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

MYDAYIS (mixed salts of a single-entity amphetamine product) extended-release capsules, for oral use, CII
Initial U.S. Approval: 2001

WARNING: ABUSE AND DEPENDENCE
See full prescribing information for complete boxed warning.

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

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

MYDAYIS is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 13 years and older. (1)

Limitations of Use:

Pediatric patients 12 years and younger experienced higher plasma exposure than patients 13 years and older at the same dose and experienced higher rates of adverse reactions, mainly insomnia and decreased appetite. (8.4)

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

- MYDAYIS should be taken once daily upon awakening**.**

	Recommended Starting Dose	Titration Schedule	Maximum Daily Dose
Adults	12.5 mg	12.5 mg weekly	50 mg
Pediatrics (13 to 17)	12.5 mg	12.5 mg weekly	25 mg

- In adult patients with severe renal impairment the maximum dose should not exceed 25 mg daily. Use in adult patients with ESRD is not recommended. (2.6, 8.6)
- The maximum dose in pediatric patients with severe renal impairment is 12.5 mg daily. Use in pediatric patients with ESRD is not recommended. (2.6, 8.6)
- Patients are advised to take consistently either with or without food. (2.2)
- Administer upon awakening because the effects may last up to 16 hours and there is the potential for insomnia. (2.2)
- Prior to treatment, assess for presence of cardiac disease. (2.1)
- 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. (2.7)

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

- Extended-release capsules: 12.5 mg, 25 mg, 37.5 mg, 50 mg (3)

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

- Known hypersensitivity to amphetamine products or other ingredients in MYDAYIS. (4)
- Use with monoamine oxidase (MAO) inhibitors, or within 14 days of the last MAO inhibitor dose. (4, 7.1)

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

- *Serious Cardiovascular Reactions:* Sudden death has been reported in association with CNS stimulant treatment at recommended doses in pediatric patients with structural cardiac abnormalities or other serious heart problems. In adults, sudden death, stroke, and myocardial infarction have been reported. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, or coronary artery disease. (5.2)
- *Blood Pressure and Heart Rate Increases:* Monitor blood pressure and pulse. Consider benefits and risks before use in patients for whom blood pressure increases may be problematic. (5.3)
- *Psychiatric Adverse Reactions:* May cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to stimulant use. (5.4)
- *Long-Term Suppression of Growth:* Monitor height and weight in pediatric patients during treatment. (5.5)
- *Peripheral Vasculopathy, including Raynaud's phenomenon:* Stimulants used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Careful observation for digital changes is necessary during treatment with ADHD stimulants. (5.6)
- *Seizures:* May lower the convulsive threshold. If a seizure occurs, discontinue MYDAYIS. (5.7)
- *Serotonin Syndrome:* Increased risk when co-administered with serotonergic agents (e.g., SSRIs, SNRIs, triptans), but also during overdosage situations. If it occurs, discontinue MYDAYIS and initiate supportive treatment. (5.8)

----------ADVERSE REACTIONS----------

Most common adverse reactions in patients with ADHD (incidence ≥5% and at a rate at least twice placebo) are:

- Pediatrics (13 years and older): insomnia, decreased appetite, decreased weight, irritability, and nausea. (6.1)
- Adults: insomnia, decreased appetite, decreased weight, dry mouth, increased heart rate, and anxiety. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Shire US Inc. at 1-800-828-2088 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) decrease amphetamine blood levels, while alkalinizing agents (GI and urinary) increase amphetamine blood levels. Adjust MYDAYIS dosage accordingly. (2.5, 7.1)

----------USE IN SPECIFIC POPULATIONS----------

- *Pregnancy:* Based on animal data, may cause fetal harm. (8.1)
- *Lactation:* Breastfeeding not recommended. (8.2)
- *Renal Impairment:* Dose adjustment is needed in patients with severe renal insufficiency. Use of MYDAYIS in patients with ESRD is not recommended. (2.6, 8.6)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 06/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: ABUSE AND DEPENDENCE

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE AND DEPENDENCE

CNS stimulants, including MYDAYIS, 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, 9.3), and Drug Abuse and Dependence (9.2, 9.3)]*.

1 INDICATIONS AND USAGE

MYDAYIS is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 13 years and older *[see Clinical Studies (14)]*.

Limitations of Use

Pediatric patients 12 years and younger experienced higher plasma exposure than patients 13 years and older at the same dose, and experienced higher rates of adverse reactions, mainly insomnia and decreased appetite *[see Use in Specific Populations (8.4)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Important Information Prior to Initiating Treatment

Prior to initiating treatment with MYDAYIS, assess for the presence of cardiac disease (e.g., 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 MYDAYIS use *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9)]*.

