



PDL NEW DRUG REVIEW

Proprietary Name: Evekeo®

Common Name: amphetamine sulfate

PDL Category: Stimulant- Amphetamines, Short Acting

<u>Comparable Products</u>	<u>Preferred Drug List Status</u>
Amphetamine-Dextroamphetamine	Preferred with Conditions
Dextroamphetamine Sulfate	Non-Preferred with Conditions

Summary

Indications and Usage: For narcolepsy AND Attention Deficit Disorder with Hyperactivity (ADDH) as an integral part of a total treatment program AND for exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction for patients refractory to alternative therapy (e.g. repeated diets, group programs, and other drugs). The limited usefulness of amphetamines should be weighed against possible risk inherent in use of the drug.

This is a pregnancy category C medication. The long-term effects of amphetamines in children have not been well established. Amphetamines are not recommended for use as anorectic agents in children <12 years of age or in children <3 years of age with ADDH. Use is not recommended in children <12 years of age for exogenous obesity.

Dosage Forms: Tablets: 5mg, 10mg

Recommended Dosage: *For Narcolepsy:* 5-60mg per day in divided doses per individual response. While narcolepsy does not typically occur in children <12 years of age, Evekeo® may be used if it does, with the suggested initial dose in those 6-12 years of age being 5mg daily and increasing by 5mg at weekly increments as needed. In children >12 years of age, start with 10mg daily and increase by 10mg at weekly intervals. Give the first dose upon awakening and then additional doses at intervals of 4-6 hours. *For ADDH:* In children 3-5 years, initiate treatment with 2.5mg QD. In children 6 years or older, it is recommended to start with 5mg QD or BID; only in rare cases should the total daily dose exceed 40mg/day. Give the initial dose upon awakening and additional doses at intervals of 4-6 hours. *For exogenous obesity:* Take up to 30mg daily in divided doses of 5-10mg given 30-60 minutes before a meal.

Drug Interactions: Gastrointestinal acidifying agents and urinary acidifying agents lower blood levels and efficacy of amphetamines. Gastrointestinal and urinary alkalinizing agents increase blood levels of amphetamines and thus potentiate their activity. Amphetamines may enhance the activity of TCAs or sympathomimetic agents and cardiovascular effects can be potentiated. MAO inhibitors slow amphetamine metabolism and a variety of neurological toxic effects and malignant hyperpyrexia can occur. The following are listed as drug interactions but dose adjustments are not listed: antihistamines, antihypertensives, chlorpromazine, ethosuximide, haloperidol, lithium carbonate, meperidine, methamphetamine, norepinephrine, phenobarbital, phenytoin, propoxyphene, and Veratrum alkaloids.

Common Adverse Drug Reactions: *Note that there was not placebo data available.* The most commonly reported adverse events included palpitations, tachycardia, elevation of blood pressure, overstimulation, restlessness, dizziness, insomnia, euphoria, dyskinesia, dysphoria, tremor, headache, exacerbation of motor and phonic tics and Tourette's syndrome, dry mouth, unpleasant taste, diarrhea, constipation, other GI disturbances, anorexia, weight loss, urticaria, impotence, changes in libido, and frequent/prolonged erections.

There are warnings of serious cardiovascular events with CNS stimulants, including sudden death at usual doses in children/adolescents with structural cardiac abnormalities or other serious heart problems. Patients being considered for treatment with stimulants should have a careful history and physical exam to assess for the presence of cardiac disease and should receive further cardiac evaluation if findings suggest such disease. Stimulants can cause an increase in hypertension.

While long-term suppression of growth has been observed in patients treated with methylphenidate, data are inadequate to determine if chronic use of amphetamines may cause a similar suppression in growth. Nevertheless, it is anticipated that amphetamines may have the same effect. It is therefore recommended that growth be monitored during treatment with stimulants. Patients not growing as expected may need to have treatment interrupted.

Contraindications: Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, or known hypersensitivity or idiosyncrasy to the sympathomimetic amines; Agitated states; Patients with a history of drug abuse; During or within 14 days following the administration of monoamine oxidase inhibitors.

Manufacturer: Arbor Pharmaceuticals

Analysis: Amphetamine sulfate, the active ingredient of Evekeo[®], is a sympathomimetic amino of the amphetamine group with CNS stimulant activity. It is a 1:1 racemic mixture of dextroamphetamine and levo-amphetamine. Evekeo[®] is a Schedule II controlled substance. Amphetamines have been extensively abused, and tolerance and extreme psychological dependence have occurred with their use. Evekeo[®] also has a box warning regarding the high potential for abuse with amphetamines and that administration for long periods of time may lead to drug dependence and must be avoided. Misuse of amphetamine may cause sudden death and serious cardiovascular adverse events.

Place in Therapy: There are numerous medications available to treat ADHD, including but not limited to stimulants, atomoxetine, clonidine, and guanfacine. Stimulants include methylphenidate and amphetamines. Evekeo[®] is a short-acting amphetamine approved for narcolepsy, ADDH, and exogenous obesity as a short-term adjunct.

There is no evidence at this time to support that Evekeo[®] is safer or more effective than the currently available, more cost effective medications, based on data reviewed from the package insert. It is therefore recommended that Evekeo[®] remain non-preferred and require prior authorization and be available to the few who are unable to tolerate or who have failed on preferred medications.

PDL Placement: Preferred
 Non-Preferred with Conditions
 Preferred with Conditions

References

¹ Evekeo [package insert]. Atlanta, FA: Arbor Pharmaceuticals, LLC; 2014.