Australian Government
Department of Health, Disability and Ageing
Therapeutic Goods Administration

Australian Public Assessment Report for ENOXACOR, ENOXAJECT and CLASTO

Active ingredient: Enoxaparin

Sponsor: Pharmacor Pty Ltd

July 2025

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health, Disability and Ageing and is responsible for regulating therapeutic goods, including medicines, medical devices, and biologicals.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety, and efficacy.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to the Australian public outweigh any risks associated with the use of therapeutic goods.
- The TGA relies on the public, healthcare professionals and industry to report problems with therapeutic goods. The TGA investigates reports received to determine any necessary regulatory action.
- To report a problem with a therapeutic good, please see the information on the TGA website.

About AusPARs

- The Australian Public Assessment Report (AusPAR) provides information about the evaluation of a prescription medicine and the considerations that led the TGA to approve or not approve a prescription medicine submission. Further information can be found in Australian Public Assessment Report (AusPAR) guidance.
- AusPARs are prepared and published by the TGA.
- AusPARs are static documents that provide information that relates to a submission at a particular point in time. The publication of an AusPAR is an important part of the transparency of the TGA's decision-making process.
- A new AusPAR may be provided to reflect changes to indications or major variations to a prescription medicine subject to evaluation by the TGA.

Contents

List of abbreviations

Abbreviation	Meaning
ARTG	Australian Register of Therapeutic Goods
$AUEC_{0-t}$	Area under the effect–time curve from time 0 to the time of the last quantifiable concentration
C_{max}	Maximum measured concentration
PCI	Percutaneous coronary intervention
Ph. Eur.	European Pharmacopoeia
STEMI	ST-segment Elevation Myocardial Infarction
TFPI	Tissue factor pathway inhibitor
TGA	Therapeutic Goods Administration
USP	United States Pharmacopeia

CLASTO, ENOXACOR and ENOXAJECT (enoxaparin) submission

Type of submission:	New biosimilar (to CLEXANE)
Product name:	CLASTO, ENOXACOR, ENOXAJECT
Active ingredient:	enoxaparin
Decision:	Approved
Date of decision:	31 January 2025
Date of entry onto ARTG:	17 February 2025
ARTG numbers:	422248 - CLASTO enoxaparin sodium 20mg/0.2mL solution for injection syringe with safety lock system 423430 - CLASTO enoxaparin sodium 40mg/0.4mL solution for injection syringe with safety lock system 423431 - CLASTO enoxaparin sodium 60mg/0.6mL solution for injection syringe with safety lock system 423432 - CLASTO enoxaparin sodium 80mg/0.8mL solution for injection syringe with safety lock system 423433 - CLASTO enoxaparin sodium 100mg/1mL solution for injection syringe with safety lock system 423550 - ENOXACOR enoxaparin sodium 20mg/0.2mL solution for injection syringe with safety lock system 423551 - ENOXACOR enoxaparin sodium 40mg/0.4mL solution for injection syringe with safety lock system 423552 - ENOXACOR enoxaparin sodium 60mg/0.6mL solution for injection syringe with safety lock system 423553 - ENOXACOR enoxaparin sodium 80mg/0.8mL solution for injection syringe with safety lock system 423554 - ENOXACOR enoxaparin sodium 100mg/1mL solution for injection syringe with safety lock system 423555 - ENOXAJECT enoxaparin sodium 20mg/0.2mL solution for injection syringe with safety lock system 423556 - ENOXAJECT enoxaparin sodium 40mg/0.4mL solution for injection syringe with safety lock system 423557 - ENOXAJECT enoxaparin sodium 60mg/0.6mL solution for injection syringe with safety lock system 423558 - ENOXAJECT enoxaparin sodium 80mg/0.8mL solution for injection syringe with safety lock system 423559 - ENOXAJECT enoxaparin sodium 100mg/1mL solution for injection syringe with safety lock system 432813 - CLASTO enoxaparin sodium 120mg/0.8mL solution for injection syringe with safety lock system

