5.13 CICLOSPORIN
Eye drops 1 mg per mL, 2 mL
Vevye®,
AFT Pharmaceuticals (AU) Pty Ltd

1 Purpose of Submission

1.1 The Category 4 submission requested to list a new form of ciclosporin eye drops bottle for the treatment of dry eye disease with keratitis in adult patients whose condition has not been adequately controlled by monotherapy with an artificial tears substitute. The submission proposed listing ciclosporin 1 mg per mL, 2 mL (Vevye) under the same circumstances as the currently PBS-listed Ikervis and Cequa ciclosporin eye drops.

1.2 Listing was requested on the basis of a cost-minimisation basis versus Ikervis and Cequa.

2 Current Situation

2.1 The submission stated that there is considerable variation between patients in terms of tolerability to treatment with the different ciclosporin eye drop formulations. The submissions stated that the water-free vehicle in the Vevye product reduces friction, which reduces instillation site pain and contributes to efficacy and tolerability and that Vevye expands treatment options for patients who cannot tolerate existing PBS-listed therapies.

Registration status

2.2 Vevye was TGA registered on 21 October 2025 for adult patients for the treatment of moderate to severe dry eye disease (keratoconjunctivitis sicca) which has not improved despite treatment with tear substitutes.

Previous PBAC consideration

2.3 Vevye has not been considered by the PBAC previously.

2.4 Ikervis was considered by the PBAC at its March 2021 meeting and was recommended for the treatment of severe keratitis with dry eye disease.

2.5 Cequa was considered by the PBAC at its March 2022 and was recommended for the treatment of chronic severe dry eye disease with keratitis on the basis of a CMA versus Ikervis.

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

3 Requested listing

3.1 The submission proposed for a General Schedule Authority Required (telephone/electronic) listing that aligns with the current PBS restrictions for Ikervis and Cequa. Suggested additions are in italics and removals in strikethrough.

MEDICINAL PRODUCT **medicinal product pack**		**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
CICLOSPORIN						
ciclosporin 0.1% eye drops, 2 mL ~~bottle~~		*NEW*	1	1	5	Vevye
Concept ID (for internal Dept. use)	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)					
	Prescriber type: ☒Medical Practitioners ☒Optometrists					
	Restriction type: ☒Authority Required (telephone/online PBS Authorities system)					
	Prescribing rule					
	Caution: *It is recommended that the potential for immunosuppression with long term use of this drug be clinically reviewed after at least 24 months of treatment, if not already reviewed.*					
	Administrative Advice: *Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.*					
	Indication: Chronic severe dry eye disease with keratitis					
	Treatment Phase: Initial treatment for up to the first 180 days of treatment					
	Clinical criteria:					
	Patient must have a corneal fluorescein staining (CFS) grade of 4 at treatment initiation, using at least one of: (i) the Oxford scale, (ii) the modified Oxford scale, (iii) an equivalent scale to the Oxford scale as determined by the prescriber					
	AND					
	Clinical criteria:					
	Patient must have an ocular surface disease index (OSDI) score of at least 23 at treatment initiation					
	AND					
	Clinical criteria:					
	The condition must be inadequately controlled by monotherapy with a preservative free artificial tears substitute					
	AND					
	Clinical criteria:					
	The treatment must be the sole PBS-subsidised therapy for this condition.					
	Treatment criteria:					
	Patient must be undergoing simultaneous treatment with a preservative free artificial tears substitute					
	AND					
	Treatment criteria:					
	Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist; OR					
	Must be treated by an optometrist in accordance with Optometry Board of Australia guidelines					
	AND					
	Treatment criteria:					

