

5.14 APOMORPHINE

**Injection containing apomorphine hydrochloride
30 mg in 3 mL pre-filled pen,
MOVAPO[®] PEN,
STADA Pharmaceuticals Australia Pty Ltd**

1 Purpose of Application

- 1.1 The minor submission requested a Section 100 Highly Specialised Drugs Program Authority Required listing of a new form of apomorphine (30 mg in 3 mL) delivered in a disposable multiple dose pen injector system for the treatment of Parkinson's disease (PD).

2 Requested listing

- 2.1 The submission requested the listing of the following new form, 30 mg in 3 mL, with the same restrictions as the existing listing:
- 2.2 Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
A POMORPHINE apomorphine hydrochloride 30 mg/ 3 mL injection cartridge, 5 × 3 mL pens	72 60	5	\$9,793.44 \$8,167.80* (Public hospital) \$9,840.94 \$8215.15* (Private hospital)	MOVAPO® PEN Stada Pharmaceuticals Australia Pty Ltd

* recalculated on a cost per mg vs comparator basis with reduced Maximum Quantity

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Parkinson Disease
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input checked="" type="checkbox"/> Authority Required – Emergency <input checked="" type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined (Public only)
Clinical criteria:	Patient must have experienced severely disabling motor fluctuations which have not responded to other therapy

- 2.3 In the Pre-PBAC response, the sponsor accepted the Secretariat suggested Maximum Quantity as appropriate for the listing to give the same quantity in milligrams as other forms of the same drug currently listed on the PBS.

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

3 Background

- 3.1 Apomorphine injectables have been registered with the Therapeutic Goods Administration (TGA) since they were grandfathered onto the Australian Register of Therapeutic Goods (ARTG) on 8 October 1991 for the treatment of patients with PD with severely disabling motor fluctuations which have not responded to other therapy.
- 3.2 Apomorphine is currently available in ampoule forms (20 mg/2 mL, 50 mg/5 mL and 100 mg/20 mL) for continuous and intermittent subcutaneous injection and in a pre-filled syringe form (50 mg/10 mL) for continuous subcutaneous infusion.
- 3.3 Apomorphine 30 mg in 3 mL injection cartridge delivered in a disposable multiple dose pen injector system was registered on the ARTG on 3 November 2017.
- 3.4 This formulation of apomorphine has not previously been considered by the PBAC.

- 3.5 The PBAC most recently considered the 100 mg/20 mL vial form at the November 2016 PBAC meeting where it was recommended on an equivalent cost per milligram basis with the 10 mg/mL forms (Public Summary Document apomorphine November 2016). The PBAC considered the 50 mg/10 mL syringe form at the July 2016 meeting where it was recommended on an equivalent cost per milligram basis with the 50 mg/5 mL vial form for which it was considered to be most likely to be substituted (Public Summary Document apomorphine July 2016).

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

4 Comparator

- 4.1 The minor submission nominated apomorphine hydrochloride 20 mg/2 mL ampoule as the main comparator.
- 4.2 The sponsor claimed that the apomorphine 30 mg in 3 mL multi-dose injector pen is as safe and as effective as other forms of apomorphine.
- 4.3 The PBAC considered that all other forms of apomorphine would also be appropriate comparators.

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.

Consumer comments

- 5.2 The PBAC noted that there were no consumer comments for this submission.

Clinical trials

- 5.3 The submission stated that the apomorphine multiple dose pen injection delivers the same medicine as provided in the PBS-listed formulation, therefore no clinical trials were presented in the submission. The PBAC noted that this form has a different delivery method, self/carer-injection, as compared to all other forms of apomorphine listed on the PBS that require either extraction from a vial by the patient or a carer or continuous subcutaneous infusion. In the Pre-PBAC response, the sponsor stated that the multi-dose pen injector has been approved for use by several overseas regulatory agencies for over 15 years and is available in over 30 countries.
- 5.4 The PBAC noted that sodium bisulfite 1.51 mg/mL is included in the formulation used in the multiple dose pen injector instead of sodium metabisulfite 1 mg/mL used in the other formulations. The submission stated that contraindications relating to

hypersensitivity to these antioxidants are not expected to have any impact on the circumstances of use of these products.

