Press Release

Hikma receives FDA approval and launches the generic version of Victoza®, Liraglutide, in the US

London, 26 December 2024 – Hikma Pharmaceuticals PLC (Hikma), the multinational pharmaceutical company, has received FDA approval for and launched its generic version of Victoza®, Liraglutide Injection, in a 6 mg/mL dosage in the US. Liraglutide Injection, a Glucagon-Like Peptide-1 (GLP-1) product, is indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.

“We are very pleased to launch Liraglutide Injection immediately upon receiving US FDA approval, providing US healthcare professionals and patients with this important generic treatment of diabetes,” said Dr Bill Larkins, President of Injectables. “This launch is the latest example of our actions to expand our portfolio in growing therapeutic areas like diabetes and to provide customers and patients with affordable access to a reliable supply of high-quality essential medicines.”

According to IQVIA, US sales of Liraglutide Injection, 6 mg/mL, were approximately $1.3 billion in the 12 months ending October 2024.

Hikma is a top three supplier of generic injectable medicines by volume in the US[1], with a growing portfolio of more than 170 products. We are continuously expanding our portfolio of essential medicines and introducing new dosage forms that enhance patient care.

- ENDS –

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.

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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 45 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 North America, the Middle East

[1] Source: IQVIA MAT October 2024, generic injectable volumes by eaches, excluding branded generics and Becton Dickinson

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 9,100 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

Important Safety Information for Liraglutide Injection, 6 mg/mL:

Please see package insert for referenced section/section numbering, where appropriate.

BOXED WARNING

WARNING: RISK OF THYROID C-CELL TUMORS

- **Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether liraglutide injection causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined *[see Warnings and Precautions (5.1) and Nonclinical Toxicology (13.1)].***
- **Liraglutide injection is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of liraglutide injection and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with liraglutide injection *[see Contraindications (4) and Warnings and Precautions (5.1)].***

CONTRAINDICATIONS

Liraglutide injection is contraindicated in patients with a:

- personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) *[see Warnings and Precautions (5.1)]*.
- serious hypersensitivity reaction to liraglutide or to any of the excipients in liraglutide injection. Serious hypersensitivity reactions including anaphylactic reactions and angioedema have been reported with liraglutide injection *[see Warnings and Precautions (5.6)].*

WARNINGS & PRECAUTIONS

- **Risk of Thyroid C-cell Tumors –** Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice. Malignant thyroid C-cell carcinomas were detected in rats and mice. It is unknown whether liraglutide injection will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide induced rodent thyroid C-cell tumors has not been determined. Cases of MTC in patients treated with liraglutide injection have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and liraglutide injection use in humans.
- **Pancreatitis –** Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with liraglutide injection. Liraglutide injection has been studied in a limited number of patients with a history of pancreatitis. It is unknown if patients with a history of pancreatitis are at higher risk for development of pancreatitis on liraglutide injection.
- **Never Share a Liraglutide Injection Pen Between Patients –** Liraglutide injection pens must never be shared between patients, even if the needle is changed. Pen sharing poses a risk for transmission of blood-borne pathogens.
- **Hypoglycemia –** Adult patients receiving liraglutide injection in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. In pediatric patients 10 years of age and older, the risk of hypoglycemia was higher with liraglutide injection regardless of insulin and/or metformin use.
- **Acute Kidney Injury –** Liraglutide injection has not been found to be directly nephrotoxic in animal studies or clinical trials. There have been postmarketing reports of acute renal failure and worsening of chronic renal

failure, which may sometimes require hemodialysis in liraglutide injection-treated patients. Some of these events were reported in patients without known underlying renal disease.

- **Hypersensitivity Reactions –** There have been postmarketing reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema) in patients treated with liraglutide injection.
- **Acute Gallbladder Disease –** Acute events of gallbladder disease such as cholelithiasis or cholecystitis have been reported in GLP-1 receptor agonist trials and postmarketing.
- **Pulmonary Aspiration During General Anesthesia or Deep Sedation –** Liraglutide injection delays gastric emptying. There have been rare postmarketing reports of pulmonary aspiration in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation who had residual gastric contents despite reported adherence to preoperative fasting recommendations.

ADVERSE REACTIONS

The following serious adverse reactions are described below or elsewhere in the prescribing information:

- Risk of Thyroid C-cell Tumors *[see Warnings and Precautions (5.1)]*
- Pancreatitis *[see Warnings and Precautions (5.2)]*
- Hypoglycemia *[see Warnings and Precautions (5.4)]*
- Acute Kidney Injury *[see Warnings and Precautions (5.5)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.6)]*
- Acute Gallbladder Disease *[see Warnings and Precautions (5.7)]*
- Pulmonary Aspiration During General Anesthesia or Deep Sedation *[see Warnings and Precautions (5.8)]*

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 practice.