	Patient must not be undergoing treatment with this drug under this treatment phase beyond day 180 of treatment
	Population criteria:
	Patient must be at least 18 years of age
	Prescribing instructions: *Prescribing instruction:* *State in the first authority application for this drug, for the purpose of having a baseline measurement to assess response to treatment under the Continuing treatment listing, each of: (i) the qualifying corneal fluorescein staining grade (a numerical value no less than 4), (ii) the qualifying ocular surface disease index score (a numerical value no less than 23).*
	Administrative Advice: *The Oxford scale, modified Oxford scale and Ocular Surface Disease Index (OSDI) were relied upon in the submission supporting initial PBS listing.* *The Oxford scale uses a chart system consisting of a series of panels, labelled A to E in order of increasing severity. In each chart, staining is represented by dots. To grade staining, comparisons are made between the panels and the appearance of staining on the exposed interpalpebral conjunctiva and cornea of the patient. The details of the chart are presented in Figure 1 and, in a simplified form in Figure 4 (where the criteria, dot count and log columns are not displayed), in the following literature article: Bron A, Evans V, Smith, J. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea. 2003;22(7):640-650.* *The modified Oxford scale is as above, but with the first grade depiction (Grade 0), termed 'Grade 0.5'.* *A list of equivalent scales to the Oxford scale is not provided. Prescribers should be satisfied that a scale other than the Oxford scale, if used, is equivalent to the Oxford scale.* *The Ocular Surface Disease Index (OSDI) is a 12-item questionnaire created by the Outcomes Research Group at Allergan Inc, Irvine, CA, USA, to assess dry eye symptoms and the effects on vision-related function.* *The questionnaire has 3 subscales: ocular symptoms, vision-related function, and environmental triggers. Patients rate their responses on a 0 to 4 scale with 0 corresponding to 'none of the time' and 4 corresponding to 'all of the time'. A final score is calculated which ranges from 0 to 100 with scores 0 to 12 representing normal, 13 to 22 representing mild dry eye disease, 23 to 32 representing moderate dry eye disease, and greater than 33 representing severe dry eye disease.* *The OSDI questionnaire asks the following:* *Presence of ocular symptoms - Have you experienced any of the following during the last week?* *1. Eyes that are sensitive to light* *2. Eyes that feel gritty* *3. Painful or sore eyes* *4. Blurred vision* *5. Poor vision* *Impact on daily activities - Have you had problems with your eyes limited you in performing any of the following during the last week?* *1. Reading* *2. Driving at night* *3. Working with a computer or bank machine (ATM)* *4. Watching TV* *Environmental factors - Have your eyes felt uncomfortable in any of the following situations during the last week?* *1. Windy conditions* *2. Places or areas with low humidity (very dry)* *3. Areas that are airconditioned* *Rate responses on a scale of 0 to 4; 0 = none of the time, 1 = some of the time, 2 = half of the time, 3 = most of the time, and 4 = all of the time.* *Further information on this index is in the following literature article: Walt J, Rowe M, Stern K. Evaluating the functional impact of dry eye: the Ocular Surface Disease Index. Drug Information Journal. 1997;31:1436*

	The 'Dry Eye OSDI 'Questionnaire' app developed by Allergan Inc is available to download for iPhone.
	Administrative Advice: *If the maximum number of repeats stated in this listing is not requested in this application, further supplies can be obtained through this treatment phase listing to continue treatment for up to the first 180 days of treatment, but the OSDI score and CFS grade need not be re-stated. Alternatively, treatment may be continued under the 'Continuing treatment' phase listing, provided the patient meets all eligibility criteria specified in that treatment phase listing.*
Concept ID (for internal Dept. use)	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners ☒Optometrists
	Restriction type: ☒Authority Required (telephone/online PBS Authorities system)
	Indication: Chronic severe dry eye disease with keratitis
	Treatment Phase: Continuing treatment
	Clinical criteria:
	Patient must have received PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	The condition must have improved to an extent that corneal fluorescein staining, using the same scale used at the time of the first authority application, shows an improvement (reduction) by at least 3 grades from baseline (the grade stated in the first authority application) - the improvement need only be demonstrated by staining once only with the first Continuing treatment authority application
	AND
	Clinical criteria:
	The condition must have improved to an extent that the patient's ocular surface disease index score at the time of this authority application, has improved (reduced) by at least 30% compared to the value stated in the first authority application (i.e. baseline)
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised therapy for this condition.
	Treatment criteria:
	Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist; OR
	Must be treated by an optometrist in accordance with Optometry Board of Australia guidelines
	Prescribing instructions: *Prescribing instruction:* *State in the first continuing treatment authority application for this drug:* *(i) an improved corneal fluorescein staining grade (a numerical value that has improved by 3 grades from that provided in the first Initial 1 treatment authority application).* *State in all continuing treatment authority applications:* *(ii) the ocular surface disease index score at the time of this authority application (a numerical value that is at least 30% lower than that stated in the first Initial 1 treatment authority application).*

