

## **5.17 CARMELLOSE**

**Eye drops containing carmellose sodium 5 mg per mL,  
10 mL**

**Evolve® carmellose 0.5%**

## **HYPROMELLOSE**

**Eye drops containing hypromellose 3 mg per mL,  
10 mL**

**Evolve® hypromellose 0.3%,  
Contact Lens Centre Australia**

### **1 Purpose of Application**

- 1.1 The minor submission requested General Schedule Authority Required (STREAMLINED) listings for carmellose (Evolve® carmellose 0.5%) and hypromellose (Evolve® hypromellose 0.3%) in multi-use eye drops for the treatment of severe dry eye syndrome in patients who are sensitive to preservatives.

### **2 Requested listing**

- 2.1 The submission requested the same PBS listing as the sodium hyaluronate containing formulations, Hylo-Fresh® and Hylo-Forte®.
- 2.2 Although the sponsor did not specifically request optometrist prescribing, this has been included in the suggested restriction wording to align with the other PBS-listed preservative-free ocular lubricants.
- 2.3 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 Manufacturer	Name and
CARMELLOSE SODIUM carmellose sodium 0.5% (5 mg/mL) eye drops, 10 mL 0.5% w/v, 10mL	1	5	\$33.56	Evolve® carmellose 0.5%	Contact Lens Centre Australia
HYPROMELLOSE hypromellose 0.3% (3 mg/mL) eye drops, 10 mL 0.3% w/v, 10mL	1	5	\$33.56	Evolve® hypromellose 0.3%	

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input checked="" type="checkbox"/> Optometrists
<b>Severity:</b>	N/A Severe
<b>Condition:</b>	Severe d Dry eye syndrome
<b>PBS Indication:</b>	Severe dry eye syndrome
<b>Restriction Level / Method:</b>	<input checked="" type="checkbox"/> Streamlined
<b>Clinical criteria:</b>	Patient must be sensitive to preservatives in multi-dose eye drops.

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

### 3 Background

- 3.1 Carmellose 0.5% and hypromellose 0.3% were approved by the TGA and registered on the Australian Register of Therapeutic Goods on 17 October 2017 for use in the relief of discomfort that arises from dry eye sensations.
- 3.2 These brands of drugs have not previously been considered by the PBAC.
- 3.3 At its November 2014 meeting, the PBAC considered a Drug Utilisation Sub-Committee (DUSC) utilisation analysis of ocular lubricants. The PBAC recommended that all ocular lubricants should be considered equivalent for pricing purposes, including those that contain a preservative, those that are preservative-free, multi-dose products and single dose unit products. The PBAC also considered that no evidence was presented to conclude any difference in patient outcomes between the various ocular lubricants (November 2014 Public Summary Document on ocular lubricants).

## 4 Comparator

- 4.1 The minor submission nominated the PBS-listed sodium hyaluronate products (Hyo-Fresh and Hylo-Forte) as comparators on the basis that they are both preservative-free multi-dose ocular lubricants.
- 4.2 Perfluorohexyloctane, another preservative-free ocular lubricant in a multi-dosing system, received a positive recommendation for the same indication at the March 2018 PBAC meeting. In considering this submission, the PBAC was of the view that all of the other preservative-free multi-dose ocular lubricants were appropriate comparators for perfluorohexyloctane.
- 4.3 The submission assumed that carmellose 0.5% and hypromellose 0.3% will replace the existing single dose carmellose and hypromellose products, as well as the sodium hyaluronate products.
- 4.4 The PBAC considered that carmellose 0.5% and hypromellose 0.3% could replace any of the PBS-listed ocular lubricants, and hence they should be cost-minimised against the lowest cost ocular lubricant.

*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 as it was a minor submission.

### ***Consumer comments***

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

### ***Clinical trials***

- 5.3 The submission claimed non-inferiority between the requested drugs and the nominated comparators. No clinical evidence was presented to support this claim.

### ***Economic analysis***

- 5.4 The submission requested the same price as the comparator as follows:
  - 10 mL of carmellose 0.5% is equivalent to 10 mL of sodium hyaluronate 0.1%
  - 10 mL of carmellose 0.5% is equivalent to 10 mL of sodium hyaluronate 0.2%
  - 10 mL of hypromellose 0.3% is equivalent to 10 mL of sodium hyaluronate 0.1%
  - 10 mL of hypromellose 0.3% is equivalent to 10 mL of sodium hyaluronate 0.2%

- 5.5 The shelf life for the carmellose 0.5% and hypromellose 0.3% is three months after opening, which is half the duration of the shelf life of sodium hyaluronate and other preservative-free multi-dose ocular lubricants. The submission claimed that multiple drops per eye per day are usually required and therefore the likelihood of wastage is low.
- 5.6 The requested comparator, hyaluronic acid, has a higher DPMQ than other available preservative-free ocular lubricants. The table below summarises the preservative-free ocular lubricants that are currently listed on the PBS and their DPMQs.