Common Adverse Reactions

The safety of liraglutide injection in patients with type 2 diabetes mellitus was evaluated in 5 glycemic control, placebo-controlled trials in adults and one trial of 52 weeks duration in pediatric patients 10 years of age and older.

Table 1 of the package insert shows common adverse reactions in adults, excluding hypoglycemia, associated with the use of liraglutide injection for the treatment of type 2 diabetes mellitus. These adverse reactions occurred more commonly on liraglutide injection than on placebo and occurred in at least 5% of patients treated with liraglutide injection. Overall, the type, and severity of adverse reactions in pediatric patients 10 years of age and older and above were comparable to that observed in the adult population.

In an analysis of placebo- and active-controlled trials, the types and frequency of common adverse reactions, excluding hypoglycemia, were similar to those listed in Table 1 of the package insert.

Other Adverse Reactions

Other Adverse Reactions from the clinical trials are detailed in the package insert and include Gastrointestinal Adverse Reactions, Injection site reactions, Hypoglycemia, Papillary thyroid carcinoma, and Cholelithiasis and cholecystitis.

Laboratory Tests

Laboratory Tests affected from the clinical trials are detailed in the package insert and include Bilirubin, Calcitonin, and Lipase and Amylase.

Vital signs

Liraglutide injection did not have adverse effects on blood pressure. Mean increases from baseline in heart rate of 2 to 3 beats per minute have been observed in adult patients treated with liraglutide injection compared to placebo.

Postmarketing Experience

The following additional adverse reactions have been reported during post-approval use of liraglutide injection. Because these events are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal: Acute pancreatitis, hemorrhagic and necrotizing pancreatitis sometimes resulting in death, ileus
General Disorders and Administration Site Conditions: Allergic reactions: rash and pruritus

Hepatobiliary: Elevations of liver enzymes, hyperbilirubinemia, cholestasis, cholecystitis, cholelithiasis requiring cholecystectomy, hepatitis
Immune system: Angioedema and anaphylactic reactions
Metabolism and nutrition: Dehydration resulting from nausea, vomiting and diarrhea
Neoplasms: Medullary thyroid carcinoma
Nervous system: Dysgeusia, dizziness
Pulmonary: Pulmonary aspiration has occurred in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation
Renal and urinary: Increased serum creatinine, acute renal failure or worsening of chronic renal failure, sometimes requiring hemodialysis
Skin and subcutaneous tissue: Cutaneous amyloidosis

DRUG INTERACTIONS

Effects of Delayed Gastric Emptying on Oral Medications
Liraglutide injection causes a delay of gastric emptying, and thereby has the potential to impact the absorption of concomitantly administered oral medications. In clinical pharmacology trials, liraglutide injection did not affect the absorption of the tested orally administered medications to any clinically relevant degree. Nonetheless, caution should be exercised when oral medications are concomitantly administered with liraglutide injection.

Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin
Liraglutide injection stimulates insulin release in the presence of elevated blood glucose concentrations. Patients receiving liraglutide injection in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. When initiating liraglutide injection, consider reducing the dose of concomitantly administered insulin secretagogues (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia.

USE IN SPECIFIC POPULATIONS

Pregnancy
Risk Summary
Based on animal reproduction studies, there may be risks to the fetus from exposure to liraglutide injection during pregnancy. Liraglutide injection should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Clinical Considerations
Disease-associated maternal and/or embryo/fetal risk
Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, pre-eclampsia, spontaneous abortions, preterm delivery, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, still birth, and macrosomia related morbidity.

Lactation
Risk Summary
There are no data on the presence of liraglutide injection in human milk, the effects on the breastfed infant, or the effects on milk production. Liraglutide was present in milk of lactating rats. Developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for liraglutide injection and any potential adverse effects on the breastfed infant from liraglutide injection or from the underlying maternal condition.

Pediatric Use
The safety and effectiveness of liraglutide injection as an adjunct to diet and exercise to improve glycemic control in type 2 diabetes mellitus have been established in pediatric patients 10 years of age and older. The safety and effectiveness of liraglutide injection have not been established in pediatric patients less than 10 years of age.

Geriatric Use
In the liraglutide injection treatment arms of the glycemic control trials, a total of 832 (19.3%) of the patients were 65 to 74 years of age and 145 (3.4%) were 75 years of age and over. No overall differences in safety or effectiveness for liraglutide injection have been observed between patients 65 years of age and older and younger patients.

Renal Impairment
No dose adjustment of liraglutide injection is recommended for patients with renal impairment. There is limited experience with liraglutide injection in patients with end stage renal disease. There have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis. Use caution in patients who experience dehydration.

