

## 5.17 PERFLUOROHEXYLOCTANE

### Eye drops containing perfluorohexyloctane 1 mL per mL, 3 mL NovaTears<sup>®</sup>, AFT Pharmaceuticals Pty Ltd

#### 1 Purpose of Application

- 1.1 The minor submission requested a General Schedule and an Optometric Schedule Authority Required (STREAMLINED) listing for the treatment of severe dry eye syndrome in patients who are sensitive to preservatives in multi dose eye drops.

#### 2 Requested listing

- 2.1 The submission requested the same PBS listing as sodium hyaluronate and soy lecithin containing formulations.
- 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 Manufacturer	Name and
PERFLUOROHEXYLOCTANE eye drops, 1 mL per 1 mL (100% v/v), 3 mL	1	5	██████*	NovaTears®	AFT Pharmaceuticals Pty Ltd

\* as calculated based on the requested AEMP.

<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
<b>Severity:</b>	Severe
<b>Condition:</b>	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>	<i>The in-use shelf life of Novatear is 6 months from the date of opening.</i>

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input checked="" type="checkbox"/> Optometrists
<b>Severity:</b>	Severe
<b>Condition:</b>	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>	<i>The in-use shelf life of Novatear is 6 months from the date of opening.</i>

*For more detail on PBAC’s view, see section 7 PBAC outcome.*

### **3 Background**

3.1 This drug had not previously been considered by the PBAC.

### **4 Population and disease**

4.1 Dry eye syndrome was defined by the International Dry Eye Workshop (2007) as ‘a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbances and tear-film instability with potential damage to the ocular surface. It is accompanied by increased osmolality of the tear film and inflammation of the ocular surface’<sup>1</sup>. These symptoms can have a considerable impact on patient’s visual function, daily activities and quality of life.

4.2 The submission’s proposed place in therapy for perfluorohexyloctane was as a preservative-free ocular lubricant, for the treatment of severe dry eye syndrome in patients who are sensitive to preservatives. Perfluorohexyloctane can be an alternative option for these patients to manage their dry eye in order to reduce risk of allergies or adverse reactions associated with preservatives.

*For more detail on PBAC’s view, see section 7 PBAC outcome.*

### **5 Comparator**

5.1 The minor submission nominated soy lecithin as the comparator as both products are primarily used for evaporative dry eye syndrome. The Secretariat notes that products containing sodium hyaluronate should also be considered a comparator as they are both preservative free multi-dose ocular lubricants with over 280 doses (per eye) with a 6 month shelf life after opening.

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<sup>1</sup> “The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye Workshop” *The Ocular Surface* ISSN: 1542-0124. 2007;5(2):75-92.

- 5.2 While the PBAC considered that soy lecithin was an appropriate comparator for the submission, the Committee also considered that the other preservative free multi-dose ocular lubricants were also appropriate comparators.

*For more detail on PBAC's view, see section 7 PBAC outcome.*

## **6 Consideration of the evidence**

### ***Sponsor hearing***

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

### ***Consumer comments***

- 6.2 The PBAC noted that there was no consumer comment for this submission.

### ***Clinical trials***

- 6.3 As a minor submission, no clinical trials were presented in the submission.
- 6.4 The submission claimed that the drug is clinically validated by a significant improvement in the signs and symptoms in evaporative dry eye disease and Meibomian Gland Dysfunction (MGD) in trials NT-001 and NT-002. In the pre-PBAC response, the sponsor stated that both studies were published in peer-review journals. The PBAC noted that the both clinical trials are single arm studies which were conducted in Germany and these studies were not independently validated by the Department.

### ***Economic analysis***

- 6.5 The submission did not specify a particular economic analysis, it presented a cost comparison across a number of PBS listed preservative-free ocular lubricants and perfluorohexyloctane (Table 1) with a proposed AEMP of \$ [REDACTED].
- 6.6 The submission stated that due to the nature of packaging of preservative-free ocular lubricant solutions, the majority of PBS listed items are available in single use containers to prevent contamination. The Sponsor stated that single use containers may contain an excess ocular lubricant solution, and are associated with unnecessary wastage and higher treatment costs.

