7.16 PROPRANOLOL
oral liquid, 3.75 mg/mL, 120 mL x 2
Hemangiol®, Pierre Fabre Australia Pty Ltd

1 Purpose of Application

1.1 The minor submission sought a higher price than recommended in the March 2015 meeting.

2 Background

2.1 Propranolol liquid (Hemangiol®) listed on the ARTG on 25 June 2015 for the following indications:
Treatment of proliferating infantile hemangioma requiring systemic therapy:
Life-threatening hemangioma.
Ulcerated hemangioma with pain and/or lack of response to simple wound care measures.
Hemangiomas with a risk of permanent scars or disfigurement.

2.2 At its March 2015 meeting, the PBAC recommended the listing of propranolol oral liquid (Hemangiol) as an Authority Required (telephone) item on the general schedule.

2.3 The PBAC was satisfied that Hemangiol provides the same benefits as seen with either of the currently available alternatives, namely, Auspman propranolol solution or compounded propranolol liquid, and that these are the therapies most likely to be replaced. Auspman propranolol solution or compounded propranolol liquid are therefore the most appropriate comparators.

2.4 The PBAC noted the clinical need for a product to treat infantile haemangiomas in high risk patients.

2.5 The PBAC noted that PBS listing is unlikely to change the current treatment algorithm for infantile haemangioma as patients would otherwise be treated with an alternative compounded product.

2.6 The PBAC considered that the PBS restriction should mirror the TGA indication: that is, for the treatment of patients requiring systemic therapy with life threatening haemangiomas, ulcerated haemangiomas with pain, or haemangiomas with risk of permanent scarring or disfigurement.

2.7 The PBAC agreed that the maximum quantity of 240mL as proposed in the submission was appropriate, but considered it appropriate for up to 2 repeats to be issued to allow patients to complete 6 months of treatment if required.

2.8 The PBAC recommended use should be limited to prescribing only by a doctor with expertise in the diagnosis, treatment and management of infantile haemangiomas, or

by a General Practitioner in consultation with a doctor with expertise in the diagnosis, treatment and management of infantile haemangiomas.

2.9 The PBAC considered that Hemangiol should be cost minimised against the currently available Auspman propranolol solution with a modest price premium to be negotiated between the sponsor and the Department in acknowledgement that Hemangiol is a commercially available product which is likely to have benefits for patients in terms of access. The PBAC noted that cost consequence method used to derive the proposed price was unsubstantiated and resulted in an unacceptably high price, noting that the proposed price of Hemangiol is over [redacted] times the price of propranolol tablets (at the ex-manufacturer level). The PBAC considered a price premium of this magnitude to be unjustified, although a small price premium for oral liquids over tablets is reasonable. The price of Hemangiol was considered in the context of the ratio of the solution price per milligram compared to the tablet price per milligram for other liquid dosage form products, which demonstrated that the ratio requested is significantly higher for Hemangiol (see table below).

Drug	Form, including strength	Mg per pack	Ex-man price per pack	Price per mg	Ratio of solution price per mg to tablet price per mg
Propranolol	Oral liquid, 3.75 mg/1 mL, 120 mL	450 mg	$[redacted]	$[redacted]	[redacted]
	Tablet 10 mg, 100	1,000 mg	$3.05	$0.003	
Digoxin	Oral solution, 50 mcg/1 mL, 60 mL	3 mg	$14.04	$4.68	18:1
	Tablet 62.5 mcg, 200	12.5 mg	$3.24	$0.26	
Diazepam	Oral liquid, 1 mg/1 mL, 100 mL	100 mg	$29.63	$2.96	32:1
	Tablet 2 mg, 50	100 mg	$0.94	$0.094	
Naproxen	Oral suspension, 125 mg/5 mL, 474 mL	11,850 mg	$102.47	$0.01	50:1
	Tablet 250 mg, 50	12,500 mg	$2.80	$0.0002	

2.10 The PBAC noted that the estimated total number of prescriptions was based on patient weight. While the total patient population is likely to be small, the PBAC considered that there was a risk of Hemangiol use in patients with less severe, non-fatal haemangiomas. The Committee considered that the basis for the financial estimates should be reviewed in the context of negotiations of pricing with the Department.