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

4 Comparator

4.1 The submission nominated Ikervis and Cequa as the comparators.

4.2 The submission presented comparative efficacy information comparing with Vevye with a vehicle (placebo) only. Comparative safety versus Ikervis and Cequa was assessed using the approved TGA Product Information leaflets. The submission presented a cost minimisation approach (CMA) versus Ikervis and Cequa.

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.

Consumer inputs

5.2 The PBAC noted and welcomed the input from one organisation via the Office of Health Technology Assessment Consultation Hub. The input from the National Paediatric Medicines Forum supported the submission and requested an age agnostic listing, noting that children and adolescents are often refractory to the currently available ciclosporin treatments.

Clinical trials

5.3 The submission noted there were no head-to-head randomised trials between Vevye and the PBS-listed comparators, Ikervis and Cequa.

5.4 The submission was based on 2 randomised controlled trials, ESSENCE-1 and ESSENCE-2, and a long-term open-label extension (ESSENCE-2-OLE) that evaluated Vevye ophthalmic solution for moderate to severe dry eye disease compared to a vehicle.

5.5 The ESSENCE-1 Phase 2b/3 trial involved 328 patients in a prospective, 12-week, multicentre, randomised, double-masked, vehicle-controlled clinical study and assessed the efficacy and safety of Vevye applied twice daily compared to a vehicle for the treatment of signs and symptoms of dry eye disease.

5.6 The ESSENCE-2 Phase 3 trial involved 834 patients in a 29-day multicentre, randomised, double-masked, vehicle-controlled clinical study to assess the efficacy, safety and tolerability of Vevye applied twice daily compared to a vehicle for the treatment of signs and symptoms of dry eye disease.

5.7 The ESSENCE-2-OLE Phase 3 open label extension study involved 175 patients in a 52-week prospective, multicentre, open-label, clinical study to demonstrate the long-term safety, tolerability, and efficacy Vevye in patients with dry eye disease.

Table 1: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
ESSENCE-1 NCT03292809	ESSENCE-1 Sheppard et al. A Water-free 0.1% Cyclosporine A Solution for Treatment of Dry Eye Disease: Results of the Randomized Phase 2B/3 ESSENCE Study	January 2021 *Cornea*. 2021; 1;40(10):1290-1297
ESSENCE-2 NCT04523129	ESSENCE-2 Akpek et al. Efficacy and Safety of a Water-Free Topical Cyclosporine, 0.1%, Solution for the Treatment of Moderate to Severe Dry Eye Disease: The ESSENCE-2 Randomized Clinical Trial	May 2023 *JAMA Ophthalmol.* 2023; May 1;141(5):459-466.
ESSENCE-2-OLE NCT04523142	ESSENCE-2-OLE Wirta et al. Long-Term Safety and Efficacy of a Water-Free Cyclosporine 0.1% Ophthalmic Solution for Treatment of Dry Eye Disease: ESSENCE-2 OLE	May 2024 *Cornea* 2024; 21;44(6):692-700.

Source: pp7-9 of the submission.

5.8 The submission's request was based on the outcomes of the ESSENCE-1, ESSENCE-2, and ESSENCE-2-OLE trials only. No comparisons were presented comparing Vevye with the nominated comparators, Ikeris or Cequa.

Comparative effectiveness

5.9 The primary endpoint in both ESSENCE-1 and ESSENCE-2 was the change from baseline in total corneal fluorescein staining (tCFS) score at Day 29 (see **Error! Reference source not found.**).

