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6.06 EFGARTIGIMOD ALFA, Solution for subcutaneous injection 1,000 mg in 5.6 mL vial, Injection 1,000 mg in 5 mL pre-filled syringe, Vyvgart®, ARGENX AUSTRALIA PTY. LTD.

1 Purpose of submission

1.1 The Category 1 submission requested a Section 85 Authority Required (Written, Telephone, Electronic) listing for efgartigimod alfa (herein referred to as efgartigimod) for the treatment of patients with active chronic inflammatory demyelinating polyneuropathy (CIDP) who have progressive, relapsing or refractory symptoms despite immunoglobulin treatment or who are intolerant to immunoglobulin products. The Pre-Sub-Committee Response (PSCR) updated the requested population to remove the sub-group of relapsed patients as the targeted population are patients who cannot access immunoglobulin (see paragraph 3.1).

1.2 The submission claimed that there is a high unmet clinical need for additional treatment options for patients who fail to achieve adequate disease control with immunoglobulin products. The Sub-Committees considered that the refined population represents the patient group with the greatest need.

1.3 Listing was requested on the basis of a cost analysis versus intravenous immunoglobulin (IVIg).

Table 1: Key components of the clinical issue addressed in the submission

Component	Description
Population	Patients with active CIDP who have progressive or refractory symptoms despite immunoglobulin treatment (either alone or in combination with other therapies) or who are intolerant to immunoglobulin products.
Intervention	Monotherapy with efgartigimod (1,000 mg vial or pre-filled syringe) co-formulated with vorhyaluronidase alfa for subcutaneous injection. Treatment is initiated with a weekly dose regimen and may be adjusted to every other week based on clinical evaluation.
Comparator	IVIg/SCIg (variable dosing) or placebo
Outcomes	Reduction in disease relapses, disability and muscle impairment as well as improvements in quality of life.
Clinical claim	Efgartigimod is superior in terms of efficacy and non-inferior in terms of safety compared to both IVIg/SCIg and placebo

Source: Table 1.1-1, p19 of the submission (relapsing population was removed per the PSCR)
Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin

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2 Background

Registration status

2.1 Efgartigimod was assessed by the TGA under the Comparable Overseas Regulator pathway (EMA assessment). At the time of PBAC consideration, the outcome from the TGA's Clinical Evaluation Report was available. The requested indication for efgartigimod (1,000 mg vials co-formulated with vorhyaluronidase alfa for subcutaneous injection) was 'monotherapy for the treatment of adult patients with progressive or relapsing active chronic inflammatory demyelinating polyneuropathy (CIDP) after prior treatment with corticosteroids or immunoglobulins'.

The draft Product Information (PI) and TGA requests for further information from the sponsor were available during the evaluation process. [redacted]

2.2 An alternative presentation of efgartigimod (1,000 mg pre-filled syringes co-formulated with vorhyaluronidase alfa for subcutaneous injection) was also separately assessed by the TGA under the Comparable Overseas Regulator pathway (EMA assessment).

2.3 Efgartigimod (400 mg concentrated vials for intravenous infusion and 1,000 mg vials co-formulated with vorhyaluronidase alfa for subcutaneous injection) is currently TGA approved for the treatment of generalised myasthenia gravis.

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

3 Requested listing

MEDICINAL PRODUCT medicinal product pack	Dispensed price for Max. qty		Max. qty packs	Max. qty units	№.of Rpts	Available brands
	Published	Effective				
EFGARTIGIMOD						
Initial treatment						
Efgartigimod, 1,000 mg solution in 5.6 mL (180 mg/mL) vial for subcutaneous injection	$[redacted]	$[redacted]	1	4	2	Vyvgart
Efgartigimod, 1,000 mg solution in 5.0 mL (200 mg/mL) pre-filled syringe for subcutaneous injection	$[redacted]	$[redacted]	1	4	2	
Grandfathering, first continuation, subsequent continuation						
Efgartigimod, 1,000 mg solution in 5.6 mL (180 mg/mL) vial for subcutaneous injection	$[redacted]	$[redacted]	1	4	5	Vyvgart
Efgartigimod, 1,000 mg solution in 5.0 mL (200 mg/mL) pre-filled syringe for subcutaneous injection	$[redacted]	$[redacted]	1	4	5	
Category / Program: General Schedule						
Prescriber type: Medical Practitioners						

