Press Release

Hikma launches Clindamycin in 5% Dextrose Injection in the US

London, 3 September 2024 – Hikma Pharmaceuticals PLC (Hikma), the multinational pharmaceutical company, has launched Clindamycin in 5% Dextrose Injection, in 300mg/50mL, 600mg/50mL and 900mg/50mL doses. The product has been launched in the US and will be available in a vial.

Clindamycin in 5% Dextrose Injection is indicated for the treatment of numerous infections, including but not limited to septicemia, intra-abdominal infections, lower respiratory infections, gynecological infections, bone and joint infections, and skin and skin structure infections.

According to IQVIA, US sales of Clindamycin Injection, 300mg/50mL, 600mg/50mL and 900mg/50mL were approximately $22 million in the 12 months ending June 2024.

Hikma is a top three supplier of generic injectable medicines by volume in the US[1], with a growing portfolio of more than 160 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 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

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

hikma.

bring innovative health technologies to people around the world. For more information, please visit: www.hikma.com

Important Safety Information for Clindamycin in 5% Dextrose Injection, 300mg/50mL, 600mg/50mL and 900mg/50mL:

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

BOXED WARNING

WARNING
***Clostridioides difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin in 5% dextrose injection and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.**

Because clindamycin in 5% dextrose injection therapy has been associated with severe colitis which may end fatally, it should be reserved for serious infections where less toxic antimicrobial agents are inappropriate, as described in the INDICATIONS AND USAGE section. It should not be used in patients with nonbacterial infections such as most upper respiratory tract infections.

***C. difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.**

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

CONTRAINDICATIONS

This drug is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin.

WARNINGS & PRECAUTIONS

- ***Clostridioides difficile*-Associated Diarrhea –** *Clostridioides difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin in 5% dextrose injection, and may range in severity from mild diarrhea to fatal colitis.
- **Anaphylactic and Severe Hypersensitivity Reactions –** Anaphylactic shock and anaphylactic reactions have been reported. Severe hypersensitivity reactions, including severe skin reactions such as toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and Stevens-Johnson syndrome (SJS), some with fatal outcome, have been reported.
- **Nephrotoxicity –** Clindamycin is potentially nephrotoxic and cases with acute kidney injury have been reported.
- **Usage in Meningitis** – Since clindamycin does not diffuse adequately into the cerebrospinal fluid, the drug should not be used in the treatment of meningitis.
- **General –** Clindamycin in 5% dextrose injection products should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis, and in atopic individuals. Clindamycin in 5% dextrose injection should not be injected intravenously undiluted as a bolus, but should be infused over at least 10 to 60 minutes. Clindamycin dosage modification may not be necessary in patients with renal disease. Prescribing clindamycin in 5% dextrose injection in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
- **Laboratory Tests –** During prolonged therapy periodic liver and kidney function tests and blood counts should be performed.

ADVERSE REACTIONS

The following reactions have been reported with the use of clindamycin.

Infections and Infestations: *Clostridioides difficile* colitis
Gastrointestinal: Antibiotic-associated colitis, pseudomembranous colitis, abdominal pain, nausea, and vomiting. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment. An unpleasant or metallic taste has been reported after intravenous administration of the higher doses of clindamycin phosphate.
Hypersensitivity Reactions: Maculopapular rash and urticaria have been observed during drug therapy. Generalized mild to moderate morbilliform-like skin rashes are the most frequently reported of all adverse reactions. Severe skin reactions such as Toxic Epidermal Necrolysis, some with fatal outcome, have been reported. Cases of Acute Generalized Exanthematous Pustulosis (AGEP), erythema multiforme, some resembling Stevens-Johnson syndrome, have been associated with clindamycin. Anaphylactic shock, anaphylactic reaction and hypersensitivity have also been reported.
Skin and Mucous Membranes: Pruritus, vaginitis, angioedema and rare instances of exfoliative dermatitis have been reported.
Liver: Jaundice and abnormalities in liver function tests have been observed during clindamycin therapy.
Renal: Acute kidney injury.
Hematopoietic: Transient neutropenia (leukopenia) and eosinophilia have been reported. Reports of agranulocytosis and thrombocytopenia have been made. No direct etiologic relationship to concurrent clindamycin therapy could be made in any of the foregoing.
Immune System: Drug reaction with eosinophilia and systemic symptoms (DRESS) cases have been reported.
Local Reactions: Injection site irritation, pain, induration and sterile abscess have been reported after intramuscular injection and thrombophlebitis after intravenous infusion. Reactions can be minimized or avoided by giving deep intramuscular injections and avoiding prolonged use of indwelling intravenous catheters.
Musculoskeletal: Polyarthritis cases have been reported.
Cardiovascular: Cardiopulmonary arrest and hypotension have been reported following too rapid intravenous administration.

