

5.17 ENOXAPARIN

Injection containing enoxaparin sodium 20 mg (2,000 I.U. anti-Xa) in 0.2 mL pre-filled syringe,
Injection containing enoxaparin sodium 40 mg (4,000 I.U. anti-Xa) in 0.4 mL pre-filled syringe,
Injection containing enoxaparin sodium 60 mg (6,000 I.U. anti-Xa) in 0.6 mL pre-filled syringe,
Injection containing enoxaparin sodium 80 mg (8,000 I.U. anti-Xa) in 0.8 mL pre-filled syringe,
Injection containing enoxaparin sodium 100 mg (10,000 I.U. anti-Xa) in 1.0 mL pre-filled syringe,
Injection containing enoxaparin sodium 120 mg (12,000 I.U. anti-Xa) in 0.8 mL pre-filled syringe,
Injection containing enoxaparin sodium 150 mg (15,000 I.U. anti-Xa) in 1 mL pre-filled syringe,
Enoxapo[®],
Apotex Pty Ltd.

1 Purpose of Application

- 1.1 The minor submission requested the PBS listing of a new biosimilar brand of enoxaparin (Enoxapo[®]) on the General Schedule (Section 85) for the same indications and level of restrictions as its comparator, Clexane Safety-Lock[®].
- 1.2 The Sponsor also requested listing of two new strengths of enoxaparin that are not currently listed on the PBS: 120 mg and 150 mg.

2 Background

Registration status and previous PBAC consideration

- 2.1 Enoxapo was TGA registered on 10 February 2020 for the same indications for which Clexane Safety-Lock is TGA-registered:
 - Prevention of thromboembolic 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).
- 2.2 The TGA-approved Product Information (PI) for Enoxapo states that it is a biosimilar medicine to Clexane®.
- 2.3 The PBAC has not previously considered an application for Enoxapo.
- 2.4 There are currently three PBS-listed brands for enoxaparin: Clexane, Clexane Safety-Lock and Enoxaparin Winthrop®. The three PBS-listed brands for enoxaparin are listed on the General Schedule as Unrestricted Benefits and also Restricted Benefits for the treatment of haemodialysis in the 20 mg/0.2 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL and 100 mg/mL strengths.
- 2.5 Both the 120 mg/0.8 mL and 150 mg/mL strengths of enoxaparin were recommended for an Unrestricted Benefit listing by the PBAC in July 2019 for Clexane Forte®, Enoxaparin Winthrop and Clexane Safety-Lock, but are yet to be listed on the PBS (para 6.1, enoxaparin Public Summary Document (PSD), July 2019 PBAC Meeting). The sponsor, Sanofi-Aventis Australia Pty Ltd, did not request Restricted Benefit listings of the 120 mg and 150 mg strengths for the indication of haemodialysis in its July 2019 submission. The submission considered that enoxaparin 120 mg and 150 mg would predominantly be used in deep vein thrombosis (para 4.1, enoxaparin PSD, July 2019 PBAC Meeting).

For more detail on PBAC's view, see section 6 PBAC outcome.

3 Requested listing

- 3.1 The submission requested listing Enoxapo with the same restriction as the currently listed PBS brand Clexane Safety-Lock and the addition of two new strengths of enoxaparin: 120 mg/0.8 mL and 150 mg/mL.
- 3.2 The requested restriction is shown below. Secretariat suggested additions are in italics and deletions are in strikethrough.

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Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ENOXAPARIN enoxaparin sodium 20 mg/0.2 mL injection, 10 x 0.2 mL syringes	8558K	2	20	1	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 40 mg/0.4 mL injection, 10 x 0.4 mL syringes	8510X	2	20	1	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 60 mg/0.6 mL injection, 10 x 0.6 mL syringes	8262W	1	10	1	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 80 mg/0.8 mL injection, 10 x 0.8 mL syringes	8263X	1	10	1	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 100 mg/mL injection, 10 x 1 mL syringes	8264Y	1	10	1	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 120 mg/0.8 mL injection, 10 x 0.8 mL syringes	NEW	1	10	1	Enoxapo
enoxaparin sodium 150 mg/mL injection, 10 x 1 mL syringes	NEW	1	10	1	Enoxapo

