

**14.03(f) TERBUTALINE,
Powder for oral inhalation in breath actuated device
containing terbutaline sulfate 500 micrograms per
dose, 120 doses,
Bricanyl® M3 Turbuhaler,
AstraZeneca Pty Ltd**

1 Purpose of Application

- 1.1 The committee secretariat submission requested Authority Required (STREAMLINED) listing of a new inhaler device Bricanyl® M3 Turbuhaler (referred to as M3 Turbuhaler from herein) under the same eligibility criteria as the current inhaler presentation Bricanyl® M2 Turbuhaler (referred to as M2 Turbuhaler from herein).

2 Background

- 2.1 The Turbuhaler device is an inspiratory flow-driven, multi-dose, dry-powder inhaler which dispenses a small dose of dry powder when the patient inhales through the mouthpiece.
- 2.2 The submission stated that the M2 Turbuhaler device was updated following a recommendation from the European Medicines Agency (EMA) Pharmacovigilance Working Party (PhVWP) in April 2011 to mitigate the potential risk of excessive dose delivery if the device is dropped at the end of inhaler life. The report recommended a stop to the availability of the Bricanyl® Turbuhaler 200 actuations and supported using only a pack size of 100 actuations (EMA PhVWP April 2011 plenary meeting monthly report, p4). The submission considered the M3 Turbuhaler (120 actuations) a technical improvement over the M2 Turbuhaler with improved robustness and more accurate dose indicator.

Previous PBAC consideration

- 2.3 Terbutaline powder for oral inhalation was previously considered by the PBAC at its July 2019 meeting. A summary of the previous PBAC consideration is provided below.

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Table 1: Previous PBAC considerations

Meeting date	Request	Outcome	Detail
July 2019	<ul style="list-style-type: none"> • Sponsor requested a price increase from AEMP \$3.75 to \$6.82 on the basis of commercial viability. • PBAC was requested to consider whether terbutaline should be retained on the PBS and to advise the eligible patient population. 	Recommended	<p>Terbutaline powder for oral inhalation to be retained for the following patient groups:</p> <ul style="list-style-type: none"> • Patients unable to use a pMDI; • Patients who suffer from adverse effects with the use of salbutamol; and • Patients who experience paradoxical bronchoconstriction with pMDI. <p>The benefit listing be amended from unrestricted to Authority Required (STREAMLINED).</p>

Abbreviation: pMDI = pressurised metered-dose inhaler.

Registration status

- 2.4 M3 Turbuhaler was TGA registered on 9 April 2020 for the same indication as M2 Turbuhaler. The TGA concluded that therapeutic equivalence of terbutaline sulfate was established between the M2 and M3 devices (TGA Delegate’s Note, p5).

3 Requested listing

- 3.1 The submission requested the M3 Turbuhaler to be listed under the same listing conditions as the existing listing for the M2 Turbuhaler. M2 Turbuhaler is currently listed on the PBS as an Authority Required (STREAMLINED) listing as a reliever inhaler for the management of bronchospasm.
- 3.2 The sponsor argued that the two products should not be substitutable at the pharmacy level (‘a’ flagged) because the maximum quantity of the drug supplied per dispensing is different (p3, pre-PBAC response).
- 3.3 The M2 and M3 Turbuhaler both deliver 400 mcg of terbutaline sulfate per inhalation. However, the current product label for M2 Turbuhaler displays a metered dose of 500 mcg, whilst the M3 Turbuhaler displays the ‘delivered dose of 400 mcg (corresponding to 500 mcg metered dose)’. The TGA supported the proposal that the same ‘Bricanyl Turbuhaler 500’ product label, which refers to the metered dose of 500 mcg, be applied to the M3 Turbuhaler (TGA Delegate’s Note, p2). The submission stated this would minimise confusion when patients transition from the M2 to the M3 device and was supported by the product label provided in the pre-PBAC response (p1). The sponsor noted they will work with the Australian Digital Health Agency to make the terminology consistent with the existing listing.

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

4 Comparator

- 4.1 The committee secretariat submission nominated M2 Turbuhaler as the comparator. This was considered appropriate.

