

**6.07 CALCIPOTRIOL with BETAMETHASONE DIPROPIONATE  
Gel containing calcipotriol 50 micrograms with  
betamethasone 500 micrograms (as dipropionate)  
per g, 60 g,  
Daivobet<sup>®</sup>, LEO Pharma**

**1 Purpose of Application**

- 1.1 The minor submission requested an amendment to the PBS listing of calcipotriol 0.005% with betamethasone dipropionate 0.05% gel, 60 g (thereafter referred to as calcipotriol + betamethasone) to facilitate access to increased quantities, based on the proportion of the body surface area (BSA) affected by psoriasis.

**2 Requested listing**

- 2.1 The submission requested the following restrictions.
- 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.

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| Name, Restriction, Manner of administration and form   | Max. Qty | No. of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|--|----------|-------------|------------------------------|-----------------------------------|
| CALCIPOTRIOL + BETAMETHASONE DIPROPIONATE<br>Calcipotriol 0.005% + betamethasone (as dipropionate) 0.05% gel, 60 g | 2        | 1           | \$ [REDACTED]                | Daivobet Leo Pharma               |

|                                    |  |
|------------------------------------|--|
| <b>Category / Program</b>          | GENERAL – General Schedule (Code GE)   |
| <b>Prescriber type:</b>            | <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists<br><input type="checkbox"/> Midwives   |
| <b>Condition:</b>                  | Chronic stable plaque type psoriasis vulgaris  |
| <b>PBS Indication:</b>             | Chronic stable plaque type psoriasis vulgaris  |
| <b>Treatment phase:</b>            | Initial or continuing  |
| <b>Restriction Level / Method:</b> | <input type="checkbox"/> Restricted benefit<br><input type="checkbox"/> Authority Required - In Writing<br><input type="checkbox"/> Authority Required - Telephone<br><input type="checkbox"/> Authority Required – Emergency<br><input type="checkbox"/> Authority Required - Electronic<br><input checked="" type="checkbox"/> Streamlined |
| <b>Clinical criteria:</b>          | The condition must be inadequately controlled by potent topical corticosteroid monotherapy, AND<br>The condition must cover 7-13% of the patient's body surface area.  |

| Name, Restriction, Manner of administration and form   | Max. Qty | No. of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|--|----------|-------------|------------------------------|-----------------------------------|
| CALCIPOTRIOL + BETAMETHASONE DIPROPIONATE<br>Calcipotriol 0.005% + betamethasone (as dipropionate) 0.05% gel, 60 g | 3        | 1           | \$ [REDACTED]                | Daivobet Leo Pharma               |

|                                    |  |
|------------------------------------|--|
| <b>Category / Program</b>          | GENERAL – General Schedule (Code GE)   |
| <b>Prescriber type:</b>            | <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists<br><input type="checkbox"/> Midwives   |
| <b>Condition:</b>                  | Chronic stable plaque type psoriasis vulgaris  |
| <b>PBS Indication:</b>             | Chronic stable plaque type psoriasis vulgaris  |
| <b>Treatment phase:</b>            | Initial or continuing  |
| <b>Restriction Level / Method:</b> | <input type="checkbox"/> Restricted benefit<br><input type="checkbox"/> Authority Required - In Writing<br><input type="checkbox"/> Authority Required - Telephone<br><input type="checkbox"/> Authority Required – Emergency<br><input type="checkbox"/> Authority Required - Electronic<br><input checked="" type="checkbox"/> Streamlined |

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|                           |  |
|---------------------------|--|
| <b>Clinical criteria:</b> | The condition must be inadequately controlled by potent topical corticosteroid monotherapy, AND<br>The condition must cover 13-19% of the patient's body surface area. |
|---------------------------|--|

| Name, Restriction, Manner of administration and form   | Max. Qty | No. of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|--|----------|-------------|------------------------------|-----------------------------------|
| CALCIPOTRIOL + BETAMETHASONE DIPROPIONATE<br>Calcipotriol 0.005% + betamethasone (as dipropionate) 0.05% gel, 60 g | 4        | 1           | \$ [REDACTED]                | Daivobet Leo Pharma               |