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners
Benefit Type: <input checked="" type="checkbox"/> Unrestricted benefit
Administrative Advice: Biosimilar prescribing policy <i>Prescribing of the biosimilar brand Apotex Enoxapo is encouraged for treatment naive patients.</i> <i>Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).</i>

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Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ENOXAPARIN enoxaparin sodium 20 mg/0.2 mL injection, 10 x 0.2 mL syringes	8716R	2	20	3	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 40 mg/0.4 mL injection, 10 x 0.4 mL syringes	8639Q	2	20	3	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 60 mg/0.6 mL injection, 10 x 0.6 mL syringes	8640R	2	20	3	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 80 mg/0.8 mL injection, 10 x 0.8 mL syringes	5434B	2	20	3	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 100 mg/mL injection, 10 x 1 mL syringes	5435C	2	20	3	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners
Benefit Type: <input checked="" type="checkbox"/> Restricted benefit
Indication: Haemodialysis
Treatment criteria: Patient must be undergoing haemodialysis treatment AND Must be treated in a haemodialysis in clinic; OR Must be treated in a home dialysis setting AND Must be treated by a renal practitioner; OR Must be treated by a patient/carer trained in home haemodialysis
Clinical criteria: Patient must be diagnosed with chronic renal failure requiring haemodialysis treatment either in-centre or at home AND Home patient must be suitably trained by renal practitioner on performing haemodialysis treatment at home, including the use of anticoagulants
Administrative Advice: Biosimilar prescribing policy Prescribing of the biosimilar brand Apotex Enoxapo is encouraged for treatment naive patients. Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).

- 3.3 The sponsor supported the proposed inclusion of an administrative note encouraging the use of biosimilar medicines for treatment-naïve patients, in line with the Department’s Biosimilar Awareness Initiative (pg 1, pre-PBAC response).

For more detail on PBAC’s view, see section 6 PBAC outcome.

4 Comparator

- 4.1 The minor submission nominated Clexane Safety-Lock as the main comparator.
- 4.2 Clexane Safety-Lock has an automatic safety-lock system which retracts and seals the needle once the dose is administered, which is similar to the presentation of Enoxapo (pre-filled syringe with automatic safety device).

For more detail on PBAC’s view, see section 6 PBAC outcome.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

- 5.2 The PBAC noted that no consumer comments were received for this item.

Clinical claim

- 5.3 The Sponsor claimed that Enoxapo was non-inferior in terms of efficacy and safety compared to the comparator, Clexane Safety-Lock. The minor submission did not provide any clinical evidence in support of this claim. The sponsor provided the TGA approval letter which stated that Enoxapo had undergone an evaluation and was approved as a biosimilar medicine to Clexane.
- 5.4 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.
- 5.5 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Estimated PBS usage & financial implications

- 5.6 The Sponsor requested that the ex-manufacturer prices for the 20 mg/0.2 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL and 100 mg/mL formulations of Enoxapo be equivalent to the price of the corresponding PBS listed formulation of Clexane Safety-Lock.
- 5.7 For the 120 mg and 150 mg formulations, the proposed price was calculated on a cost-minimisation basis against the 100 mg formulation, as the 100 mg therapy was the least expensive item on a cost per milligram basis. This is consistent with the PBAC’s previous recommendation, that the listing of the 120 mg and 150 mg strengths for the

current PBS-listed enoxaparin brands should be cost minimised against the 100 mg price (para 6.4, enoxaparin PSD, July 2019 PBAC meeting). The calculation of these prices is shown in the table below.

Table 1: Proposed PBS pricing for Enoxapo 120 mg and 150 mg strengths

Brand name, strength	mg per syringe	Pack quantity	Total mg per pack (mg)	AEMP	Price per mg	Note
Clexane Safety Lock, 100 mg/mL	100	10	1000	\$69.27	\$0.069	Currently listed price
Enoxapo, 120 mg/0.8 mL	120	10	1200	\$83.12	\$0.069	Priced at same cost per mg as 100mg
Enoxapo, 150 mg/mL	150	10	1500	\$103.91	\$0.069	Priced at same cost per mg as 100mg

Source: Table 11, p 15 of the submission.

