5.17 ANIFROLUMAB, Solution for subcutaneous injection 120 mg in 0.8 mL, Saphnelo®, AstraZeneca Pty Ltd.

1 Purpose of submission

1.1 The Category 3 submission requested a Section 85 Authority Required listing for anifrolumab pre-filled pen auto-injector for subcutaneous injection (referred to as anifrolumab SC) for the treatment of adults with severe systemic lupus erythematosus (SLE) and high disease activity despite the standard of care as an alternative to the currently Section 100-listed anifrolumab for intravenous administration (anifrolumab IV).

1.2 Although the dose of anifrolumab SC was higher (480 mg versus 300 mg every four weeks), the SC and IV preparations were considered equivalent by the TGA evaluation.

1.3 Listing was requested on the basis of a cost-equivalence analysis including the administration costs of the IV form to calculate the price per pre-filled pen autoinjector over a 28 day period.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Adult patients with severe SLE with a high degree of disease activity (SLEDAI-2K ≥10) despite SoC (triple therapy)
Intervention	Anifrolumab 120 mg subcutaneous injection every week added to SoC
Comparator	Anifrolumab 300 mg intravenous infusion every four weeks added to SoC
Outcomes	BICLA Response at Week 52 Proportion of Patients who are BICLA Responders at Week 52 and Have Maintained Low (or reduced) OCS Use Through Week 52 Time to BICLA response sustained through Week 52 Time to First Flare through Week 52 OCS Response Annualised flare rate SRI(4) DORIS Remission LLDAS AEs
Clinical claim	Non-inferior effectiveness and safety

Source: Table 1.1, p27 of the submission. BICLA = British Isles lupus assessment group composite lupus assessment; BILAG = British Isles Lupus Assessment Group; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; LLDAS, low lupus disease activity state; OCS = oral corticosteroids; PGA = physician's global assessment; SLE = Systemic Lupus Erythematosus; SLEDIA-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SoC = standard of care; SRI(4) = 4-point reduction on the SLE Responder Index; Q4W = every 4 weeks.

2 Background

Registration status

2.1 Anifrolumab 300 mg vial was TGA-registered on 29 March 2022 for add on treatment of adult patients with moderate to severe, active SLE despite standard therapy. The approved dose is 300 mg given intravenously every 4 weeks. Lupus nephritis and central nervous system lupus were excluded from the approved indications due to a lack of data.[1]

2.2 Anifrolumab SC was TGA-registered on 7 May 2026 for add on treatment of adult patients with moderate to severe, active SLE, despite standard therapy.

2.3 Anifrolumab SC was approved in the European Union in December 2025.

2.4 Anifrolumab SC was not approved by the US FDA in October 2025 because of "critical data quality issues that affect key analyses, including the primary endpoint"[2]. These issues were identified in an amendment "submitted late in the review cycle" (the date is redacted in the published FDA Complete Response letter). The sponsor has stated that it has provided the FDA with a corrected dataset and the re-analyses required for resubmission and that a decision is expected "in the first half of 2026".[3]

2.5 The CSR for the TULIP-SC trial included in the submission was labelled Edition Number 1 and dated 21 October 2025 and was stated by the submission to use a data cut-off date of 23 August 2025. It is not clear whether this document is the original version, the amended version given to the FDA late in the first review cycle, or the corrected version for the FDA resubmission.

Previous PBAC consideration

2.6 Anifrolumab IV for the treatment of SLE was considered by PBAC in July 2022 and March 2023 but not recommended for listing. The PBAC considered that although there appeared to be improvement in some patients, the "magnitude of benefit was modest and uncertain" (Paragraph 7.1, Anifrolumab Public Summary Document [PSD], July 2022 PBAC Meeting; Paragraphs 7.1 and 7.4, Anifrolumab PSD, March 2023 PBAC Meeting).

2.7 In July 2023, the PBAC convened a clinical consultation meeting to seek further information about SLE treatments and the related aspects of clinical efficacy and measures of benefits from treatments. The clinical consultation meeting was attended by clinicians with significant expertise in the management of SLE. The clinicians noted challenges with SLE related to the management and assessment of outcomes, clinical

[1] NCT05138133, a trial of anifrolumab in lupus nephritis is scheduled for completion in early 2027.
[2] https://download.open.fda.gov/crl/CRL_BLA761451_20251010.pdf accessed 20 March 2026.
[3]https://www.astrazeneca.com/media-centre/press-releases/2026/update-on-saphnelo-subcutaneous-administration.html accessed 20 March 2026.

experience with belimumab and anifrolumab and the clinical relevance of Lupus Low Disease Activity State (LLDAS). The clinicians indicated that the achievement and maintenance of LLDAS as a clinical outcome would be relevant for a future PBAC submission to consider and could be incorporated into economic models.

2.8 Anifrolumab IV was recommended for listing in March 2024 after a price reduction and with a Risk Sharing Agreement.

2.9 The PBAC noted that the March 2024 resubmission included data for the outcome of LLDAS not included in the previous submissions and considered that this was clinically meaningful and informative (Paragraph 7.3, Anifrolumab PSD, March 2024 PBAC Meeting).

3 Requested listing

3.1 The submission proposed restrictions for initial treatment in a new patient, initial treatment for a patient changing treatment and for continuing treatment as well as flow-on changes to the restriction of IV anifrolumab to allow for switching between the SC and IV forms.

3.2 The restrictions were modelled on the current Section 100 restriction for anifrolumab.

3.3 The PBAC has previously noted that given only a small subset of SLE patients are expected to meet the proposed eligibility criteria [...] there is potential for use outside of the requested restrictions (Paragraph 3.6, Anifrolumab PSD, July 2022 PBAC Meeting).

3.4 The sponsor's proposed restrictions are presented below. Suggested additions from the Secretariat are in italics and deletions are in strikethrough.

Option 1: Amendments to Sponsor's Proposed Restrictions

Initial Treatment – New Patient (anifrolumab SC)

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
ANIFROLUMAB					
Anifrolumab 120 mg/0.8 mL pre-filled pen	NEW	4	4	5	Saphnelo
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Benefit type: ☒Authority Required (FULL assessment) in writing only via post/HPOS upload)				
	Prescribing rule level:				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
	Restriction Summary / Treatment of Concept				
	Indication: Systemic lupus erythematosus				
	Treatment Phase: Initial Treatment				
	Clinical Criteria				

	Patient must have a confirmed and documented diagnosis of systemic lupus erythematosus (SLE) according to the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) SLE Classification Criteria 2019
	AND
	Clinical Criteria
	Patient must have persistent disease activity as supported by a SLE Disease Activity Index 2000 (SLEDAI-2K) score of at least 10 points
	AND
	Clinical Criteria
	Patient must be currently receiving hydroxychloroquine, with treatment received for at least 12 weeks, unless contraindicated/intolerant necessitating treatment withdrawal
	AND
	Clinical Criteria
	Patient must be currently receiving immunosuppressant medication, with treatment received for at least 12 weeks, with either: (i) minimum dose of methotrexate 20 mg per week, (ii) azathioprine 100 mg per day, (iii) mycophenolate 1,000 mg per day unless contraindicated/intolerant necessitating treatment withdrawal
	AND
	Clinical Criteria
	Patient must be currently receiving prednisolone or equivalent of at least 7.5 mg per day, with treatment received for at least 4 weeks, unless contraindicated/intolerant necessitating treatment withdrawal
	AND
	Clinical Criteria
	Patient must not have either: (i) severe active lupus nephritis, (ii) severe active central nervous system systemic lupus erythematosus
	Treatment Criteria
	Must be treated by a specialist physician experienced in the management of this condition
	Prescribing Instructions If prednisolone or equivalent is contraindicated according to the Therapeutic Goods Administration (TGA)-approved Product Information or cannot be tolerated of at least 7.5 mg per day, the patient must have received at least 12 weeks of continuous treatment with each of at least 2 of the following: (i) hydroxychloroquine; (ii) methotrexate at a dose of at least 20 mg per week; (iii) azathioprine at a dose of at least 100 mg per day; (iv) mycophenolate at a dose of at least 1,000 mg per day. Where two of: (i) hydroxychloroquine; (ii) methotrexate at a dose of at least 20 mg per week; or (iii) azathioprine at a dose of at least 100 mg per day; (iv) mycophenolate at a dose of at least 1,000 mg per day, are either contraindicated according to the relevant TGA-approved Product Information or cannot be tolerated at the doses specified above in addition to having a contraindication or intolerance to prednisolone or equivalent: at least one of the remaining tolerated therapies must be trialled at a minimum dose as mentioned above. If the patient has a contraindication/severe intolerance to each of: (i) prednisolone or equivalent of at least 7.5 mg per day; (ii) hydroxychloroquine; (iii) methotrexate at a dose of at least 20 mg per week; (iv) azathioprine at a dose of at least 100 mg per day; (v) mycophenolate at a dose of at least 1,000 mg per day; in such cases, provide details for each of the contraindications/severe intolerances claimed in the authority application.

	Prescribing Instructions The authority application must be made in writing via HPOS form upload or mail and must include: (a) details of the ACR/EULAR SLE Classification Criteria 2019 confirming diagnosis of SLE; (b) details (date and score) of the completed SLEDAI-2K score sheet; (c) details of current systemic therapy used (dosage, date of commencement and duration of therapy including prior anifrolumab use); (d) details of contraindication/intolerances to prior therapies (drug name, the degree of toxicity and dose). All the reports must be documented in the patient's medical records.
	Prescribing Instructions If the application is submitted through HPOS form upload or mail, it must include: (i) ~~A completed authority prescription form~~ *details of the proposed prescription*; and (ii) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Administrative Advice SLEDAI-2K can be accessed via Gladman 2002 J. Rheumatol. 29 (2) 288-291 or from AstraZeneca Medical Information on 1800 805 342.
	Administrative Advice Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001

Continuing Treatment (anifrolumab SC)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ANIFROLUMAB					
Anifrolumab 120 mg/0.8 mL pre-filled pen	NEW	4	4	5	Saphnelo
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Benefit type: ☒ Authority required (Telephone/Online PBS Authorities immediate assessment)				
	Prescribing rule level:				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
	Restriction Summary / Treatment of Concept				
	Indication: Systemic lupus erythematosus				
	Treatment Phase: Continuing or recommencement of treatment (within 12 months of a treatment break)				
	Clinical Criteria				
	Patient must have previously been issued with an authority prescription for this drug for this condition				
	AND				

