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Press Release

Hikma launches generic version of Vyvanse® following FDA approval

London, 31 August 2023 – Hikma Pharmaceuticals PLC (Hikma), the multinational pharmaceutical company, announces it has received FDA approval for and launched its generic version of Vyvanse® (lisdexamfetamine dimesylate) 20mg, 30mg, 40mg, 50mg, 60mg, and 70mg capsules in the US.

Lisdexamfetamine is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older and Moderate to Severe Binge Eating Disorder (BED) in adults.

“We are pleased to have launched our generic version of Vyvanse® today immediately upon receiving FDA approval, providing one of the first generic versions of this important medicine to patients and health care providers in the US,” said Brian Hoffmann, President, Generics. “This launch is the latest example of our ability to successfully deliver on our pipeline and launch new products, expanding access to needed medicines for our customers and their patients.”

“Patients across the US are currently experiencing shortages of ADHD medicines like lisdexamfetamine,” continued Mr. Hoffmann. “We are eager to work with the US Drug Enforcement Administration to obtain adequate supplies of raw materials that would enable Hikma to expediently use its strong US-based manufacturing and distribution capabilities to help address shortages of this essential medicine.”

According to IQVIA, US sales of Vyvanse® were approximately $5.1 billion in the 12 months ending June 30, 2023.

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About Hikma
(LSE: HIK) (NASDAQ Dubai: HIK) (OTC: HKMPY) (rated BBB-/stable S&P and BBB-/positive Fitch)

Hikma helps put better health within reach every day for millions of people around the world. For more than 40 years, we've been creating high-quality medicines and making them accessible to the people who need them. Headquartered in the UK, we are a global company with a local presence across the North America, the Middle East and North Africa (MENA) and Europe, and we use our unique insight and expertise to transform cutting-edge science into innovative solutions that transform people's lives. We're committed to our customers, and the people they care for, and by thinking creatively and acting practically, we provide them with a broad range of branded and non-branded generic medicines. Together, our 8,800 colleagues are helping to shape a healthier world that enriches all our communities. We are a leading licensing partner, and through our venture capital arm, are helping bring innovative health technologies to people around the world. For more information, please visit: www.hikma.com

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This product has been approved for marketing in the United States by the US FDA. This product approval does not confer the right on Hikma, or any other party, to market this product outside the United States.

Important Safety Information for LISDEXAMFETAMINE DIMESYLATE capsules, for oral use, CII:

WARNING: ABUSE AND DEPENDENCE

CNS stimulants, including lisdexamfetamine dimesylate, 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.

CONTRAINDICATIONS

Lisdexamfetamine dimesylate capsules are contraindicated in patients with:

- Known hypersensitivity to amphetamine products or other ingredients of lisdexamfetamine dimesylate capsules. Anaphylactic reactions, Stevens-Johnson Syndrome, angioedema and urticaria have been observed.

- 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.

WARNINGS AND PRECAUTIONS

- **Potential for Abuse and Dependence**

Central nervous system (CNS) stimulants, including lisdexamfetamine dimesylate capsules, 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.

- **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 attention-deficit/hyperactivity disorder (ADHD). Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease and other serious heart problems. Evaluate patients who develop exertional chest pain, unexplained syncope or arrhythmias during lisdexamfetamine dimesylate capsules treatment.

- **Blood Pressure and Heart Rate Increases**

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

- **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 for risk factors for developing a manic episode (eg, 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 (eg, hallucinations, delusional thinking or mania) in patients with no prior history of psychotic illness or mania. If such symptoms occur, consider discontinuing lisdexamfetamine dimesylate capsules.

- **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 lisdexamfetamine dimesylate capsules.

Patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted. Lisdexamfetamine dimesylate capsules are not approved for use in pediatric patients below 6 years of age.

- **Impairment in Ability to Operate Machinery or Vehicles**

Advise patients that lisdexamfetamine dimesylate may impair their ability to engage in potentially dangerous activities such as operating machinery or vehicles. Instruct patients to find out how lisdexamfetamine dimesylate will affect them before engaging in potentially dangerous activities.

- **Peripheral Vasculopathy, including Raynaud's Phenomenon**

Stimulants, including lisdexamfetamine dimesylate capsules, 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. Signs and symptoms generally improve after reduction in dose or discontinuation of drug. Careful observation for digital changes is necessary during treatment with stimulants. Further evaluation (eg, rheumatology referral) may be appropriate for certain patients.

- **Serotonin Syndrome**

Serotonin syndrome, a potentially life-threatening reaction, may occur when 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. The co-administration with cytochrome P450 2D6 (CYP2D6) inhibitors may also increase the risk with increased exposure to the active metabolite of lisdexamfetamine dimesylate capsules (dextroamphetamine). In these situations, consider an alternative non-serotonergic drug or an alternative drug that does not inhibit CYP2D6.

Serotonin syndrome symptoms may include mental status changes (eg, agitation, hallucinations, delirium and coma), autonomic instability (eg, tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (eg, tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea).

Concomitant use of lisdexamfetamine dimesylate capsules with MAOI drugs is contraindicated.

Discontinue treatment with lisdexamfetamine dimesylate capsules and any concomitant serotonergic agents immediately if symptoms of serotonin syndrome occur and initiate supportive symptomatic treatment. If concomitant use of lisdexamfetamine dimesylate capsules with other serotonergic drugs or CYP2D6 inhibitors is clinically warranted, initiate lisdexamfetamine dimesylate capsules with lower doses, monitor patients for the emergence of serotonin syndrome and inform patients of the increased risk for serotonin syndrome.