432814 - ENOXACOR enoxaparin sodium 120mg/0.8mL solution for injection syringe with safety lock system

432815 - ENOXAJECT enoxaparin sodium 120mg/0.8mL solution for injection syringe with safety lock system

432816 - CLASTO enoxaparin sodium 150mg/1.0mL solution for injection syringe with safety lock system

432817 - ENOXACOR enoxaparin sodium 150mg/1.0mL solution for injection syringe with safety lock system

432818 - ENOXAJECT enoxaparin sodium 150mg/1.0mL solution for injection syringe with safety lock system

476368 - CLASTO enoxaparin sodium 20mg/0.2mL solution for injection syringe without safety lock system

476369 - CLASTO enoxaparin sodium 40mg/0.4mL solution for injection syringe without safety lock system

476370 - CLASTO enoxaparin sodium 60mg/0.6mL solution for injection syringe without safety lock system

476371 - CLASTO enoxaparin sodium 80mg/0.8mL solution for injection syringe without safety lock system

476372 - CLASTO enoxaparin sodium 100mg/1mL solution for injection syringe without safety lock system

476379 - CLASTO enoxaparin sodium 120mg/0.8mL solution for injection syringe without safety lock system

476380 - CLASTO enoxaparin sodium 150mg/1.0mL solution for injection syringe without safety lock system

476381 - ENOXACOR enoxaparin sodium 20mg/0.2mL solution for injection syringe without safety lock system

476382 - ENOXACOR enoxaparin sodium 40mg/0.4mL solution for injection syringe without safety lock system

476383 - ENOXACOR enoxaparin sodium 60mg/0.6mL solution for injection syringe without safety lock system

476384 - ENOXACOR enoxaparin sodium 80mg/0.8mL solution for injection syringe without safety lock system

476385 - ENOXACOR enoxaparin sodium 100mg/1mL solution for injection syringe without safety lock system

476386 - ENOXACOR enoxaparin sodium 120mg/0.8mL solution for injection syringe without safety lock system

476387 - ENOXACOR enoxaparin sodium 150mg/1.0mL solution for injection syringe without safety lock system

476388 - ENOXAJECT enoxaparin sodium 20mg/0.2mL solution for injection syringe without safety lock system

476395 - ENOXAJECT enoxaparin sodium 40mg/0.4mL solution for injection syringe without safety lock system

	476396 - ENOXAJECT enoxaparin sodium 60mg/0.6mL solution for injection syringe without safety lock system 476397 - ENOXAJECT enoxaparin sodium 80mg/0.8mL solution for injection syringe without safety lock system 476398 - ENOXAJECT enoxaparin sodium 100mg/1mL solution for injection syringe without safety lock system 476399 - ENOXAJECT enoxaparin sodium 120mg/0.8mL solution for injection syringe without safety lock system 476400 - ENOXAJECT enoxaparin sodium 150mg/1.0mL solution for injection syringe without safety lock system.
▼*Black Triangle Scheme*	No
Sponsor's name and address:	Pharmacor Pty Ltd, Suite 803, Level 8, Tower A, The Zenith, 821 Pacific Highway, Chatswood NSW 2067
Dose form:	Solution
Approved therapeutic use for the current submission:	*Prevention of thrombo-embolic disorders of venous origin in patients undergoing orthopaedic and general surgery.* *Prophylaxis of venous thromboembolism in medical patients bedridden due to acute illness.* *Prevention of thrombosis in extra-corporeal circulation during haemodialysis.* *Treatment of established deep vein thrombosis.* *Treatment of unstable angina and non-Q-wave myocardial infarction, administered concurrently with aspirin.* *Treatment of acute ST-segment Elevation Myocardial Infarction (STEMI) as an adjunctive to thrombolytic treatment, including patients to be managed medically or with subsequent Percutaneous Coronary Intervention (PCI).*
Route of administration:	Subcutaneous, intravenous
Dosage:	For further information regarding dosage, refer to the Product Information.
Pregnancy category:	Category C Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. The use of any medicine during pregnancy requires careful consideration of both risks and benefits by the treating health professional. The pregnancy database must not be used as the sole basis of decision making in the use of medicines during pregnancy. The TGA does not provide advice on the use of medicines in pregnancy for specific cases. More information is available from obstetric drug information services in your state or territory.