Table 2: Mean least square change from baseline in total corneal fluorescein straining at Day 29

		Vevye	Vehicle	Difference (95% CI); p-value
ESSENCE-1	Baseline	11.5	11.5	
	Mean LS change at Day 29	-3.5	-2.6	-0.8 (-1.3, -0.4); 0.0002
ESSENCE-2	Baseline	11.5	11.5	
	Mean LS change at Day 29	-3.5	-3.6	-0.4 (-0.8, -0.0); 0.0278

Source: p9 of the Submission
Abbreviations: LS: least squares, CI: confidence interval

5.10 Both trials reported a statistically significant reduction in tCFS at Day 29 in favour of Vevye, with a least square (LS) mean change from baseline of -0.8 (95% CI: -1.3, -0.4) in the ESSENCE-1 trial and -0.4 (95% CI -0.8, -0.0) in the ESSENCE-2 trial.

5.11 The clinical efficacy of Vevye was also assessed using primary symptom endpoints, including ocular surface disease index (OSDI, range 0-100) in ESSENCE-1 and dryness score (visual analogue scale, range 0-100) in ESSENCE- 2. Vevye showed non-statistically significant improvements in both endpoints compared to vehicle.

5.12 ESSENCE-2-OLE did not have primary efficacy endpoints or a control group.

5.13 The submission stated that after 6 months, 86.4% of patients using Vevye experienced a clinically meaningful corneal staining improvement (≥3 grades in tCFS) and a 1% discontinuation rate, compared to 28.6% of patients using Ikervis experiencing a

clinically meaningful improvement (≥2 grades in CFS) and a 10-15% discontinuation rate using Ikervis (based on the SANSIKA trial[1]).

Comparative harms

5.14 Instillation-site pain (7.9%) and blurred vision (0.7%) were the most common ocular-related adverse events (AEs) in ESSENCE-1 and ESSENCE-2. The most common non-ocular AEs were seasonal infections (1.4% nasopharyngitis and 1.4% upper respiratory tract infection). AEs contributed to a discontinuation rate of 1% across the ESSENCE 1 and 2 studies.

5.15 The submission compared rates of instillation-site pain and discontinuation due to AEs for Vevye, Ikervis and Cequa from the relevant Product Information leaflets (see **Error! Reference source not found.**).

Table 3: Rates of instillation-site pain and discontinuation rate due to adverse events of Vevye, Ikervis and Cequa

	Vevye	Ikervis	Cequa
Instillation site pain, %	7.9%	19%	21.8%
Discontinuation rate due to AEs, %	1%	10-15%	4.2%

Source: p10 of the Submission
Abbreviations: AE = adverse event

5.16 Site pain and blurred vision were the most common ocular-related adverse events (AEs) in ESSENCE-1 and ESSENCE-2. The submission stated that Vevye appears to offer a more favourable tolerability profile, which may translate into better patient compliance.

Clinical claims

5.17 The submission claimed that compared to Ikervis and Cequa, Vevye offers comparable efficacy in the treatment of the clinical signs of dry eye disease and may provide improved tolerability, with lower rates of instillation-site pain and treatment discontinuation.

5.18 Noting that no comparative evidence was provided in the submission to support the clinical claim, the PBAC considered that, based on the previous decision that Ikervis was non-inferior to Cequa, it was likely that Vevye was comparable to Ikervis and Cequa in terms of efficacy and safety.

Economic analysis

5.19 The submission presented a simple cost-minimisation approach based on the ex-manufacturer price of Ikervis and Cequa to determine the price of Vevye (**Error! Reference source not found.**). The submission did not present equi-effective doses but assumed that the daily dose of Vevye was equivalent to the daily dose of Ikervis or Cequa. The assumed equi-effective doses were:

[1] Leonardi A, et al. Efficacy and safety of 0.1% cyclosporine A cationic emulsion in the treatment of severe dry eye disease: a multicenter randomized trial. Eur JOphthalmol. 2016;26(4):287-296.

1 mg per mL ciclosporin one drop twice daily (Vevye) =

1 mg per mL ciclosporin one 0.3 mL ampoule (i.e. one drop) once daily (Ikervis) =

900 mcg per mL ciclosporin one 0.25 mL ampoule (i.e. one drop) twice daily (Cequa)

Table 4: Cost-minimisation approach of Vevye vs. Ikervis and Cequa

	Vevye	Ikervis	Cequa
EMP	$61.00 ($60.76)	$65.00	$65.00
Pack size	2 mL	30 x 0.3 mL ampoules	60 x 0.25 mL ampoules
Strength	0.1%	0.1%	0.09%
Daily dose	1 drop twice daily	1 ampoule/drop daily	1 ampoule/drop twice daily
Number of days treatment per supply	28	30	30
Cost per day	$2.18 ($2.17)	$2.17	$2.17

Source: p3 of the submission
Abbreviations: EMP = ex-manufacturer price

5.20 Based on the daily cost of Ikervis and Cequa ($2.17) the EMP of Vevye should be $60.76, rather than the $61.00 proposed in the submission.