DRUG INTERACTIONS

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, it should be used with caution in patients receiving such agents.

Clindamycin is metabolized predominantly by CYP3A4, and to a lesser extent by CYP3A5, to the major metabolite clindamycin sulfoxide and minor metabolite N-desmethylclindamycin. Therefore, inhibitors of CYP3A4 and CYP3A5 may increase plasma concentrations of clindamycin and inducers of these isoenzymes may reduce plasma concentrations of clindamycin. In the presence of strong CYP3A4 inhibitors, monitor for adverse reactions. In the presence of strong CYP3A4 inducers such as rifampicin, monitor for loss of effectiveness.

In vitro studies indicate that clindamycin does not inhibit CYP1A2, CYP2C9, CYP2C19, CYP2E1 or CYP2D6 and only moderately inhibits CYP3A4.

USE IN SPECIFIC POPULATIONS

Carcinogenesis, Mutagenesis, Impairment of Fertility
Long term studies in animals have not been performed with clindamycin to evaluate carcinogenic potential.

Pregnancy
Teratogenic effects
In clinical trials with pregnant women, the systemic administration of clindamycin during the second and third trimesters, has not been associated with an increased frequency of congenital abnormalities.

Clindamycin should be used during the first trimester of pregnancy only if clearly needed. There are no adequate and well-controlled studies in pregnant women during the first trimester of pregnancy.

Nursing Mothers
Limited published data based on breast milk sampling reports that clindamycin appears in human breast milk in the range of less than 0.5 to 3.8 mcg/mL at dosages of 150 mg orally to 600 mg intravenously. Clindamycin has the potential to cause adverse effects on the breast-fed infant’s gastrointestinal flora. If oral or intravenous clindamycin

is required by a nursing mother, it is not a reason to discontinue breastfeeding, but an alternate drug may be preferred.

Pediatric Use
When clindamycin in 5% dextrose injection sterile solution is administered to the pediatric population (birth to 16 years) appropriate monitoring of organ system functions is desirable.

Geriatric Use
Clinical studies of clindamycin did not include sufficient numbers of patients age 65 and over to determine whether they respond differently from younger patients. However, other reported clinical experience indicates that antibiotic-associated colitis and diarrhea (due to *Clostridium difficile*) seen in association with most antibiotics occur more frequently in the elderly (>60 years) and may be more severe.

DOSAGE AND ADMINISTRATION

If diarrhea occurs during therapy, this antibiotic should be discontinued.

Adults: Parenteral (IV Administration): Serious infections due to aerobic gram-positive cocci and the more susceptible anaerobes (NOT generally including *Bacteroides fragilis*, *Peptococcus* species and *Clostridium* species other than *Clostridium perfringens*): 600 to 1200 mg/day in 2, 3 or 4 equal doses.

More severe infections, particularly those due to proven or suspected *Bacteroides fragilis, Peptococcus* species, or *Clostridium* species other than *Clostridium perfringens*: 1200 to 2700 mg/day in 2, 3 or 4 equal doses.

For more serious infections, these doses may have to be increased. In life-threatening situations due to either aerobes or anaerobes these doses may be increased. Doses of as much as 4800 mg daily have been given intravenously to adults. See **Infusion Rates** section of package insert.

Alternatively, drug may be administered in the form of a single rapid infusion of the first dose followed by continuous IV infusion as per the package insert.

Pediatric patients 1 month of age to 16 years: Parenteral (IV) Administration: 20 to 40 mg/kg/day in 3 or 4 equal doses. The higher doses would be used for more severe infections. Clindamycin should be dosed based on total body weight regardless of obesity. As an alternative to dosing on a body weight basis, pediatric patients may be dosed on the basis of square meters body surface: 350 mg/m^2/day for serious infections and 450 mg/m^2/day for more severe infections.

Parenteral therapy may be changed to oral clindamycin palmitate hydrochloride granules or clindamycin hydrochloride capsules when the condition warrants and at the discretion of the physician.

In cases of β-hemolytic streptococcal infections, treatment should be continued for at least 10 days.