Proposed indication

This AusPAR describes the submission by Pharmacor Pty Ltd (the Sponsor)[1] to register a new biosimilar medicine (of enoxaparin sodium with the same strengths, indications, doses, and routes of administration as the Australian reference product, CLEXANE), CLASTO, ENOXACOR, and ENOXAJECT (enoxaparin), for the following proposed indications:

> *Prevention of thrombo-embolic disorders of venous origin in patients undergoing orthopaedic and general surgery.*
> *Prophylaxis of venous thromboembolism in medical patients bedridden due to acute illness.*
> *Prevention of thrombosis in extra-corporeal circulation during haemodialysis.*
> *Treatment of established deep vein thrombosis.*
> *Treatment of unstable angina and non-Q-wave myocardial infarction, administered concurrently with aspirin.*
> *Treatment of acute ST-segment Elevation Myocardial Infarction (STEMI) as an adjunctive to thrombolytic treatment, including patients to be managed medically or with subsequent Percutaneous Coronary Intervention (PCI).*

Regulatory status

This application was submitted to TGA on 11 September 2023. Various trade names were proposed during the course of the application, and the following trade names are proposed for registration: CLASTO, ENOXAJECT, and ENOXACOR.

The reference product, CLEXANE, was first registered in Australia on 12 February 1993.

Several enoxaparin biosimilar products are registered in Australia. ENOXAPO was registered on 10 February 2020 following a complex regulatory history (rejection by initial delegate, rejection confirmed by s60 delegate, review by AAT, then approval by delegate of Minister). EXARANE and EXARANE FORTE were registered on 28 July 2023

Australian regulatory status

This product is a new biosimilar medicine for Australian regulatory purposes.

International regulatory status

USA: Approved 6 June 2023 (applicant BE Pharmaceuticals, ANDA-214646).

Canada: Approved 26 October 2022 (ELONOX, ELONOX HP, Sponsored by Fresenius Kabi).

EU/UK: Applications via the decentralised process in the EU and UK were withdrawn in 2023 for commercial reasons.

Registration timeline

Table 1 captures the key steps and dates for this submission.

This submission was evaluated under the standard prescription medicines registration process.

[1] A Sponsor is a person or company who does one or more of the following: a) exports therapeutic goods from Australia, b) imports therapeutic goods into Australia, c) manufactures therapeutic goods for supply in Australia or d) elsewhere arranges for another party to import, export or manufacture therapeutic goods

Table 1: Registration timeline for CLASTO, ENOXACOR and ENOXAJECT (enoxaparin), submission PM-2023-04221-1-3

Description	Date
Submission dossier accepted and evaluation commenced	31 October 2023
Evaluation completed	26 August 2024
Registration decision (Outcome)	31 January 2025
Registration in the ARTG completed	17 February 2025
Number of working days from submission dossier acceptance to registration decision*	318 days

*Statutory timeframe for standard submissions is 255 working days

Assessment overview

Quality evaluation summary

Enoxaparin sodium is the sodium salt of depolymerised heparin. It is a mixture of heterogeneous oligosaccharide chains which vary in molecular weight, chain length, degree of sulfation and disaccharide unit composition. The majority of the components have a 4-enopyranose urinate structure at the nonreducing end of their chain. About 20% of the materials contain a 1,6-anhydro derivative on the reducing end of the chain, the range being between 15% and 25%.