Drug cost/patient/year: $1,035.48

5.21 The estimated cost per patient per year of Vevye is $1,035.48 based on a submission's proposed DPMQ of $79.38 and the claim that a patient uses one bottle every 28 days (i.e. $79.38/28 * 365.25).

5.22 The estimated cost per patient per year of Ikervis and Cequa is $1,018.80 (DPMQ of $83.68/30 * 365.25).

Estimated PBS usage and financial implications

5.23 As the price of Vevye was based on a cost minimisation approach to Ikervis and Cequa, the cost to the PBS/RPBS of listing Vevye was expected to be approximately cost-neutral (**Error! Reference source not found.**).

5.24 Utilisation of Ikervis (October 2021 to August 2025) and Cequa (June 2023 to August 2025) was obtained from PBS statistics report and demonstrated sustained and growing demand of ciclosporin eye drops. The submission assumed that Vevye will have a market share of [redacted]% in Year 1, increasing to [redacted]% in Year 6. No further information was provided on the market share approach utilised.

Table 5: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Total ciclosporin scripts dispensed	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Vevye scripts	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]
Estimated financial implications of Vevye						
Cost to PBS/RPBS less co-payments	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]
Estimated treatment replaced						
Cequa	[redacted][6]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Ikervis	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]
Total scripts	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]
Estimated financial implications of treatment replaced						
Cequa	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]
Ikervis	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]
Cost to PBS/RPBS less co-payments	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][5]	-$[redacted][7]
Net financial implications						
Net cost to PBS/RPBS	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]	-$[redacted][7]

Abbreviations: MBS = Medical Benefits Scheme; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

Source: Table 6, p13 of the submission

The redacted values correspond to the following ranges:

[1] *20,000 to < 30,000*

[2] *30,000 to < 40,000*

[3] *500 to < 5,000*

[4] *5,000 to < 10,000*

[5] *$0 to < $10 million*

[6] *< 500*

[7] *net cost saving*

Quality use of medicines

5.25 The submission stated that quality use of medicines will by promoting the safe, effective, and appropriate use of its products through clear, evidence-based information and education for healthcare professionals.

5.26 The submission stated that robust pharmacovigilance systems to monitor adverse events and real-world outcomes, using this data to inform risk management and update product information as needed.

5.27 The submission stated that ongoing collaboration with healthcare providers, regulators, and consumers, will ensure continuous improvement in medicine safety and patient outcomes.

Financial Management – Risk Sharing Arrangements

5.28 There is currently a Risk Sharing Arrangement (RSA) in place for Ikervis and Cequa.

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

6 PBAC Outcome

6.1 The PBAC recommended the listing of ciclosporin eye drops (Vevye) for the treatment of chronic severe dry eye disease with keratitis in adult patients whose condition has not been adequately controlled by monotherapy with an artificial tears substitute. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Vevye would be acceptable if it were cost-minimised against the ciclosporin eye drops that are currently listed on the PBS for the same indication (Ikervis and Cequa). The PBAC advised that Vevye should join the existing risk sharing arrangement (RSA) for ciclosporin eye drops and that there should be no increase to the expenditure caps.

6.2 The PBAC noted the consumer input from the National Paediatric Medicines Forum which requested an age agnostic restriction. However, the PBAC noted that neither the submission nor the TGA Clinical Evaluation Report presented data on the use of Vevye in paediatrics. Further, the PBAC noted that the restrictions for Ikervis and Cequa include a clinical criterion stating that "Patient must be at least 18 years of age". Thus, the PBAC recommended that the restriction should remain limited to adult patients.

6.3 In addition, the PBAC recommended that the General Schedule Authority Required (telephone/electronic) restriction should include the Secretariat suggested changes outlined in Section 3 above.