Clinical claim

- 5.5 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of the apomorphine 30 mg/3 mL compared with the other existing formulations of apomorphine. The PBAC noted that no clinical trials were supplied with this submission to support efficacy and safety of the proposed self-administered form over the current forms which require extraction.
- 5.6 In the Pre-PBAC response, the sponsor described an open label study involving 546 participants from 61 centres in the United States, which was to assess the safety and adverse effects of subcutaneous apomorphine injections over a six-year period. The sponsor concluded that no differences in the delivery method were noted. However, the study was not supplied with the response nor was it independently validated by the Department in the evaluation process.

Economic analysis

- 5.7 An economic comparison was considered, by the submission, to not be relevant due to the new form of apomorphine being expected to only replace the existing listings and therefore be cost neutral to the Government.

Drug cost/patient/ year: \$ 3,312.09

- 5.8 The sponsor calculated drug cost at the same price per mg as the 20 mg in 2 mL ampoule form on a cost-minimisation approach.
- 5.9 Although the submission stated that the daily dose was typically in the range of 3 to 30 mg/day, the presented calculation assumed an estimate of 10 mg/day as the equi-effective dose. In the Pre-PBAC response, due to a calculation error, the sponsor adjusted the drug cost/patient/year to \$3,312.09 on the basis of an AEMP of \$136.02 per pack.
- 5.10 As part of the evaluation process, the Department conducted an utilisation analysis of apomorphine based on Medicare statistic between the years 2014 to 2017. The PBAC noted that the analysis indicated an average cost of around \$18,000 per patient per year, which was significantly higher than the submission's estimate. The PBAC considered that the submissions' estimated daily dose of 10 mg/day apomorphine, and hence the drug cost/patient/year was underestimated.
- 5.11 The result of the utilisation analysis is summarised in Table 1 below:

Table 1. Utilisation analysis of apomorphine between 2014 and 2017.

	2014	2015	2016	2017
Prescriptions	2,180	2,034	1,853	1,776
Govt Expenditure	\$7,321,184	\$7,787,513	\$6,348,543	\$6,965,389
Govt Exp per Script	\$3,358	\$3,829	\$3,426	\$3,922
Patients	411	407	381	388
Prescriptions per patient	5.30	5.00	4.86	4.58
Govt Exp per patient	\$17,813	\$19,134	\$16,663	\$17,952

Source: DHS Prescription database (2014 to 2017 based on date of supply)"

Estimated PBS usage & financial implications

5.12 The minor submission used a market share approach, and estimated that there would be no financial implications to the PBS as the requested listing would partially replace existing PBS-listed formulations, but would not be expected to increase the PD market beyond the current growth rate. The Secretariat noted that this would be the first non-extractable self-administered form of apomorphine available on the PBS and therefore the assumption of no growth in the PD market may not be reasonable due to the ease of use in this setting and the possibility of use in patients with less severe disease.

5.13 The submission also assumed that no net change in MBS items was estimated because all services associated with eligibility, monitoring, clinical management, administration of the medicine, and AEs were assumed to remain the same as those associated with the currently listed apomorphines.

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

6 PBAC Outcome

6.1 The PBAC recommended the Authority Required listing of a new form of apomorphine (30 mg in 3 mL) delivered in a disposable multiple dose pen injector system for the treatment of Parkinson's disease (PD), on the basis that it should be available under Section 100, Highly Specialised Drugs (HSD) Program.

6.2 The PBAC was satisfied that the new form would provide a wider dosing range for apomorphine and a more convenient delivery method to PD patients and their carers.

6.3 The PBAC considered that the maximum quantity should be consistent with other forms of apomorphine listed on the PBS (i.e. equivalent to maximum quantity of 60 and a total of 300 units for a total of 9,000 mg apomorphine) at the same cost per mg as the currently listed forms of apomorphine.

6.4 The PBAC noted that this was the first form of apomorphine that was not specifically for either extraction, from a vial and caregiver/patient administration or continuous subcutaneous injection which may be beneficial to some patients and the carers.

6.5 The PBAC noted that there may be a potential risk of leakage to less severe PD

patients due to the convenient delivery method. However, the PBAC considered that this risk would be relatively low because of the estimated small patient population for this indication.

- 6.6 The PBAC advised that the Early Supply Rule should not apply as it currently does not apply to Section 100 items or for the other forms of apomorphine.
- 6.7 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
A POMORPHINE apomorphine hydrochloride 30 mg/ 3 mL injection cartridge, 5 × 3 mL pens	60	5	MOVAPO® PEN	Stada Pharmaceuticals Australia Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
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Clinical criteria:	Patient must have experienced severely disabling motor fluctuations which have not responded to other therapy

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.