|                                    |  |
|------------------------------------|--|
| <b>Category / Program</b>          | GENERAL – General Schedule (Code GE)   |
| <b>Prescriber type:</b>            | <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists<br><input type="checkbox"/> Midwives   |
| <b>Condition:</b>                  | Chronic stable plaque type psoriasis vulgaris  |
| <b>PBS Indication:</b>             | Chronic stable plaque type psoriasis vulgaris  |
| <b>Treatment phase:</b>            | Initial or continuing  |
| <b>Restriction Level / Method:</b> | <input type="checkbox"/> Restricted benefit<br><input type="checkbox"/> Authority Required - In Writing<br><input type="checkbox"/> Authority Required - Telephone<br><input type="checkbox"/> Authority Required – Emergency<br><input type="checkbox"/> Authority Required - Electronic<br><input checked="" type="checkbox"/> Streamlined |
| <b>Clinical criteria:</b>          | The condition must be inadequately controlled by potent topical corticosteroid monotherapy, AND<br>The condition must cover <del>more than</del> 20% or more of the patient's body surface area.   |
| <b>Prescriber Instructions</b>     | Note: When using calcipotriol containing products, the maximum daily dose should not exceed 15 g and the maximum weekly dose should not exceed 100 g. The total body surface area treated with calcipotriol should not exceed 30%.   |

### 3 Background

- 3.1 Calcipotriol + betamethasone is TGA registered for topical treatment of scalp psoriasis and mild to moderate plaque psoriasis on the body. The gel should be applied to the affected areas of the scalp once daily for up to 4 weeks with use beyond this period according to need under medical supervision (Daivobet® Product Information[PI]). For psoriasis of the body, the gel should be applied to the affected areas once daily for up to 8 weeks (Daivobet® PI). Due to the content of calcipotriol, the maximum daily dose should not exceed 15 g and the maximum weekly dose should not exceed 100 g (Daivobet® PI). The total BSA treated with calcipotriol should not exceed 30% (Daivobet® PI).
- 3.2 Calcipotriol + betamethasone is currently listed on the PBS for chronic stable plaque type psoriasis vulgaris in a 30 g (1 + 1 repeat) and a 60 g (1 + 1 repeat) presentation. The submission proposes that, due to the proportion of BSA affected by the condition, many patients with psoriasis require more than 60 g of the product per

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month for appropriate treatment. The submission proposes that patients with 7–13%, 13–19% and more than 20% of their BSA affected by the condition would be eligible for a maximum quantity of 2, 3 and 4 presentations of the 60 g gel respectively, each with 1 repeat.

- 3.3 From 1 July 2016, betamethasone dipropionate and three other class III potency corticosteroids have been made available as Authority Required (Streamlined) benefits for higher quantities based on the proportion of BSA affected by the condition to be treated. The submission suggested that the proposed Authority Required (Streamlined) listings for calcipotriol + betamethasone will align with the class III potency corticosteroid listings. The submission proposed that the requested amendment will support patients with more extensive psoriasis to obtain 4 weeks supply of calcipotriol + betamethasone based on their clinical need.
- 3.4 The PBAC recommended a 30 g calcipotriol + betamethasone ointment formulation for listing in July 2009 with the 30 g gel presentation recommended on a cost-minimisation basis to the ointment in 2010 (between the July and November PBAC meetings). In March 2013 there were two minor submissions, one requesting listing for the 60 g gel and the second requesting full body use. Both minor submissions were rejected and then in November 2013 PBAC recommended listing of the 60 g gel for plaque psoriasis of the scalp. On 1 October 2015, the 60 g gel was listed on the PBS as an Authority Required (Streamlined) benefit for plaque psoriasis of the scalp, from the previous Authority Required listing. At its November 2015 meeting the PBAC recommended extending the listing of the 30 g and 60 g gel presentation for the treatment of the scalp to a listing for the treatment of the whole body.

*For more detail on PBAC's views, see section 5 PBAC Outcome.*

## **4 Consideration of the evidence**

### ***Sponsor hearing***

- 4.1 There was no hearing for this item as it was a minor submission.

### ***Consumer comments***

- 4.2 The PBAC noted that no consumer comments were received for this item.

### ***Clinical trials***

- 4.3 The minor submission presented the following clinical trials. These trials were included in those presented to the November 2015 PBAC meeting in the major submission for Daivobet<sup>®</sup> gel, which requested an extension to the listing to include treatment of the whole body.

