Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:
KAREMEGA 4 INJECTION

2. Qualitative and quantitative composition
Each vial contains Benzylpenicillin Sodium 1,000,000 IU (600mg) and Procaine Penicillin 3,000,000IU (3g).

For a full list of excipients, see section 6.1.

3. Pharmaceutical form
Powder for injection

4. Clinical particulars

4.1 Therapeutic indications
Treatment of a wide variety of infections including: Pneumococcal pneumonia, Streptococcal pharyngitis, Syphilis, Gonorrhea strains. Treatment of enterococcal infections (requires the addition of an aminoglycoside). Prevention of rheumatic fever. Should not be used as a single agent to treat anthrax.

4.2 Posology and method of administration
IM (Adults): Moderate or severe infections—600,000– 1.2 million units/day, single dose or 2 divided doses. Neurosyphilis—2.4 million units/day with 500 mg probenecid PO 4 times daily for 10– 14 days. IM (Children): Congenital syphilis—50,000 units/kg/day for 10– 14 days.

Method of administration
Intramuscular

4.3 Contraindications
Previous hypersensitivity to penicillins (cross-sensitivity exists with cephalosporins and other beta-lactam antibiotics); Hypersensitivity to procaine.

4.4 Special warnings and precautions for use
Use Cautiously in: Severe renal insufficiency (dosage reduction recommended);
OB: Although safety not established, has been used safely; Lactation: Safety not established;
Geriatric: Consider decreased body mass, age-related decrease in renal/hepatic/cardiac function, inter-current diseases and drug therapy

4.5 Interaction with other medicinal products and other forms of interaction
Drug-Drug: Penicillin may reduce effectiveness of oral contraceptive agents. Probenecid reduce renal excretion and increase blood levels of penicillin (therapy may be combined for this purpose). Neomycin may

reduce absorption of penicillin. Concurrent use with methotrexate reduce methotrexate elimination and increase risk of serious toxicity.

- Lab Test Considerations: May cause positive direct Coombs' test results.
- Monitor serum sodium concentrations in patient with hypertension or HF. Hypernatremia may develop after large doses of penicillin sodium.
- May cause increased AST, ALT, LDH, and serum alkaline phosphatase concentrations.
- May cause leukopenia and neutropenia, especially with prolonged therapy or hepatic impairment.

4.6 Pregnancy and Lactation

Teratogenic Effects

Reproduction studies performed in the mouse, rat, and rabbit have revealed no evidence of impaired fertility or harm to the fetus due to penicillin G. Human experience with the Penicillins during pregnancy has not shown any positive evidence of adverse effects on the fetus. There are, however, no adequate and well-controlled studies in pregnant women showing conclusively that harmful effects of these drugs on the fetus can be excluded. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Penicillins are excreted in human milk. Caution should be exercised when penicillins are administered to a nursing woman.

4.7 Effects on ability to drive and use machines

Not stated

4.8 Undesirable effects

CNS: Seizures.
GI: diarrhea, epigastric distress, nausea, vomiting, pseudomembranous colitis.
GU: interstitial nephritis.
Derm: rash, urticaria.
Hemat: eosinophilia, leukopenia. Local: pain at IM site.
Misc: allergic reactions including ANAPHYLAXIS and SERUM SICKNESS, superinfection.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via National Pharmacovigilance Electronic Reporting Systems' to the respective National Regulatory Authorities.

4.9 Overdose

Symptoms of overdose may include the following:
Twitching
Seizures

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Penicillins with extended spectrum;
ATC code: J01CA04

Mechanism of Action It exerts a bactericidal action against penicillin-susceptible microorganisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell-wall peptidoglycan, rendering the cell wall osmotically unstable.

Mechanism of Resistance
Penicillin is not active against penicillinase-producing bacteria, or against organisms resistant to beta-lactams because of alterations in the penicillin-binding proteins. Resistance has not been reported in Streptococcus pyogenes.

5.2 Pharmacokinetic properties

Penicillin G procaine is an equimolecular compound of procaine and penicillin G, administered intramuscularly. It dissolves slowly at the site of injection, giving a plateau type of blood level at about 4 hours which falls slowly over a period of the next 15 to 20 hours.

Approximately 60% of penicillin G is bound to serum protein. The drug is distributed throughout the body tissues in widely varying amounts. Highest levels are found in the kidneys with lesser amounts in the liver, skin, and intestines. Penicillin G penetrates into all other tissues to a lesser degree with a very small level found in the cerebrospinal fluid.

With normal kidney function, the drug is excreted rapidly by tubular excretion. In neonates and young infants and in individuals with impaired kidney functions, excretion is considerably delayed. Approximately 60 to 90 percent of a dose of parenteral penicillin G is excreted in the urine within 24 to 36 hours.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. Pharmaceutical Particulars

6.1 List of Excipients

Not Applicable

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life
36 months

6.4 Special Precautions for storage
Store in a cool dry place below 30°C, Out of direct sunlight, keep medicines out of reach of children.

6.5 Nature and Content of container
Packed in glass vial contained in a unit carton with literature insert.

6.6 Special precautions for disposal and other handling
Not applicable

7. Marketing Authorization Holder
Karemax Industrial Limited

8. Marketing Authorization Number
H2022/CTD8738/18836

9. Date of first authorization/renewal of the authorization
09/11/2023

10. Date of revision of the text
09/11/2023