The enoxaparin sodium drug substance is manufactured at Biological E. Ltd. (India). The active ingredient is derived from heparin sodium sourced from porcine intestinal mucosa, which is the same starting material in the drug substance manufacturing process as for CLEXANE. The overall quality of the active substance was demonstrated via adequate controls of the starting material, control of critical steps and intermediates, process validation, extensive characterisation using orthogonal and state-of-the-art analytical methods, control of impurities and contaminants, generation of robust reference materials and batch analyses that covered multiple manufacturing campaigns. Stability data have been generated under real time and stressed conditions to characterise the stability profile of the active ingredient and to establish a shelf life. The real time data submitted support a shelf life for the drug substance of 48 months when stored at ≤ 25°C.

The proposed drug product enoxaparin sodium injection USP 20 mg/0.2 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/1 mL (100 mg/mL) and 120 mg/0.8 mL, 150 mg/1 mL (150 mg/mL) is a clear, colourless to pale yellow coloured solution. The drug product is presented in Type I glass barrel, 27 G ½ Inch needle with rigid needle shield, plunger stopper and a plunger rod with a safety device (PREVENTIS) and without a safety device. The composition of the drug product has been developed as per the reference product CLEXANE, with same active ingredient and excipient. The only excipient used is water for injections, which is compliant with Ph. Eur. and USP. The container closure is considered suitable for its intended use as demonstrated by compatibility and stability studies.

The enoxaparin sodium drug product is manufactured at Biological E. Ltd. (India). The drug substance is subject to compounding, filtration, filling and packaging during the manufacturing of enoxaparin sodium drug product. The description of the manufacturing process has been provided in sufficient details. All analytical methods used for testing of the finished product are

satisfactorily described in the dossier. Stability data have been generated under stressed and real time conditions to characterise the stability profile of the drug product. The recommended storage condition of the drug product is 36 months when stored at ≤25°C. The product labels are acceptable.

There are no outstanding issues from the secondary quality evaluations (infectious disease/viral safety, container safety, microbiology (sterility), endotoxin).

Approval is recommended from a quality perspective.

Biosimilarity

During development of the proposed enoxaparin sodium, German CLEXANE, UK CLEXANE, and USA LOVENOX were used in comparisons to demonstrate biosimilarity in the quality and non-clinical comparability exercise. An additional bridging comparability study was performed between EU CLEXANE and Australian CLEXANE.

The biosimilarity assessment covers comparative analyses of physicochemical and biological attributes of the proposed biosimilar product and CLEXANE (and other brands of enoxaparin sodium), which is comprehensive. Samples have been assessed for similarity with respect to molecular weight distribution, overall chemical composition, starting material, mode of depolymerisation, disaccharide building blocks, fragment mapping profiles, biological and biochemical assays. Extensive characterisation studies involving comparison of primary, secondary and tertiary structures, physicochemical properties and biological activities showed that the proposed product and the reference medicine CLEXANE are generally similar.

Overall, the Sponsor has demonstrated that the proposed product is comparable to CLEXANE in terms of structure, species, function and degradation profile (i.e. physicochemically and biologically).

The proposed Product Information is acceptable from a quality perspective. The proposed trade names CLASTO, ENOXACOR, and ENOXAJECT are acceptable.

Nonclinical evaluation summary

The scope of the non-clinical program is adequate under the relevant EU guideline. The non-clinical dossier contained comparative in vitro and in vivo immunogenicity studies which indicated that the biosimilar enoxaparin and the reference product (EU-sourced CLEXANE) were comparable. Comparability of EU-sourced and Australian-sourced CLEXANE was confirmed in the quality evaluation.

There are no objections on nonclinical grounds to the registration of the proposed product.

Clinical evaluation summary

The clinical dossier included a randomised, two-period, two-sequence, single-dose, cross-over study comparing PD parameters of the test product to EU-sourced CLEXANE. A justification for use of an overseas reference product, including a bridging study assessing physicochemical, structural and functional similarity of EU- and AU-sourced CLEXANE, was assessed by the quality Evaluator. The application did not include a clinical efficacy and safety study.