	Clinical Criteria
	Patient must be responding to treatment if they have received less than 12 months of treatment with this drug for this condition; OR
	Patient must have attained a Lupus Low Disease Activity State (LLDAS) and maintained this state while on treatment
	Treatment Criteria
	Must be treated by a specialist physician experienced in the management of this condition
	Prescribing Instructions Lupus Low Disease Activity State (LLDAS) is defined as: (a) Total SLEDAI-2K of not greater than 4, with no major activity in major organ systems (renal, central nervous system (CNS), cardiopulmonary, vasculitis, fever); and (b) No new features of lupus disease activity compared with the previous assessment, and (c) Physician Global Assessment (PGA) of not greater than 1, and (d) Current prednisolone (or equivalent) dose of not greater than 7.5 mg daily, and (e) Well tolerated standard maintenance doses of anti-malarial and immunosuppressive drugs are allowed.
	Prescribing Instructions Where retreatment with anifrolumab after a break in PBS-subsidised treatment with anifrolumab is being sought, the date of cessation of the previous treatment course with anifrolumab must be included in the application. Recommencement of treatment with anifrolumab for severe SLE is within 12 months from the date that treatment was ceased.
	Administrative Advice SLEDAI-2K can be accessed via Gladman 2002 J. Rheumatol. 29 (2) 288-291 or from AstraZeneca Medical Information on 1800 805 342.
	Administrative Advice PGA can be accessed via Petri 2005 N Engl J Med 353: 2550-8.
	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 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

Change/Switch from anifrolumab IV to anifrolumab SC (after initial phase)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ANIFROLUMAB					
Anifrolumab 120 mg/0.8 mL pre-filled pen	NEW	4	4	5	Saphnelo
	Category / Program: ☒ Section 85 – General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Benefit type: ☒ Authority required ~~(Telephone/Online PBS Authorities immediate assessment)~~ *(FULL assessment) in writing only via post/HPOS upload)*				
	Authority type: ☒ Complex Authority Required (CAR)				
	Prescribing rule level:				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				

	Restriction **Summary / Treatment of Concept**
	Indication: Systemic lupus erythematosus
	Treatment Phase: ~~Initial treatment (CHANGE treatment)~~ *Change in route of administration following initial treatment with intravenous anifrolumab (i.e. switching from intravenous anifrolumab to subcutaneous anifrolumab)*
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with intravenous anifrolumab (300 mg/2 mL injection) for this condition
	AND
	Clinical criteria:
	Patient must be responding to treatment if they have received less than 12 months of treatment with intravenous anifrolumab (300 mg/2 mL injection) for this condition; OR
	Patient must have attained a Lupus Low Disease Activity State (LLDAS) and maintained this state while on treatment with intravenous anifrolumab (300 mg/2 mL injection) for this condition
	Treatment criteria:
	Must be treated by a specialist physician experienced in the management of this condition
	Prescribing Instructions *Lupus Low Disease Activity State (LLDAS) is defined as:* *(a) Total SLEDAI-2K of not greater than 4, with no major activity in major organ systems (renal, central nervous system (CNS), cardiopulmonary, vasculitis, fever); and* *(b) No new features of lupus disease activity compared with the previous assessment, and* *(c) Physician Global Assessment (PGA) of not greater than 1, and* *(d) Current prednisolone (or equivalent) dose of not greater than 7.5 mg daily, and* *(e) Well tolerated standard maintenance doses of anti-malarial and immunosuppressive drugs are allowed.*
	Administrative Advice *SLEDAI-2K can be accessed via Gladman 2002 J. Rheumatol. 29 (2) 288-291 or from AstraZeneca Medical Information on 1800 805 342.*
	Administrative Advice *PGA can be accessed via Petri 2005 N Engl J Med 353: 2550-8.*
	Prescribing Instructions: The authority application must be made in writing via HPOS form upload or mail and must include: (a) details of the ACR/EULAR SLE Classification Criteria 2019 confirming diagnosis of SLE; (b) details (date and score) of the completed SLEDAI-2K score sheet; (c) details of current systemic therapy used (dosage, date of commencement and duration of therapy including prior anifrolumab use); (d) details of contraindication/intolerances to prior therapies (drug name, the degree of toxicity and dose). All the reports must be documented in the patient's medical records.
	Prescribing Instructions: If the application is submitted through HPOS form upload or mail, it must include: (i) ~~A completed authority prescription form~~ *details of the proposed prescription*; and (ii) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice). (iii) the details of prior biological medicine treatment including the details of date and duration of treatment.

	Administrative Advice Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001

3.5 The Secretariat noted that the 'change/switch from anifrolumab IV to anifrolumab SC' restriction is requested as Authority Required (Telephone/Online). The submission stated that this restriction is based on the continuing treatment restriction (which is a telephone/online authority), however the Secretariat proposed Full written authority as the prescribing instructions are based on a written authority restriction.

3.6 The Secretariat noted that the TGA Product Information (PI) states the following:

'Transitioning between routes of administration

- If transitioning a patient from intravenous administration to subcutaneous administration, the first subcutaneous injection should be administered approximately 2 weeks after the last intravenous dose.
- If transitioning a patient from subcutaneous administration to intravenous administration, the first intravenous infusion should be administered approximately 3 to 4 weeks after the last subcutaneous dose.'

As such, the Secretariat considered that it may be inappropriate to describe the treatment phase as 'initial' treatment with respect to the 'change/switch from anifrolumab IV to anifrolumab SC' restriction.

3.7 The submission also stated that patients only have one opportunity to achieve and maintain a response to treatment with anifrolumab (regardless of mode of administration). The Secretariat considered that if a patient can swap only after completing initial treatment with anifrolumab IV, and the patient must have demonstrated a response in order to be allowed to switch, then the treatment phase should be amended to:

'Change in route of administration following initial treatment with intravenous anifrolumab (i.e. switching from intravenous anifrolumab to subcutaneous anifrolumab)'

3.8 The submission stated that a flow on change to anifrolumab IV listings on the PBS is proposed to allow for switching between anifrolumab SC and anifrolumab IV. The submission proposed that an initial restriction be added to the PBS which allows switching from anifrolumab SC to anifrolumab IV consistent with the switching restriction from IV to SC.

Change/Switch from anifrolumab SC to anifrolumab IV

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ANIFROLUMAB					
Anifrolumab 300 mg/2 mL injection	NEW (Public) NEW (Private)	1	1	5	Saphnelo
	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)				
	Prescriber type: ☒Medical Practitioners				
	Benefit type: ☒ Authority required ~~(Telephone/Online PBS Authorities immediate assessment)~~ *(FULL assessment) in writing only via post/HPOS upload)*				
	Authority type: ☒ Complex Authority Required (CAR)				
	Prescribing rule level:				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
	Restriction Summary / Treatment of Concept				
	Indication: Systemic lupus erythematosus				
	Treatment Phase: ~~Initial treatment (CHANGE treatment)~~*Change in route of administration following initial treatment with subcutaneous anifrolumab (i.e. switching from subcutaneous anifrolumab to intravenous anifrolumab)*				
	Clinical criteria:				
	Patient must have received prior PBS-subsidised treatment with subcutaneous anifrolumab (120 mg/0.8 mL pre-filled pen) for this condition				
	AND				
	Clinical criteria:				
	Patient must be responding to treatment if they have received less than 12 months of treatment with subcutaneous anifrolumab (120 mg/0.8 mL pre-filled pen) for this condition; OR				
	Patient must have attained a Lupus Low Disease Activity State (LLDAS) and maintained this state while on treatment with subcutaneous anifrolumab (120 mg/0.8 mL pre-filled pen) for this condition				
	Treatment criteria:				
	Must be treated by a specialist physician experienced in the management of this condition				
	Prescribing Instructions *Lupus Low Disease Activity State (LLDAS) is defined as:* *(a) Total SLEDAI-2K of not greater than 4, with no major activity in major organ systems (renal, central nervous system (CNS), cardiopulmonary, vasculitis, fever); and* *(b) No new features of lupus disease activity compared with the previous assessment, and* *(c) Physician Global Assessment (PGA) of not greater than 1, and* *(d) Current prednisolone (or equivalent) dose of not greater than 7.5 mg daily, and* *(e) Well tolerated standard maintenance doses of anti-malarial and immunosuppressive drugs are allowed.*				
	Administrative Advice *SLEDAI-2K can be accessed via Gladman 2002 J. Rheumatol. 29 (2) 288-291 or from AstraZeneca Medical Information on 1800 805 342.*				
	Administrative Advice *PGA can be accessed via Petri 2005 N Engl J Med 353: 2550-8.*				

	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 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).*
	Prescribing Instructions: *The authority application must be made in writing via HPOS form upload or mail and must include:* *(a) details of the ACR/EULAR SLE Classification Criteria 2019 confirming diagnosis of SLE;* *(b) details (date and score) of the completed SLEDAI-2K score sheet;* *(c) details of current systemic therapy used (dosage, date of commencement and duration of therapy including prior anifrolumab use);* *(d) details of contraindication/intolerances to prior therapies (drug name, the degree of toxicity and dose).* *All the reports must be documented in the patient's medical records.*
	Prescribing Instructions: If the application is submitted through HPOS form upload or mail, it must include: (i) ~~A completed authority prescription form~~ *details of the proposed prescription*; and (ii) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice). (iii) the details of prior biological medicine treatment including the details of date and duration of treatment.
	Administrative Advice Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001

3.9 The Secretariat noted the TGA PI and its advice regarding transitioning between routes of administration and considered that it may be inappropriate to describe the treatment phase as 'initial' treatment with respect to the 'change/switch from anifrolumab SC to anifrolumab IV' restriction.

3.10 As the 'change/switch from anifrolumab IV to anifrolumab SC' restriction is based on the continuing treatment restriction, the submission stated that switching patients must meet the same criteria as continuing patients (e.g. patients must be responding to treatment if they have received less than 12 months of treatment, or have attained and maintained an LLDAS while on treatment). If this is the intended approach, the Secretariat considered that a separate switch treatment phase may not be required. Patients receiving continuing treatment with anifrolumab IV could access the proposed anifrolumab SC continuing treatment listing, and vice versa, as the relevant clinical criterion (concept ID 10971) refers broadly to a previous authority prescription "for this drug" and does not specify the route of administration.

	Clinical Criteria

	Patient must have previously been issued with an authority prescription **for this drug** for this condition

3.11 Alternatively, if switching during initial treatment is intended, an additional set of restrictions would be required for both forms of anifrolumab. The Secretariat noted this would need to be structured as a Balance of Supply listing, allowing patients to access the balance of up to six months of treatment to complete the initial treatment phase, as shown in the alternative restriction option below (option 2 restrictions).

Option 2: Secretariat Proposed Restrictions (if switching is permitted during initial and continuing treatment)

Switching during continuing treatment occurs within the continuing treatment phase (no requirement for an additional switch treatment phase); switching during initial treatment would require a Balance of Supply option.