Restriction type: ☒Authority Required (telephone/online PBS Authorities system) ☒Authority Required (in writing only via post/HPOS upload)
Severity: Progressive, relapsing and refractory
Condition: Chronic Inflammatory Demyelinating Polyneuropathy
Indication: Chronic Inflammatory Demyelinating Polyneuropathy
Treatment Phase: Initial
Clinical criteria:
Patient must have a diagnosis of CIDP made by a neurologist using the EAN/PNS Diagnostic Guideline criteria.
AND
Clinical criteria:
Patient must have significant disability or compromised walking as objectively measured by an ~~Inflammatory Neuropathy Cause and Treatment (INCAT)~~ *Overall Neuropathy Limitation Scale (ONLS)* score of at least 3 points.
AND
Clinical criteria:
Patient must be refractory to immunoglobulin following a maximum of 4-month initiation treatment with immunoglobulin at or above the registered dose, where refractory is defined as: • a decrease in the ~~Overall Neuropathy Limitations Scale (~~ONLS~~)~~ of less than 1 point, or an increase in the Medical Research Council (MRC) sum score of less than 3, compared to baseline; OR • *Patient continues to meet the National Blood Authority (NBA) initiation requirements for immunoglobulins (eg ONLS score ≥3, despite experiencing a one-point decrease in ONLS.*
Patient must have progressive disease with an inadequate response to immunoglobulins (beyond the 4 months initiation period) at or above the registered dose, where inadequate response is defined as worsening of ONLS score, or MRC sum score compared to the previous assessment; OR
~~Patient must have relapsed at least 6 months after cessation of immunoglobulin treatment; OR~~
Patient must be contraindicated or intolerant to immunoglobulin.
Treatment criteria:
Must be treated by a prescriber who is either: (i) a neurologist; (ii) a clinical immunologist with expertise in the treatment of CIDP; OR
Must be treated by a medical practitioner who has consulted at least one of the above-mentioned specialist types, with an agreement reached that the patient should be treated with this pharmaceutical benefit on this occasion
Population criteria:
Patient must be 18 years or older.
Administrative Advice:
No increase in the maximum quantity or number of units may be authorised.
No increase in the maximum number of repeats may be authorised.
Special Pricing Arrangements apply.
Category / Program: General Schedule
Prescriber type: Medical Practitioners
Restriction type: ☒Authority Required (telephone/online PBS Authorities system) ☒Authority Required (in writing only via post/HPOS upload)
Severity: Progressive, relapsing and refractory
Condition: Chronic Inflammatory Demyelinating Polyneuropathy
Indication: Chronic Inflammatory Demyelinating Polyneuropathy
Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements
Clinical criteria:
Patient must have received non-PBS-subsidised treatment with this drug for this PBS indication prior to [the PBS listing date].