**Table 1: Preservative-free ocular lubricants**

Drug/ Brand name	PBS Item Code	Multi-dose or single dose presentation	Quantity	Price (DPMQ)* April 2018
Carbomer 980	5504Q, 8578L,	Single dose units	3 x 30	\$36.88
Carbomer 974	5502N, 8514D	Single dose units	3 x 30	\$35.56
Carmellose (Celluvisc, Cellufresh, Optifresh)	2324H, 5505R, 2338C, 5506T,	Single dose units	3 x 30	\$31.63
Carmellose (Theratears)	5509Y, 8823J, 5510B, 8824K	Single dose units	4 x 24 3 x 28	\$39.19 \$33.94
<b>Hyaluronic acid (Hylo-Fresh, Hylo-Forte)</b>	<b>2181T, 2184Y, 2171G, 2253N</b>	<b>Multi-dose</b>	<b>1 x 10 mL</b>	<b>\$33.56</b>
Hypromellose with dextran	5521N, 8299T	Single dose units	3 x 28 3 x 28 x 0.4 mL	\$35.98
Paraffin	2167C, 2222Y, 2202X, 1754H, 5523Q, 1750D, 5522P, 9218E, 9217D,	Multi-dose (ointment) Multi-dose (ointment) Multi-dose (ointment)	2 x 5 g 2 x 3.5 g 2 x 3.5 g	\$23.97 \$23.97 \$23.42
Polyethylene glycol 400 with propylene glycol	5532E, 9170P	Single dose units	2 x 28	\$33.95
Soy lecithin	5545W, 9448G	Multi-dose (eye spray)	2 x 10 mL	\$35.59
Perfluorohexyloctane (NovaTears®)	TBA	Multi-dose	3 mL	n/a

\*Brand price premiums excluded. 2018 prices from April 2018 Pharmaceutical Benefits Schedule  
Source: modified from Table 1.2 pg 12 of the submission.

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

- 5.7 The minor submission estimated a net save to the PBS of less than \$10 million in Year 5 of listing, with a total net saving to the PBS of less than \$10 million over the first 5 years of listing, based on substitution for eye drops that are more expensive than the requested listing.

Table 2: Estimated market prescriptions:

	Year 1	Year 2	Year 3	Year 4	Year 5
<b>Estimated script VOLUMES (based on the estimated scripts of displaced drugs<sup>a</sup>)</b>	████████	████████	████████	████████	████████
<b>Estimated net cost of new listing</b>					
to PBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
to RPBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
to the PBS/RPBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
Less co-payments	-\$ ██████████	-\$ ██████████	-\$ ██████████	-\$ ██████████	-\$ ██████████
Net cost to PBS/RPBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
<b>Estimated net costs of displaced medicines</b>					
to PBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
to RPBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
to the PBS/RPBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
Less co-payments	-\$ ██████████	-\$ ██████████	-\$ ██████████	-\$ ██████████	-\$ ██████████
Net cost to PBS/RPBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
<b>Overall net saving to the PBS/RPBS</b>					
to PBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
to RPBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
to the PBS/RPBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
Less co-payments	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████
Net saving to PBS/RPBS	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████	\$ ██████████

<sup>a</sup> The submission assumed that carmellose 0.5% and hypromellose 0.3% would substitute the existing single dose carmellose (Celluvisc, Cellufresh, Optifresh and Theratears) and hypromellose (hypromellose with dextran) products, as well as the sodium hyaluronate products

Source: adapted from the financial model spreadsheet provide in the submission

5.8 The submission assumed that carmellose 0.5% and hypromellose 0.3% would substitute for the existing single dose carmellose (Celluvisc®, Cellufresh®, Optifresh® and TheraTears®) and hypromellose (hypromellose with dextran) products, as well as the sodium hyaluronate products.

5.9 Using a market share approach, the sponsor assumed that the carmellose 0.5% and hypromellose 0.3% multi-dosing eye drops would displace the current single dose units for carmellose and hypromellose. The expected market share will be 40% in the first year of listing to 65% in year five. The sponsor claimed that the large market uptake is due to the convenience of the multi-dose device of the carmellose 0.5% and hypromellose 0.3% products. The sponsor also assumed that only 4%-10% of the sodium hyaluronate market would be displaced by these new listings as patients familiar and comfortable with those products are unlikely to switch to carmellose 0.5% and hypromellose 0.3%.