Balance of supply for Initial Treatment (Change/Switch from anifrolumab IV to anifrolumab SC)

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
ANIFROLUMAB					
Anifrolumab 120 mg/0.8 mL pre-filled pen	NEW	4	4	5	Saphnelo

	Category / Program: Section 85 – General Schedule (Code GE)
	Prescriber type: Medical Practitioners
	Benefit type: Authority required (Telephone/Online PBS Authorities immediate assessment)
	Authority type: Complex Authority Required (CAR)
	Prescribing rule level:
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Restriction Summary / Treatment of Concept
	Indication: Systemic lupus erythematosus
	Treatment Phase: Balance of Supply - Change in route of administration (i.e. switching from intravenous anifrolumab to subcutaneous anifrolumab)
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with intravenous anifrolumab (300 mg/2 mL injection) for this condition
	AND
	Clinical criteria:

	Patient must have received insufficient therapy with this drug for this condition under the Initial restriction to complete 24 weeks treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restrictions
	Treatment criteria:
	Must be treated by a specialist physician experienced in the management of this condition
	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 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

Balance of supply for Initial Treatment (Change/Switch from anifrolumab SC to anifrolumab IV)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ANIFROLUMAB					
Anifrolumab 300 mg/2 mL injection	NEW (Public) NEW (Private)	1	1	5	Saphnelo

	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒Medical Practitioners
	Benefit type: ☒ Authority required (Telephone/Online PBS Authorities immediate assessment)
	Authority type: ☒ Complex Authority Required (CAR)
	Prescribing rule level:
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Restriction Summary / Treatment of Concept
	Indication: Systemic lupus erythematosus
	Treatment Phase: Balance of Supply - Change in route of administration (i.e. switching from subcutaneous anifrolumab to intravenous anifrolumab)
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with subcutaneous anifrolumab (120 mg/0.8 mL pre-filled pen) for this condition
	AND
	Clinical criteria:
	Patient must have received insufficient therapy with this drug for this condition under the Initial restriction to complete 24 weeks treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restrictions

	Treatment criteria:
	Must be treated by a specialist physician experienced in the management of this condition
	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 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

4 Population and disease

4.1 SLE is a complex, chronic autoimmune disease with diverse clinical manifestations and a fluctuating and unpredictable course. The disease may involve muscles and joints, skin, gastrointestinal tract, kidneys, brain, and heart and blood vessels. Constitutional symptoms include fatigue, fever, malaise, arthralgia, myalgia, headache and weight loss. Mortality rates are two to three times higher than those of the general population and maternal and foetal outcomes of pregnancy are adversely affected.

4.2 The prevalence of SLE is of the order of 0.1% of the population. SLE is about ten times more common in females than in males and is more common and more severe in Aboriginal and Torres Strait Islander people and Asians. Onset is typically in early adult life, but SLE also affects children, in whom it is more often severe, and older adults. Of the order of one third of Australian patients have disease severe enough to satisfy the PBS criteria for use of anifrolumab, as judged by treatment with antimalarials + steroids + one of azathioprine, methotrexate, ciclosporin, mycophenolate, or tacrolimus (Ciciriello, 2023).

4.3 The cause of SLE is unknown, but autoantibody production and regulation are abnormal. Among the factors leading to autoantibody production is over-production of tissue necrosis factor (TNF), interleukin-1, B cell activating factor (BAFF), and Type I interferons (IFN- α and IFN-β), which promote survival of autoreactive B cells.

4.4 Anifrolumab is an antibody to Type I IFN receptors. Type I IFN are important in control of viral infections and may play a role in tumour surveillance, and malignancy and infections are possible risks of treatment.

4.5 The proposed algorithm differs from the current algorithm only in adding anifrolumab 120 mg weekly SC as an alternative to anifrolumab 300 mg 4 weekly IV. Both algorithms assume that anifrolumab is the only option when disease is not controlled by anti-malarial + steroid + immunosuppressant, which does not reflect Australian practice (Ciciriello, 2023). The anifrolumab IV submissions had noted that for a subset of patients, belimumab and/or off-label rituximab may also be treatment options, however the IV submissions defined these treatments as outside preferred 'standard of care' (comprising triple therapy with hydroxychloroquine + immunosuppressant + prednisone). The PBAC considered that triple therapy was the appropriate comparator for its consideration of anifrolumab IV (Paragraph 5.2, Anifrolumab PSD, March 2024 PBAC Meeting).

5 Comparator

5.1 The nominated comparator was anifrolumab IV.

5.2 Rituximab (off-label) and belimumab could potentially be considered as comparators. Belimumab and rituximab are recommended for refractory SLE by the 2023 EULAR guidelines relied on by the submission (Fanouriakis, 2023).

5.3 Rituximab is a CD20 antagonist and depletes B cells. Rituximab is not TGA-approved for SLE but off-label use was recorded in the OPAL dataset (Table 3, Ciciriello, 2023), and it has an unrestricted PBS listing. For these reasons its use is likely to be displaced by PBS-listing of anifrolumab SC and it may be considered a potential comparator.

5.4 Belimumab is an inhibitor of BAFF, and is TGA-approved for the same indication as anifrolumab; it was not recommended for listing for the treatment of SLE by PBAC because it was too expensive, although when considering anifrolumab the committee noted that its efficacy was similar to that of anifrolumab (Paragraphs 6.15, 6.16, Anifrolumab PSD, March 2023 PBAC Meeting). No patients in the OPAL dataset were reported as using belimumab (Table 3, Ciciriello, 2023) but it may be used in public hospitals.[4]

5.5 Obinutuzumab could potentially be considered as a near-market comparator. Obinutuzumab is also a CD20 antagonist, but it more effectively depletes B cells and causes fewer infusion reactions than rituximab.[5] It is effective in lupus nephritis and in active SLE.[6,7] Obinutuzumab is TGA-approved and PBS-listed for chronic lymphocytic leukemia and follicular lymphoma. Obinutuzumab is TGA-approved for the treatment of lupus nephritis and was recommended for PBS listing at the March 2026 PBAC meeting (PBAC Outcomes, March 2026 Meeting).

5.6 In the context of the cost-minimisation approach taken by the submission, a further consideration for PBAC is that, under Section 101(3B) of the National Health Act 1953, when the proposed medicine is substantially more costly than an alternative therapy, the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy. If the committee is so satisfied, it must make a statement to this effect.

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[4]https://au.gsk.com/en-au/media/press-releases/new-medicine-for-lupus-now-available-in-australia/ accessed 21 March 2026.

[5] Wallace DJ, Systemic lupus erythematosus in adults: Overview of the management and prognosis. In: Connor RF, ed, UpToDate, Wolters Kluwer, accessed 21 March 2026.

[6] Furie RA, Rovin BH, Garg JP, et al. Efficacy and safety of obinutuzumab in active lupus nephritis. *N Engl J Med* 2025; 392:1471.

[7] Furie RA, Dall'Era M, Vital EM, et al. Efficacy and safety of obinutuzumab in active systemic lupus erythematosus. *N Engl J Med* 2026; doi/full/10.1056/NEJMoa2516150.

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer inputs

6.2 The PBAC noted and welcomed the input from individuals (8), health care professionals (5) and organisations (4) via the Office of Health Technology Assessment Consultation Hub. Access and equity were key themes across input; the SC formulation is expected to improve access by reducing reliance on hospital-based infusion services, supporting rural and regional patients, lessening financial and transport burden, and freeing infusion capacity for patients with more complex needs.

6.3 The PBAC noted the input received from the Australasian Society of Clinical Immunology and Allergy (ASCIA) that stated the SC form of anifrolumab should: enable patients with severe SLE to be treated in the home, which will result in cost savings to the patient and the health system; and facilitate optimal and timely treatment of patients with severe SLE and therefore reduce costs due to delayed and inadequate treatment.

Clinical trials

6.4 The submission was based on the TULIP-SC trial comparing anifrolumab SC to placebo (N = 367) and an indirect treatment comparison (ITC) using the placebo-controlled trials of anifrolumab IV, TULIP-1 and TULIP-2. The TULIP-1 and TULIP-2 trials were reviewed by PBAC when it considered anifrolumab IV (July 2022, March 2023, March 2024). Details of the trials presented in the submission are provided in Table 2.

6.5 The submission stated that because PBAC has reviewed the TULIP-1 and TULIP-2 trials recently the data from these studies were not presented in the submission. However, the TULIP-1 and 2 results used for the ITC were from an individual patient meta-analysis and differed from those of the pooled analysis using aggregate data seen previously by PBAC.

6.6 Pharmacokinetic data and dose-response data from TULIP-1 and 2 and TULIP-SC were presented in the submission to support the claim of non-inferior efficacy. The submission noted that the TGA evaluation considered that because what was proposed was a new route of administration (SC) and dosing regimen without changing the formulation or indication, only limited pharmacokinetic and pharmacodynamic data were required for registration purposes.

6.7 The patients in all three TULIP trials had less severe disease than the PBS-eligible population: SLEDAI-2K had to be ≥6 rather than ≥10, and only one of corticosteroids, antimalarials or immunosuppressants had to be used, rather than all three. In TULIP-1 and 2, 149/726 (20.5%) patients and in TULIP-SC 88/367 (23.9%) met the PBS eligibility criteria.

6.8 Two possibly relevant studies, NCT02962960 and NCT01438489, were excluded.

6.9 NCT02962960 was a Phase 2 study comparing anifrolumab SC 150 mg q2wk and 300 mg q2wk with placebo. The submission stated that this study was excluded because it used the wrong dose - i.e., neither 300 mg q4wk nor 120 mg weekly. The study was small (N = 36), required a high Type I interferon gene signature, used a different clinical eligibility criterion to the TULIP trials, was double-blind only for the first 12 weeks, and included a corticosteroid taper beginning at 12 weeks. The exclusion of this study was reasonable.

6.10 NCT01438489 (MUSE) was a randomised controlled trial (N = 305) with similar eligibility criteria to the TULIP trials comparing anifrolumab 300 mg or 1000 mg 4 weekly with placebo. MUSE was presented in the anifrolumab submissions considered by PBAC, but it was not referred to in the present submission and no reason for its exclusion was offered. Exclusion of MUSE was not appropriate, but it is unlikely that its inclusion in the ITC would have had any material impact on the result.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
TULIP-SC NCT04877691	A Multicentre, Randomised, Double-blind, Placebo-controlled, Phase 3 Study Evaluating the Efficacy and Safety of Subcutaneous Anifrolumab in Adult Patients with Systemic Lupus Erythematosus.	21 October 2025
	Manzi S, Bruce I, Morand E, et al. Efficacy and safety of subcutaneous anifrolumab in systemic lupus erythematosus: the randomized, Phase 3, TULIP-SC study.	*Arthritis & Rheumatology* 2025; https://doi.org/10.1002/art.70041.

Source: Table 2-3, p49 of the submission.

6.11 The key features of the included trials, including those previously reviewed by the PBAC, are summarised in Table 3.

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use
Anifrolumab SC vs Placebo						
TULIP-SC	367	R 1:1 vs placebo, DB, MC, 52 wk + OLE 52 wk with ANI	Low	Age 18-70; autoantibody positive; SLEDAI-2K ≥6; treated with OCS ≥7.5 mg/day **or** antimalarials **or** immunosuppressant;	Primary: BICLA response at 52 wk Secondary: % BICLA responders; % reduced OCS; time to flare.	ITC compared TULIP-1 and 2 with TULIP-SC, using the placebo arms as common comparator.
Anifrolumab IV vs Placebo						
TULIP-1	457	R 2:1:2 placebo, ANI 150 mg or ANI 300 mg q4wk, MC, DB; 52 wk	Unclear	Age 18-70, SLEDAI-2K ≥6, autoantibody positive; treated with OCS **or** antimalarials **or** immunosuppressant	Primary: SRI(4) at 52 wk Secondary: OCS dose; flare rate; BICLA	IP meta-analysis of data for 300 mg q4wk and TULIP-2 outcomes used for ITC.
TULIP-2	362	R 1:1 ANI 300 mg or placebo q4wk; MC; DB; 52 wk	Unclear	Age 18-70, SLEDAI-2K ≥6, autoantibody positive; treated with OCS ≥ **or** antimalarials **or** immunosuppressant	Primary: BICLA at 52 wk Secondary: OCS dose; flare rate; SRI(4)	

Source: Manzi, 2025; Table 3, Anifrolumab PSD, July 2022 PBAC Meeting
ANI = anifrolumab; BICLA = British Isles Lupus Assessment Group-2004-based Combined Lupus Assessment; DB = double-blind; IP = individual patient; ITC = indirect treatment comparison; MC = multi-centre; OCS = oral corticosteroid; OLE = open-label extension; R = randomised; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SRI(4) = Systemic Lupus Erythematosus Responder Index of ≥ 4.