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

5 Consideration of the evidence

5.1 As a committee secretariat submission, a clinical evaluation was not performed.

Sponsor hearing

5.2 There was no hearing for this item as it was a committee secretariat submission.

Consumer comments

5.3 The PBAC noted and welcomed the input from an organisation (1) via the Consumer Comments facility on the PBS website. Lung Foundation Australia described that the new device with dosage counter and additional inhalations would improve patient experience and adherence, particularly for patients with chronic obstructive pulmonary disease (COPD).

Clinical claim

5.4 The submission claimed that the M3 Turbuhaler provided equivalent effectiveness and safety to the M2 Turbuhaler. The TGA concluded that therapeutic equivalence of terbutaline sulfate was established between the M2 and M3 devices and that the M3 Turbuhaler had a consistent safety profile and did not raise any major safety concerns (TGA Delegate’s Note, p5).

Pricing considerations

5.5 The submission requested a 20% increase in the AEMP for M3 Turbuhaler with 120 actuations, which is proportional to the current AEMP of M2 Turbuhaler with 100 actuations.

Table 2: Proposed pricing for terbutaline Bricanyl® Turbuhalers

Drug, form and strength	AEMP (per Turbuhaler)	AEMP (per MQ)	Price to pharmacy (per Turbuhaler)	Price to pharmacy (per MQ)	DPMQ
Bricanyl M2 Turbuhaler, 100 actuations	\$6.82	\$13.64	\$7.34	\$14.67	\$26.15
Bricanyl M3 Turbuhaler, 120 actuations	\$8.19	\$16.37	\$8.80	\$17.60	\$29.08

Source: Main submission document, page 4.

Abbreviations: AEMP = Agreed ex-manufacturer price; DPMQ = Dispensed price for maximum quantity; MQ = maximum quantity

- 5.6 In January 2019, the sponsor requested an 82% price increase from AEMP \$3.75 to AEMP \$6.82 for the M2 Turbuhaler on the basis of commercial viability. This was implemented in November 2019. The price increase was based on the increase to the cost of goods following a production site move. The evaluation considered that the cost of goods per actuation for the M3 Turbuhaler was expected to decrease with the increased actuations per manufactured device, resulting in a lower AEMP per dose of the M3 Turbuhaler compared to the M2 Turbuhaler. However, the pre-PBAC response (p1) disagreed and argued that the variable cost components of the device would rise in proportion to the quantity of materials in the product; and that any decrease in cost per actuation would be negated by the increase in the number of actuations in the M3 device.
- 5.7 The commercial costings for the M3 Turbuhaler could not be verified.

Estimated PBS usage & financial implications

- 5.8 The submission estimated there to be no financial implications to the PBS. The listing of the M3 Turbuhaler is not expected to increase the current market. However, the submission expected a decrease in dispensing frequency proportional to the 20% increase in the number of doses per pack and given that terbutaline is only used when required. Additionally, the reduced number of dispensings is expected to have financial impacts to the PBS, as it would reduce the number of co-payments. The pre-PBAC response (p2) provided financial estimates and stated that a reduction in script numbers of 12% would negate the increased DPMQ at the proposed price, resulting in a nil net financial impact to the Commonwealth.

Table 3: Utilisation and expected financial implications from pre-PBAC response

	Govt cost @ current DPMQ	Govt cost @ proposed DPMQ with 20% fewer scripts
PBS General		
Scripts		
Costs (DPMQ)	\$	\$
PBS General Safety Net		
Scripts		
Costs (DPMQ)	\$	\$
PBS Concessional		
Scripts		
Costs (DPMQ)	\$	\$
PBS Concessional Safety Net (zero copayment)		
Scripts		
Costs (DPMQ)	\$	\$
RPBS Ordinary		
Scripts		
Costs (DPMQ)	\$	\$
RPBS Entitlement (zero copayment)		
Scripts		
Costs (DPMQ)	\$	\$
Totals		
Scripts		
Govt cost	\$	\$
Difference in Govt cost		\$

Source: Table 1 from pre-PBAC response based on 2019 Bricanyl M2 script volumes.

Government costs calculated by deducting 2019 PBS/RPBS copayment (appropriate to patient category) from current and proposed DPMQs. PBS General scripts had no copayment deducted, as Bricanyl M2 is priced below General copayment.

The redacted table shows that at the current DPMQ the estimated total number of scripts is 80,000 to < 90,000 and the government cost would be \$0 to < \$10 million; and at the proposed DPMQ with 20% fewer scripts the estimated total number of scripts is 60,000 to < 70,000 and the government cost would be \$0 to < \$10 million.