2.2 General Instructions for Use

Because the effects of MYDAYIS may last up to 16 hours and there is potential for insomnia, administer once daily in the morning upon awakening. In the event of a missed dose, do not administer later in the day. Do not administer additional medication to make up for the missed dose *[see Adverse Reactions (6.1), Clinical Studies (14)]*.

Pharmacological treatment of ADHD may be needed for an extended period. Periodically re-evaluate the long-term use of MYDAYIS and adjust dosage as needed.

2.3 Administration Instructions

Administer MYDAYIS orally with or without food. Advise patients to take MYDAYIS consistently either with food or without food *[see Clinical Pharmacology (12.3)]*.

MYDAYIS may be administered in one of the following ways:

- Swallow MYDAYIS capsules whole, or
- Open capsule and sprinkle the entire contents over a spoonful of applesauce. The sprinkled applesauce should be consumed immediately; it should not be stored. Patients should take the sprinkled applesauce in its entirety without chewing.
- The dose of a single capsule should not be divided.

2.4 Dosing Information

Adult Use (18 to 55 years)

The recommended starting dose of MYDAYIS is 12.5 mg once daily in the morning upon awakening. Initial doses of 25 mg once daily may be considered for some patients. Dosage may be adjusted in increments of 12.5 mg no sooner than weekly, up to a maximum dose of 50 mg once daily, based on the therapeutic needs and response of the patient. Doses above 50 mg daily have shown no additional clinically meaningful benefit.

Pediatric Use (13 to 17 years)

The recommended starting does is 12.5 mg once daily in the morning upon awakening. Dosage may be adjusted in increments of 12.5 mg no sooner than weekly, up to a recommended maximum dose of 25 mg once daily. The dose should be individualized according to the needs and response of the patient. Doses higher than 25 mg have not been evaluated in clinical trials in pediatric patients.

2.5 Dosage Modifications due to Drug Interactions

Agents that alter gastrointestinal and 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 MYDAYIS dosage accordingly *[see Drug Interactions (7.1)]*.

2.6 Dosage in Patients with Renal Impairment

In adult patients with severe renal impairment (GFR between 15 to < 30 mL/min/1.73 m^2), the recommended starting dose of MYDAYIS is 12.5 mg daily with a maximum recommended dose of 25 mg daily. MYDAYIS is not recommended for use in patients with end stage renal disease (ESRD < 15 ml/min/1.73 m^2). In pediatric patients (13 to 17 years) with severe renal impairment, the maximum dose is 12.5 mg, if tolerated *[see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)]*.

2.7 Switching from other Amphetamine Products

For patients switching from another medication or any other amphetamine products, discontinue that treatment, and titrate with MYDAYIS using the titration schedule *[see Dosage and Administration (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), Description (11), Clinical Pharmacology (12.3)]*.

3 DOSAGE FORMS AND STRENGTHS

- Extended-release capsules 12.5 mg: green body/green cap (imprinted with SHIRE 465 and 12.5 mg)
- Extended-release capsules 25 mg: ivory body/green cap (imprinted with SHIRE 465 and 25 mg)
- Extended-release capsules 37.5 mg: ivory body/light caramel cap (imprinted with SHIRE 465 and 37.5 mg)
- Extended-release capsules 50 mg: ivory body/purple cap (imprinted with SHIRE 465 and 50 mg)

4 CONTRAINDICATIONS

MYDAYIS is contraindicated in patients with:

- Known hypersensitivity to amphetamine, or other components of MYDAYIS. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with other amphetamine products *[see Adverse Reactions (6.2)]*.
- Concomitant treatment with monoamine oxidase inhibitors (MAOIs), and also within 14 days following discontinuation of treatment with a monoamine oxidase inhibitor, because of an increased risk of hypertensive crisis *[see Drug Interactions (7.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Potential for Abuse and Dependence

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

5.2 Serious Cardiovascular Reactions

Sudden death, stroke and myocardial infarction have been reported in adults with CNS stimulant treatment at recommended doses. Sudden death has been reported in pediatric patients with structural cardiac abnormalities and other serious heart problems while 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 MYDAYIS 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 *[see Adverse Reactions (6.1)]*.

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 mixed/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 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 a prior history of psychotic illness or mania. If such symptoms occur, consider discontinuing MYDAYIS. 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 MYDAYIS. In a 4-week, placebo-controlled trial of MYDAYIS in patients ages 6 to 17 years old with ADHD, there was a decrease in weight in the MYDAYIS groups compared to weight gain in the placebo group *[see Adverse Reactions (6.1)]*.

Patients who are not growing or gaining weight as expected may need to have their treatment interrupted. MYDAYIS is not approved for use in pediatric patients 12 years and younger *[Use in Specific Populations (8.4)]*.

5.6 Peripheral Vasculopathy, including Raynaud's Phenomenon

Stimulants, including MYDAYIS, 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

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