6.12 Baseline characteristics were well-matched between the anifrolumab-treated and placebo-treated groups.

Comparative effectiveness

6.13 The outcomes used in the trials were those previously considered by the PBAC. Efficacy results for TULIP-SC are shown in Table 4.

Table 4: Efficacy outcomes for TULIP-SC

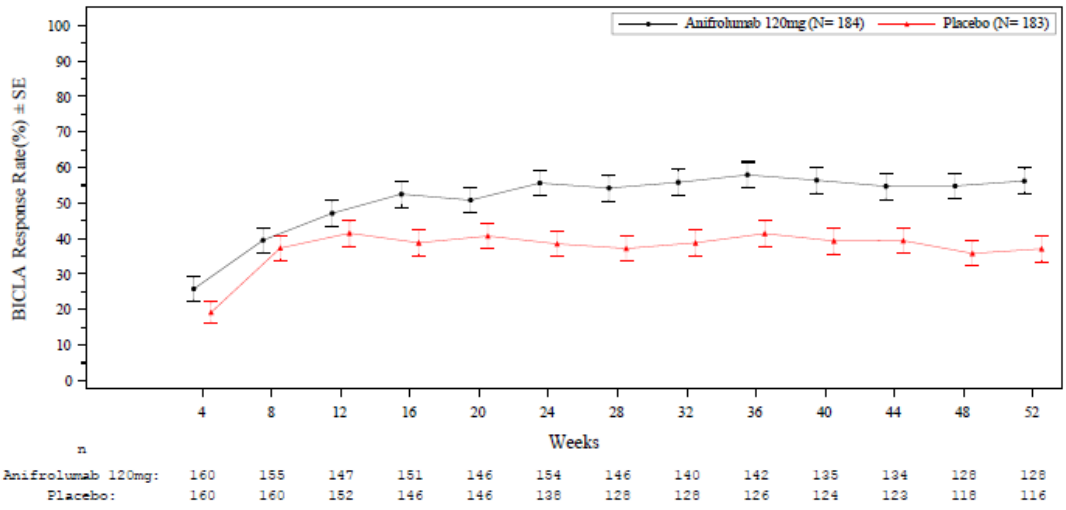
	Anifrolumab 120 mg weekly N = 184	Placebo N = 183
BICLA response at 52 weeks, n (%)	103 (56.2%)	68 (37.1%)
Difference (95% CI) in BICLA response rate	**19.1 (9.0, 29.2)**	-
BICLA response at 52 weeks in patients with baseline SLEDAI-2K ≥10, n/N (%)	72/125 (57.9%)	45/125 (35.9%)
Difference (95% CI) in BICLA response rate	**22.1 (9.9, 34.2)**	-
BICLA response at 52 weeks in patients with baseline SLEDAI-2K <10, n/N (%)	31/59 (52.6%)	23/58 (39.7%)
Difference (95% CI) in BICLA response rate	12.9 (-5.3, 31.1)	-
BICLA response at 52 weeks for Asian patients, n/N (%)	7/17 (39.1%)	6/15 (40.0%)
BICLA response at 52 weeks for Black patients, n/N (%)	4/10 (40%)	3/7 (37.1%)
BICLA response before 52 weeks sustained to 52 weeks, n (%)	76 (41.3%)	40 (21.9%)
Hazard Ratio (95% CI)	**2.16 (1.48, 3.20)**	-
LLDAS at 52 weeks, n (%)	74 (40.2%)	48 (26.2%)
Difference (95% CI) in LLDAS response rate	**14.1 (4.6, 23.6)**	-

	Anifrolumab 120 mg weekly N = 184	Placebo N = 183
DORIS remission, n (%)	53 (28.8%)	27 (14.7%)
Difference (95% CI) in DORIS rate	**14.2 (5.6, 22.8)**	-
Subjects with Flare, n (%)	74 (40.2%)	87 (47.5%)
Hazard Ratio (95% CI)	0.76 (0.55, 1.03)	-
Flares, events/years of exposure	90/158	110/151
Flare rate (95% CI) events/year	0.60 (0.47, 0.76)	0.76 (0.61, 0.95)
Rate Ratio (95% CI)	0.78 (0.57, 1.08)	-

Source: TULIP-SC CSR, Table 15, p69; Table 18, p75; Table 20, p79; Table 23, p83; Table 26, p85; Figure 3, p71.
A flare was one or more new BILAG grade of A or two or more new grades of B since last assessment.
BICLA = British Isles Lupus Assessment Group Combined Lupus Assessment; CI = confidence interval; DORIS = definition of remission in SLE; LLDAS = Lupus Low Disease Activity State.
Results in **bold** are statistically significant.

6.14 The proportions of anifrolumab-treated and placebo-treated patients with BICLA responses were about 50% and about 35% respectively at all time points after 16 weeks (Figure 1). Lower proportions of anifrolumab-treated and placebo-treated patients had a BICLA response before 52 weeks and sustained that response until 52 weeks (41% and 22% respectively), so a significant proportion of patients in both treatment groups relapsed after achieving a response.

Figure 1: BICLA responses by study visit.



Source: TULIP-SC CSR, Figure 2, p70. Note that error bars are standard error of the mean.

6.15 Fewer anifrolumab-treated patients had a disease flare, and the annualised flare rate was lower in anifrolumab-treated patients, but neither result was statistically significant.

6.16 Patients could lose BICLA response status without having a flare, since BICLA required no new BILAG2004 grade A or B domain, while a flare required one new grade A or two new grade B domains.

6.17 No comparison of anifrolumab SC and placebo for the PBS-eligible population was provided. Anifrolumab-treated patients with baseline SLEDAI-2K ≥10 were more likely to have a BICLA response at 52 weeks than patients with SLEDAI-2K <10. The pooled TULIP-1 and 2 data did not show a difference in results between SLEDAI-2K <10 versus ≥10 (this result was not provided for the results of the new individual patient meta-analysis).

6.18 There was no benefit of anifrolumab SC in Black or in Asian patients, due to lower frequency of BICLA responses with active treatment. Similar differences between results in Black or Asian patients and the overall population were also seen for BICLA response with maintained low corticosteroid use, for BICLA response before week 52 sustained until week 52, and for time to first disease flare.

6.19 The TULIP-1 and 2 trials enrolled larger numbers of Asian and Black patients (76 and 94, respectively) than TULIP-SC. In the pooled TULIP-1 and 2 trials, there was no meaningful difference in the rates of BICLA responses at 52 weeks in anifrolumab-treated Black, Asian, and white patients, although the effect of anifrolumab did not reach statistical significance in Black patients. The difference (95% CI) vs placebo in BICLA response rate was 15.5 (-4.4, 35.5) for Black patients; 29.1 (7.8, 50.5) for Asian patients; and 14.8 (6.2, 23.5) for white patients.

6.20 No data for quality of life or time lost from work or study were reported.

6.21 Data were presented for the relationship between anifrolumab dose regimens, pharmacokinetic parameters, and efficacy outcomes.

6.22 Data were provided for anifrolumab 150 mg IV q4wk and anifrolumab 300 mg IV q 4 wk from TULIP-1, anifrolumab 300 mg IV q 4 wk from TULIP-2, and anifrolumab 120 mg SC weekly from TULIP-SC.

6.23 Anifrolumab 120 mg weekly SC was associated with higher average steady state concentration (Cave,ss), higher steady state area under the curve (AUCss), and, as expected, lower maximum concentration (Cmax,ss) and much higher minimum concentration (Cmin,ss) at steady state than 300 mg q4wk IV.

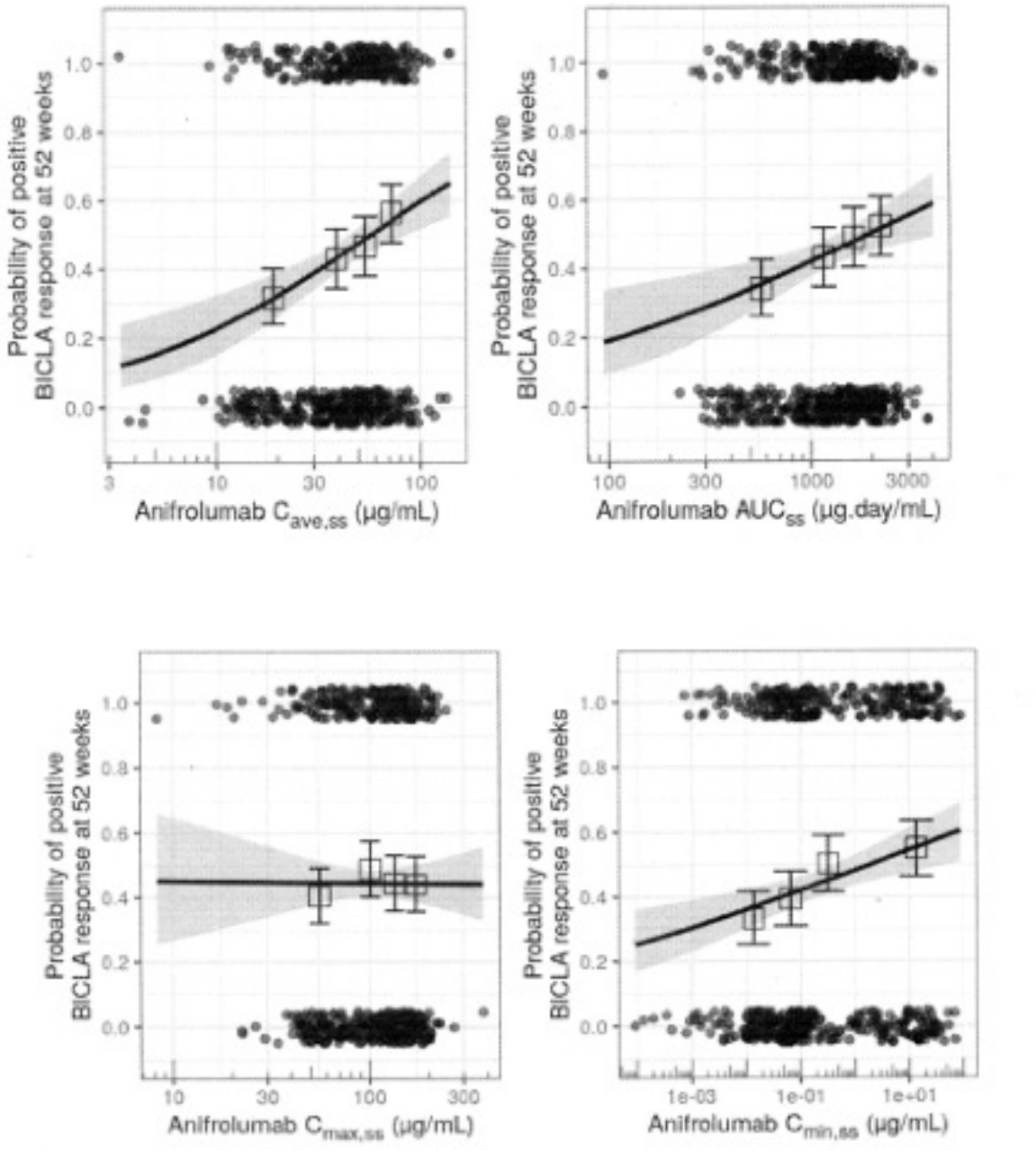
6.24 The data relating the quartiles of these parameters to BICLA at 52 weeks are shown in Figure 2.

