

12.01 SALBUTAMOL

**Pressurised inhalation 100 micrograms (as sulfate) per dose with dose counter, 200 doses (CFC-free formulation),
Ventolin[®],
GlaxoSmithKline Australia Pty Ltd.**

An addendum to this Public Summary Document (PSD) has been included at the end of the document.

1 Purpose

- 1.1 The PBAC was asked to consider correspondence received from GlaxoSmithKline Australia Pty Ltd (GSK). GSK have sought reconsideration of the PBAC's advice at its November 2019 meeting that the cost-effectiveness of salbutamol pressurised inhalation 100 micrograms (as sulfate) per dose with dose counter (Ventolin DC) would be acceptable if it was priced with a small premium (█%) over the currently PBS listed salbutamol pressurised inhalation 100 micrograms (as sulfate) per dose (Ventolin MDI) price.

2 Background

- 2.1 Two brands of salbutamol pressurised inhalation 100 micrograms (as sulfate) per dose, 200 doses (CFC-free formulations) are currently listed on the PBS and available over-the-counter (Ventolin MDI and Asmol). Asmol is manufactured by GSK on behalf of Alphapharm Pty Ltd (Alphapharm). The current presentations of Ventolin and Asmol MDIs do not have a dose counter.
- 2.2 At its November 2019 meeting, the PBAC considered a submission from GSK for a presentation of salbutamol pressurised inhalation with a dose counter (Ventolin DC).
- 2.3 In its November 2019 submission, GSK stated that Ventolin DC was intended to replace Ventolin MDI listing on the PBS. The submission stated that a phasing-in approach would see both presentations available on the PBS in 2020 (Year 1), followed by 100% supply of Ventolin DC from 2021 (Year 2). The submission stated that Ventolin MDI would be de-listed in Year 2. The submission anticipated that a DC version of the Asmol MDI from Alphapharm would also become available.
- 2.4 In recommending Ventolin DC, the PBAC considered the evidence provided in the submission was insufficient to support the AEMP requested in the submission. However, the PBAC pragmatically advised that a small price premium of no more than █% over the existing Ventolin MDI price would be acceptable.

Table 1: PBAC matters of concern in previous consideration (November 2019)

Matters of concern	How the resubmission addresses it
The PBAC noted the studies identified by the submission to provide evidence on the impact of a dose counter in an MDI device on patient satisfaction (Wasserman 2006) and healthcare utilisation (Chipps 2017, Kerwin 2017, Lachman 2018, Price 2016). The PBAC considered the risk of bias to be high and in favour of Ventolin DC in the non-controlled, unblinded patient satisfaction study.	No change. Sponsor has reiterated its November 2019 submission.
The PBAC noted that all four healthcare utilisation studies (Chipps 2017, Kerwin 2017, Lachman 2018, Price 2016) were conducted in the United States and considered that differences in healthcare settings may limit applicability to the Australian setting.	No further information provided.
The PBAC also considered that despite the large sample size (n=422,548) in the Kerwin 2017 study the differences were small for the odds of experiencing a respiratory-related hospitalisation (DC vs no DC, adjusted OR 0.92; 95% CI 0.88-0.96) or emergency department visit (adjusted OR 0.92; 95% CI 0.90-0.94) with the upper 95% confidence intervals close to the null value. The PBAC also noted that Price 2016 reported no differences in the rates of severe exacerbations or the rates of acute respiratory events between DC versus no DC MDI use. The PBAC noted the remaining two studies (Chipps 2017, Lachmann 2018) were provided in abstract form only. The PBAC considered that the evidence supporting a reduction in healthcare utilisation as a result of an integrated DC was limited.	No further information provided.
The PBAC noted the cost-effectiveness analysis provided in the pre-PBAC response based on the Kerwin 2017 study to ascertain cost per ED visit avoided. In addition to the concerns raised regarding the applicability of the Kerwin 2017 study to the Australian setting, the PBAC considered that differences in baseline inhaled corticosteroid use and the proportion using no asthma therapy likely favoured Ventolin DC in this study.	No change. The correspondence from GSK did not present any additional evidence.
In considering the financial estimates, the PBAC noted the potential for devices like Ventolin DC to over count doses (see paragraph 5.15) and advised that this may result in an increase in utilisation in clinical practice. Accordingly, the PBAC considered that the submission had underestimated total utilisation for the salbutamol MDI market but considered that any increase in the market as a result of listing Ventolin DC was likely to be relatively small.	The correspondence from the sponsor provided an updated summary of financial impacts at a new proposed price of \$ [REDACTED] (ex-man), but this did not provide any additional increase in utilisation due to potential over-counting.