5.8 The submission argued that the financial impact would be a minor cost save because the 120 mg and 150 mg strengths would replace additive therapies of lower strengths with a higher cost per milligram (120 mg would replace 2 x 60 mg; 150 mg would replace 2 x 80 mg).

5.9 The minor submission estimated that Enoxapo would be costs saving over the first six years of listing. This is summarised in the table below.

Table 2: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of units dispensed ^a						
Estimated financial implications of Enoxapo						
to PBS	\$	\$	\$	\$	\$	\$
to RPBS	\$	\$	\$	\$	\$	\$
to PBS/RPBS	\$	\$	\$	\$	\$	\$
Estimate financial implications of other PBS listed brands of enoxaparin						
to PBS	\$	\$	\$	\$	\$	\$
to RPBS	\$	\$	\$	\$	\$	\$
to PBS/RPBS	\$	\$	\$	\$	\$	\$
Net financial implications						
to PBS	\$	\$	\$	\$	\$	\$
to RPBS	\$	\$	\$	\$	\$	\$
to PBS/RPBS	\$	\$	\$	\$	\$	\$

^a Assuming one unit (10 syringes) per script as estimated by the submission.

Source: Enoxaparin utilisation and cost model workbook attachment, p 3a,3b,4b,5 of the workbook.

The redacted table shows that at Year 6, the estimated number of units dispensed was 60,000 to < 70,000 and the net financial implications would be a net cost saving.

5.10 The submission noted that overall usage of enoxaparin had decreased by 2.38% per year since 2014 according to PBS services data. However, the Sponsor estimated that the market share of Enoxapo would increase over the six-year period due to the rate of displacement of the current PBS listed enoxaparin formulations.

5.11 The submission argued that the PBS listing of Enoxapo was not expected to grow the market as the prevalence of the conditions for which enoxaparin is prescribed and the

large number of treatment options for these conditions means that the market is mature and well defined.

Quality Use of Medicines

- 5.12 The Sponsor claimed that the listing of Enoxapo 120 mg/0.8 mL and 150 mg/mL injections would reduce treatment burden on patients in need of higher doses of enoxaparin, while increasing patient compliance, clinical outcomes and cost savings for patients.
- 5.13 The sponsor stated that the listing of Enoxapo would offer more options and contingencies in the event of medicines shortages, as all three of the currently PBS-listed brands are manufactured by the one sponsor.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended the enoxaparin biosimilar (Enoxapo[®]) be listed on the General Schedule (Section 85) on a cost-minimisation basis under the same circumstances for which the reference product Clexane Safety-Lock[®] is currently PBS listed, and for the same circumstances as outlined in the July 2019 PBAC recommendation relating to the 120 mg and 150 mg strengths.
- 6.2 The PBAC advised that the listing of the 20 mg/0.2 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL and 100 mg/mL formulations of Enoxapo be based on equi-effective doses of each corresponding PBS listed formulation of Clexane Safety-Lock.
- 6.3 The PBAC recommended the listing of Enoxapo 120 mg/0.8 mL and 150 mg/mL be on a cost-minimisation basis with enoxaparin 100 mg/mL, with maximum quantities of 1 (pack) / 10 (units) and 1 repeat for these two strengths for the Unrestricted Benefit, and a maximum quantity of 2 (packs) / 20 (units) and 3 repeats for the Restricted Benefit for treatment of haemodialysis.
- 6.4 The PBAC noted that the listing of Enoxapo 120 mg/0.8 mL and 150 mg/mL would offer cost savings as they would replace the use of multiple lower strengths (with a higher cost per mg) for patients requiring higher doses of enoxaparin.
- 6.5 In Australia, decisions about indication extrapolation for biosimilar medicines are made by the TGA. The PBAC noted that no clinical evidence was provided with the submission, however the TGA-approved PI stated that Enoxapo was biosimilar to Clexane.
- 6.6 The PBAC advised that the addition of an administrative note to encourage the uptake of biosimilar prescribing for treatment naïve patients would be appropriate, in accordance with the Department's Biosimilar Awareness Initiative. The PBAC noted that it is not possible to implement the other biosimilar uptake driver of a less restrictive Authority Required type listing in this instance.