Hepatic Impairment
There is limited experience in patients with mild, moderate or severe hepatic impairment. Therefore, liraglutide injection should be used with caution in this patient population. No dose adjustment of liraglutide injection is recommended for patients with hepatic impairment.

Gastroparesis
Liraglutide injection slows gastric emptying. Liraglutide injection has not been studied in patients with pre-existing gastroparesis.

DOSAGE AND ADMINISTRATION

Recommended Dosage
Adult Patients
- The recommended starting dosage of liraglutide injection is 0.6 mg injected subcutaneously once daily for one week. The 0.6 mg once daily dosage is intended to reduce gastrointestinal symptoms during initial titration and is not effective for glycemic control in adults.
- After one week at the 0.6 mg once daily dosage, increase the dosage to 1.2 mg injected subcutaneously once daily.
- If additional glycemic control is required, increase the dosage to the maximum recommended dosage of 1.8 mg injected subcutaneously once daily after at least one week of treatment with the 1.2 mg once daily dosage.

Pediatric Patients Aged 10 Years and Older
- The recommended starting dosage of liraglutide injection is 0.6 mg injected subcutaneously once daily.
- If additional glycemic control is required, increase the dosage in 0.6 mg increments after at least one week on the current dosage.
- The maximum recommended dosage is 1.8 mg injected subcutaneously once daily.

Recommendations Regarding Missed Dose
- Instruct patients who miss a dose of liraglutide injection to resume the once-daily dosage regimen as prescribed with the next scheduled dose. Do not administer an extra dose or increase the dose to make up for the missed dose.
- If more than 3 days have elapsed since the last liraglutide injection dose, reinitiate liraglutide injection at 0.6 mg once daily to mitigate any gastrointestinal symptoms associated with reinitiation of treatment. Upon reinitiation, liraglutide injection should be titrated at the discretion of the healthcare provider.

Important Administration Instructions
- Inspect visually prior to each injection. Only use if solution is clear, colorless, and contains no particles.
- Inject liraglutide injection subcutaneously once daily at any time of day, independently of meals.
- Inject liraglutide injection subcutaneously in the abdomen, thigh or upper arm. No dosage adjustment is needed if changing the injection site and/or timing.
- Rotate injection sites within the same region in order to reduce the risk of cutaneous amyloidosis.
- When using liraglutide injection with insulin, administer as separate injections. Never mix. It is acceptable to inject liraglutide injection and insulin in the same body region but the injections should not be adjacent to each other.

OVERDOSAGE

Overdoses have been reported in clinical trials and post-marketing use of liraglutide injection. Observed effects have included severe nausea, severe vomiting, and severe hypoglycemia. In the event of overdosage, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms.

INDICATIONS AND USAGE

Liraglutide injection is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus

Limitations of Use:
Liraglutide injection should not be used in patients with type 1 diabetes mellitus.
Liraglutide injection contains liraglutide and should not be coadministered with other liraglutide-containing products.

HOW SUPPLIED/STORAGE AND HANDLING

How Supplied
Liraglutide Injection: 18 mg/3 mL (6 mg/mL) clear, colorless solution in a pre-filled, single-patient-use pen that delivers doses of 0.6 mg, 1.2 mg, or 1.8 mg is available in the following package sizes:

2 x Liraglutide Injection pen NDC 0143-9144-02
3 x Liraglutide Injection pen NDC 0143-9144-03

Recommended Storage
Prior to first use, Liraglutide Injection should be stored in a refrigerator between 36ºF to 46ºF (2ºC to 8ºC). Do not store in the freezer or directly adjacent to the refrigerator cooling element. Do not freeze Liraglutide Injection and do not use Liraglutide Injection if it has been frozen.

After first use of the Liraglutide Injection pen, the pen can be stored for 30 days at controlled room temperature (59°F to 86°F; 15°C to 30°C) or in a refrigerator (36°F to 46°F; 2°C to 8°C). Keep the pen cap on when not in use. Protect Liraglutide Injection from excessive heat and sunlight. Always remove and safely discard the needle after each injection and store the Liraglutide Injection pen without an injection needle attached. This will reduce the potential for contamination, infection, and leakage while also ensuring dosing accuracy. Always use a new needle for each injection to prevent contamination.

ENDING INFORMATION

Patient Counseling Information should be shared with the patient prior to administration. The patient should also be advised to read the FDA-approved patient labeling (Medication Guide) and the injection pen Instructions for Use.
For additional information, please refer to the Package Insert for full prescribing information, available on www.hikma.com.

To report SUSPECTED ADVERSE REACTIONS, contact Hikma Pharmaceuticals USA Inc. at 1-877-845-0689 or FDA at 1-800 FDA-1088 or www.fda.gov/medwatch.

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