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Table 1: Trials and associated reports presented in the submission

| Trial ID   | Protocol title/ Publication title  | Publication citation                                     |
|--|--|--|
| <b>Supplementary randomised trials – indirect comparison</b> |  |  |
| LEO 80185-G23  | Calcipotriol plus betamethasone dipropionate topical suspension compared to betamethasone dipropionate in the topical suspension vehicle, calcipotriol in the topical suspension vehicle and the topical suspension vehicle alone in psoriasis vulgaris.<br><br>Menter A, Stein Gold L, Bukhalo M et al. Calcipotriene Plus Betamethasone Dipropionate Topical Suspension for the Treatment of Mild to Moderate Psoriasis Vulgaris on the Body: A Randomized, Double-Blind, Vehicle-Controlled Trial | 11 October 2011<br><br>JDD 2013; 12 (1):92-98            |
| LEO 80185-G21  | Efficacy and safety of calcipotriol plus betamethasone dipropionate gel compared with tacalcitol ointment and the gel vehicle alone in patients with psoriasis vulgaris<br><br>Langley RGB, Gupta A, Papp K et al. Calcipotriol plus Betamethasone Dipropionate Gel Compared with Tacalcitol Ointment and the Gel Vehicle Alone in Patients with Psoriasis Vulgaris: A Randomized, Controlled Clinical Trial   | 6 June 2009.<br><br>Dermatology 2011; 222:148-156        |
| MBL 0202 INT   | Calcipotriol plus betamethasone dipropionate gel compared to betamethasone dipropionate in the gel vehicle, calcipotriol in the gel vehicle and the gel vehicle alone in psoriasis vulgaris.<br><br>Fleming C, Ganslandt C, Guenther L et al. Calcipotriol plus betamethasone dipropionate gel compared with its active components in the same vehicle and the vehicle alone in the treatment of psoriasis vulgaris: a randomised, parallel group, double-blind, exploratory study                   | 16 October 2008<br><br>Eur J Dermatol 2010; 20(4):465-71 |

Source: Calcipotriol + betamethasone gel 50/500, Public Summary Document, November 2015 PBAC Meeting

4.4 The submission reported on baseline disease severity characteristics and BSA involvement for the trials listed in Table 1 along with calcipotriol + betamethasone use at week 4. A weighted average for the mean total dose in 4 weeks and the mean % BSA affected were then determined (Table 2).

Table 2: Combined results of usage across Daivobet® gel trials

| Study ID                               | N   | Mean total dose in 4 weeks (28 days) | Mean % BSA affected                  |
|--|-----|--------------------------------------|--------------------------------------|
| <b>Weighted averages</b>               |     | 110.8                                | 11.40%                               |
| LEO 80185-G23                          | 482 | 120.7                                | 12.3%                                |
| LEO 80185-G21                          | 183 | 103.4                                | 9.0%                                 |
| MBL 0202 1 <sup>st</sup> 4 weeks usage | 162 | 89.3                                 | NR, but similar PASI to other trials |

Source: Table 5, Calcipotriol + betamethasone gel 50/500, Submission to the March 2018 PBAC Meeting

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- 4.5 Using data in Table 2, the submission proposed that for a mean weighted usage of 110.8 g in 28 days, where there is a mean weighted % BSA of 11.4%, the amount required per 1% BSA per day is 0.35 g.
- 4.6 The submission used the estimate of 0.35 g per 1% BSA to determine the number of units of 60 g required for 4 weeks treatment per % BSA (Table 3).

**Table 3: Number of units of 60 g required for 4 weeks treatment per % BSA**

| <b>Daivobet gel 60 g</b> |  |                      |   |
|--------------------------|--|----------------------|---|
| <b>% BSA</b>             | <b>g of calcipotriol + betamethasone used over 28 days</b> | <b>Units of 60 g</b> | <b>Dispensed units of 60 g required</b> |
| 2                        | 19.4   | 0.32                 | 1                                       |
| 4                        | 38.9   | 0.65                 | 1                                       |
| 5                        | 48.6   | 0.81                 | 1                                       |
| <b>7</b>                 | <b>68.1</b>  | <b>1.13</b>          | <b>2</b>                                |
| 10                       | 97.2   | 1.62                 | 2                                       |
| 12                       | 116.7  | 1.94                 | 2                                       |
| <b>13</b>                | <b>126.9</b>   | <b>2.11</b>          | <b>3</b>                                |
| 15                       | 145.8  | 2.43                 | 3                                       |
| <b>19</b>                | <b>184.7</b>   | <b>3.08</b>          | <b>4</b>                                |
| 20                       | 194.4  | 3.24                 | 4                                       |

Source: Table 6, Calcipotriol + betamethasone gel 50/500, Submission to the March 2018 PBAC Meeting