AND
Clinical criteria:
Patient must have a diagnosis of CIDP made by a neurologist using the EAN/PNS Diagnostic Guideline criteria.
AND
Clinical criteria:
Patient must have significant disability or compromised walking as objectively measured by an ~~Inflammatory Neuropathy Cause and Treatment (INCAT)~~ *Overall Neuropathy Limitation Scale (ONLS)* score of at least 3 points.
AND
Clinical criteria:
Patient must be refractory to immunoglobulin following a maximum of 4-month initiation treatment with immunoglobulin at or above the registered dose, where refractory is defined as a decrease in the ~~Overall Neuropathy Limitations Scale (~~ONLS~~)~~ of less than 1 point, or an increase in the Medical Research Council (MRC) sum score of less than 3, compared to baseline; OR
Patient must have progressive disease with an inadequate response to immunoglobulins (beyond the 4 months initiation period) at or above the registered dose, where inadequate response is defined as worsening of ONLS score, or MRC sum score compared to the previous assessment; OR
~~Patient must have relapsed at least 6 months after cessation of immunoglobulin treatment; OR~~
Patient must be contraindicated or intolerant to immunoglobulin.
Treatment criteria:
Must be treated by a prescriber who is either: (i) a neurologist; (ii) a clinical immunologist with expertise in the treatment of CIDP; OR
Must be treated by a medical practitioner who has consulted at least one of the above-mentioned specialist types, with an agreement reached that the patient should be treated with this pharmaceutical benefit on this occasion
Population criteria:
Patient must be 18 years or older.
Administrative Advice:
No increase in the maximum quantity or number of units may be authorised.
No increase in the maximum number of repeats may be authorised.
Special Pricing Arrangements apply.
Category / Program: General Schedule
Prescriber type: Medical Practitioners
Restriction type: ☒Authority Required (telephone/online PBS Authorities system) ☒Authority Required (in writing only via post/HPOS upload)
Severity: Progressive, relapsing and refractory
Condition: Chronic Inflammatory Demyelinating Polyneuropathy
Indication: Chronic Inflammatory Demyelinating Polyneuropathy
Treatment Phase: First continuing
Clinical criteria:
Patient must have previously received PBS-subsidised treatment with this drug for this condition
AND
Clinical criteria:
Patient must have achieved *an improvement in disability, as measured by a* decrease in the ~~Inflammatory Neuropathy Cause and Treatment (INCAT)~~ *Overall Neuropathy Limitation Scale (ONLS)* score of one or more points; ***OR*** *by an increase in the Medical Research Council (MRC) sum score by at least three points, as compared to the qualifying assessment.*
Treatment criteria:
Must be treated by a prescriber who is either: (i) a neurologist; (ii) a clinical immunologist with expertise in the treatment of CIDP.

Administrative Advice:
No increase in the maximum quantity or number of units may be authorised.
No increase in the maximum number of repeats may be authorised.
The number of repeats should provide sufficient treatment for six months.
Special Pricing Arrangements apply.
Category / Program: General Schedule
Prescriber type: Medical Practitioners
Restriction type: ☒Authority Required (telephone/online PBS Authorities system) ☒Authority Required (in writing only via post/HPOS upload)
Severity: Progressive, relapsing and refractory
Condition: Chronic Inflammatory Demyelinating Polyneuropathy
Indication: Chronic Inflammatory Demyelinating Polyneuropathy
Treatment Phase: Subsequent continuing
Clinical criteria:
Patient must have previously received PBS-subsidised treatment with this drug for this condition
AND
Clinical criteria:
Patient must have demonstrated stabilisation or continued improvement in disease as measured by the ~~Inflammatory Neuropathy Cause and Treatment (INCAT)~~ *Overall Neuropathy Limitation Scale (ONLS)* score, **OR** *the Medical Research Council (MRC) sum score compared to the previous review score,.*
Treatment criteria:
Must be treated by a prescriber who is either: (i) a neurologist; (ii) a clinical immunologist with expertise in the treatment of CIDP.
Administrative Advice:
No increase in the maximum quantity or number of units may be authorised.
No increase in the maximum number of repeats may be authorised.
The number of repeats should provide sufficient treatment for six months.
Special Pricing Arrangements apply.

Italics = additions proposed in the PSCR
Strikethrough = deletions proposed in the PSCR

3.1 The submission's original proposed clinical criteria would have allowed efgartigimod to be used in patients who relapsed at least 6 months after cessation of immunoglobulin treatment. The submission had claimed that these patients were not eligible for further immunoglobulin treatment under the NBA. However, correspondence with the NBA during the evaluation process indicated this was incorrect and these patients can receive further immunoglobulin (i.e. IVIg/subcutaneous immunoglobulin [SCIg]) treatment as long as they re-qualify under the NBA treatment initiation criteria. The PSCR withdrew this population (i.e. patients who relapse at least 6 months after receiving immunoglobulin treatment), given they are eligible for retreatment with immunoglobulin. The PSCR noted that patients demonstrating an inadequate response to retreatment would be eligible to access efgartigimod via the other proposed criteria.

3.2 The requested PBS restriction for efgartigimod requires a confirmed diagnosis of CIDP according to the European Academy of Neurology (EAN)/Peripheral Nerve Society

(PNS) guidelines[1], limits treatment to patients with significant disability or compromised walking, does not allow corticosteroid treatment as a prior qualifying therapy, and includes specific clinical criteria to define relapsing, refractory, progressive and intolerant populations, as well as specific clinical criteria for treatment continuation. The Sub-Committees considered that the proposed listing (with the relapsed sub-population removed, as per paragraph 3.1) appears to align with current Australian practice for use of immunoglobulin early in the disease course and with relapses following other therapies (e.g. steroids and immunosuppressive therapies).