Source: Compiled by the Secretariat

3 Current situation

- 3.1 On 20 December 2019, GSK wrote to the PBAC Secretariat to advise that the [REDACTED]% price premium over Ventolin MDI (resulting in AEMPs between \$ [REDACTED] and \$ [REDACTED]) as per the PBAC’s November 2019 recommendation, was not commercially viable, since the proposed AEMP range was less than their reported cost of goods of \$ [REDACTED] for Ventolin DC.
- 3.2 GSK subsequently proposed an AEMP of \$ [REDACTED], which represents a \$ [REDACTED] (or [REDACTED]%) increase on the current price of Ventolin MDI, based on the currently listed ex-manufacturer price of \$3.90.

4 Consideration of the evidence

Clinical trials

Evidence previously considered by the PBAC

- 4.1 The sponsor's correspondence referred to evidence presented in its November 2019 submission, which included evidence on patient satisfaction (Wasserman 2006) and healthcare utilisation (Chipps 2017, Kerwin 2017, Lachman 2018, Price 2016). *PBAC's views on this evidence is at Table 1 above.*

New evidence provided by GSK

- 4.2 In its correspondence, the sponsor referred to a review by Connor 2013¹, which estimated the extent of inadvertent non-adherence to MDIs to be up to 40%. It also referred to a New Zealand study (Holt et al 2005)² which found that rather than count doses, most patients use the 'shaking method' to determine remaining doses. GSK argued that patients often discard their inhaler with less than 200 doses which leads to wastage.
- 4.3 The sponsor's letter also stated there are anecdotal reports that patients stockpile inhalers, as they are anxious about running out of doses. GSK also noted there have been reports on social media from consumers using non-validated techniques to estimate the remaining contents of Ventolin inhalers, including dismantling inhalers to weight aerosol canisters and/or to float aerosol canisters in water to estimate remaining doses.
- 4.4 The sponsor also stated that the dose counter results in reduced ED visits.
- 4.5 The sponsor referred to a number of other issues, including TGA registration, cost of goods, as well as increase in demand for salbutamol, as the number of scripts dispensed for Ventolin DC increased during the recent bushfires.

Pricing considerations

- 4.6 The current AEMP for Salbutamol MDI is \$3.90. Since September 2012 (when prices began to be reported in AEMP), the AEMP has increased twice as outlined in table 2.
- 4.7 The price increase of 15.4% in December 2016 resulted in an additional cost to the PBS of less than \$10 million per year. And resulted in an increase in the ex-man price from \$2.99 to \$3.45.
- 4.8 The price increase of 13% in April 2019 resulted in an additional cost to the PBS of less than \$10 million per year. And resulted in an increase in the ex-man price from \$3.45 to \$3.90.

¹ Connor, J. and Buck, P. 2013. "Improving asthma management: The case for Mandatory Inclusion of Dose counters on all rescue bronchodilators." *Journal of Asthma* 6 (50): 658-663.

² Holt, S. Holt, A. Weatherall, M. et al. "Metered dose inhalers: A need for dose counters", *Respirology* (2005), 10, 105-106.

Table 2: Price increase history of salbutamol without a dose counter

Date of increase	Increase amount	AEMP	Additional cost to PBS per year	Reported cost of goods from Alphapharm who requested increase	Requested AEMP by Alphapharm
Dec 2016	+\$0.46 or +15.4%	\$3.45	less than \$10 million	\$ [REDACTED]	\$ [REDACTED]
Apr 2019	+\$0.45 or +13.0%	\$3.90	less than \$10 million	\$ [REDACTED]	\$ [REDACTED]

Abbreviations: AEMP, Approved Ex-Manufacturer Price; PBS, Pharmaceutical Benefits Scheme

Source: Compiled by the Secretariat

4.9 The sponsor claimed that the cost of goods for the Ventolin DC will be \$ [REDACTED] per unit.

4.10 Ventolin MDI is currently listed on the PBS with a brand premium (BP) of \$1.29 for the prescriber bag item (3495Y) and \$2.58 for the general schedule item (8288F). A history of the brand premium for Ventolin MDI is outlined in table 3.

4.11 The BP means that the actual price paid for Ventolin MDI is higher than the ex-man price being requested by the sponsor for Ventolin DC. The Secretariat noted that while not a matter for PBAC, it would be open to the sponsor to request a brand premium on the GSK brand, should more than one brand of salbutamol DC become available on the PBS.