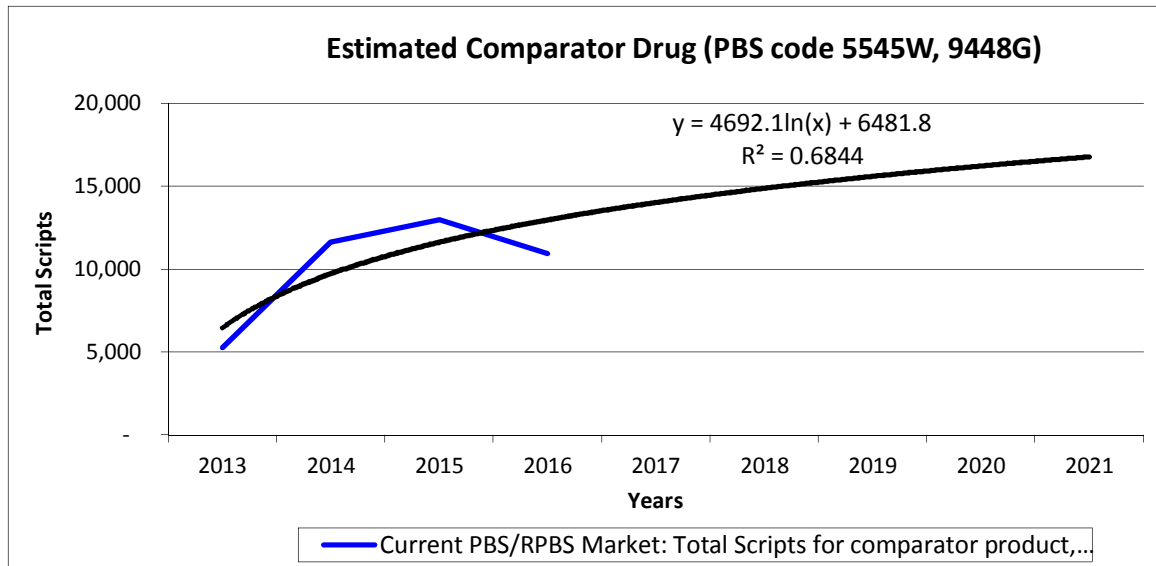
**Table 1. Cost comparison across PBS listed preservative free ocular lubricants and NovaTears®.**

Brand Name	PBS Item number	Form and strength	Packaging	AEMP	Total number of treatments (Both eyes) per pack	Cost per treatment (both eyes) per pack (\$)
Bion Tears	8299T 5521N	Dextran 1mg + Hypromellose 3mg/ml	28 single use containers x 0.4ml each	\$7.72	28	\$0.275
Optifresh Plus	2324H 5505R	Carmellose sodium 1% (4 mg/0.4 mL)	30 single use containers x 0.4ml each	\$6.37	30	\$0.212
Optifresh Tears	2338C 5506T	Carmellose sodium 0.5% (2 mg/0.4 mL)	30 single use containers x 0.4ml each	\$6.37	30	\$0.212
Theratears	8823J 5509Y	Carmellose sodium 0.25% (1.5 mg/0.6 mL)	24 single use containers x 0.6ml each	\$6.53	24	\$0.272
Theratears	8824K 5510B	Carmellose sodium 1% (6 mg/0.6 mL)	28 single use containers x 0.6ml each	\$7.09	24	\$0.295
Viscotears Gel PF	8578L 5504Q	Carbomer-980 0.2%	30 single use containers x 0.6ml each	\$8.00	30	\$0.267
Systane	9170P 5532E	Polyethylene Glycol 400 0.4% + Propylene Glycol 0.3%	28 single use containers x 0.8ml each	\$10.63	28	\$0.400
TearsAgain	5545W 9448G	Soy Lecithin 1% + tocopherol 0.002% + vitamin A pamate 0.025%	Eye Spray, 100 actuations	\$11.39	50	\$0.228
Hyo-Fresh and Hyo-Forte	2171G 2181T 2184Y 2253N	Sodium Hyaluronate 1mg/ml and 2mg/ml	Single drop COMOD value system – 300 drops total	\$22.00	150	\$0.147
NovaTears®		Perfluorohexyloctane (100% v/v) in 3mL sterile bottle	EyeSol® drug delivery technology –280 total single	\$ [REDACTED]	140	\$ [REDACTED]