6.25 There was an exposure-response relationship for average concentration and AUC, but not for Cmax.

6.26 The proportion of patients in the highest quartile who had received anifrolumab 300 mg q4wk or anifrolumab 120 mg weekly varied with parameter. For AUCss and Cave,ss patients receiving anifrolumab SC were over-represented in the highest quartile, while for Cmax,ss very few patients in the highest quartile received anifrolumab SC and for Cmin,ss nearly all patients in the highest quartile received anifrolumab SC. The claim

made by the submission that these results suggest that "the regimens can be used interchangeably" was not supported.

Figure 2: BICLA at 52 weeks versus pharmacokinetic parameters in TULIP-1, TULIP-2 and TULIP-SC



Source: Figure 3, pp18-19, Submission Attachment 6. Each dot is a patient with a BICLA response at 52 weeks and a pharmacokinetic measurement, squares with error bars are the observed probability of response at each exposure quartile. The black lines are the logistic regression between two variables and the grey area represents the associated confidence interval.
AUCss = area under the curve at steady state; BICLA = British Isles Lupus Assessment Group Combined Lupus Assessment; Cave, ss = average concentration at steady state; Cmax,ss = maximum concentration at steady state; Cmin,ss = minimum concentration at steady state.

Comparative harms

6.27 Adverse events in TULIP-SC, TULIP-1 and TULIP-2, and MUSE are shown in Table 5.

Table 5: Adverse events in TULIP-SC, TULIP-1 and TULIP-2, and MUSE

	TULIP-SC		TULIP-1 and TULIP-2		MUSE	
	Placebo N = 183	Anifrolumab 120 mg SC weekly N = 184	Placebo N = 364	Anifrolumab 300 mg IV q4wk N = 360	Placebo N = 101	Anifrolumab 300 mg IV q4w N = 99
Any AE, n (%)	143 (78.6%)	159 (85.9%)	297 (81.6%)	320 (87.9%)	78 (77.2%)	84 (84.8%)
Any SAE, n (%)	19 (10.4%)	22 (11.9%)	61 (16.8%)	40 (11.1%)	19 (18.8%)	16 (16.2%)
AE leading to death, n (%)	0	1 (0.5%)	2 (0.5%)	0	0	0
AE leading to study discontinuation, n (%)	8 (4.4%)	14 (7.6%)	18 (4.9%)	16 (4.4%)	2 (2%)	1 (1%)
Any AE of special interest, n (%)	37 (20.3%)	45 (24.3%)	33 (9.1%)	47 (13.1%)	12 (11.9%)	10 (10.1%)
Herpes zoster, n (%)	2 (1.1%)	7 (3.8%)	5 (1.4%)	23 (6.4%)	2 (2.0%)	5 (5.1%)
Infusion or Injection Site Reactions, n (%)	28 (15.4%)	29 (15.7%)	27 (7.4%)	41 (11.4%)	6 (6%)	2 (2%)
Non-opportunistic serious infections, n (%)	6 (3.3%)	13 (7.0%)	18 (4.9%)	14 (3.9%)	NR	NR

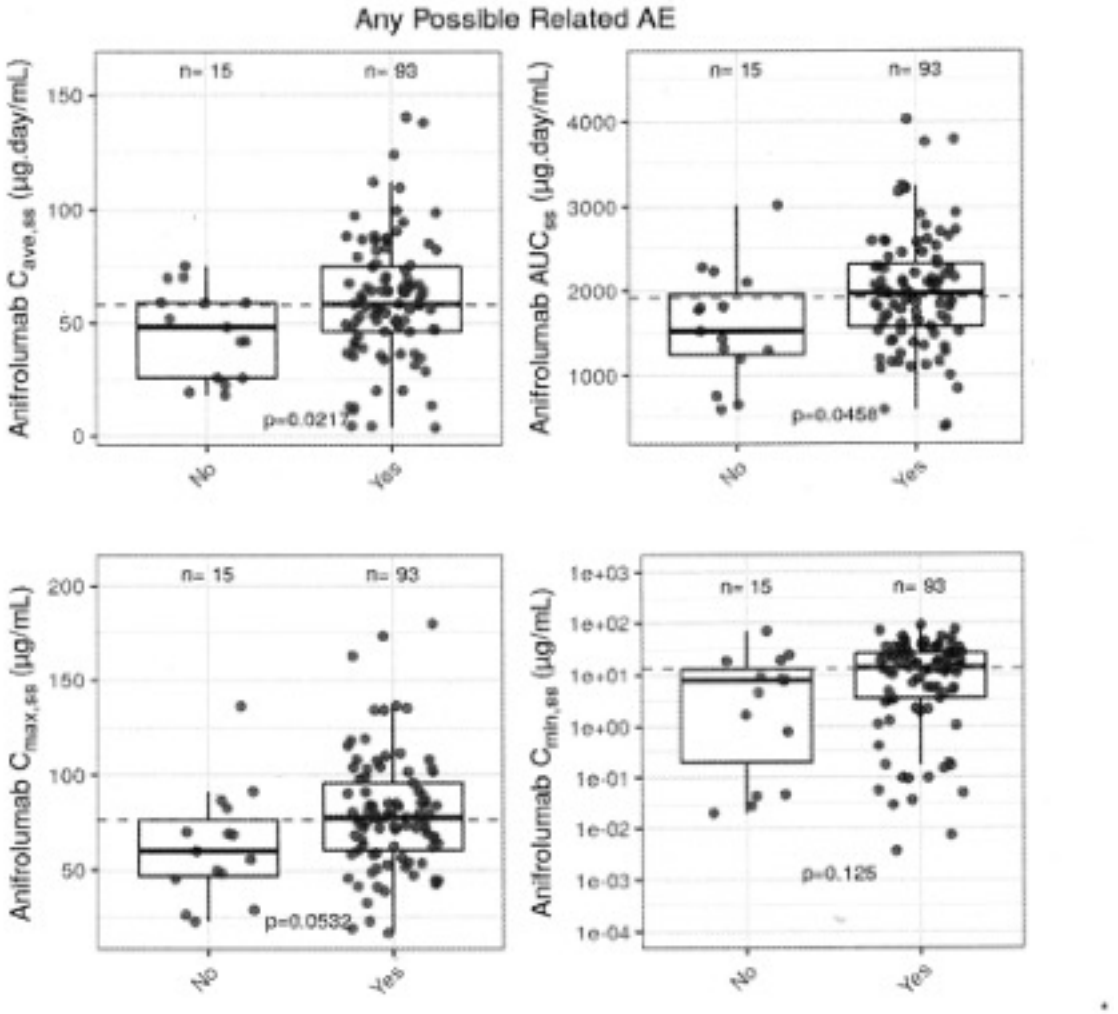
Source: TULIP-SC CSR, Table 30, p95; Tables 2-38, 2-39, 2-40, p170, Submission Attachment 4.
Adverse events of special interest were non-opportunistic serious infections, major adjudicated cardiovascular events, malignancy, herpes zoster, tuberculosis including latent tuberculosis, and injection site reactions.
AE = adverse event; NR = not reported; SAE = serious adverse event.

6.28 Adverse events were more common with anifrolumab IV/SC than placebo but serious adverse events and adverse events leading to study discontinuation were not. The only adverse event clearly associated with anifrolumab was herpes zoster. This is a well-known risk associated with the mechanism of action of anifrolumab and did not appear to be more common with the higher dose and SC administration.

6.29 The relationship between pharmacokinetic parameters and the risk of any adverse event considered by the investigator to be at least possibly related to anifrolumab is shown in Figure 3.

6.30 Patients with adverse events had higher values for all pharmacokinetic parameters. For three of four parameters, the higher quartiles contained more patients receiving anifrolumab SC.

Figure 3: Pharmacokinetic parameters in patients in TULIP-1, TULIP-2 and TULIP-SC with and without any adverse event at least possibly related to anifrolumab.



Source: Figure 5, p21, Submission Attachment 6. The dots represent the values observed in a single patient. The middle line of the box is the median, the lower and upper borders of the box are the 25% and 75% percentiles, and the lower and upper whiskers are the median–1.5 IQR and median+1.5 IQR. The dashed line represents the global median.
AE = adverse event; AUCss = area under the curve at steady state; Cave,ss = average concentration at steady state; Cmax,ss = maximum concentration at steady state; Cmin,ss = minimum concentration at steady state.

Extended Assessment of Harms

6.31 The Periodic Safety Update Report (PSUR) for anifrolumab for the period July 2024 to July 2025 was provided. Patient exposure in this period was estimated to be 17,045 patient years. Patient exposure from the anifrolumab international birth date in July 2021 to July 2024 was estimated to be 16,124 patient years - i.e., use of anifrolumab has risen recently. None of the post-marketing data reported in the PSUR related to anifrolumab SC.

6.32 The PSUR included 408 adverse event reports of lack of efficacy, of which 28 were serious adverse events.

6.33 Herpes zoster is known to be a risk of anifrolumab and in the randomised trials was clearly more common among anifrolumab-treated patients.

6.34 There were 160 post-marketing reports of herpes zoster in the year to July 2025, including four of ophthalmic herpes and two of disseminated varicella-zoster virus infection; 33/160 were serious. In the controlled trials TULIP-1+TULIP-2+TULIP-SC the incidence of herpes zoster in the double-blind phase was 6.1% in anifrolumab-treated patients, although data from the open-label extension studies suggested that herpes zoster was commonest early in anifrolumab treatment. The reported rate from post-marketing surveillance was much lower than that seen in the controlled trials, which could reflect a lower risk with long-term treatment or under-reporting of a well-known risk.

6.35 Type I interferons play a role in tumour surveillance and are used in the treatment of a number of malignancies. For this reason, malignancy is defined as an important potential risk of anifrolumab. In the double-blind phases of TULIP-1+2+SC malignancy developed in 6/635 anifrolumab-treated patients and 3/636 placebo-treated patients, with an excess in anifrolumab-treated patients of 0.5 malignancies per 100 patient years. There were 27 case reports of malignancy in the year to July 2025; 18 cases had been reported between the international birth date of anifrolumab in July 2021 and July 2024.

