

## 5.13 ENOXAPARIN

**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, Clexane Forte<sup>®</sup>, Enoxaparin Winthrop<sup>®</sup>, Clexane Forte Safety -Lock<sup>®</sup>, Sanofi-aventis Australia Pty Ltd.**

### 1 Purpose of Application

- 1.1 The minor submission requested an unrestricted benefit listing of two new higher strength pre-filled syringes of enoxaparin, 120 mg in 0.8 mL and 150 mg in 1 mL, for each of the Clexane Forte, Enoxaparin Winthrop and Clexane Forte Safety-Lock brands.

### 2 Requested listing

- 2.1 The submission requested the new listings on the same basis as the current unrestricted benefit listings for 60 mg, 80 mg and 100 mg prefilled syringes of enoxaparin.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
ENOXAPARIN				
enoxaparin sodium 120 mg/mL injection, 10 x 0.8 mL syringes	1	1	██████████	Clexane Forte <sup>®</sup> Clexane Forte <sup>®</sup> Safety-lock
enoxaparin sodium 150 mg/mL injection, 10 x 1 mL syringes	1	1	██████████	Enoxaparin Winthrop <sup>®</sup> Sanofi-aventis Australia Pty Ltd

<b>Category / Program:</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Restriction level</b>	<input checked="" type="checkbox"/> Unrestricted Benefit

### 3 Background

- 3.1 Enoxaparin 120 mg and 150 mg injections were first TGA registered in May 2000, with additional brands and the safety-lock device registered in October 2017.

3.2 Enoxaparin is currently PBS listed as an unrestricted benefit listing, and as a restricted benefit listing for haemodialysis. It is TGA registered for the following indications:

- thromboembolic disorders in patients undergoing surgery
- prophylaxis of venous thromboembolism
- prevention of thrombosis during haemodialysis
- deep vein thrombosis (DVT)
- unstable angina
- non-Q-wave myocardial infarction (in combination with aspirin)
- treatment of acute ST-segment elevation myocardial infarction (STEMI) as an adjunctive to thrombolytic treatment.

## **4 Population and disease**

4.1 The submission considered that enoxaparin 120 mg and 150 mg would predominantly be used in DVT.

4.2 For DVT, the PI-recommended dose is a weight-based subcutaneous injection at 1.5 mg/kg once daily or 1 mg/kg twice daily. The submission argued that patients over 100 kg requiring treatment for DVT must administer two syringes per administration to achieve optimal dosing either by having multiple prescriptions dispensed or by prescribers applying for authority to prescribe an increased maximum quantity.

## **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 the Medical Oncology Group of Australia (MOGA) indicated its support for the listing of new enoxaparin strengths as it would allow many patients to administer once daily instead of using multiple injections.

### ***Clinical claim***

5.3 The submission claimed that the availability of higher strength formulations of enoxaparin would advantage patients who currently administer two injections per dose to achieve a therapeutic dose, as the current situation may lead to lower compliance, increasing the DVT risk in these patients.

**Economic analysis**

5.4 The submission requested pricing based on an average of the per mg prices of the 60 mg, 80 mg and 100 mg strengths of enoxaparin as outlined below.

**Table 1: Proposed per mg pricing calculation**

	<b>60 mg</b>	<b>80 mg</b>	<b>100 mg</b>
DPMQ	\$64.48	\$72.48	\$85.81
Ex-manufacturer price	\$49.43	\$56.87	\$69.27
Maximum quantity units	10	10	10
Total mg	600	800	1,000
Price/mg (ex-man)	\$0.082	\$0.071	\$0.069
<b>Proposed price/mg: Average price/mg (ex man)</b>	<b>\$0.074</b>		

Source: Table 2.3 p15 of the submission (pricing calculations)

**Drug cost/patient/course: \$ [redacted] (120 mg); \$ [redacted] (150 mg)**

5.5 The drug cost per patient per course was derived from the requested DPMQ, with two packs considered to be one course, consistent with maximum quantity and repeats for current listings.

**Estimated PBS usage & financial implications**

5.6 The minor submission assumed that the introduction of the new strengths would not grow the overall enoxaparin market, but instead that patients who require higher doses would switch to these alternative formulations, resulting in fewer instances of multiple prescriptions and authorities for increased quantities being required.

5.7 The submission assumed that the market was trending towards decline over the long term, and used a linear function of 2011 – 2017 data to extrapolate the direction of the market out to 2024.

