
mannitol (UNII: 3OWL53L36A)	
microcrystalline cellulose (UNII: OP1R32D61U)	
crospovidone (UNII: 2S7830E561)	
ethylcellulose, unspecified (UNII: 7Z8S9VYZ4B)	
dimethylaminoethyl methacrylate - butyl methacrylate - methyl methacrylate copolymer (UNII: 905HNO1SIH)	
anhydrous citric acid (UNII: XF417D3PSL)	
magnesium stearate (UNII: 70097M6I30)	
dibutyl sebacate (UNII: 4W5IH7FLNY)	
malic acid (UNII: 817L1N4CKP)	
sucralose (UNII: 96K6UQ3ZD4)	

Product Characteristics

Color	WHITE (white to off-white)	Score	no score
Shape	ROUND (flat-faced, radius-edged)	Size	7mm
Flavor		Imprint Code	5;EVI
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:24338-031-01	1 in 1 CARTON	06/28/2019	
1	NDC:24338-031-30	1 in 1 CASE		
1		30 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	NDA209905	06/28/2019	

EVEKEO ODT

amphetamine sulfate tablet, orally disintegrating

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:24338-033
Route of Administration	ORAL	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMPHETAMINE SULFATE (UNII: 6DPV8NK46S) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE SULFATE	10 mg

Inactive Ingredients

Ingredient Name	Strength
mannitol (UNII: 3OWL53L36A)	
microcrystalline cellulose (UNII: OP1R32D61U)	
crospovidone (UNII: 2S7830E561)	
ethylcellulose, unspecified (UNII: 7Z8S9VYZ4B)	
dimethylaminoethyl methacrylate - butyl methacrylate - methyl methacrylate copolymer (UNII: 905HNO1SIH)	
anhydrous citric acid (UNII: XF417D3PSL)	
magnesium stearate (UNII: 70097M6I30)	
dibutyl sebacate (UNII: 4W5IH7FLNY)	
malic acid (UNII: 817L1N4CKP)	
sucralose (UNII: 96K6UQ3ZD4)	

Product Characteristics

Color	WHITE (white to off-white)	Score	no score
Shape	ROUND (flat-faced, radius-edged)	Size	8mm
Flavor		Imprint Code	10;EVI
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:24338-033-01	1 in 1 CARTON	06/28/2019	
1	NDC:24338-033-30	1 in 1 CASE		
1		30 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	NDA209905	06/28/2019	

EVEKEO ODT

amphetamine sulfate tablet, orally disintegrating

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:24338-035
Route of Administration	ORAL	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMPHETAMINE SULFATE (UNII: 6DPV8NK46S) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE SULFATE	15 mg

Inactive Ingredients

Ingredient Name	Strength
mannitol (UNII: 3OWL53L36A)	
microcrystalline cellulose (UNII: OP1R32D61U)	
crospovidone (UNII: 2S7830E561)	
ethylcellulose, unspecified (UNII: 7Z8S9VYZ4B)	
dimethylaminoethyl methacrylate - butyl methacrylate - methyl methacrylate copolymer (UNII: 905HNO1SIH)	
anhydrous citric acid (UNII: XF417D3PSL)	
magnesium stearate (UNII: 70097M6I30)	
dibutyl sebacate (UNII: 4W5IH7FLNY)	
malic acid (UNII: 817L1N4CKP)	
sucralose (UNII: 96K6UQ3ZD4)	

Product Characteristics

Color	WHITE (white to off-white)	Score	no score
Shape	ROUND (flat-faced, radius-edged)	Size	10mm
Flavor		Imprint Code	15;EVI
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:24338-035-01	1 in 1 CARTON	06/28/2019	
1	NDC:24338-035-30	1 in 1 CASE		
1		30 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	NDA209905	06/28/2019	

EVEKEO ODT
amphetamine sulfate tablet, orally disintegrating

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:24338-037
Route of Administration	ORAL	DEA Schedule	CII

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
AMPHETAMINE SULFATE (UNII: 6DPV8NK46S) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE SULFATE	20 mg

Inactive Ingredients	
Ingredient Name	Strength
mannitol (UNII: 3OWL53L36A)	
microcrystalline cellulose (UNII: OP1R32D61U)	
crospovidone (UNII: 2S7830E561)	
ethylcellulose, unspecified (UNII: 7Z8S9VYZ4B)	
dimethylaminoethyl methacrylate - butyl methacrylate - methyl methacrylate copolymer (UNII: 905HNO1SIH)	
anhydrous citric acid (UNII: XF417D3PSL)	
magnesium stearate (UNII: 70097M6I30)	
dibutyl sebacate (UNII: 4W5IH7FLNY)	
malic acid (UNII: 817L1N4CKP)	
sucralose (UNII: 96K6UQ3ZD4)	

Product Characteristics			
Color	WHITE (white to off-white)	Score	no score
Shape	ROUND (flat-faced, radius-edged)	Size	10mm
Flavor		Imprint Code	20;EVI
Contains			

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date

1	NDC:24338-037-02	2 in 1 CARTON	06/28/2019	
1	NDC:24338-037-15	1 in 1 CASE		
1		15 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	NDA209905	06/28/2019	

EVEKEO ODT

amphetamine sulfate tablet, orally disintegrating

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:24338-045
Route of Administration	ORAL	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMPHETAMINE SULFATE (UNII: 6DPV8NK46S) (AMPHETAMINE - UNII:CK833KGX7E)	AMPHETAMINE SULFATE	2.5 mg

Inactive Ingredients

Ingredient Name	Strength
mannitol (UNII: 3OWL53L36A)	
microcrystalline cellulose (UNII: OP1R32D61U)	
crospovidone (UNII: 2S7830E561)	
ethylcellulose, unspecified (UNII: 7Z8S9VYZ4B)	
dimethylaminoethyl methacrylate - butyl methacrylate - methyl methacrylate copolymer (UNII: 905HNO1SIH)	
anhydrous citric acid (UNII: XF417D3PSL)	
magnesium stearate (UNII: 70097M6I30)	
dibutyl sebacate (UNII: 4W5IH7FLNY)	
malic acid (UNII: 817L1N4CKP)	
sucralose (UNII: 96K6UQ3ZD4)	

Product Characteristics

Color	WHITE (white to off-white)	Score	no score
Shape	ROUND (flat-faced, radius-edged)	Size	7mm
Flavor		Imprint Code	2;E
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:24338-045-01	1 in 1 CARTON	08/30/2021	
1	NDC:24338-045-30	1 in 1 CASE		
1		30 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	NDA209905	08/30/2021	

Labeler - Arbor Pharmaceuticals (781796417)

Revised: 3/2022

Arbor Pharmaceuticals