- 5.10 The PBAC noted that the sodium hyaluronate products are also multi-dose devices that have been listed on the PBS since 2012, and therefore some displacement of single dose units due to the convenience of multi-dose devices would likely have already occurred. It is therefore possible that the sponsor has overestimated the potential market share for the carmellose 0.5% and hypromellose 0.3% products, and also overestimated the potential net savings to the PBS.
- 5.11 The sponsor estimated that the market of the carmellose and hypromellose single dose units would be relatively stable in the next five years. The sponsor also assumed that the current sodium hyaluronate market would continue to grow but at a reduced rate, decreasing to 5% by year 5.

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

## **6 PBAC Outcome**

- 6.1 The PBAC recommended General Schedule Authority Required (STREAMLINED) listings for carmellose (Evolve<sup>®</sup> carmellose 0.5%) and hypromellose (Evolve<sup>®</sup> hypromellose 0.3%) multi-use ocular lubricants for the treatment of severe dry eye syndrome in patients who are sensitive to preservatives in multi dose eye drops.
- 6.2 The PBAC recalled its previous recommendation that all ocular lubricants should be considered equivalent for pricing purposes, including those that contain a preservative, those that are preservative-free, multi-dose products and single dose unit products (November 2014 public summary document on ocular lubricants). The PBAC therefore advised that any of the PBS-listed ocular lubricants could be appropriate comparators for carmellose 0.5% and hypromellose 0.3%.
- 6.3 The PBAC noted that the nominated comparator, hyaluronic acid, has a higher DPMQ than other PBS-listed ocular lubricants. The PBAC also noted that if treatment with carmellose 0.5% and hypromellose 0.3% were substantially more costly than any of the relevant comparators, the PBAC could only recommend listing carmellose 0.5% and hypromellose 0.3% if it was satisfied that carmellose 0.5% and hypromellose 0.3% provide, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies (*National Health Act 1953, Section 101(3B)*). The PBAC noted that the submission did not provide clinical evidence to support a claim of superiority of carmellose 0.5% or hypromellose 0.3% compared to any of the currently PBS-listed ocular lubricants. The PBAC therefore advised, under Section 101(3B) of the National Health Act 1953, that carmellose 0.5% and hypromellose 0.3% should be cost-minimised against the lowest cost ocular lubricant.
- 6.4 The PBAC advised that an additional administrative advice stating “The in-use shelf life of Evolve<sup>®</sup> carmellose 0.5% and Evolve<sup>®</sup> hypromellose 0.3% is 3 months from the date of opening” in the restriction would be appropriate, consistent with the PBS

restrictions for other preservative-free eye drops (e.g. sodium hyaluronate listings Hylo-Fresh and Hylo-Forte, which have a 6 month shelf life).

- 6.5 The PBAC recalled that at its April 2010 Special meeting, it recommended that eye lubricants be included for prescribing by nurse practitioners. This has been included in the suggested restriction.
- 6.6 The PBAC considered that, in line with other ocular lubricants, carmellose 0.5% and hypromellose 0.3% eye drops be included for prescribing by optometrists.
- 6.7 The PBAC noted that the Early Supply Rule currently does not apply to any eye drop formulations and considered that carmellose 0.5% and hypromellose 0.3% should also be exempt from the Early Supply Rule.
- 6.8 The PBAC considered, under Section 101(3BA) of the National health Act, 1953 carmellose 0.5% and hypromellose 0.3% and other PBS-listed preservative free multi-dose ocular lubricants should be treated as interchangeable on an individual patient basis.
- 6.9 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**

Recommended

## 7 Recommended listing

Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
CARMELLOSE SODIUM carmellose sodium 0.5% (5 mg/mL) eye drops, 10 mL 0.5% w/v, 10mL	1	5	Evolve® carmellose 0.5%	Contact Lens Centre Australia
HYPROMELLOSE hypromellose 0.3% (3 mg/mL) eye drops, 10 mL 0.3% w/v, 10mL	1	5	Evolve® hypromellose 0.3%	

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input checked="" type="checkbox"/> Optometrists
<b>Severity:</b>	<del>N/A</del> Severe
<b>Condition:</b>	<del>Severe</del> Dry eye syndrome
<b>PBS Indication:</b>	Severe dry eye syndrome
<b>Restriction Level / Method:</b>	<input checked="" type="checkbox"/> Streamlined
<b>Clinical criteria:</b>	Patient must be sensitive to preservatives in multi-dose eye drops.
<b>Administrative Advice:</b>	The in-use shelf life of Evolve® carmellose 0.5% and Evolve® hypromellose 0.3% is 3 months from the date of opening

## 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

Contact Lens Centre Ltd welcomes the PBAC's decision to recommend Evolve eyes drops for Australian patients and looks forward to a PBS listing at the earliest opportunity.