Pharmacology

Pharmacodynamics

Study 0356-18

This was an open label, balanced, randomised, two-treatment, two-period, two-sequence, single dose, crossover, bioequivalence study assessing pharmacodynamic (PD) end points in healthy adults. The study was conducted in January 2020 in India. The study objectives were to compare and characterise the PD profile of the test product with the reference product in normal, healthy, adult, human subjects under fasting conditions and to assess the bioequivalence with respect to PD end points, and to monitor the adverse events, clinically significant deviations from laboratory examinations and physical examinations for the evaluation of safety.

The study compared single 100 mg/1 mL doses of enoxaparin sodium manufactured by Biological E Limited and CLEXANE sourced from Germany, administered by subcutaneous injection. There was a washout period of 7 days between the successive dosing days. 40 subjects were dosed in Period I, and 39 were dosed in Period II and completed the study (1 subject discontinued from the study on own accord in Period II).

Bioequivalence was concluded based on the 95% CIs for the geometric mean ratio (GMR) for ln-transformed Anti-Xamax and $AUEC_{0-t}$ being within the acceptance range of 80-125%. Supportive measures were the geometric mean ratio (GMR) (95% CI) for ln-transformed parameters for anti-IIa, baseline corrected and uncorrected data of tissue factor pathway inhibitor (TFPI), and ratio of anti-Xa to anti-IIa activities.

The statistical analysis was performed using an analysis of variance (ANOVA) model. The model included Sequence, Period, Formulation and Subject as fixed effects. Each analysis of variance was included for calculation of least-squares means, the difference between adjusted formulation means and the standard error associated with this difference. An F-test was to be performed to determine the statistical significance of the effects involved in the model at a significance level of 2.5% (α= 0.025).

Bioequivalence was demonstrated for all anti-Xa parameters (Table 2). Statistically significant effects were observed for formulation, sequence, period and subject (Table 3). Significant fixed effects for subject and formulation are acceptable as the 95% confidence intervals are within the acceptance criteria. An effect for period might indicate a carryover effect from the previous treatment period, a deterioration in the drug products between treatment periods (e.g. spoilage due to inappropriate storage conditions), or different conditions on the study day (e.g. collection, storage and analysis of study samples). Sequence effect might indicate a difference between the two sequences (i.e., subjects in one of the sequences were more affected than in the other by a period effect). The presence of a significant sequence or period effect would tend to increase the variability in the data. The 95% confidence intervals for anti-Xa_{max} and $AUEC_{0-t}$ were narrow and well within the acceptance range of 80% to 125%. Consequently, the presence of sequence and period effects are considered unlikely to have biased the results. Bioequivalence was also demonstrated for all anti-IIa (Table 4, Table 5) and TFPI (Table 6, Table 7) parameters, and for InC_{max} and $InAUEC_{0-t}$ for ratio of anti-Xa to anti-IIa activity (Table 8, Table 9).

The PD findings satisfactorily demonstrate bioequivalence of the proposed product to EU-CLEXANE. Similarity of EU- and AU-CLEXANE was addressed in the quality evaluation.

Table 2. Relative Bioavailability Results for Anti-Xa activity (N = 39)

Parameters	Geometric Least Squares Means			95% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R)%			
lnAnti-Xa_{max}	1.767	1.659	106.5	103 - 110	7.6	100.0
$lnAUEC_{0-t}$	15.548	13.938	111.5	108 - 115	7.2	100.0
$lnAUEC_{0-\infty}$	17.643	15.452	114.2	110 - 118	7.9	100.0

Table 3. ANOVA p-values for Anti-Xa activity

Parameters	ANOVA (p-value)			
	Formulation	Sequence	Period	Subject (Seq)
lnAnti-Xa_{max}	0.0007	<0.0001	0.0119	<0.0001
$lnAUEC_{0-t}$	<0.0001	<0.0001	0.0009	<0.0001
$lnAUEC_{0-\infty}$	<0.0001	<0.0001	0.0018	<0.0001

Note: p-value is statistically significant if it is < 0.025.