6.36 Type I interferons are important in the innate immune response to viral infections and may play a role in bacterial and fungal infections. This is most obvious in relation to herpes zoster, but serious infection of any aetiology is defined as an important potential risk of anifrolumab. In the double-blind phases of TULIP-1+2+SC there was no increased risk of serious infections, which occurred in 34/635 anifrolumab-treated patients and 32/636 placebo-treated patients. However, there were 275 reported cases of serious infection in the year to July 2025; 212 cases had been reported between July 2021 and July 2024. Ten patients died of serious infection during the year to July 2025.

6.37 The plausible mechanisms for anifrolumab increasing the risk of malignancy and serious infections, the clinically (though not statistically) significant increase in risk of malignancy in the randomised controlled trials, and the association of increasing post-marketing reports of malignancy and serious infections with increasing anifrolumab use suggest that the possibility of an increased risk of malignancy and serious infections with anifrolumab should be an ongoing concern.

6.38 In the controlled trials, adverse events were related to anifrolumab exposure (paragraph 6.32). The adverse event experience in clinical trials may not reflect adverse events in clinical use of the higher dose used for anifrolumab SC.

Indirect Treatment Comparison (ITC)

6.39 The ITC compared TULIP-1 and 2 with TULIP-SC, using the placebo arms as common comparator. Individual patient data from all three trials were used, with patients in TULIP-1 and 2 treated as a single population.

6.40 The primary outcome of TULIP-1 and of TULIP-2 as it was originally designed was a Systemic Lupus Erythematosus Responder Index of ≥ 4. TULIP-1 did not find a statistically significant effect of anifrolumab on this outcome but did find significant differences in some secondary outcomes, including BICLA. The primary outcome of TULIP-2 was changed to BICLA based on the results of TULIP-1. Although this change was made before data lock and unblinding in TULIP-2, "the amended analysis was akin to a *post-hoc* analysis given the trial was already nearing completion at the time of the change" (Paragraph 6.10, Anifrolumab PSD, July 2022 PBAC Meeting).

6.41 In both TULIP-1 and TULIP-2 patients who used pre-specified restricted medications during the trial could not be counted as responders. After TULIP-1 was analysed, the investigators concluded that the rules for restricted medications had been too restrictive and performed post hoc analyses with less restrictive rules. The revised rules strongly favoured anifrolumab. The TULIP-2 protocol was amended to use the new rules, and although this change was made before unblinding it was made after most of the data had been collected under the unrevised rules.

6.42 The designs of TULIP-1 and 2 were presented as having been similar, but this was correct only as regards the post hoc analyses of TULIP-1.

6.43 The pooled data from TULIP-1 and 2 and the individual patient data used for the ITC in the submission were analysed using the TULIP-2 outcomes and revised medication restriction rules - i.e., were post hoc analyses of TULIP-1. Because of the protocol changes, PBAC previously graded the risk of bias for TULIP-1 as Unclear (Paragraph 6.10, Anifrolumab PSD, July 2022 PBAC Meeting), and the risk of bias for the pooled data and the data used in the ITC is also Unclear.

6.44 The use of the TULIP-1 post hoc analysis favoured anifrolumab IV versus placebo and would disadvantage anifrolumab SC in the ITC.

6.45 There were meaningful differences between the baseline characteristics of patients in TULIP-1 and 2 and those in TULIP-SC; in particular, in TULIP-SC there was a lower mean baseline SLEDAI-2K, a lower mean baseline oral corticosteroid dose, and a higher proportion of patients receiving antimalarials. For this reason, two ITCs were presented: a "naive" ITC using the Bucher method, and an adjusted ITC in which patients in TULIP-SC were weighted to reduce the effect of differences in baseline characteristics; this was referred to as the TULIP IV Estimand. A sensitivity analysis was done in which TULIP-1 and 2 data were weighted to match TULIP-SC data, referred to as the TULIP-SC Estimand.

6.46 The results of the individual patient re-analyses of efficacy outcomes for TULIP-1 and 2 and TULIP-SC used in the ITC differed from those reported previously in the case of

pooled TULIP-1 and 2 data and from the CSR in the case of TULIP-SC. The results are shown in Table 6.

Table 6: Efficacy outcomes in pooled TULIP-1 and 2 data seen previously by PBAC and in TULIP-SC CSR vs those used in the ITC

	TULIP-1 & 2 as seen November 2023	TULIP-1 & 2 in ITC	TULIP-SC in CSR	TULIP-SC in ITC weighted by TULIP IV Estimand
BICLA at 52 weeks	ANI 46.9% PBO 30.6%	ANI 47.5% PBO 30.6%	ANI 56.2% PBO 37.1%	ANI 60.9% PBO 38.8%
LLDAS at 52 weeks	ANI 30.9% PBO 19.6%	ANI 30.9% PBO 19.7%	ANI 40.1% PBO 26.0%	ANI 45.1% PBO 28.4%
DORIS remission	ANI 15.3% PBO 7.6%	ANI 15.3% PBO 6.6%	ANI 29.0% PBO 14.7%	ANI 32.1% PBO 16.9%
Annualised flare rate	ANI 0.51 PBO 0.67	ANI 0.58 PBO 0.76	ANI 0.57 PBO 0.73	ANI 0.57 PBO 0.73

Source: Submission Attachment 4, Table 2-19, p133; Table 2-24, p145; Figure 2-22, p152; Table 2-31, p159; Submission Attachment 7, Table 9.1, p29. A flare was one or more new BILAG grade of A or two or more new grades of B since last assessment.
ANI = anifrolumab; BICLA = British Isles lupus assessment group combined lupus assessment; CSR = clinical study report; DORIS = definition of remission in systemic lupus erythematosus; ITC = individual treatment comparison; LLDAS = lupus low disease activity state; PBO = placebo.

6.47 There were minor differences between the individual patient re-analysis of TULIP-1 and 2 and the previous pooled analysis, but the weighted analysis of TULIP-SC substantially favoured anifrolumab SC.

6.48 Results of the ITC were presented as odds ratios or rate ratios for anifrolumab IV versus anifrolumab SC. Results for the whole population and for the PBS-eligible sub-group using the Bucher method and the two weighted populations are shown in Table 7.

6.49 There were no statistically significant differences between anifrolumab SC and anifrolumab IV.

Table 7: Results of the ITC of anifrolumab SC vs anifrolumab IV

	Whole Population			PBS-Eligible Population	
	Bucher Method	**Weighted, TULIP IV Estimand**	**Weighted, TULIP-SC Estimand**	**Bucher Method**	**Weighted, TULIP IV Estimand**
BICLA at 52 weeks, OR (95% CI)	1.17 (0.70, 1.97)	1.31 (0.74, 2.33)	1.35 (0.78, 2.35)	0.86 (0.28, 2.66)	1.02 (0.27, 3.87)
Annualised rate of flare, Rate Ratio (95% CI)	1.06 (0.72, 1.54)	0.89 (0.59, 1.35)	1.01 (0.67, 1.51)	1.04 (0.51, 2.14)	0.72 (0.31, 1.66)
LLDAS at 52 weeks, OR (95% CI)	1.18 (0.68, 2.06)	1.05 (0.57, 1.93)	1.45 (0.81, 2.61)	2.12 (0.62, 7.28)	2.87 (0.71, 11.60)
DORIS remission at 52 weeks, OR (95% CI)	0.90 (0.44, 1.83)	1.13 (0.53, 2.42)	0.94 (0.94, 2.02)	0.92 (0.21, 4.10)	0.70 (0.18, 2.76)

Source: Table 2-30, p100 of the submission.
A flare was one or more new BILAG grade of A or two or more new grades of B since last assessment.
OR > 1 indicates anifrolumab 120 mg SC weekly was superior.
RR < 1 indicates anifrolumab 120 mg SC weekly was superior. Severe BILAG flare was

BICLA = British Isles Lupus Assessment Group Combined Lupus Assessment; BILAG = British Isles Lupus Assessment Group; CI = confidence interval; DORIS = Definition of Remission in Systematic Lupus Erythematosus; ITC = indirect treatment comparison; IV = intravenous; LLDAS = Lupus Low Disease Activity State; OR = odds ratio.

6.50 No ITC for adverse events was presented.

Benefits/harms

6.51 A benefits/harms table is not provided because the submission made a claim of non-inferiority.

Clinical claim

6.52 The submission described anifrolumab SC as non-inferior in terms of effectiveness compared to anifrolumab IV. The evaluation considered that this claim was adequately supported. However, the data presented for anifrolumab SC do not alter the conclusion PBAC reached in relation to anifrolumab IV: some patients appear to benefit but the magnitude of the effect is uncertain.

6.53 The submission described anifrolumab SC as non-inferior in terms of safety compared to anifrolumab IV. The evaluation considered that this claim was adequately supported with regard to adverse events in the controlled trials, but concern remains with regard to the safety of the higher dose of anifrolumab in long-term use, especially with regard to the risk of malignancy.

Economic analysis

6.54 The submission presented what it described as a 'cost-equivalence' analysis to calculate the price of anifrolumab SC based on the cost of the IV formulation plus the administration cost (effectively, a cost-minimisation approach).

6.55 The equi-effective doses were anifrolumab 120 mg SC weekly as equivalent to the 300 mg IV infusion given every 4 weeks, so that four prefilled 120 mg pens (i.e., total dose 480 mg) are equivalent to the 300 mg infusion over a 28-day period. These doses were based on the results of the indirect treatment comparison.

6.56 The cost-minimisation approach included the costs of the IV infusion based on MBS Item 105 but no other costs. The results of the analysis are shown in Table 8.

6.57 Where an IV formulation of a drug is already PBS listed, in some cases, the PBAC has previously considered that it would be appropriate to derive the SC formulation ex-manufacturer price based on drug costs only (for example: efgartigimod alfa SC, November 2025 PBAC Meeting; ocrelizumab SC, July 2025 PBAC Meeting; natalizumab SC, March 2023 PBAC Meeting; daratumumab SC, July 2021 PBAC Meeting). In the case of efgartigimod alfa, the PBAC considered that the medicine was expected to continue to be administered by a healthcare professional, even with its SC presentation.

6.58 In its resubmission for anifrolumab IV, the sponsor had used MBS Item 105 for the cost of administration (adjusted by 9/13, assuming that 9 out of 13 administrations would

incur an additional cost, with 4 specialist visits a year assumed to be standard practice) (Paragraph 6.64, Anifrolumab PSD, March 2024 PBAC Meeting).

6.59 As with other SC formulations considered by the PBAC, the evaluation considered it is unclear whether the proposed savings to the MBS would be realised in practice.

6.60 If the costs of IV administration are excluded, the resulting AEMP/120 mg vial would be $[redacted]. If the cost of administration are adjusted to align with the approach used in the March 2024 submission model, that is, allowing for only approximately 9 additional consultations per year rather than one for every IV dose, the cost per administration is approximately $[redacted], with the resulting AEMP for the 120mg SC being $[redacted].