Source: modified from Table 1 and Table 2, pg 3-4 of the submission

6.7 The Sponsor claimed that there would be a potential PBS cost saving for listing perfluorohexyloctane based on an economic model between perfluorohexyloctane and soy lecithin. The economic model forecasted the perfluorohexyloctane utilisation based on the extrapolation of the Medicare script data for soy lecithin (PBS item 5545W and 944eG) between the year 2013 and 2016 (Figure 1). The submission assumed that 50% of the comparator scripts would be switching to the perfluorohexyloctane.

Figure 1. Forecast utilisation for the nominated comparator, soy lecithin (Sourced from Economic Evaluation Model from the submission)



- 6.8 The PBAC noted that there was an assumption in the submission that perfluorohexyloctane would only replace soy lecithin. The sponsor acknowledged that there are a number of similar products containing different drugs available on the PBS with the same restriction and indication) including ones with a lower cost per treatment than the nominated comparator. This was again acknowledged by the sponsor in its pre-PBAC response.
- 6.9 While the PBAC considered that there was a level of uncertainty in the financial estimates from patients switching between different lubricants, it considered that the cost implications would be minimal.

**Estimated PBS usage & financial implications**

- 6.10 The minor submission estimated a net save to the PBS of less than \$10 million per year 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. This is summarised in Table 2 below based of the expected prescription numbers. The PBAC noted that the Department had identified multiple errors in the economic model of the submission.

**Table 2. Estimated market prescriptions: based on the assumption of 50% for perfluorohexyloctane and 50% for comparator, soy lecithin on PBS**

	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated 50% of soy lecithin PBS scripts (assumed to be substituted by perfluorohexyloctane)	█	█	█	█	█
Original cost of soy lecithin PBS scripts <sup>a</sup>	\$█	\$█	\$█	\$█	\$█
Estimated total cost to the PBS if proposed perfluorohexyloctane <sup>b</sup> recommended	\$█	\$█	\$█	\$█	\$█
<b>Overall cost savings to the PBS</b>	\$█	\$█	\$█	\$█	\$█
Substitution of 50% of soy lecithin RPBS scripts (assumed to be substituted by perfluorohexyloctane)	█	█	█	█	█
Original cost of soy lecithin PBS scripts	\$█	\$█	\$█	\$█	\$█
Estimated total cost to the PBS if proposed perfluorohexyloctane <sup>a</sup> recommended	\$█	\$█	\$█	\$█	\$█
<b>Overall cost savings to the RPBS</b>	\$█	\$█	\$█	\$█	\$█
<b>Overall cost savings to PBS/RPBS</b>	\$█	\$█	\$█	\$█	\$█

<sup>a</sup> the cost was calculated based on a DPMQ of \$20.50 for soy lecithin

<sup>b</sup> the cost was calculated based on a DPMQ of \$█ for perfluorohexyloctane,

Data was modified from the Economic Evaluation Model spreadsheet provided by the submission

- 6.11 The PBAC noted that the DPMQ of soy lecithin in the submitted economic model was \$20.50 (due to errors in the cost calculation in the model), instead of \$35.59 as published in the February 2018 Ex-manufacturer pricing spreadsheet (PBS Pharmaceutical costs workbook from Economic Evaluation Model).
- 6.12 The PBAC noted that the DPMQ of perfluorohexyloctane in the economic model was \$█ (based off an incorrect script correction in the model compounded by the use of an incorrect value for cost of soy lecithin), which was significantly lower than the proposed AEMP of \$█. The model used a script conversion rate (50/140) based off a script for soy lecithin of only one 10 mL container while a script is for a maximum quantity of 2 x 10 mL containers which would result in a script conversion of 100/140).
- 6.13 In the pre-PBAC response, the sponsor acknowledged the above corrections from the Department.
- 6.14 The PBAC noted the Department had adjusted the pricing calculations in the model to reflect the proposed price for perfluorohexyloctane and the published DPMQ for soy lecithin, no adjustment was made for other assumptions in the model. The proposed cost saving to the PBS was reduced by approximately 50% per year (Table 3). The PBAC considered that the Departmental adjusted model was more likely to be an accurate representation of what would be realised in practice.