Table 3: Brand premium changes to GSK's Ventolin MDI

Event	Dispense setting	AEMP	Effective date	Previous BP	New BP	Claimed price
AEMP increase from \$2.99 to \$3.45 & BP increase	General schedule	\$3.45	1 December 2016	\$2.04	\$2.54	\$4.63
BP increase	General schedule	\$3.45	1 February 2018	\$2.54	\$3.54	\$5.11
AEMP increased from \$3.45 to \$3.90, however, claimed price remained the same	General schedule	\$3.90	1 April 2019	\$3.54	\$2.58	\$5.10
BP increase	General schedule	\$3.90	1 August 2019	\$2.58	\$3.66	\$5.60

Abbreviations: AEMP, Approved Ex-Manufacturer Price; BP, Brand premium; PBS, Pharmaceutical Benefits Scheme

Source: Compiled by the Secretariat

4.12 The subsidised price for salbutamol without a dose counter in New Zealand is AUD \$3.64 (or NZD \$3.80).

4.13 GSK advised in their letter that the price of Ventolin DC in the United States is \$ [REDACTED] AUD. The Secretariat could not verify this claim.

Estimated PBS usage & financial implications

4.14 In its correspondence, GSK proposed a revised AEMP of \$ [REDACTED] (reduced from \$ [REDACTED]). GSK presented revised budget impact figures which are presented in Table 4.

4.15 The Secretariat could not verify these financial estimates, as the sponsor did not provide the revised financial impact spreadsheet. Based on the proportion of reduction, the adjusted estimates presented appear to only incorporate the new proposed ex-manufacturer price, with no further adjustments to the budget impact.

Table 4: Summary of Net Impact of listing Ventolin DC at an AEMP of \$ [REDACTED]

	2020	2021	2022	2023	2024	2025
PBS						
New listing	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Changed listing	(\$ [REDACTED])	(\$ [REDACTED])	(\$ [REDACTED])	(\$ [REDACTED])	(\$ [REDACTED])	(\$ [REDACTED])
Net cost to PBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
RPBS						
New listing	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Changed listing	(\$ [REDACTED])	(\$ [REDACTED])	(\$ [REDACTED])	(\$ [REDACTED])	(\$ [REDACTED])	(\$ [REDACTED])
Net cost to PBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Net cost to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

Source: Table 1, p4 of letter from GSK dated 20 December 2019

The redacted table shows that at Year 6, the estimated net cost to the PBS/RPBS would be less than \$10 million.

4.16 The additional cost to the PBS of various AEMPs are outlined in table 5.

Table 5: Additional costs to PBS based on different approved ex-manufacturer prices of salbutamol with a dose counter

AEMP	\$ increase over Ventolin MDI	% increase over Ventolin MDI	Projected additional cost to PBS per year
\$3.90	-	-	-
\$4.10	+\$0.20	+5.00%	less than \$10 million
\$4.29	+\$0.39	+10.00%	less than \$10 million
\$4.68	+\$0.78	+20.00%	less than \$10 million
\$ [REDACTED] (proposed by GSK)	+\$ [REDACTED]	+ [REDACTED] %	less than \$10 million
\$ [REDACTED] (original proposal)	+\$ [REDACTED]	+ [REDACTED] %	less than \$10 million

Abbreviations: AEMP, Approved Ex-Manufacturer Price; PBS, Pharmaceutical Benefits Scheme

Source: Compiled by the Secretariat

5 PBAC Outcome

5.1 The PBAC noted the sponsor’s correspondence of 20 January 2020 that it was unable to list Ventolin DC on the PBS with only a [REDACTED] % increase compared to the Ventolin MDI, as in the sponsor’s view it did not reflect the added safety value for this product.

5.2 The PBAC recalled that when making its November 2019 recommendation for listing Ventolin DC with a small premium ([REDACTED] %) over the current Ventolin MDI price was based on, among other matters, the potential health benefits related to the likely risk