Table 4. Relative Bioavailability results for Anti-IIa activity (N = 28) [Excluding subjects having pre-dose concentration > 5% of C_{max}]

Parameters	Geometric Least Squares Means			95% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R)%			
lnAnti-IIa_{max}	0.309	0.291	106.2	92 - 123	27.3	91.4
$lnAUEC_{0-t}$	2.194	2.283	96.1	90 - 102	11.5	100.0
$lnAUEC_{0-\infty}$	2.900	2.940	98.6	87 - 112	22.8	97.2

Table 5. Relative Bioavailability Results for Anti-IIa activity (N = 39) [Including subjects having pre-dose concentration > 5% of C_{max}]

Parameters	Geometric Least Squares Means			95% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R)%			
lnAnti-IIa_{max}	0.313	0.295	106.3	95 - 119	24.3	99.0
$lnAUEC_{0-t}$	2.324	2.393	97.1	92 - 103	12.5	100.0
$lnAUEC_{0-\infty}$	3.169	3.100	102.2	90 - 116	27.6	97.0

Table 6. Relative Bioavailability Results for TFPI (Baseline corrected data)

Parameters	Geometric Least Squares Means			95% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R) %			
lnC_{max}	75506.406	68174.243	110.8	105 – 117	12.3	100.0
$lnAUEC_{0-t}$	477213.883	432912.090	110.2	104 - 117	12.2	100.0
$lnAUEC_{0-\infty}$	481256.894^	446862.767^	107.7	102 - 114	12.6	100.0

^N = 38

Table 7. Relative Bioavailability Results for TFPI (Baseline uncorrected data)

Parameters	Geometric Least Squares Means			95% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R) %			
lnC_{max}	100847.650	94484.127	106.7	102 – 112	9.9	100.0
$lnAUEC_{0-t}$	1056799.875	1031405.140	102.5	100 -105	6.3	100.0
$lnAUEC_{0-\infty}$	1434420.861^	1397800.652^	102.6	94 -112	18.2	100.0

^N = 38

Table 8. Relative Bioavailability Results for Ratio of Anti-Xa to Anti-IIa activity (N=28) [excluding subjects having pre-dose concentration >5% of Cmax for Anti-IIa activity]

Parameters	Geometric Least Squares Means			95% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R)%			
lnC_{max}	9.638	8.709	110.7	102 - 120	14.7	100.0
$lnAUEC_{0-t}$	96.611	84.726	114.0	104 - 125	17.5	99.8
$lnAUEC_{0-\infty}$	280.565^	189.599^	148.0	86 - 254	96.5	19.8

Table 9. Relative Bioavailability Results for Ratio of Anti-Xa to Anti-IIa activity (N=39) [including subjects having pre-dose concentration >5% of Cmax for Anti-IIa activity]

Parameters	Geometric Least Squares Means			95% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R) %			
lnC_{max}	9.602	8.603	111.6	105- 119	13.5	100.0
$lnAUEC_{0-t}$	99.027	88.569	111.8	102- 122	19.3	99.9
$lnAUEC_{0-\infty}$	233.754^	176.217^	132.7	91- 194	81.6	31.2

^N=30

Efficacy and safety

No clinical efficacy and safety study was conducted. Efficacy and safety are expected to be similar to CLEXANE based on the findings of similar physicochemical properties, functional characteristics, and PD profiles. Immunogenicity was assessed in comparative in vitro and in vivo immunogenicity studies in Module 4. No new safety concerns were identified in the PD equivalence study. Post-market safety findings presented in the Quarterly Adverse Drug Experience Report for the period 6 March 2024 to 5 June 2024 did not change the safety profile.

Risk-benefit analysis

Biosimilarity

The Sponsor presented comprehensive comparative analyses of physicochemical and biological attributes demonstrating similarity of the proposed product to the reference product CLEXANE, including a bridging study demonstrating similarity of EU-CLEXANE and AU-CLEXANE. The findings from the comprehensive quality and non-clinical comparability exercise support a conclusion of biosimilarity. The non-clinical evaluation concluded that immunogenicity was satisfactorily addressed in comparative in vitro and in vivo immunogenicity studies.

