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5.22 ELTROMBOPAG, Tablet 75 mg (as olamine), Revolade®, Novartis Pharmaceuticals Australia Pty Limited

1 Purpose of Submission

1.1 The Category 4 submission sought to list eltrombopag 75 mg tablet (as olamine) (Revolade®) under the same circumstances as the PBS-listed eltrombopag 25 mg and 50 mg tablets.

1.2 The submission noted that patients taking eltrombopag frequently require multiple tablets to reach their individualised target dose (usually 12.5mg – 150mg). The submission claimed the introduction of a 75 mg tablet will reduce pill burden, enhance compliance whilst ensuring cost neutrality to the PBS relative to existing strengths.

1.3 Listing was requested based on a cost-minimisation approach versus current strengths of the drug.

2 Background

2.1 Eltrombopag is currently listed on the PBS as a Section 100 Highly Specialised Drug (HSD) listing for severe thrombocytopenia (ITP) and severe aplastic anaemia (SAA).

Registration status

2.2 Eltrombopag is TGA-registered for the following indications:

• paediatric patients with chronic immune thrombocytopaenia who have failed other treatments and either (a) need an increased platelet concentration for a planned procedure or (b) are at a high risk of bleeding;

• adult patients with ITP who have had an inadequate response or are intolerant to corticosteroids and immunoglobulins;

• thrombocytopenia in adult patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy;

• severe aplastic anaemia in combination with standard immunosuppressive therapy for the first-line treatment of adult and paediatric patients 2 years and older;

• adult patients with SAA who have had an insufficient response to immunosuppressive therapy.

2.3 Eltrombopag (25 mg and 50 mg film-coated tablets) was first TGA registered on 16 July 2010 for the treatment of adult patients with chronic ITP who have an inadequate response or are intolerant to corticosteroids and immunoglobulins.

2.4 Eltrombopag 75 mg film-coated tablet was TGA registered on 27 August 2013.

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Previous PBAC consideration

2.5 At its November 2010 meeting, the PBAC did not recommend eltrombopag for adult patients with chronic ITP on the basis of uncertain clinical effectiveness compared to romiplostim.

2.6 At its March 2011 meeting, the PBAC recommended eltrombopag for chronic ITP based on acceptable cost effectiveness at the revised price (less effective but less expensive compared to romiplostim).

2.7 At its May 2022 meeting, the PBAC recommended an extension of restrictions of romiplostim and eltrombopag to match more current clinical practice:

- switching between eltrombopag and romiplostim be allowed at any time and wording in the restriction about switching within 24 weeks be removed to mitigate any confusion among prescribers
- the wording in the restriction regarding prior splenectomy or contraindication to splenectomy use be removed
- children be included in the updated restrictions by removing age limits
- restrictions on platelet count specified in continuing treatment be removed, and treatment be allowed to continue if the patient can maintain platelet count sufficient to prevent clinically significant bleeding
- the requirement to stipulate toxicity to corticosteroid and immunoglobulin be removed.

2.8 At its November 2023 meeting, the PBAC recommended listing eltrombopag for the treatment of SAA, as first-line treatment in combination with horse anti thymocyte globulin (hATG) and ciclosporin A (CsA), and as a second-line treatment in patients with an inadequate response to immunosuppressive therapy (IST).

3 Requested listing

3.1 The submission requested an addition of a new dosage strength, eltrombopag 75 mg to the existing listings. The number of repeats requested is the same as existing listings with respect to the treatment phases.

3.2 As the submission did not request changes to the restrictions, the full text of the restrictions have not been reproduced here. Suggested additions are in italics.

Add new medicinal product as follows:

Severe thrombocytopenia

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ELTROMBOPAG					
eltrombopag 75 mg tablet, 28	*NEW (Public)*	*1*	*28*	*5*	*Revolade®*
eltrombopag 75 mg tablet, 28	*NEW (Private)*	*1*	*28*	*5*	*Revolade®*
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (in writing only via post/ HPOS upload)				
	Indication: Severe thrombocytopenia				
	Treatment phase: Initial treatment – New patient				
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/Online PBS Authorities system)				
	Indication: Severe thrombocytopenia				
	Treatment phase: First Continuing treatment or Re-initiation of interrupted continuing treatment				
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/Online PBS Authorities system)				
	Indication: Severe thrombocytopenia				
	Treatment phase: Second or Subsequent Continuing treatment				
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/Online PBS Authorities system)				
	Indication: Severe thrombocytopenia				
	Treatment phase: Balance of supply or change of therapy				