**Table 3. Adjusted cost saving to the PBS from listing perfluorohexyloctane.**

	Year 1	Year 2	Year 3	Year 4	Year 5
<b>Overall cost savings to the PBS</b>	\$█	\$█	\$█	\$█	\$█
<b>Overall cost savings to the RPBS</b>	\$█	\$█	\$█	\$█	\$█
<b>Overall cost savings to PBS/RPBS</b>	\$█	\$█	\$█	\$█	\$█

<sup>a</sup> the cost was calculated based on a DPMQ of \$35.59 for soy lecithin

<sup>b</sup> the cost was calculated based on a DPMQ of \$ [REDACTED] for perfluorohexyloctane, Data was modified from the Economic Evaluation Model spreadsheet provided by the submission

The redacted tables above show that at Year 5, the estimated number of dispensed scripts was less than 10,000 per year, and the net savings to the PBS would be substantially less than \$10 million per year.

- 6.15 The PBAC also noted that the saving in the proposed financial estimates may have been overestimated, as the submission did not compare perfluorohexyloctane against the drug with the lowest cost per treatment sodium hyaluronate. The substitution of sodium hyaluronate by perfluorohexyloctane would change the proposed cost saving to the PBS however, the magnitude of this change was uncertain. The PBAC considered that there was some uncertainty in regards to patients switching between different lubricants; the Committee considered the cost implications would be minimal.

*For more detail on PBAC's view, see section 7 PBAC outcome.*

## **7 PBAC Outcome**

- 7.1 The PBAC recommended a General Schedule and an Optometric Schedule Authority Required (STREAMLINED) listing of perfluorohexyloctane for the treatment of severe dry-eye syndrome in patients who are sensitive to preservatives in multi-dose eye drops.
- 7.2 The PBAC noted that the submission did not specify the maximum quantity or number of repeats for the proposed restriction. The PBAC considered that the maximum quantity should be consistent with other multi-dose preservative-free ocular lubricants on the PBS with a maximum quantity of 1 and the number of repeats should be limited to 5.
- 7.3 The PBAC considered an additional NOTE stating “The in-use shelf life of Novatears is 6 months from the date of opening” in the restriction would be appropriate, consistent with the PBS restriction for sodium hyaluronate with same shelf life.
- 7.4 The PBAC considered the risk of wastage in the request would be relatively low because patients would be using the drug for a chronic condition.
- 7.5 While the PBAC agreed that there was uncertainty in the financial estimates due to patients switching between different lubricants, it considered the cost implications would be minimal.
- 7.6 The PBAC noted that, at the April 2010 Special PBAC meeting, the Committee had previously recommended that eye lubricants be included for prescribing by nurse practitioners within collaborative arrangements. Hence, the PBAC considered that perfluorohexyloctane was suitable for inclusion in the PBS medicines for prescribing by nurse practitioners within collaborative arrangements

- 7.7 The PBAC noted that the Early Supply Rule currently does not apply to any eye drop formulations and considered that perfluorohexyloctane should also be exempt from the Early Supply Rule.
- 7.8 The PBAC considered, under Section 101(3BA) of the *National Health Act, 1953* perfluorohexyloctane and other PBS-listed preservative free multi-dose ocular lubricants should be treated as interchangeable on an individual patient basis.
- 7.9 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**

Recommended

## 8 Recommended listing

Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
PERFLUOROHEXYLOCTANE eye drops, 1 mL per 1 mL (100% v/v), 3 mL	1	5	NovaTears®	AFT Pharmaceuticals Pty Ltd

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<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>	<i>The in-use shelf life of Novatear is 6 months from the date of opening.</i>

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
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<b>Severity:</b>	Severe
<b>Condition:</b>	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>	<i>The in-use shelf life of Novatears is 6 months from the date of opening.</i>

## 9 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.

## 10 Sponsor's Comment

The sponsor had no comment.