Table 8: Results of the cost-minimisation approach, effective AEMP

Component	Anifrolumab 300 mg IV	Anifrolumab 120 mg SC
Drug cost per pack	$[redacted]	$[redacted]
Drug cost per 28-day cycle	$[redacted]	$[redacted]
Administration cost per dose (MBS item 105)	$50.95	$0
Total cost per 28-day cycle	$[redacted]	$[redacted]
Difference in cost per 28-day cycle	-	$0
Administration cost removed, equivalent AEMP/28 days	$[redacted]	$[redacted]
Administration cost adjusted as per March 2024 model equivalent AEMP/28 days	$[redacted] *+$35= $[redacted]*	$[redacted]

Source: Submission Workbook, PBAC Anifrolumab SC Cost Equivalence.
Italics = calculated during the evaluation.

Drug cost/patient/course

6.61 At the time of the evaluation, the cost per patient per 28-day cycle of treatment for anifrolumab SC listed on Section 85 would be an effective DPMQ of $[redacted], while the Section 100 listing for the IV form had an effective DPMQ of $[redacted] in the public hospital and $[redacted] in the private hospital setting.

Estimated PBS usage & financial implications

6.62 This submission was not considered jointly by DUSC and ESC.

6.63 The submission presented a market share approach to estimate the PBS usage and financial implications of listing anifrolumab 120 mg SC pre- filled autoinjector. The key inputs used in the estimates are shown in Table 9.

Table 9: Key inputs for financial estimates

Parameter	Value	Source	Comment
Market:			
Existing Market	1894 Scripts in 2025 calendar year	PBS item codes 14189T 14195D Medicare Statistics for July 2024 – June 2025, and July 2025 – December 2025.	Appropriate
% Growth Rate	Yr 1: 16.0% Yr 2: 14.1% Yr 3: 12.7% Yr 4: 11.5% Yr 5: 11.0% Yr 6: 10.3%	Extrapolation using a Linear/logarithmic trend, allowing for observed increase in market growth compared to predicted for IV form in March 2024 submission.	May be an over or underestimate, although uptake of SC may be greater than IV.
% Treatment Uptake Rate	Yr 1: [redacted]% Yr 2: [redacted]% Yr 3: [redacted]% Yr 4: [redacted]% Yr 5: [redacted]% Yr 6: [redacted]%	Sponsor Assumption	Claims it is based on other markets but may be an underestimate given difference between Section 100 and Section 85 listings.
Script Equivalence	1:1	TGA Product Information	Appropriate
MBS Impacts	MBS Item number 105 for IV administration: 1 per IV service, cost of $40.76 (80% of fee)	MBS	Appropriate

Source: Tables 4.1, 4.6, 4.8, 4.15, pp 123, 127, 130, 135 of the submission.

6.64 The submission compared the estimates in the March 2024 submission for IV anifrolumab with the actual uptake and noted that the actual script numbers were much less than predicted. However, the submission also pointed out that the year-on-year growth rate for year 1 to year 2 was 183% and therefore it was reasonable to assume that actual utilisation of anifrolumab will approach the March 2024 predictions. The estimates of patient numbers provided in the March 2024 submission and the actual patient numbers, based on an analysis of data by the DUSC Secretariat are shown in Table 10 below.

Table 10; Comparison of 2024 estimates with actual use

	Year 1 2024/25	Year 2 2025/26	Year 3 2026/27	Year 4 2027/28	Year 5 2028/29	Year 6 2029/30
March 2024 – initiating patients	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
March 2024 – continuing patients	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Actual use – initiating 2024/25 (Year 1)	*177*	*131 (to end Feb 2026)*				
Prevalent patients	*177*	*287 (to end Feb 2026)*				

Source: Table 4.2, p125 of the submission, and in *italics data provided by the DUSC Secretariat, 22 April 2026.*
The redacted values correspond to the following ranges:
[1] 500 to < 5,000
[2] < 500

6.65 The observed data for initiating patients are substantially less than the predicted uptake, however if the current dispensing arrangements were amended, the uptake is likely to be substantially higher. In this scenario it may be reasonable to conclude that the market growth rates are underestimated.

6.66 The estimated use and financial impact of listing anifrolumab SC are shown in Table 11.

Table 11: Estimated use and financial implications, effective DPMQ $[redacted]

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use – scripts						
March 2024 submission, IV	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]
Actual use yr 1, projected use yr 2	[redacted][1]	[redacted][1]				
Projected use IV 2027-2032	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Projected use SC 2027-2032	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]
Estimated financial implications of SC anifrolumab						
Cost to PBS/RPBS less copayments ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]
Estimated financial implications for IV anifrolumab						
Cost to PBS/RPBS less copayments ($)	-[redacted][5]	-[redacted][5]	-[redacted][5]	-[redacted][5]	-[redacted][5]	[redacted][5]
Net financial implications						
Net cost to PBS/RPBS ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Net cost to MBS ($)	-[redacted][5]	-[redacted][5]	-[redacted][5]	-[redacted][5]	-[redacted][5]	-[redacted][5]
Net cost to PBS/RPBS/MBS ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Revised Overall Net cost ($) to PBS/RPBS based on revised effective price as per Table 8 ($[redacted])	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]

Source: Tables 4.4, 4.5, 4.7, 4.8, 4.11, 4.14, 4.15, 4.16., pp126,128,130, 133, 134, 135, 36 of the submission.
Italics: Revised estimates from the pre-PBAC response
The redacted values correspond to the following ranges:
[1] 5,000 to < 10,000
[2] 10,000 to < 20,000
[3] $0 to < $10 million
[4] $10 million to < $20 million

[5] *net cost saving*

6.67 The total cost to the PBS/RPBS of listing anifrolumab SC was estimated to be $10 million to < $20 million in Year 6, and a total of $50 million to < $60 million in the first 6 years of listing. Allowing for the reduction in use of IV anifrolumab, the submission estimated a net total cost over 6 years of $$0 to < $10 million, attributed to the difference in administration costs incorporated in the cost-minimisation equivalence analysis, and the difference in dispensing fees and mark-ups associated with Section 85 and Section 100 listings.

6.68 Noting the difference between the estimated use in the March 2024 submission and the actual use of IV anifrolumab since listing, it would appear that the use of anifrolumab SC may be overestimated. However, the differences between access via Section 100 listing and access via Section 85 listing as well the SC formulation compared to the IV formulation, may result in actual use being closer to the predicted use in the current submission.

6.69 The submission presented sensitivity analyses varying the size of the anifrolumab IV market, the substitution rate of the SC for the IV formulation, and the market growth rates. These results are shown in Table 12. Market growth has the largest impact on the financial estimates.

Table 12: Sensitivity analyses on the net financial impact to the PBS

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Base case ($)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Size of the underlying anifrolumab IV market (base case: based on estimates in Ratified Minutes for March 2024 PBAC submission for anifrolumab IV)						
25% smaller market ($)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
25% larger market ($)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Substitution rates (base case 50-75%)						
40-65% ($)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
60-85% ($)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Market growth due to anifrolumab SC listing (base case 0%)						
10% ($)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
20% ($)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]

Source: Table 1.17, p136 of the submission. IV = intravenous; SC = subcutaneous.

The redacted values correspond to the following ranges:

[1] *$0 to < $10 million*

Quality Use of Medicines

6.70 The submission did not present any information concerning the quality use of medicines with respect to anifrolumab SC.

Financial Management – Risk Sharing Arrangements

6.71 The submission proposed that anifrolumab SC enter the RSA currently in place for anifrolumab IV, with no change to the current expenditure caps or rebates above the caps. The expenditure caps in the current Deed of Agreement are shown in Table 13.

Table 13: Subsidisation Caps in the current Deed of Agreement for anifrolumab

Anifrolumab	Year 1	Year 2	Year 3	Year 4	Year 5
Cap Year Start	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cap Year End	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Annual Subsidisation Cap ($)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Rebate above caps	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%

Source: Table 4.18, p137 of the submission.

7 PBAC Outcome

7.1 The PBAC recommended the Section 85 Authority Required listing for anifrolumab pre-filled pen auto-injector for subcutaneous injection (referred to as anifrolumab SC) for the treatment of adults with severe systemic lupus erythematosus (SLE) and high disease activity despite the standard of care. The PBAC recommended the listing on a cost-minimisation basis to the currently Section 100-listed anifrolumab for intravenous administration (anifrolumab IV). The PBAC advised the equi-effective doses to be anifrolumab 120 mg SC weekly as equivalent to the 300 mg IV infusion given every 4 weeks, so that four prefilled 120 mg pens (i.e., total dose 480 mg) are equivalent to the 300 mg infusion over a 28-day period.

7.2 The PBAC noted that anifrolumab SC was TGA-registered on 7 May 2026 for add on treatment of adult patients with moderate to severe, active SLE, despite standard therapy. Although the dose of anifrolumab SC was higher (480 mg versus 300 mg every four weeks), the SC and IV preparations were considered equivalent by the TGA evaluation.

7.3 In terms of the requested listing, the PBAC agreed with the Secretariat's proposed amendments to the restrictions (Section 3). The pre-PBAC response confirmed that patients may switch formulations during the initial treatment phase and agreed that an additional set of restrictions, structured as a Balance of Supply listing, would be required for both forms of anifrolumab (Option 2 restrictions proposed by the Secretariat for 'switching' with revisions on the number of repeats to zero consistent with Balance of Supply settings). The PBAC considered this was appropriate.

7.4 As stated in the pre-PBAC response, the PBAC noted that the sponsor intends to submit a TGA variation application for an additional pack size comprising one pack containing four anifrolumab syringes.

7.5 The PBAC considered that the nominated comparator of anifrolumab IV was appropriate. The PBAC recalled that other PBS (or near PBS listed drugs) had not been deemed appropriate comparators during the anifrolumab IV consideration (Paragraph

7.4, Anifrolumab PSD, July 2022 PBAC meeting; Paragraph 5.2, Anifrolumab PSD, March 2024 PBAC Meeting).

7.6 The PBAC noted that the submission was based on the TULIP-SC trial comparing anifrolumab SC to placebo (N = 367) and an indirect treatment comparison (ITC) using the placebo-controlled trials of anifrolumab IV, TULIP-1 and TULIP-2 (which were previously reviewed in the context of the anifrolumab IV consideration). The PBAC also noted the evaluation found that efficacy in the overall trial population was modest and the difference versus placebo was sensitive to the outcome measure chosen and to the rules for restricted medication use. The PBAC recalled its previous conclusion for anifrolumab IV that some patients appear to benefit but the magnitude of the effect is uncertain (paragraph 7.7, anifrolumab PSD, March 2024 PBAC meeting).

7.7 The PBAC also recalled it had previously acknowledged that the low level of certainty in the evidence and the modest and uncertain incremental benefit between anifrolumab and placebo likely reflected, in part, the complex and variable nature of the condition and the challenges associated with assessing outcomes in SLE (paragraph 7.10, anifrolumab PSD, March 2023 PBAC meeting; paragraph 7.3, anifrolumab PSD, March 2024 PBAC meeting).

7.8 The PBAC noted the evaluation found that no comparison of anifrolumab SC and placebo for the PBS-eligible population was provided. The pre-PBAC response stated that the ITC for the PBS-relevant subgroups was in an appendix to the submission. Notwithstanding that it should have been in the main body of the submission, the PBAC considered that this ITC indicated similarity across outcomes. Overall, the PBAC considered it was reasonable to conclude (including the TGA's position) that the claim of non-inferior comparative effectiveness was adequately supported by the data.