Severe aplastic anaemia

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ELTROMBOPAG					
eltrombopag 75 mg tablet, 28	*NEW (Public)*	*2*	*56*	*5*	*Revolade®*
eltrombopag 75 mg tablet, 28	*NEW (Private)*	*2*	*56*	*5*	*Revolade®*
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/ Online PBS Authorities system)				
	Indication: Severe aplastic anaemia				
	Treatment phase: First line treatment				
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/ Online PBS Authorities system)				
	Indication: Severe aplastic anaemia				
	Treatment phase: Continuing treatment – Second line treatment				

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ELTROMBOPAG					
eltrombopag 75 mg tablet, 28	*NEW (Public)*	*2*	*56*	*3*	*Revolade®*
eltrombopag 75 mg tablet, 28	*NEW (Private)*	*2*	*56*	*3*	*Revolade®*
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (in writing only via post/ HPOS upload)				
	Indication: Severe aplastic anaemia				
	Treatment phase: Initial treatment – Second line treatment				

4 Comparator

4.1 The submission proposed a new 75 mg strength tablet of eltrombopag and compared this to the currently listed 25 mg and 50 mg strengths of the same drug. The new strength has the same intended population. The PBAC considered this comparison to be appropriate.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer input

5.2 The PBAC noted and welcomed the input from individuals (5) and organisations (1) via the Consumer Comments facility on the PBS website. The comments described the disease burden of ITP on patients and families, including: ongoing worry about sudden deterioration and hospitalisation; difficulty planning daily life and travel; health anxiety

5.3 Contributions from parents described the benefits of simplified treatment regimens for children and young people with ITP.

5.4 One consumer organisation (ITP Australia and New Zealand) stated introducing a 75 mg tablet would reduce pill burden, simplify dosing schedules, and lower the risk of medication errors. Also, a 75 mg tablet would reduce the financial and administrative burden on patients who currently require two separate prescriptions each month to make up their dose.

Clinical claim

5.5 The submission did not include new clinical efficacy or safety data as the efficacy and safety of eltrombopag has been established in earlier submissions. The submission claimed the 75 mg strength tablet requested in this submission is equivalent to the 25 mg and 50 mg tablets when given at the same daily dose.

5.6 The submission noted that based on the product information, no clinically meaningful pharmacokinetic or pharmacodynamic differences are expected when a total daily dose of 75 mg is administered as one 75 mg tablet or as a combination of one 50 mg tablet plus one 25 mg tablet.

5.7 The PBAC considered that the clinical claims in the submission were supported.

5.8 The PBAC noted that the equi-effective dose is one 75 mg tablet = one 50 mg tablet plus one 25 mg tablet.

Pricing considerations

5.9 Eltrombopag has a Special Pricing Arrangement. The submission proposed that the new dosage strength has a price that is equivalent on a per-milligram basis to the PBS-listed eltrombopag dosage strengths. Table 1 below shows the current and proposed effective Approved Ex-Manufacturer Price (AEMP) (under the Special Pricing Arrangement) for the currently listed 25 mg and 50 mg strengths, and the proposed 75 mg strength.

Table 1: Effective AEMP of currently listed and proposed strengths of eltrombopag

	Currently listed		Proposed
Strength	25 mg, 28 tablets	50 mg, 28 tablets	75 mg, 28 tablets
AEMP ($)	$[redacted]	$[redacted]	$[redacted]

Estimated PBS usage and financial implications

5.10 The submission used a market share approach to estimate financial impact. The submission noted that eltrombopag dosing is different between the indications for ITP and SAA, and the dose regimens must be individualised based on the patient's platelet counts.

5.11 The submission assumed no changes to the current treatment algorithm and no changes in prescribing behaviour due to the introduction of the 75 mg tablet (e.g., no increase in patient numbers expected due to the availability of the 75 mg strength tablet).

5.12 For the ITP indication, it was assumed that substitution would occur in patients who take a dose of 75 mg. This patient split was assumed to be 15% in Year 1 based on PBS 10% data in 2024.

5.13 For the ITP indication, the submission noted an expected decline in proportion of patients applicable to this indication from 2025-31. The pre-PBAC response clarified that this was an extrapolation from PBS 10% dispensing data. This data had demonstrated a decline in the proportion of patients receiving a 75 mg dose from 27.1% in 2020 to 15.1% in 2024.