5.8 The submission used the DHS Processed Prescriptions database and PBS 10% sample to establish the current market for enoxaparin and estimate the proportion of patients requiring a dose greater than 100 mg. While the methodology used may identify patients who are currently receiving higher doses of enoxaparin, it cannot identify patients who require more than 100 mg enoxaparin twice daily and are not currently dosed appropriately.

5.9 The submission assumed that all requests to DHS to increase maximum quantities will be eliminated with listing the new strengths.

5.10 The table below outlines the estimated utilisation and financial implications.

**Table 2: Estimated use and financial implications**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Estimated extent of use</b>						
Scripts dispensed	████	████	████	████	████	████
Enoxaparin 120mg/0.8mL	████	████	████	████	████	████
Enoxaparin 150mg/1mL	████	████	████	████	████	████
Aggregate of replaced enoxaparin scripts	██████	██████	██████	██████	██████	██████
<b>Estimated financial implications of enoxaparin 120mg and 150mg</b>						
Cost to PBS/RPBS	██████	██████	██████	██████	██████	██████
Minus co-payments	██████	██████	██████	██████	██████	██████
Cost to PBS/RPBS less co-payments	██████	██████	██████	██████	██████	██████
<b>Estimated financial implications for other enoxaparin strengths</b>						
Cost to PBS/RPBS	██████	██████	██████	██████	██████	██████
Minus co-payments	██████	██████	██████	██████	██████	██████
Cost to PBS/RPBS less co-payments	██████	██████	██████	██████	██████	██████
<b>Net financial implications</b>						
Net cost to PBS/RPBS	██████	██████	██████	██████	██████	██████
Net cost to DHS*	██████	██████	██████	██████	██████	██████

Source: Compiled during minor overview from Attachment 3 to the submission – Utilisation and Cost model (3a, 3c, 4c);  
 \* assumes a cost per telephone authority to DHS of \$11.00 per request to increase maximum quantity, figure provided by DHS and calculated by the Secretariat.

The redacted table shows that the total estimated number of dispensed scripts over 6 years was from 10,000 – 50,000, and the net cost to the PBS was less than \$10 million per year.

5.11 A key driver of the forecast savings was the replacement of the 60 mg dose, which is more expensive per milligram than the requested price for the 120 mg and 150 mg strengths and assumed to be the most replaced in practice. Furthermore, the estimates assumed that the use of the 60 mg strength will remain relatively stable while that of the 80 mg and 100 mg strengths will decline.

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

## 6 PBAC Outcome

- 6.1 The PBAC recommended the unrestricted benefit listings of two new strengths of enoxaparin, 120 mg and 150 mg, on a cost minimisation basis with the least costly alternative presentation on a per milligram basis, enoxaparin 100 mg.
- 6.2 In making this recommendation, the PBAC considered some patients who require daily doses higher than the current available strength will have a reduced injection burden as a result of listing these new strengths.
- 6.3 The PBAC agreed the maximum quantity and repeats should align with current listings, as the intention of these new strengths is to provide the same duration of treatment as current listings.
- 6.4 Noting the price of enoxaparin differs between strengths, the PBAC considered there

was no basis upon which to recommend the two new strengths at a higher price than the least costly listed strength on a per milligram basis. On that basis, the PBAC considered that enoxaparin 120 mg and enoxaparin 150 mg should be cost-minimised to enoxaparin 100 mg.

- 6.5 The PBAC considered the utilisation and financial estimates were uncertain, as the methodology used was simplistic and was not able to identify all patients requiring doses above 100 mg. The PBAC did not consider that the estimated savings would be realised, but considered that the listing of the two new strengths would likely be cost neutral.
- 6.6 The PBAC noted that in its July 2015 consideration of nadroparin, it had advised under Section 101(3BA) of the *National Health Act 1953* that low weight molecular heparins including enoxaparin, nadroparin and dalteparin should be treated as interchangeable on an individual patient basis.
- 6.7 The PBAC advised no change to current arrangements for nurse practitioner prescribing or the Early Supply Rule.
- 6.8 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because alternative dose forms of enoxaparin are not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over alternative strengths, or not expected to address a high and urgent unmet clinical need over alternative low molecular weight heparins, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 6.9 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**

Recommended

## 7 Recommended listing

### 7.1 Add new items:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
ENOXAPARIN				
enoxaparin sodium 120 mg/mL injection, 10 x 0.8 mL syringes	1	1	Clexane Forte® Clexane Forte® Safety-lock	Sanofi-aventis
enoxaparin sodium 150 mg/mL injection, 10 x 1 mL syringes	1	1	Enoxaparin Winthrop®	Australia Pty Ltd

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## 8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

## 9 Sponsor's Comment

The sponsor had no comment.