3.3 The requested restriction states that diagnosis should be conducted by a neurologist using the EAN/PNS guidelines[1]. The evaluation considered that this was reasonable, but considered that as the current EAN/PNS guidelines include the diagnoses of CIDP and possible CIDP, there was uncertainty as to whether patients with possible CIDP could access treatment. The PSCR suggested that this could be addressed by requiring patients to explicitly meet both the clinical and neurophysiologic criteria for CIDP diagnosis under the EAN/PNS diagnostic guidelines, and noting the importance of excluding alternative diagnoses prior to commencing efgartigimod. Noting the challenges with diagnosing CIDP, the Sub-Committees considered that it may be appropriate to clarify in the restriction that CIDP must be "confirmed" and require physicians to provide documentation of the qualifying criteria. The Secretariat proposed the addition of administrative advice to refer prescribers to the relevant diagnostic resource/reference.

3.4 Given that response to treatment (particularly immunoglobulin) is part of the diagnostic guidelines, the Sub-Committees considered that the proposed restriction may target a population enriched for misdiagnosis (even with the restriction based on "confirmed" cases). The Sub-Committees considered that it was unclear whether this would impact the magnitude of the treatment effect of efgartigimod. The pre-PBAC response contended that "while a proportion of non-responders may ultimately be reclassified, non-response itself does not equate to misdiagnosis, reinforcing the importance of structured reassessment". The pre-PBAC response acknowledged the Sub-Committee's consideration that around 30% of patients not responding to immunoglobulin will likely be reclassified as not having CIDP (see Table 11), and excluded this proportion of patients from the eligible pool in revised financial estimates (increased from 19% in the submission).

3.5 In line with the draft TGA PI, the initial and grandfather restrictions require that treatment must be initiated/supervised by a physician experienced in the management of patients with neuromuscular disorders. The Secretariat questioned whether the initial and grandfather treatment phase should be restricted only to prescribing by specialist, given the risk of misdiagnosis of CIDP (i.e. remove treatment by a medical practitioner "in consultation" with specialists). The submission's

[1] The most recent version is the 2021 guidelines; however, the key clinical trial for efgartigimod used an older version of these guidelines (European Federation of Neurological Societies (EFNS)/PNS 2010). The PSCR agreed that the EAN/PNS 2021 guidelines should be the basis for CIDP diagnosis.

requested restriction required patients to have significant disability or compromised walking, as indicated by an Inflammatory Neuropathy Cause and Treatment (INCAT) score[2] ≥3, on the basis that this would target treatment to patients with higher clinical need. However, the evaluation noted that current NBA IVIg/SCIg eligibility criteria defines significant disability based on an Overall Neuropathy Limitation Scale (ONLS) score ≥2 in combination with the Medical Research Council (MRC) sum score. The PSCR stated that four neurologists consulted advised that the appropriate instrument and threshold for initiation of efgartigimod was "ONLS 3 for initiation to replace the requirement for an INCAT 3", noting that "ONLS is the primary instrument used in Australia and the ADHERE entry criteria of INCAT 3 (or 2 where the score is only from leg disability) most closely maps to an ONLS of 3". While use of the ONLS instrument is more consistent with the existing IVIg/SCIg listing under the NBA, the nominated threshold differs (efgartigimod proposed ≥3; IVIg/SCIg listing ≥2). The Sub-Committees considered that the requirement for a greater (ONLS) impairment score compared to IVIg/SCIg eligibility appropriately targets treatment to patients with higher clinical need.

3.6 The requested restriction would limit treatment to patients who have progressive or refractory symptoms despite immunoglobulin treatment, or who are intolerant to immunoglobulin products. While immunoglobulins appear to be the most widely used therapy for the treatment of CIDP in Australia, the evaluation considered that the submission did not adequately justify the exclusion of corticosteroid monotherapy as a prior qualifying therapy, and the exclusion of this group is narrower than the proposed TGA indication. The submission and the PSCR noted that the clinical survey results showed that "other treatments such as corticosteroids and immunotherapy are not used as monotherapy" in Australia.