- of having sub-therapeutic or negligible drug being available at a time of acute bronchoconstriction, and the role of a DC in this specific context to act as a reminder to replace medication.
- 5.3 The sponsor's submission referenced the evidence on the impact of a dose counter in an MDI device on healthcare utilisation (Chippis 2017, Kerwin 2017, Lachman 2018, and Price 2016) on patients who used a salbutamol MDI with a DC compared to those who used a salbutamol MDI without a dose counter.
 - 5.4 The PBAC recalled it considered the evidence from these studies at its November 2019 meeting where it noted that all four studies were conducted in the United States and as such, differences in healthcare settings may limit applicability to the Australian setting. It also recalled its conclusion that the evidence supporting a reduction in healthcare utilisation as a result of an integrated DC was limited. The PBAC noted that no new evidence was presented on this issue.
 - 5.5 The PBAC noted that in its January 2020 correspondence, the sponsor cited new evidence from a New Zealand study (Holt et al 2005) that patients use the 'shaking' method to estimate remaining medication. The PBAC noted that of the 100 patients surveyed in the study, 109 Ventolin MDI inhalers were discarded with 84% being 'more than empty'.
 - 5.6 The PBAC also noted that the sponsor's letter referred to anecdotal passive pharmacovigilance reports that patients stockpile inhalers, as they are anxious about running out of doses; as well as consumers using non-validated techniques to estimate the remaining contents of Ventolin inhalers, including dismantling inhalers to weight aerosol canisters and/or to float aerosol canisters in water to estimate remaining doses. The PBAC noted that the estimated reduction in wastage due to reduced stockpiling that might be realised from the Ventolin DC was not calculated by the sponsor, nor was the estimated increased cost to the PBS of patients purchasing Ventolin DC before all 200 doses have been used. As such the relative potential cost saving impacts of the introduction of the Ventolin DC could not be considered.
 - 5.7 The PBAC noted that no evidence was presented to support the sponsor's claim that the dose counter listing would result in reduced ED visits.
 - 5.8 The sponsor referred to a number of other issues, including TGA registration, cost of goods, as well as increase in demand for salbutamol, as the number of scripts dispensed for Ventolin DC increased during the recent bushfires. The PBAC noted that the highest number of scripts dispensed in 2019 for Ventolin MDI was in December. The PBAC considered that this may have been a response to the bushfire season, but no further data was made available on this issue.
 - 5.9 The PBAC noted the sponsor's submission that the manufacture of Ventolin DC is more complex than and the packaging is larger than that of Ventolin MDI, resulting in higher costs of manufacture and supply.

- 5.10 The PBAC noted the sponsor's comments on the value of Ventolin to the Australian community during times of natural disasters and crisis.
- 5.11 Taking into account all of the submissions made to it, the PBAC considered that it remained difficult to ascertain a cost-effectiveness premium for Ventolin DC, in particular when taken outside the disaster relief context, and therefore advised that a [REDACTED] % premium over the current Ventolin MDI price would be appropriate.

Addendum to the March 2020 PBAC PSD:

6 Background

- 6.1 At its November 2019 meeting, the PBAC considered that Ventolin DC and currently listed salbutamol MDI (Ventolin MDI, Asmol MDI) should not be considered equivalent for the purposes of substitution under Section 101(4AACD) of the *National Health Act 1953*.
- 6.2 In late 2019 and early 2020, salbutamol was in high demand during the bush fire season and then also the subject of panic buying and stockpiling in March 2020 coinciding with the outbreak of COVID-19. This has resulted in localised shortages of salbutamol inhalers.
- 6.3 If Ventolin MDI and Asmol MDI are 'a' flagged with Ventolin DC at the time of introduction of Ventolin DC into the market, this may assist with localised shortages that may continue to occur in 2020. If all brands are 'a' flagged, patients with a prescription for Ventolin MDI or Asmol MDI will be able to access Ventolin DC, should Ventolin MDI or Asmol MDI be unavailable.

7 PBAC Outcome

- 7.1 The PBAC advised that salbutamol pressurised inhalation 100 micrograms (as sulfate) per dose with dose counter, 200 doses (CFC-free formulation) (Ventolin DC) should be treated as equivalent to salbutamol pressurised inhalation 100 micrograms (as sulfate) per dose, 200 doses (CFC-free formulation) (Ventolin MDI and Asmol MDI) for the purposes of substitution under Section 101(4AACD) of the *National Health Act 1953*.
- 7.2 The PBAC noted that when providing this advice, it considered that the two products are identical apart from the dose counter, and therefore any consumer advice around the use of the dose counter presentation compared to Ventolin MDI can likely be managed at the pharmacy level, while the majority of the clinical advice to patients would still be applicable across the two presentations.
- 7.3 The PBAC further noted that while it still considered that consistent with its November 2019 advice, any additional benefit of the dose counter presentation would be lost if the patient is switched back to Ventolin MDI, this was only likely to occur for a short time until the sponsor withdraws Ventolin MDI from the market, as the sponsor had

flagged in its submissions; and only where supply of the Ventolin DC was not otherwise accessible to individual patients.

- 7.4 Finally, the PBAC noted the high need for consistent supply of this medicine.

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

GSK welcomes the PBAC recommendation. The dose-counter presentation should benefit Australian patients in terms of safety and quality use of medicine.