ADVERSE REACTIONS

The following serious adverse reactions are described in greater detail in the Full Prescribing Information for lisdexamfetamine dimesylate capsules:

- Known hypersensitivity to amphetamine products or other ingredients of lisdexamfetamine dimesylate capsules
- Hypertensive Crisis When Used Concomitantly With MAOIs
- Drug Dependence
- Serious Cardiovascular Reactions
- Blood Pressure and Heart Rate Increases
- Psychiatric Adverse Reactions
- Suppression of Growth
- Peripheral Vasculopathy, including Raynaud's Phenomenon
- Serotonin Syndrome

ADHD
The most common adverse reactions (incidence ≥5% and least twice the rate of placebo) in pediatric patients ages 6 to 17 years and/or adults with ADHD were anorexia, anxiety, decreased appetite, decreased weight, diarrhea, dizziness, dry mouth, irritability, insomnia, nausea, upper abdominal pain and vomiting.

Binge Eating Disorder (BED)
The most common adverse reactions (≥5% and least twice the rate of placebo) reported in BED clinical trials of adult patients were dry mouth, insomnia, decreased appetite, increased heart rate, feeling jittery, constipation and anxiety.

DRUG INTERACTIONS

- **MAOIs**

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. Do not administer lisdexamfetamine dimesylate during or within 14 days following the administration of MAOI.

- **Serotonergic Drugs**

The concomitant use of lisdexamfetamine dimesylate and serotonergic drugs increases the risk of serotonin syndrome. Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome, particularly during lisdexamfetamine dimesylate initiation or dosage increase. If serotonin syndrome occurs, discontinue lisdexamfetamine dimesylate and the concomitant serotonergic drugs.

- **CYP2D6 Inhibitors**

The concomitant use of lisdexamfetamine dimesylate and CYP2D6 inhibitors may increase the risk of serotonin syndrome. Initiate with lower doses and monitor patients for signs and symptoms of serotonin syndrome, particularly during lisdexamfetamine dimesylate initiation and after a dosage increase. If serotonin syndrome occurs, discontinue lisdexamfetamine dimesylate and the CYP2D6 inhibitor.

- **Alkalinizing Agents**

Urinary alkalinizing agents can increase blood levels and potentiate the action of amphetamine. Coadministration of lisdexamfetamine dimesylate and urinary alkalinizing agents should be avoided.

- **Acidifying Agents**

Urinary acidifying agents can lower blood levels and efficacy of amphetamines. Increase dose based on clinical response.

- **Tricyclic Antidepressants**

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. Monitor frequently and adjust or use alternative therapy based on clinical response.

USE IN SPECIFIC POPULATIONS

- **Pregnancy**

Pregnancy Exposure Registry
Healthcare providers are encouraged to register patients exposed to ADHD medicine during pregnancy with the National Pregnancy Registry for Psychostimulants by phone at 1-866-961-2388 or online at https://womensmentalhealth.org/research/pregnancyregistry/.

Risk Summary
Adverse pregnancy outcomes, including premature delivery and low birth weight, have been seen in infants born to mothers dependent on amphetamines.

Clinical Considerations
Fetal/Neonatal Adverse Reactions
Amphetamines such as lisdexamfetamine dimesylate cause vasoconstriction and thereby may decrease placental perfusion. In addition, amphetamines can stimulate uterine contractions, increasing the risk of premature delivery. Infants born to amphetamine-dependent mothers 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.

- **Lactation**

Risk Summary
Breastfeeding is not recommended during treatment with lisdexamfetamine dimesylate.

- **Pediatric Use**

ADHD
Safety and effectiveness of lisdexamfetamine dimesylate have not been established in pediatric patients below the age of 6 years.

BED
Safety and effectiveness of lisdexamfetamine dimesylate have not been established in patients younger than 18 years of age.

- **Geriatric Use**

Clinical studies of lisdexamfetamine dimesylate capsules did not include sufficient numbers of patients 65 years and older to determine whether they respond differently from younger subjects.

In general, dose selection for an elderly patient should start at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

- **Renal Impairment**

Due to reduced clearance in patients with severe renal impairment, the maximum dose should not exceed 50 mg/day. The maximum recommended dose in patients with end-stage renal disease patients is 30 mg/day. Lisdexamfetamine dimesylate and d-amphetamine are not dialyzable.

DRUG ABUSE AND DEPENDENCE

- **Controlled Substance**

Lisdexamfetamine dimesylate capsules contain lisdexamfetamine, a prodrug of amphetamine, a Schedule II controlled substance.

- **Abuse**

CNS stimulants, including lisdexamfetamine dimesylate capsules, have a high potential for abuse. Both abuse and misuse may lead to addiction, and some individuals may develop addiction even when taking lisdexamfetamine dimesylate capsules as prescribed.

Abusers of CNS stimulants may chew, snort, inject or use other unapproved routes of administration, which can result in overdose and death.

To reduce the abuse of CNS stimulants, including lisdexamfetamine dimesylate capsules, assess the risk of abuse prior to prescribing. After prescribing, keep careful prescription records and 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 lisdexamfetamine dimesylate capsules use.

- **Dependence**

Physical Dependence
Lisdexamfetamine dimesylate capsules may produce physical dependence from continued therapy. Withdrawal symptoms after abrupt cessation following prolonged high-dosage administration of CNS stimulants include extreme fatigue and depression.

Tolerance
Lisdexamfetamine dimesylate capsules may produce tolerance from continued therapy.

OVERDOSAGE
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. Serotonin syndrome has been reported with amphetamine use, including lisdexamfetamine dimesylate. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea and abdominal cramps. Fatal poisoning is usually preceded by convulsions and coma.

Lisdexamfetamine and d-amphetamine are not dialyzable.

For more information, please see the Full Prescribing Information, including the Boxed Warning.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit https://www.fda.gov/medwatch or call 1-800-FDA-1088.

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