Pediatric Patients less than 1 month: The recommended dosage is 15 to 20 mg/kg/day in 3 to 4 equal doses. See Table 3 of package insert regarding the dosing regimen for pediatric patients with post menstrual age (PMA) less than or equal to 32 weeks, or greater than 32 weeks to less than or equal to 40 weeks.

Infusion Rates: Infusion rates for Clindamycin in 5% Dextrose Injection should not exceed 30 mg per minute. The usual infusion dilutions and rates are provided in the package insert. Administration of more than 1200 mg in a single 1-hour infusion is not recommended.

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

Compatibility: Physical and biological compatibility studies monitored for 24 hours at room temperature have demonstrated no inactivation or incompatibility with the use of clindamycin in 5% dextrose injection sterile solution (clindamycin phosphate) in IV solutions containing sodium chloride, glucose, calcium or potassium, and solutions containing vitamin B complex in concentrations usually used clinically. No incompatibility has been demonstrated with the antibiotics cephalothin, kanamycin, gentamicin, penicillin or carbenicillin.

The following drugs are physically incompatible with clindamycin phosphate: ampicillin sodium, phenytoin sodium, barbiturates, aminophylline, calcium gluconate, and magnesium sulfate. The compatibility and duration of stability of drug admixtures will vary depending on concentration and other conditions.

OVERDOSAGE

Significant mortality was observed in mice at an intravenous dose of 855 mg/kg and in rats at an oral or subcutaneous dose of approximately 2618 mg/kg. In the mice, convulsions and depression were observed. Hemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum.

INDICATIONS AND USAGE

Clindamycin in 5% dextrose injection is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria.

Clindamycin in 5% dextrose injection is also indicated in the treatment of serious infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Its use should be reserved for penicillin-allergic patients or other patients for whom, in the judgment of the physician, a penicillin is inappropriate. Because of the risk of antibiotic-associated pseudomembranous colitis, as described in the **BOXED WARNING**, before selecting clindamycin the physician should consider the nature of the infection and the suitability of less toxic alternatives (e.g., erythromycin).

Bacteriologic studies should be performed to determine the causative organisms and their susceptibility to clindamycin. Indicated surgical procedures should be performed in conjunction with antibiotic therapy.

Clindamycin in 5% dextrose injection is indicated in the treatment of serious infections caused by susceptible strains of the designated organisms in the conditions listed below:

- Lower respiratory tract infections including pneumonia, empyema, and lung abscess caused by anaerobes, *Streptococcus pneumoniae,* other streptococci (except *E. faecalis*), and *Staphylococcus aureus.*
- Skin and skin structure infections caused by *Streptococcus pyogenes, Staphylococcus aureus*, and anaerobes.
- Gynecological infections including endometritis, nongonococcal tubo-ovarian abscess, pelvic cellulitis, and postsurgical vaginal cuff infection caused by susceptible anaerobes.
- Intra-abdominal infections including peritonitis and intra-abdominal abscess caused by susceptible anaerobic organisms.
- Septicemia caused by *Staphylococcus aureus*, streptococci (except *Enterococcus faecalis*), and susceptible anaerobes.
- Bone and joint infections including acute hematogenous osteomyelitis caused by *Staphylococcus aureus* and as adjunctive therapy in the surgical treatment of chronic bone and joint infections due to susceptible organisms.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of clindamycin in 5% dextrose injection and other antibacterial drugs, clindamycin in 5% dextrose injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

DIRECTIONS FOR USE

Premixed clindamycin in 5% dextrose injection IV solution is for intravenous administration using sterile equipment. If leaks are found, discard solution as sterility may be impaired. Do not add supplementary medication. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Do not use unless solution is clear and seal is intact.

Caution: Do not use in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is complete.

HOW SUPPLIED/STORAGE AND HANDLING

Clindamycin in 5% Dextrose Injection is a sterile solution of clindamycin phosphate with 5% dextrose. It is

available in 50 mL clear molded glass vial fitted with an injection stopper. Single-dose vials are intended for single use only and are available as follows:

Strength	Total Clindamycin/Vial	Cap Color	NDC#
6 mg/mL	300 mg/50 mL	Light Blue	0143-9267-01
12 mg/mL	600 mg/50 mL	Blue	0143-9268-01
18 mg/mL	900 mg/50 mL	Brown	0143-9269-01

Exposure of pharmaceutical products to heat should be minimized.

Storage: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Avoid temperatures above 30°C. Discard unused portion.

ENDING INFORMATION

Patient counseling information should be shared with the patient prior to administration. 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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