***Estimated PBS usage & financial implications***

- 4.7 The submission proposed that there is significant dispensing of increased quantities of calcipotriol + betamethasone currently taking place. Using prescription data from the IQVIA® NostraData database, the submission reported that █% of calcipotriol + betamethasone 60 g gel dispensing events between October 2016 and November 2017 have two or more units dispensed on the same day (increased quantities). Overall, the average units of calcipotriol + betamethasone 60 g gel per dispensing event was █. Of those receiving increased quantities, the units per dispensing event was █.
- 4.8 Data provided by the Drug Utilisation Sub Committee (DUSC) Secretariat indicated that the proportion of prescriptions for increased quantities was overestimated. PBS prescription data for Item 10075G were extracted from the Department of Human Services prescription database for date of supply between October 2016 and November 2017. Of the █ supplies (defined as all prescriptions to a patient on a day) over this period, the majority (█%) involved the supply of one unit (i.e. one 60 g pack). The weighted average quantity per supply over this period was █ units. Of those receiving increase quantities, the average quantity per supply was █ units.
- 4.9 The utilisation estimates in the submission assumed █% of current dispensings of calcipotriol + betamethasone 60 g gel (Item 10075G) are for increased quantities, at a rate of █ units/service. Services for increased quantities were allocated a proxy

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item number (10075G-Incr). The proxy item number was allocated a DPMQ for an MQ of [REDACTED]. It was assumed that [REDACTED]% of services for increased quantities would move from the proxy item 10075G-Incr (currently accessing increased quantities) to the proposed Authority required (Streamlined) listings. Market growth was approximated at [REDACTED]% based on existing growth for Item 10075G. The Secretariat noted that the estimate of market growth has not been independently evaluated.

- 4.10 The Secretariat noted that the utilisation estimates are likely overestimated as, based upon the data provided by the DUSC Secretariat, the assumption that [REDACTED]% of current dispensings of calcipotriol + betamethasone 60 g gel are for increased quantities may not be valid.
- 4.11 The minor submission estimated a net save to the PBS/RPBS of less than \$10 million in Year 6 of listing, with a total net save to the PBS/RPBS of less than \$10 million over the first 6 years of listing. In addition, the submission proposed the net saving will be accompanied by a reduction in processing of Authority prescriptions for increased quantities. The Secretariat noted that, as the utilisation estimates are likely overestimated, the proposed net savings and reductions in the processing of Authority prescriptions are unlikely to be realised.
- 4.12 In the pre-PBAC response the sponsor acknowledged and accepted the results of the data provided by the DUSC Secretariat indicating that [REDACTED]% of calcipotriol + betamethasone supplies involve increased quantities. The pre-PBAC response noted that, due to an interpretation error identified on confirmation of the original analysis, the estimate of [REDACTED]% of dispensing events comprising increased quantities was erroneous. In addition, the pre-PBAC response states that, although the proportion of dispensing events involving increased quantities is lower than initially estimated, the benefit of the proposed amendment to this group of patients remains valid.

*For more detail on PBAC's views, see section 5 PBAC Outcome.*

## **5 PBAC Outcome**

- 5.1 The PBAC did not recommend amending the listing of calcipotriol + dipropionate to facilitate access to increased quantities based on the proportion of BSA affected by psoriasis.
- 5.2 The PBAC noted that in the pre-PBAC response the sponsor accepted the utilisation data regarding the proportion of prescriptions for increased quantities provided by the DUSC Secretariat. The PBAC considered that there was limited clinical need for the amendment as the utilisation data provided by the DUSC Secretariat indicated the majority of patients were covered by existing arrangements.
- 5.3 The PBAC further noted that, where there is a clinical need, access to increased quantities of calcipotriol + betamethasone is available via an Authority PBS prescription for patients who require more than 60 g per prescription.

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- 5.4 The PBAC noted that, due to the content of calcipotriol, the total BSA treated with calcipotriol + betamethasone should not exceed 30%. The PBAC considered that BSA measurement may not always be undertaken accurately and hence broader access to larger quantities of calcipotriol + betamethasone may potentially increase the risk of toxicity associated with calcipotriol.
- 5.5 The PBAC noted that this submission is not eligible for an Independent Review as the requested listing is for the same condition for which calcipotriol + betamethasone is currently subsidised.

**Outcome:**

Rejected

## **6 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.

## **7 Sponsor's Comment**

LEO Pharma is disappointed by this outcome and remains committed to working with the PBAC to provide the best outcomes for Australian patients.