6.4 The PBAC noted the statement in the submission that there was a clinical need for better tolerated treatments and considered the rationale of enhanced tolerability with the water-free formulation of Vevye to be appropriate. The PBAC considered that the addition of Vevye to the PBS would expand the treatment options for patients who cannot tolerate the existing PBS-listed therapies.

6.5 The PBAC considered that the nominated comparators, Ikervis and Cequa to be appropriate. The PBAC noted the current PBS listed comparators are in the form of single dose ampoules compared to the multi-dose form of Vevye (bottle). The PBAC considered the multi-dose form to be more sustainable than the comparators.

6.6 The PBAC noted that the submission was based on two randomised controlled trials, ESSENCE-1 and ESSENCE-2, and a long-term open-label extension (ESSENCE-2-OLE), that evaluated Vevye ophthalmic solution for moderate to severe dry eye disease compared to a vehicle. The PBAC noted that the submission did not present a treatment comparison versus the nominated comparators, Ikervis and Cequa.

6.7 Although no comparative evidence was presented in the submission, the PBAC considered that, based on the previous decision that Ikervis was non-inferior to Cequa, it was likely that Vevye was comparable to Ikervis and Cequa in terms of efficacy and safety.

6.8 The PBAC accepted the cost minimisation approach presented in the submission and considered that the equi-effective doses were:

1 mg per mL ciclosporin one drop twice daily (Vevye) =

1 mg per mL ciclosporin one 0.3 mL ampoule (i.e. one drop) once daily (Ikervis) =

900 µg per mL ciclosporin one 0.25 mL ampoule (i.e. on drop) twice daily (Cequa)

6.9 In terms of the financial impact of listing Vevye on the PBS, the PBAC agreed with the submission and considered that the listing of Vevye should be approximately cost neutral.

6.10 The PBAC advised that Vevye should join the existing Risk Sharing Arrangement (RSA) for ciclosporin eye drops with no increase to the expenditure caps.

6.11 As Vevye is 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.

6.12 This submission does not meet the criteria for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

7 Recommended listing

7.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
CICLOSPORIN					
ciclosporin 0.1% eye drops, 2 mL	NEW	1	1	5	Vevye
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Optometrists				
	Restriction type: ☒Authority Required (telephone/online PBS Authorities system)				
	Prescribing rule				
	Caution: It is recommended that the potential for immunosuppression with long term use of this drug be clinically reviewed after at least 24 months of treatment, if not already reviewed.				
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.				
	Indication: Chronic severe dry eye disease with keratitis				
	Treatment Phase: Initial treatment for up to the first 180 days of treatment				
	Clinical criteria:				
	Patient must have a corneal fluorescein staining (CFS) grade of 4 at treatment initiation, using at least one of: (i) the Oxford scale, (ii) the modified Oxford scale, (iii) an equivalent scale to the Oxford scale as determined by the prescriber				
	AND				
	Clinical criteria:				
	Patient must have an ocular surface disease index (OSDI) score of at least 23 at treatment initiation				
	AND				
	Clinical criteria:				
	The condition must be inadequately controlled by monotherapy with a preservative free artificial tears substitute				
	AND				
	Clinical criteria:				
	The treatment must be the sole PBS-subsidised therapy for this condition.				
	Treatment criteria:				
	Patient must be undergoing simultaneous treatment with a preservative free artificial tears substitute				
	AND				
	Treatment criteria:				
	Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist; OR				
	Must be treated by an optometrist in accordance with Optometry Board of Australia guidelines				
	AND				
	Treatment criteria:				
	Patient must not be undergoing treatment with this drug under this treatment phase beyond day 180 of treatment				
	Population criteria:				

