Press Release

Hikma launches Alvimopan Capsules in the US

London, 13 February 2024 – Hikma Pharmaceuticals PLC (Hikma), the multinational pharmaceutical company, has launched Alvimopan Capsules, in 12mg doses. The product has been launched in the US and is indicated to accelerate the time to upper and lower gastrointestinal recovery following surgeries that include partial bowel resection with primary anastomosis.

According to IQVIA, US sales of Alvimopan Capsules were approximately $43 million in the 12 months ending November 2023.

Hikma is a top-10 U.S. generics manufacturer[1] supplying a broad range of non-injectable products to the US market, and has expertise in complex technologies, such as nasal sprays, where we are one of the largest suppliers in the US. We have a state-of-the-art manufacturing facility in Columbus, Ohio and we market both generic and specialty branded products.

- ENDS -

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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 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

[1] IQVIA MAT November 2023, includes all generic injectable and non-injectable products

hikma.

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 Alvimopan Capsules:

WARNING: POTENTIAL RISK OF MYOCARDIAL INFARCTION WITH LONG-TERM USE:
FOR SHORT-TERM HOSPITAL USE ONLY

There was a greater incidence of myocardial infarction in alvimopan-treated patients compared to placebo-treated patients in a 12-month clinical trial, although a causal relationship has not been established. In short-term trials with alvimopan, no increased risk of myocardial infarction was observed.

Because of the potential risk for myocardial infarction with long-term use, alvimopan is available only through a restricted program for short-term use (15 doses) under a Risk Evaluation and Mitigation Strategy (REMS) called the Alvimopan REMS Program.

CONTRAINDICATIONS

Alvimopan capsules are contraindicated in patients who have taken therapeutic doses of opioids for more than 7 consecutive days immediately prior to taking alvimopan capsules.

WARNINGS AND PRECAUTIONS

- **Potential Risk of Myocardial Infarction With Long-Term Use**

There were more reports of myocardial infarctions in patients treated with alvimopan 0.5 mg twice daily compared with placebo-treated patients in a 12-month study of patients treated with opioids for chronic non-cancer pain. A causal relationship with alvimopan with long-term use has not been established.

- **Alvimopan REMS Program**

Due to the potential risk of myocardial infarction with long-term use, alvimopan capsules are available only through the Alvimopan REMS Program. For more information about the Alvimopan REMS Program, please see the Full Prescribing Information for alvimopan capsules.

- **Gastrointestinal-Related Adverse Reactions in Opioid-Tolerant Patients**

Patients recently exposed to opioids are expected to be more sensitive to the effects of alvimopan. Signs and symptoms of increased sensitivity would be related to the gastrointestinal tract (e.g., abdominal pain, nausea and vomiting, diarrhea). Patients receiving more than 3 doses of an opioid within the week prior to surgery should be monitored for gastrointestinal adverse reactions.

- **Risk of Serious Adverse Reactions in Patients With Severe Hepatic Impairment**

Alvimopan is not recommended for use in patients with severe hepatic impairment.

- **End-Stage Renal Disease**

Alvimopan is not recommended for use in patients with end-stage renal disease.

- **Risk of Serious Adverse Reactions in Patients with Complete Gastrointestinal Obstruction**

Alvimopan is not recommended for use in patients with complete gastrointestinal obstruction or in patients who have had surgery for correction of complete bowel obstruction.

- **Risk of Serious Adverse Reactions in Pancreatic and Gastric Anastomoses**

Alvimopan is not recommended for use in patients having pancreatic or gastric anastomosis.

ADVERSE REACTIONS

The following clinically significant adverse reactions are described in greater detail in the Full Prescribing Information for alvimopan capsules:

- Potential Risk of Myocardial Infarction With Long-Term Use
- Gastrointestinal-Related Adverse Reactions in Opioid-Tolerant Patients
- Risk of Serious Adverse Reactions in Patients with Severe Hepatic Impairment
- Risk of Serious Adverse Reactions in Patients with Complete Gastrointestinal Obstruction
- Risk of Serious Adverse Reactions in Pancreatic and Gastric Anastomoses

Among alvimopan-treated patients undergoing surgeries that included a bowel resection, the most common adverse reaction (incidence ≥1.5%) occurring with a higher frequency than placebo was dyspepsia (alvimopan, 1.5%; placebo, 0.8%).

DRUG INTERACTIONS

- **Effects of Alvimopan on Intravenous Morphine**

Coadministration of alvimopan does not appear to alter the pharmacokinetics of morphine and its metabolite to a clinically significant degree when morphine is administered intravenously. Dosage adjustment for intravenously administered morphine is not necessary when it is coadministered with alvimopan.

- **Effects of Concomitant Acid Blockers or Antibiotics**

A population pharmacokinetic analysis suggests that the pharmacokinetics of alvimopan were not affected by concomitant administration of acid blockers or antibiotics. No dosage adjustments are necessary in patients taking acid blockers or antibiotics with alvimopan.

USE IN SPECIFIC POPULATIONS

- **Pregnancy**

Available data regarding use of alvimopan in pregnant women are insufficient to inform a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

- **Lactation**

There are no data on the presence of alvimopan in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for alvimopan and any potential adverse effects on the breastfed child from alvimopan or from the underlying maternal condition.

- **Pediatric Use**

Safety and effectiveness in pediatric patients have not been established.

- **Geriatric Use**

No overall differences in safety or effectiveness were observed between patients 65 years of age and older and younger patients, but greater sensitivity of some older individuals cannot be ruled out. No dose adjustment based on increased age is required.

- **Hepatic Impairment**

Alvimopan is not recommended for use in patients with severe hepatic impairment. Patients with mild-to-moderate hepatic impairment should be closely monitored for possible adverse reactions (eg, diarrhea, gastrointestinal pain, cramping) that could indicate high alvimopan or 'metabolite' concentrations. Alvimopan should be discontinued if adverse reactions occur.

- **Renal Impairment**

Alvimopan is not recommended for use in patients with end-stage renal disease. Patients with mild-to-severe renal impairment should be monitored for adverse reactions. Patients with severe renal impairment should be closely monitored for possible adverse reactions (eg, diarrhea, gastrointestinal pain, cramping) that could indicate high alvimopan or 'metabolite' concentrations. Alvimopan should be discontinued if adverse reactions occur.

- **Race/Ethnicity**

The exposure to alvimopan in Japanese healthy male subjects was approximately 2-fold greater than in Caucasian subjects. Japanese patients should be closely monitored for possible adverse reactions (eg, diarrhea, gastrointestinal pain, cramping) that could indicate high alvimopan or 'metabolite' concentrations. Alvimopan should be discontinued if adverse reactions occur.

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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