7.9 The PBAC noted that no ITC for adverse events was presented. The PBAC also noted that adverse events were more common with anifrolumab IV/SC than placebo but serious adverse events and adverse events leading to study discontinuation were not. Similarly, the PBAC considered that the claim of non-inferior comparative safety was likely reasonable.

7.10 The PBAC noted that the submission presented what it described as a 'cost-equivalence' analysis to calculate the price of anifrolumab SC based on the cost of the IV formulation plus the administration cost (effectively, a cost-minimisation approach). The PBAC noted that a revised AEMP of $[redacted] for anifrolumab SC was calculated during the evaluation (see Table 8). This was based on the fact that in its resubmission for anifrolumab IV, the sponsor had used MBS Item 105 for the cost of administration (adjusted by 9/13, assuming that 9 out of 13 administrations would incur an additional cost, with 4 specialist visits a year assumed to be standard practice) (Paragraph 6.64, Anifrolumab PSD, March 2024 PBAC Meeting). The pre-PBAC was supportive of this revised approach.

7.11 The PBAC considered that the proposed anifrolumab SC formulation removes the need for regular IV infusions administered in a healthcare setting. In addition to any

healthcare resource savings, the PBAC also considered there is an expected patient benefit through greater convenience, reduced treatment burden and increased flexibility associated with self-administration. This view was consistent with that provided through consumer inputs. For these reasons, and for consistency with the previous anifrolumab IV consideration, the PBAC considered it would be reasonable for the cost-minimisation approach to include an adjusted administration cost of 9 MBS items as per the March 2024 model.

7.12 The PBAC noted that the estimated total cost of anifrolumab SC to the PBS/RPBS in the first 6 years of listing was $50 million to < $60 million, though when the existing cost of anifrolumab is offset, the net cost was approximately $0 to < $10 million over 6 years. The PBAC also noted that when expected reductions in infusion-related MBS expenditure are included, the net additional cost reduces to approximately $0 to < $10 million over 6 years (by offsetting 9/13 MBS attendance items), a portion of which is associated with the difference in dispensing fees and mark-ups associated with Section 85 and Section 100 listings (see revised estimates in Table 11). The PBAC considered this incremental cost to be reasonable in the context of patient benefits associated with anifrolumab SC.

7.13 The PBAC noted that the submission proposed that anifrolumab SC enter the RSA currently in place for anifrolumab IV, with no change to the current expenditure caps or rebates above the caps. The pre-PBAC response stated that any increased usage could be managed within the current RSA caps. The PBAC considered this approach was reasonable.

7.14 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because anifrolumab SC is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over anifrolumab IV, or 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 2022* for Pricing Pathway A were not met.

7.15 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

8 Recommended listing

8.1 Add new item:

Initial Treatment – New Patient (anifrolumab subcutaneous)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ANIFROLUMAB					
Anifrolumab 120 mg/0.8 mL pre-filled pen	NEW	4	4	5	Saphnelo

	Category / Program: ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Benefit type: ☒Authority Required (FULL assessment) in writing only via post/HPOS upload/Online PBS Authorities system)
	Prescribing rule level:
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Restriction Summary / Treatment of Concept
	Indication: Systemic lupus erythematosus
	Treatment Phase: Initial Treatment
	Clinical Criteria
	Patient must have a confirmed and documented diagnosis of systemic lupus erythematosus (SLE) according to the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) SLE Classification Criteria 2019
	AND
	Clinical Criteria
	Patient must have persistent disease activity as supported by a SLE Disease Activity Index 2000 (SLEDAI-2K) score of at least 10 points
	AND
	Clinical Criteria
	Patient must be currently receiving hydroxychloroquine, with treatment received for at least 12 weeks, unless contraindicated/intolerant necessitating treatment withdrawal
	AND
	Clinical Criteria
	Patient must be currently receiving immunosuppressant medication, with treatment received for at least 12 weeks, with either: (i) minimum dose of methotrexate 20 mg per week, (ii) azathioprine 100 mg per day, (iii) mycophenolate 1,000 mg per day unless contraindicated/intolerant necessitating treatment withdrawal
	AND
	Clinical Criteria
	Patient must be currently receiving prednisolone or equivalent of at least 7.5 mg per day, with treatment received for at least 4 weeks, unless contraindicated/intolerant necessitating treatment withdrawal
	AND
	Clinical Criteria
	Patient must not have either: (i) severe active lupus nephritis, (ii) severe active central nervous system systemic lupus erythematosus

	Treatment Criteria
	Must be treated by a specialist physician experienced in the management of this condition
	Prescribing Instructions If prednisolone or equivalent is contraindicated according to the Therapeutic Goods Administration (TGA)-approved Product Information or cannot be tolerated of at least 7.5 mg per day, the patient must have received at least 12 weeks of continuous treatment with each of at least 2 of the following: (i) hydroxychloroquine; (ii) methotrexate at a dose of at least 20 mg per week; (iii) azathioprine at a dose of at least 100 mg per day; (iv) mycophenolate at a dose of at least 1,000 mg per day. Where two of: (i) hydroxychloroquine; (ii) methotrexate at a dose of at least 20 mg per week; or (iii) azathioprine at a dose of at least 100 mg per day; (iv) mycophenolate at a dose of at least 1,000 mg per day, are either contraindicated according to the relevant TGA-approved Product Information or cannot be tolerated at the doses specified above in addition to having a contraindication or intolerance to prednisolone or equivalent: at least one of the remaining tolerated therapies must be trialled at a minimum dose as mentioned above. If the patient has a contraindication/severe intolerance to each of: (i) prednisolone or equivalent of at least 7.5 mg per day; (ii) hydroxychloroquine; (iii) methotrexate at a dose of at least 20 mg per week; (iv) azathioprine at a dose of at least 100 mg per day; (v) mycophenolate at a dose of at least 1,000 mg per day; in such cases, provide details for each of the contraindications/severe intolerances claimed in the authority application.
	Prescribing Instructions The authority application must be made in writing via HPOS form upload or mail and must include: (a) details of the ACR/EULAR SLE Classification Criteria 2019 confirming diagnosis of SLE; (b) details (date and score) of the completed SLEDAI-2K score sheet; (c) details of current systemic therapy used (dosage, date of commencement and duration of therapy including prior anifrolumab use); (d) details of contraindication/intolerances to prior therapies (drug name, the degree of toxicity and dose). All the reports must be documented in the patient's medical records.
	Prescribing Instructions If the application is submitted through HPOS form upload or mail, it must include: (i) Details of the proposed prescription; and (ii) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	Administrative Advice SLEDAI-2K can be accessed via Gladman 2002 J. Rheumatol. 29 (2) 288-291 or from AstraZeneca Medical Information on 1800 805 342.
	Administrative Advice Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001

Continuing Treatment (anifrolumab subcutaneous)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ANIFROLUMAB					
Anifrolumab 120 mg/0.8 mL pre-filled pen	NEW	4	4	5	Saphnelo

	Category / Program: ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Benefit type: ☒ Authority required (Telephone/Online PBS Authorities immediate assessment)
	Prescribing rule level:
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Restriction Summary / Treatment of Concept
	Indication: Systemic lupus erythematosus
	Treatment Phase: Continuing or recommencement of treatment (within 12 months of a treatment break)
	Clinical Criteria
	Patient must have previously been issued with an authority prescription for this drug for this condition
	AND
	Clinical Criteria
	Patient must be responding to treatment if they have received less than 12 months of treatment with this drug for this condition; OR
	Patient must have attained a Lupus Low Disease Activity State (LLDAS) and maintained this state while on treatment
	Treatment Criteria
	Must be treated by a specialist physician experienced in the management of this condition
	Prescribing Instructions Lupus Low Disease Activity State (LLDAS) is defined as: (a) Total SLEDAI-2K of not greater than 4, with no major activity in major organ systems (renal, central nervous system (CNS), cardiopulmonary, vasculitis, fever); and (b) No new features of lupus disease activity compared with the previous assessment, and (c) Physician Global Assessment (PGA) of not greater than 1, and (d) Current prednisolone (or equivalent) dose of not greater than 7.5 mg daily, and (e) Well tolerated standard maintenance doses of anti-malarial and immunosuppressive drugs are allowed.
	Prescribing Instructions Where retreatment with anifrolumab after a break in PBS-subsidised treatment with anifrolumab is being sought, the date of cessation of the previous treatment course with anifrolumab must be included in the application. Recommencement of treatment with anifrolumab for severe SLE is within 12 months from the date that treatment was ceased.
	Administrative Advice SLEDAI-2K can be accessed via Gladman 2002 J. Rheumatol. 29 (2) 288-291 or from AstraZeneca Medical Information on 1800 805 342.
	Administrative Advice PGA can be accessed via Petri 2005 N Engl J Med 353: 2550-8.

	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 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

Balance of supply for Initial Treatment (Change/Switch from anifrolumab IV to anifrolumab SC)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ANIFROLUMAB					
Anifrolumab 120 mg/0.8 mL pre-filled pen	NEW	4	4	0	Saphnelo

	Category / Program: ☒ Section 85 – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Benefit type: ☒ Authority required (Telephone/Online PBS Authorities immediate assessment)
	Authority type: ☒ Complex Authority Required (CAR)
	Prescribing rule level:
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Restriction **Summary / Treatment of Concept**
	Indication: Systemic lupus erythematosus
	Treatment Phase: Balance of Supply - Change in route of administration (i.e. switching from intravenous anifrolumab to subcutaneous anifrolumab during initial treatment)
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with intravenous anifrolumab (300 mg/2 mL injection) for this condition
	AND
	Clinical criteria:
	Patient must have received insufficient therapy with this drug for this condition under the Initial restriction to complete 24 weeks treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restrictions
	Treatment criteria:
	Must be treated by a specialist physician experienced in the management of this condition
	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 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

Balance of supply for Initial Treatment (Change/Switch from anifrolumab SC to anifrolumab IV)

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ANIFROLUMAB					
Anifrolumab 300 mg/2 mL injection	NEW (Public) NEW (Private)	1	1	0	Saphnelo

	Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
	Prescriber type: ☒Medical Practitioners
	Benefit type: ☒ Authority required (Telephone/Online PBS Authorities immediate assessment)
	Authority type: ☒ Complex Authority Required (CAR)
	Prescribing rule level:
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Restriction **Summary / Treatment of Concept**
	Indication: Systemic lupus erythematosus
	Treatment Phase: Balance of Supply - Change in route of administration (i.e. switching from subcutaneous anifrolumab to intravenous anifrolumab during initial treatment)
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with subcutaneous anifrolumab for this condition
	AND
	Clinical criteria:
	Patient must have received insufficient therapy with this drug for this condition under the Initial restriction to complete 24 weeks treatment
	AND
	Clinical criteria:
	The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restrictions
	Treatment criteria:
	Must be treated by a specialist physician experienced in the management of this condition
	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 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 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.

10 Sponsor's Comment

The sponsor had no comment.