2.11 The PBAC recommended that propranolol, in the form oral liquid, should not be treated as interchangeable with any other drugs.

2.12 The PBAC advised that propranolol oral liquid is not suitable for prescribing by nurse practitioners.

2.13 The PBAC recommended that the Safety Net 20 Day Rule should apply.

3 Summary of the minor re-submission

3.1 The re-submission sought a higher price for Hemangiol compared to what was recommended in the March meeting.

3.2 The re-submission proposed that 100% of the price for Hemangiol be based on the price of compounded propranolol solution. This proposal was based on advice from hospital pharmacists that majority of the dispensing of propranolol liquid would be from the community pharmacy setting, and that in this setting most patients would be supplied compounded propranolol liquid rather than the Auspman propranolol solution.

3.3 The re-submission proposed to establish a reference price for compounded propranolol liquid by conducting a survey of 131 community pharmacies for a 900 mg preparation – equivalent to the amount of propranolol contained in the maximum quantity of Hemangiol (2 bottles of 120 mL, 3.75 mg/mL).

3.4 The re-submission's requested price of $[redacted] (DPMQ) was based on the average price for a 900 mg preparation of compounded propranolol liquid ($[redacted]) plus a premium factor of two.

3.5 The Department explored an alternative weighting method to determine a price for Hemangiol. This method assumed the following:

- the price of Auspman oral solution as quoted in the original submission;
- the average price of compounded propranolol liquid as calculated in the re-submission;
- weightings based on the advice in the re-submission that the continued dispensing of propranolol liquid was likely to be from a community pharmacy setting (91%) using compounded propranolol liquid, with the initial script dispensed from the hospital pharmacy with the Auspman solution (9%);
- average patient would require 10 bottles of 450 mg per treatment cycle (or total propranolol content of 4,500 mg).

3.6 The alternative method results in a weighted price/mg for Hemangiol that is around double to the cost-minimised price of the March recommendation.

3.7 The proposed DPMQ prices for 2 bottles x 3.75 mg/mL x 120 mL (= 900 mg propranolol) as requested by the sponsor and as calculated by the Department's alternative method are as follows (updated using 1 July 2015 fees).

- Sponsor: $[redacted]
- Department: $[redacted]

3.8 The re-submission requested a Special Pricing Arrangement [redacted].

4 PBAC Outcome

4.1 The PBAC rejected the proposed price for Hemangiol and re-affirmed its recommendation at March 2015.

4.2 The PBAC noted the re-submission's proposed methodology to establish a reference price for compounded propranolol liquid, however it considered that the proposed price for Hemangiol, which includes a premium factor of two over the reference price of compounded propranolol liquid, to be unsubstantiated.

4.3 The PBAC considered that the price of the ready-prepared Auspman oral solution needs to be reflected in the price of Hemangiol as this is the current standard of care for this treatment setting.

4.4 The PBAC noted that Department's alternative method utilised a mixed comparator weighting based on the re-submission's assumption on the likely dispensing setting of Hemangiol, and also utilised the price of the ready-prepared Auspman from the original submission and the average price of compounded propranolol from the community pharmacy survey.

4.5 The PBAC noted the Department's alternative method would result to a price for Hemangiol that is [redacted] the price of ready-prepared Auspman oral solution.

4.6 The PBAC noted that propranolol is in the F2 formulary and the Department's advice that Special Pricing Arrangements are not normally applied to F2 medicines.

Outcome:
Rejected

5 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.

6 Sponsor's Comment

Pierre Fabre will continue to work with the Department to achieve a listing for Hemangiol