الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Saudi Public Assessment Report

(Summary Report)

Coguperin®

Type of Product: Human Biosimilar Drug.

Active Pharmaceutical Ingredient(s): Enoxaparin Sodium.

ATC code: B01AB05.

Dosage Form: Solution for injection.

Route(s) of administration: Subcutaneous.

Dosage Strength: 80 mg/0.8 ml.

Pack Size: 2.

Shelf life: 24 Months.

Storage Conditions: Store below 30°C Don't Freeze.

Reference Product in SA (if applicable): Clexane®

Marketing Authorization Holder: Venus Remedies Limited.

Manufacturer: Venus Remedies Limited.

Registration No.: 2008234002.

Date of Decision: 20/08/2023

Proposed Indications:

Enoxaparin Syringes is indicated in adults for:

- Prophylaxis of venous thromboembolic disease in moderate and high risk surgical patients, in particular those undergoing orthopaedic or general surgery including cancer surgery.
- Prophylaxis of venous thromboembolic disease in medical patients with an acute illness (such as acute heart failure, respiratory insufficiency, severe infections or rheumatic diseases) and reduced mobility at increased risk of venous thromboembolism.
- Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), excluding PE likely to require thrombolytic therapy or surgery.
- Prevention of thrombus formation in extra corporeal circulation during haemodialysis
- Acute coronary syndrome:
  - Treatment of unstable angina and Non ST-segment elevation myocardial infarction (NSTEMI), in combination with oral acetylsalicylic acid.
  - Treatment of acute ST-segment elevation myocardial infarction (STEMI) including patients to be managed medically or with subsequent percutaneous coronary intervention (PCI)

Product Background

This product is considered as a biosimilar drug for Saudi regulatory purposes qualified to follow the SFDA's Regular regulatory pathway.

The SFDA approval for Coguperin® is based on a review of the quality, safety and efficacy of the product provided as an e-CTD in accordance with the relevant guidelines, basic product information summarized hereinafter:

Quality Aspects:

Coguperin® had been developed as a biosimilar to the reference product Clexane®. Both products contain enoxaparin sodium as a drug substance. Enoxaparin sodium is the sodium salt of a low-molecular-mass heparin that consists of a complex set of oligosaccharides with an average molecular weight of about 4,500 Dalton. Enoxaparin binds to antithrombin III leading to inhibition of coagulation factors IIa and Xa. Enoxaparin inhibits the coagulation factors Xa and IIa mainly; and affects other hemostatic mechanisms slightly such as clotting time. The antithrombotic effect of enoxaparin is correlated to the inhibition of Factor Xa.

The manufacturing process of heparin sodium and enoxaparin sodium considered to be standardized with known test parameters, all the potential impurities expected during the manufacturing process of crude heparin, heparin sodium and enoxaparin sodium finished product are well controlled and relevant data submitted in a regulatory sufficient way.

The specification of API is considered comply with European Pharmacopeia monograph. The analytical procedure was appropriately described for compendial methods (appearance, solubility, 13C NMR, 1,6-anhydro derivatives, size exclusion chromatography, specific absorbance, pH, loss on drying, nitrogen content, sodium content, molar ratio of sulfate ions to carboxylate ions, benzyl alcohol content, anti-factor Xa activity assay, anti-factor IIa activity assay, free sulfates, endotoxin and microbial limit) and non-compendial methods (limit of residual solvents).

All excipients complied with the current monographs, supportive certificate of analysis had been enclosed for each excipient presented in the final formulation, including sodium hydroxide, hydrochloric acid, and water for injection.

Stability data of drug product batches conducted on long term (30°C ± 2°C / 75% RH ± 5%) and accelerated (40°C ± 2°C / 75% RH ± 5%)) conditions supporting the proposed shelf life of 24 months.

There are no issues pertaining to drug substance and drug product stability. There are no issues pertaining to drug substance and drug product specifications. All analytical procedures are validated.

Bioequivalence Study:

Ratio and 90% Confidence Intervals (CI) of Coguperin® (Enoxaparin sodium) 100mg/ml Pre-filled syringes versus Clexane® (Enoxaparin sodium) 100mg/ml Pre-filled syringes:

For Anti-Xa

Pharmacodynamics Parameter	**Point Estimate**	**90% CI**
A_{max} (IU/mL)	109.62%	105.50% - 113.90%
$AUEC_t$ (IU/mL)	107.94%	103.97% - 112.08%
$AUEC_i$ (IU/mL)	108.86%	104.72% - 113.16%

For Anti-IIa

Pharmacodynamics Parameter	**Point Estimate**	**90% CI**
A_{max} (IU/mL)	112.09%	106.56% - 117.90%
$AUEC_t$ (IU/mL)	115.78%	107.35% - 124.86%
$AUEC_i$ (IU/mL)	108.92%	92.08% - 128.84%

For Activity Ratio of Anti-Xa/ Anti-IIa

Pharmacodynamics Parameter	**Point Estimate**	**90% CI**
A_{max} (IU/mL)	97.80%	95.05% - 100.62%

$AUEC_t$ (IU/mL)	93.19%	86.21% - 100.75%
$AUEC_i$ (IU/mL)	99.29%	83.58% - 117.95%

For Corrected TFPI

Pharmacodynamics Parameter	**Point Estimate**	**90% CI**
A_{max} (pg/mL)	109.03%	102.43% - 116.05%
$AUEC_t$ (pg /mL)	114.28%	109.29% - 119.50%
$AUEC_i$ (pg /mL)	117.46%	110.14% - 125.26%

For Uncorrected TFPI

Pharmacodynamics Parameter	**Point Estimate**	**90% CI**
A_{max} (pg/mL)	105.19%	101.14% - 109.40%
$AUEC_t$ (pg /mL)	102.48%	100.96% - 104.02%
$AUEC_i$ (pg /mL)	99.25%	95.27% - 103.39%

For APTT

Pharmacodynamics Parameter	**Point Estimate**	**90% CI**
A_{max} (Sec)	114.15%	106.36% - 122.51%
$AUEC_t$ (Sec)	112.96%	98.80% - 129.14%

For Uncorrected APTT

Pharmacodynamics Parameter	**Point Estimate**	**90% CI**
A_{max} (Sec)	101.52%	99.77% - 103.30%

$AUEC_t$ (Sec)	99.74%	98.89% - 100.60%

Based on the results obtained in this study, Coguperin® (Enoxaparin sodium) 100mg/ml of Venus Remedies Limited, India is **bioequivalent** to Clexane® (Enoxaparin sodium) 100mg/ml of Chinoin Pharmaceutical and Chemical works private Co. Ltd.-A Sanofi company, Germany under fasting Conditions.

Product Information

The approved Summary of Product Characteristics (SPC) with the submission can be found in Saudi Drug Information System (SDI) at: https://sdi.sfda.gov.sa/

The date of revision of this text corresponds to that of the Saudi PAR. New information concerning the authorized medicinal product in question will not be incorporated into the Saudi PAR. New findings that could impair the medicinal product's quality, efficacy, or safety are recorded and published at (SDI or Summary Saudi-PAR report).

For inquiry and feedback regarding Saudi PAR, please contact us at Saudi.PAR@sdfa.gov.sa