Bioequivalence of PD parameters of the proposed product to CLEXANE has been satisfactorily demonstrated. The bioequivalence study evaluated doses of 100 mg by subcutaneous injection. This dose was selected as it is within the sensitive portion of the dose-response curve and within the recommended therapeutic dose range. The pharmacokinetics of enoxaparin (based on PD endpoints) is linear over the recommended dose range, including prophylactic and therapeutic doses. Extrapolation of bioequivalence to the other proposed strengths is acceptable. The 100 mg/mL and 150 mg/mL formulations contain no excipients other than water for injections. Extrapolation to other routes of administration (intravenous, and into arterial line of haemodialysis circuit) is acceptable, as bioequivalence with subcutaneous administration addresses both absorption and elimination.

There was no clinical efficacy and safety study. The demonstration of similar physicochemical properties, functional characteristics, and PD profiles to CLEXANE support a conclusion of similar efficacy and safety. Immunogenicity was satisfactorily addressed in comparative in vitro and in vivo immunogenicity studies assessed in the non-clinical evaluation. Safety data from the bioequivalence study raised no new safety concerns. This approach to determining similar efficacy and safety is consistent with the TGA-adopted guideline on non-clinical and clinical

development of similar biological medicinal products containing low molecular-weight-heparins.[2]

Assessment outcome

Based on a review of quality, safety, and efficacy, the TGA decided to register CLASTO, ENOXACOR and ENOXAJECT (enoxaparin) for the following indication:

> *Prevention of thrombo-embolic disorders of venous origin in patients undergoing orthopaedic and general surgery.*
> *Prophylaxis of venous thromboembolism in medical patients bedridden due to acute illness.*
> *Prevention of thrombosis in extra-corporeal circulation during haemodialysis.*
> *Treatment of established deep vein thrombosis.*
> *Treatment of unstable angina and non-Q-wave myocardial infarction, administered concurrently with aspirin.*
> *Treatment of acute ST-segment Elevation Myocardial Infarction (STEMI) as an adjunctive to thrombolytic treatment, including patients to be managed medically or with subsequent Percutaneous Coronary Intervention (PCI).*

Specific conditions of registration

Laboratory testing & compliance with certified product details

All batches of CLASTO, ENOXACOR and ENOXAJECT supplied in Australia must comply with the product details and specifications approved during evaluation and detailed in the Certified Product Details (CPD).

When requested by the TGA, the Sponsor should be prepared to provide product samples, specified reference materials and documentary evidence to enable the TGA to conduct laboratory testing on the Product. Outcomes of laboratory testing are published biannually in the TGA Database of Laboratory Testing Results http://www.tga.gov.au/ws-labs-index and periodically in testing reports on the TGA website.

Certified product details

The Certified Product Details (CPD), as described in Guidance 7: Certified Product Details of the Australian Regulatory Guidelines for Prescription Medicines (ARGPM), in PDF format, for the above products should be provided upon registration of these therapeutic goods. In addition, an updated CPD should be provided when changes to finished product specifications and test methods are approved in a Category 3 application or notified through a self-assessable change.

A template for preparation of CPD for biological prescription medicines can be obtained from the TGA website:

[for the form] https://www.tga.gov.au/form/certified-product-details-cpd-biological-prescription-medicines

[for the CPD guidance] https://www.tga.gov.au/guidance-7-certified-product-details

[2] European Medicines Agency. Guideline on non-clinical and clinical development of similar biological medicinal products containing low-molecular-weight-heparins - Revision 1. 10 November 2016. EMEA/CHMP/BMWP/118264/2007 Rev. 1 Committee for Medicinal products for Human (CHMP).

Product Information and Consumer Medicines Information

For the most recent Product Information (PI) and Consumer Medicines Information (CMI), please refer to the TGA PI/CMI search facility.

Therapeutic Goods Administration

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