- 5.9 As a committee secretariat submission, the financial estimates have not been independently evaluated.
- 5.10 The pre-PBAC response (p3) proposed there would be an overlap of the PBS listings for the M2 and M3 Turbuhaler to allow patients to transition onto the new device before subsequently delisting the M2 Turbuhaler.

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

6 PBAC Outcome

- 6.1 The PBAC recommended an Authority Required (STREAMLINED) listing of a new form of terbutaline, M3 Turbuhaler, under the same eligibility criteria as the currently listed form of terbutaline, M2 Turbuhaler.
- 6.2 The PBAC noted that the TGA concluded that therapeutic equivalence of terbutaline sulfate was established between the M2 and M3 devices.

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- 6.3 The PBAC considered that the M3 Turbuhaler provided equivalent efficacy and safety to the M2 Turbuhaler and the M2 Turbuhaler was the appropriate comparator.
- 6.4 The PBAC recalled the AEMP of M2 Turbuhaler increased from \$3.75 to \$6.82 on 1 November 2019, which aligned with a listing change from unrestricted to Authority Required (STREAMLINED) for bronchospasm in certain patients. The PBAC recalled the cost of goods submitted for M2 Turbuhaler was \$[REDACTED]. The PBAC also noted in its pre-PBAC response the sponsor noted the precise increase in cost of goods for M3 Turbuhaler is not yet known.
- 6.5 The PBAC noted that both the M2 Turbuhaler and the M3 Turbuhaler are used on an as needed basis as a reliever as opposed to an ongoing treatment. The PBAC noted that the sponsor also requested the same maximum quantity (2) and number of repeats (5) for M3 Turbuhaler as the M2 Turbuhaler listing. This would result in patients receiving a maximum of 240 actuations per dispense with 5 repeats (1,200 actuations in total) for M3 Turbuhaler compared with a maximum of 200 actuations per dispense with 5 repeats (1,000 actuations in total) for M2 Turbuhaler. The PBAC noted the submission did not include evidence of a clinical benefit for the additional 20 actuations per inhaler, nor evidence of a clinical benefit for the additional 200 actuations per prescription.
- 6.6 The PBAC noted that the submission did not discuss in detail the quality use of medicines impact of the additional 20 actuations per inhaler and as terbutaline is used as a reliever for the treatment of bronchospasm, did not address the potential for increased stockpiling of the medicine.
- 6.7 The PBAC recommended that the AEMP for the M3 Turbuhaler (120 actuations) should be the same as the AEMP for the M2 Turbuhaler (100 actuations). The PBAC considered it was inappropriate that the proposed AEMP for the M3 Turbuhaler be proportional to the price of M2 Turbuhaler based on the number of actuations due to a lack of information to support the purported proportional increase in cost of goods and a lack of information to support the clinical benefit for the additional actuations in the context of use on as needed basis.
- 6.8 The PBAC noted the intention of the sponsor to delist M2 Turbuhaler after a transition period, and considered that a formal request to delist M2 Turbuhaler would be required.
- 6.9 The PBAC advised, under Section 101 (4AACD) of the *National Health Act*, that terbutaline, 120 actuations and terbutaline, 100 actuations should not be considered equivalent for the purposes of substitution (i.e., 'a' flagged in the Schedule with a NOTE stating PBS of one form and PBS of another form are equivalent for the purposes of substitution) due to the different quantity of drug supplied per dispensing.
- 6.10 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because the M3 Turbuhaler is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over the M2

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Turbuhaler, 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.

- 6.11 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 item with the same restrictions as the following restriction summary:

Restriction Summary 9828/ ToC: 9828: Authority Required: Streamlined (current as of July 2020)

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Manufacturer	Name and
TERBUTALINE Terbutaline sulfate 500 mcg/actuation powder for inhalation, 120 actuations	New	2	2	5	Bricanyl Turbuhaler®	AstraZeneca Pty Ltd

Indication: Bronchospasm
Clinical criteria: Patient must be unable to achieve co-ordinated use of a metered dose inhaler containing a short-acting beta-2 agonist; or Patient must have developed a clinically important product-related adverse event during treatment with another short-acting beta-2 agonist
Prescribing Instructions: Device (inhaler) technique should be reviewed at each clinical visit and before initiating treatment with this medicine.

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.