Press Release

Hikma launches Levocarnitine Injection, USP, in the US

London, 5 October 2023 – Hikma Pharmaceuticals PLC (Hikma), the multinational pharmaceutical company, has launched Levocarnitine Injection, USP, in a 1g/5mL dose. The product has been launched in the US and is indicated for the acute and chronic treatment of patients with an inborn error of metabolism which results in secondary carnitine deficiency. It is also indicated for the prevention and treatment of carnitine deficiency in patients with end stage renal disease who are undergoing dialysis.

According to IQVIA, US sales of Levocarnitine Injection, 1g/5mL, were approximately $27 million in the 12 months ending July 2023.

Hikma is a top three supplier of generic injectable medicines by volume in the US[1], with a growing portfolio of more than 150 products. We are continuously expanding our portfolio of essential medicines and introducing new dosage forms that enhance patient care.

- ENDS -

Enquiries

Hikma Pharmaceuticals PLC

Susan Ringdal
EVP, Strategic Planning and Global Affairs
+44 (0)20 7399 2760/ +44 7776 477050
uk-investors@hikma.uk.com

Steve Weiss
David Belian
US Communications and Public Affairs
+1 732 720 2830/ +1 732 788 8279
+1 732 720 2814/+1 848 254 4875
uscommunications@hikma.com

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

[1] Source: IQVIA MAT July 2023, generic injectable volumes by eaches, excluding branded generics and Becton Dickinson

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 Levocarnitine Injection, USP, 1g/5mL:

CONTRAINDICATIONS

None known.

WARNINGS & PRECAUTIONS

- **Hypersensitivity Reactions –** Serious hypersensitivity reactions, including anaphylaxis, laryngeal edema, and bronchospasm have been reported following levocarnitine administration, mostly in patients with end stage renal disease who are undergoing dialysis. Some reactions occurred within minutes after intravenous administration of levocarnitine.
  - If a severe hypersensitivity reaction occurs, discontinue levocarnitine treatment and initiate appropriate medical treatment. Consider the risks and benefits of re-administering levocarnitine to individual patients following a severe reaction. If the decision is made to re-administer the product, monitor patients for a reoccurrence of signs and symptoms of a severe hypersensitivity reaction.

- **Carcinogenesis, Mutagenesis, Impairment of Fertility –** Mutagenicity tests performed in *Salmonella typhimurium*, *Saccharomyces cerevisiae*, and *Schizosaccharomyces pombe* indicate that levocarnitine is not mutagenic. No long-term animal studies have been performed to evaluate the carcinogenic potential of levocarnitine.

ADVERSE REACTIONS

Clinical Trials Experience
Transient nausea and vomiting have been observed. Less frequent adverse reactions are body odor, nausea, and gastritis. An incidence for these reactions is difficult to estimate due to the confounding effects of the underlying pathology.

The table in the package insert lists the adverse events that have been reported in two double-blind, placebo-controlled trials in patients on chronic hemodialysis. Events occurring at ≥5% are reported without regard to causality.

Postmarketing Experience
The following adverse reactions have been reported:

Neurologic Reactions: Seizures have been reported to occur in patients, with or without pre-existing seizure activity, receiving either oral or intravenous levocarnitine. In patients with pre-existing seizure activity, an increase in seizure frequency and/or severity has been reported.
Hypersensitivity reactions: Anaphylaxis, laryngeal edema and bronchospasm (see **WARNINGS**)

DRUG INTERACTIONS

Reports of INR increase with the use of warfarin have been observed. It is recommended that INR levels be monitored in patients on warfarin therapy after the initiation of treatment with levocarnitine or after dose adjustments.

USE IN SPECIFIC POPULATIONS

Pregnancy
Reproductive studies have been performed in rats and rabbits at doses up to 3.8 times the human dose on the basis of surface area and have revealed no evidence of impaired fertility or harm to the fetus due to levocarnitine. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers
Levocarnitine supplementation in nursing mothers has not been specifically studied. Studies in dairy cows indicate that the concentration of levocarnitine in milk is increased following exogenous administration of levocarnitine. In nursing mothers receiving levocarnitine, any risks to the child of excess carnitine intake need to be weighed against the benefits of levocarnitine supplementation to the mother. Consideration may be given to discontinuation of nursing or of levocarnitine treatment.

Pediatric Use
See DOSAGE AND ADMINISTRATION.

DOSAGE AND ADMINISTRATION

Levocarnitine Injection is administered intravenously.

Metabolic Disorders
The recommended dose is 50 mg/kg given as a slow 2 to 3 minute bolus injection or by infusion. Often a loading dose is given in patients with severe metabolic crisis, followed by an equivalent dose over the following 24 hours. It should be administered q3h or q4h, and never less than q6h either by infusion or by intravenous injection. All subsequent daily doses are recommended to be in the range of 50 mg/kg or as therapy may require. The highest dose administered has been 300 mg/kg.

It is recommended that a plasma carnitine concentration be obtained prior to beginning this parenteral therapy. Weekly and monthly monitoring is recommended as well. This monitoring should include blood chemistries, vital signs, plasma carnitine concentrations (the plasma free carnitine concentration should be between 35 and 60 µmol/L) and overall clinical condition.

ESRD Patients on Hemodialysis
The recommended starting dose is 10 to 20 mg/kg dry body weight as a slow 2 to 3-minute bolus injection into the venous return line after each dialysis session. Initiation of therapy may be prompted by trough (pre-dialysis) plasma levocarnitine concentrations that are below normal (40 to 50 µmol/L). Dose adjustments should be guided by trough (pre-dialysis) levocarnitine concentrations, and downward dose adjustments (e.g. to 5 mg/kg after dialysis) may be made as early as the third or fourth week of therapy.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Compatibility and Stability
Levocarnitine Injection is compatible and stable when mixed in parenteral solutions of Sodium Chloride 0.9% or Lactated Ringer's in concentrations ranging from 250 mg/500 mL (0.5 mg/mL) to 4200 mg/500 mL (8.0 mg/mL) and stored at room temperature (25°C) for up to 24 hours in PVC plastic bags.

OVERDOSAGE

There have been no reports of toxicity from levocarnitine overdosage. Levocarnitine is easily removed from plasma by dialysis. The intravenous LD50 of levocarnitine in rats is 5.4 g/kg and the oral LD50 of levocarnitine in mice is 19.2 g/kg. Large doses of levocarnitine may cause diarrhea.

INDICATIONS AND USAGE

For the acute and chronic treatment of patients with an inborn error of metabolism which results in secondary carnitine deficiency. For the prevention and treatment of carnitine deficiency in patients with end stage renal disease who are undergoing dialysis.

HOW SUPPLIED/STORAGE AND HANDLING

Levocarnitine Injection, USP, 200 mg per 1 mL, is available in 5 mL single dose vials packaged 10 vials per carton **NDC (0143-9852-10**).

Store vials at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Retain vial in carton until time of use. **Protect from light**. Discard unused portion of an opened vial, as they contain no preservative.
ENDING INFORMATION

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. For product inquiry call 1-877-845-0689.

Manufactured by:
HIKMA FARMACEUTICA (PORTUGAL), S.A.
Estrada do Rio da Mo, 8, 8A e 8B – Fervenca
2705-906 Terrugem SNT, PORTUGAL

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