5.14 For the SAA indication it was assumed that 100% of patients take a 150 mg dose of eltrombopag. The submission noted this is likely an overestimate but that it does not materially affect overall net impact. The PBAC considered this to be reasonable.

5.15 The submission noted several modelling challenges with using the UCM workbook. However, it assumed no additional costs for the upcoming 6 years, with eltrombopag 75 mg being a substitution option for those who are using ≥ 75mg daily. The PBAC accepted that the listing of a new 75 mg strength tablet of eltrombopag would have minimal financial impact, but noted that for the ITP population, there may be minor financial implications to the R/PBS as a result of changes in patient copayments. The financial impact to Services Australia will be determined by that agency as part of the post PBAC process.

6 PBAC Outcome

6.1 The PBAC recommended the listing of eltrombopag 75 mg tablets for severe thrombocytopenia (ITP) and severe aplastic anaemia (SAA) on the Section 100 Highly Specialised Drugs Program under the same circumstances as the eltrombopag 25 mg and 50 mg listed strengths. The PBAC accepted the clinical claims that the eltrombopag 75 mg tablet is equivalent to the eltrombopag 25 mg and 50 mg tablets when given at the same daily dose.

6.2 The PBAC considered the methodology used to calculate the financial impact to be reasonable.

6.3 The PBAC considered the estimated financial impact to be reasonable but noted there may be some minor costs to the R/PBS due to changes in co-payments in the ITP population.

6.4 The PBAC recommended that the new dosage strength have a price that is equivalent on a per-milligram basis to the PBS-listed eltrombopag dosage strengths.

6.5 The PBAC considered that the requested maximum quantities with respect to the treatment phases for severe ITP and SAA to be appropriate. The PBAC further advised aligning the number of repeats and eligibility criteria with existing eltrombopag listings. The PBAC advised that eltrombopag is suitable for prescribing by medical practitioners only.

6.6 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because eltrombopag 75 mg is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over other strengths of eltrombopag, 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 2022 for Pricing Pathway A were not met.

6.7 The PBAC recommended that the Early Supply rule should not apply.

6.8 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 medicinal product packs to **severe thrombocytopenia** and **severe aplastic anaemia** as follows:

Severe thrombocytopenia

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ELTROMBOPAG					
eltrombopag 75 mg tablet, 28	NEW (Public)	1	28	5	Revolade®
eltrombopag 75 mg tablet, 28	NEW (Private)	1	28	5	Revolade®
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (in writing only via post/ HPOS upload)				
	Indication: Severe thrombocytopenia				
	Treatment phase: Initial treatment – New patient				
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/Online PBS Authorities system)				
	Indication: Severe thrombocytopenia				
	Treatment phase: First Continuing treatment or Re-initiation of interrupted continuing treatment				
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/Online PBS Authorities system)				
	Indication: Severe thrombocytopenia				
	Treatment phase: Second or Subsequent Continuing treatment				
Restriction Summary [14128] / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/Online PBS Authorities system)				
	Indication: Severe thrombocytopenia				
	Treatment phase: Balance of supply or change of therapy				

Severe aplastic anaemia

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ELTROMBOPAG					
eltrombopag 75 mg tablet, 28	NEW (Public)	2	56	5	Revolade®
eltrombopag 75 mg tablet, 28	NEW (Private)	2	56	5	Revolade®
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/ Online PBS Authorities system)				
	Indication: Severe aplastic anaemia				
	Treatment phase: First line treatment				

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ELTROMBOPAG					
eltrombopag 75 mg tablet, 28	NEW (Public)	2	56	3	Revolade®
eltrombopag 75 mg tablet, 28	NEW (Private)	2	56	3	Revolade®
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (in writing only via post/ HPOS upload)				
	Indication: Severe aplastic anaemia				
	Treatment phase: Initial treatment – Second line treatment				

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ELTROMBOPAG					
eltrombopag 75 mg tablet, 28	NEW (Public)	2	56	5	Revolade®
eltrombopag 75 mg tablet, 28	NEW (Private)	2	56	5	Revolade®
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒ Medical Practitioners				
	Restriction type: ☒ Authority Required (Telephone/ Online PBS Authorities system)				
	Indication: Severe aplastic anaemia				
	Treatment phase: Continuing treatment – Second line treatment				

These restrictions 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.