- 6.7 The PBAC advised, under Section 101 (4AACD) of the National Health Act, that Enoxapo, Clexane, Clexane Safety-Lock and Enoxaparin Winthrop should be considered equivalent for the purposes of substitution (i.e., 'a' flagged in the Schedule with a NOTE stating PBS brand of one form and PBS brand of another form are equivalent for the purposes of substitution).
- 6.8 The PBAC advised no change to current arrangements for nurse practitioner prescribing or the Early Supply Rule for enoxaparin.
- 6.9 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Enoxapo is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over the other brands of enoxaparin, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 6.10 The PBAC noted that this submission was not eligible for an Independent Review as it received a positive recommendation

Outcome:

Recommended

7 Recommended listing

- 7.1 Add new Enoxapo brand to the existing 5 PBS item codes and add 2 new strengths (Enoxapo 120 mg and 150 mg) (shown in italics) as follows:

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enoxaparin sodium 40 mg/0.4 mL injection, 10 x 0.4 mL syringes	8510X	2	20	1	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a <i>Enoxapo</i> ^a
enoxaparin sodium 60 mg/0.6 mL injection, 10 x 0.6 mL syringes	8262W	1	10	1	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a <i>Enoxapo</i> ^a
enoxaparin sodium 80 mg/0.8 mL injection, 10 x 0.8 mL syringes	8263X	1	10	1	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a <i>Enoxapo</i> ^a
enoxaparin sodium 100 mg/mL injection, 10 x 1 mL syringes	8264Y	1	10	1	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a <i>Enoxapo</i> ^a
<i>enoxaparin sodium 120 mg/0.8 mL injection, 10 x 0.8 mL syringes</i>	<i>NEW</i>	<i>1</i>	<i>10</i>	<i>1</i>	<i>Enoxapo</i>
<i>enoxaparin sodium 150 mg/mL injection, 10 x 1 mL syringes</i>	<i>NEW</i>	<i>1</i>	<i>10</i>	<i>1</i>	<i>Enoxapo</i>

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Benefit Type: <input checked="" type="checkbox"/> Unrestricted benefit
Administrative Advice: Biosimilar prescribing policy Prescribing of the biosimilar brand Enoxapo is encouraged for treatment naive patients. Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).

7.2 Add new Enoxapo brand to the existing 5 PBS item codes and add 2 new strengths (Enoxapo 120 mg and 150 mg) as follows (shown in italics) as follows:

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enoxaparin sodium 40 mg/0.4 mL injection, 10 x 0.4 mL syringes	8639Q	2	20	3	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 60 mg/0.6 mL injection, 10 x 0.6 mL syringes	8640R	2	20	3	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 80 mg/0.8 mL injection, 10 x 0.8 mL syringes	5434B	2	20	3	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 100 mg/mL injection, 10 x 1 mL syringes	5435C	2	20	3	Clexane ^a Clexane Safety-Lock ^a Enoxaparin Winthrop ^a Enoxapo ^a
enoxaparin sodium 120 mg/0.8 mL injection, 10 x 0.8 mL syringes	NEW	2	20	3	Enoxapo
enoxaparin sodium 150 mg/mL injection, 10 x 1 mL syringes	NEW	2	20	3	Enoxapo

Restriction Summary 4910 / Treatment of Concept: 4910

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Benefit Type: <input checked="" type="checkbox"/> Restricted benefit
Indication: Haemodialysis
Administrative Advice: Biosimilar prescribing policy Prescribing of the biosimilar brand Enoxapo is encouraged for treatment naive patients. Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.