	Patient must be at least 18 years of age
	Prescribing instructions: Prescribing instruction: State in the first authority application for this drug, for the purpose of having a baseline measurement to assess response to treatment under the Continuing treatment listing, each of: (i) the qualifying corneal fluorescein staining grade (a numerical value no less than 4), (ii) the qualifying ocular surface disease index score (a numerical value no less than 23).
	Administrative Advice: The Oxford scale, modified Oxford scale and Ocular Surface Disease Index (OSDI) were relied upon in the submission supporting initial PBS listing. The Oxford scale uses a chart system consisting of a series of panels, labelled A to E in order of increasing severity. In each chart, staining is represented by dots. To grade staining, comparisons are made between the panels and the appearance of staining on the exposed interpalpebral conjunctiva and cornea of the patient. The details of the chart are presented in Figure 1 and, in a simplified form in Figure 4 (where the criteria, dot count and log columns are not displayed), in the following literature article: Bron A, Evans V, Smith, J. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea. 2003;22(7):640-650. The modified Oxford scale is as above, but with the first grade depiction (Grade 0), termed 'Grade 0.5'. A list of equivalent scales to the Oxford scale is not provided. Prescribers should be satisfied that a scale other than the Oxford scale, if used, is equivalent to the Oxford scale. The Ocular Surface Disease Index (OSDI) is a 12-item questionnaire created by the Outcomes Research Group at Allergan Inc, Irvine, CA, USA, to assess dry eye symptoms and the effects on vision-related function. The questionnaire has 3 subscales: ocular symptoms, vision-related function, and environmental triggers. Patients rate their responses on a 0 to 4 scale with 0 corresponding to 'none of the time' and 4 corresponding to 'all of the time'. A final score is calculated which ranges from 0 to 100 with scores 0 to 12 representing normal, 13 to 22 representing mild dry eye disease, 23 to 32 representing moderate dry eye disease, and greater than 33 representing severe dry eye disease. The OSDI questionnaire asks the following: Presence of ocular symptoms - Have you experienced any of the following during the last week? 1. Eyes that are sensitive to light 2. Eyes that feel gritty 3. Painful or sore eyes 4. Blurred vision 5. Poor vision Impact on daily activities - Have you had problems with your eyes limited you in performing any of the following during the last week? 1. Reading 2. Driving at night 3. Working with a computer or bank machine (ATM) 4. Watching TV Environmental factors - Have your eyes felt uncomfortable in any of the following situations during the last week? 1. Windy conditions 2. Places or areas with low humidity (very dry) 3. Areas that are airconditioned Rate responses on a scale of 0 to 4; 0 = none of the time, 1 = some of the time, 2 = half of the time, 3 = most of the time, and 4 = all of the time. Further information on this index is in the following literature article: Walt J, Rowe M, Stern K. Evaluating the functional impact of dry eye: the Ocular Surface Disease Index. Drug Information Journal. 1997;31:1436 The 'Dry Eye OSDI 'Questionnaire' app developed by Allergan Inc is available to download for iPhone.

	Administrative Advice: If the maximum number of repeats stated in this listing is not requested in this application, further supplies can be obtained through this treatment phase listing to continue treatment for up to the first 180 days of treatment, but the OSDI score and CFS grade need not be re-stated. Alternatively, treatment may be continued under the 'Continuing treatment' phase listing, provided the patient meets all eligibility criteria specified in that treatment phase listing.
	Indication: Chronic severe dry eye disease with keratitis
	Treatment Phase: Continuing treatment
	Clinical criteria:
	Patient must have received PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	The condition must have improved to an extent that corneal fluorescein staining, using the same scale used at the time of the first authority application, shows an improvement (reduction) by at least 3 grades from baseline (the grade stated in the first authority application) - the improvement need only be demonstrated by staining once only with the first Continuing treatment authority application
	AND
	Clinical criteria:
	The condition must have improved to an extent that the patient's ocular surface disease index score at the time of this authority application, has improved (reduced) by at least 30% compared to the value stated in the first authority application (i.e. baseline)
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised therapy for this condition.
	Treatment criteria:
	Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist; OR
	Must be treated by an optometrist in accordance with Optometry Board of Australia guidelines
	Prescribing instructions: Prescribing instruction: State in the first continuing treatment authority application for this drug: (i) an improved corneal fluorescein staining grade (a numerical value that has improved by 3 grades from that provided in the first Initial 1 treatment authority application). State in all continuing treatment authority applications: (ii) the ocular surface disease index score at the time of this authority application (a numerical value that is at least 30% lower than that stated in the first Initial 1 treatment authority application).

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.