3.7 The submission's proposed clinical criteria defined refractory disease as an inadequate response (less than a 1-point decrease in ONLS score or less than a 3-point increase in MRC sum score) to immunoglobulin treatment after 4 months of treatment at or above the registered dose (not defined in the restriction). The definition of inadequate response used in the restriction is consistent with current NBA eligibility criteria for IVIg (SCIg is not recommended for treatment induction). The evaluation considered it was unclear whether it would be clinically appropriate to require patients to use IVIg at or above the registered dose (refer to paragraph 3.9).

3.8 The PSCR noted that the proposed restriction would exclude patients with a high baseline ONLS who experience a one-point ONLS improvement but still have significant disability despite immunoglobulin treatment (e.g. a patient who improves from an ONLS 6 to ONLS 5). These patients are currently treated with escalating doses of immunoglobulin, often in combination with other agents. The PSCR proposed allowing access for these patients who continue to meet the NBA IVIg/SCIg initiation requirements despite receiving immunoglobulin treatment at the registered dose (1 g/kg Q3W). The Response did not provide financial estimates for this target

[2] INCAT scores are measured on a 0-10 point scale with lower scores indicating less functional impairment

population. While the Sub-Committees considered it was likely this group were already accounted for in the epidemiological approach used, it also considered that inclusion of this criterion would further increase the uncertainty with the financial estimates.

3.9 The proposed clinical criteria define progressive disease as a worsening in ONLS score or MRC sum score (no specific threshold) after at least 4 months of treatment with immunoglobulin therapy at or above the registered dose (this dose was not defined in the restriction). The evaluation noted that the definition of progression used in the restriction was broadly aligned with current NBA eligibility criteria for IVIg/SCIg (although the NBA criteria also allow IVIg/SCIg treatment to be continued if patients experience a temporary relapse or experience end-of-cycle deterioration). However, the evaluation considered it was unclear whether it would be clinically appropriate to require patients to use IVIg/SCIg at or above the registered dose. The Sub-Committees noted evidence exists that dose escalation can lead to improved response to immunoglobulin therapy; however, considered that it was not appropriate to require patients to use IVIg/SCIg above the registered dose, and that this criterion should instead specify use at the recommended dose.

3.10 Australian PI documents for IVIg and SCIg include recommended doses for CIDP but note that dosing should be individualised for each patient. Both the EAN/PNS treatment guidelines and the current NBA eligibility criteria for IVIg/SCIg treatment recommend that the dose of IVIg/SCIg should be gradually reduced over time to the lowest dose required to maintain response. The evaluation considered that selection of maintenance dosing would also be affected by a variety of other factors including whether IVIg/SCIg is being used in combination with corticosteroids and/or immunosuppressants.

3.11 The proposed clinical criteria allow efgartigimod to be used in patients who are contraindicated or intolerant to immunoglobulin. The submission claimed that this was appropriate as these patients have limited other treatment options. The submission did not provide any clinical data directly related to efgartigimod use in patients who cannot tolerate immunoglobulin therapy.

3.12 The first continuation authorisation required patients to have demonstrated a response to efgartigimod treatment as indicated by ≥1-point reduction in INCAT score after 3 months of treatment, (inconsistent with the key trial of efgartigimod which defined response based on ≥1-point reduction in adjusted INCAT score or a ≥4-point increase in Inflammatory Rasch-Built Overall Disability Scale (I-RODS) score or a ≥8 kPA increase in grip strength). The PSCR proposed amended response criterion of "Improvement in disability as measured by a reduction in the ONLS by at least one point; or an increase in the MRC sum score by at least three points, as compared to the qualifying assessment". This was in line with the NBA/BloodSTAR immunoglobulin eligibility criteria, and consistent with the current EAN/PNS 2021 guidelines which recommend that response should be assessed using both a disability measure (e.g.

INCAT, I-RODS, ONLS) and an impairment measure (e.g. MRC sum score, grip strength).

3.13 The subsequent continuation authorisation required patients to demonstrate stabilisation or continued improvement in INCAT score, but this was replaced in the PSCR to require "Stabilisation or continued improvement in disease as measured by the ONLS or the MRC sum score compared to the previous review score". The current NBA eligibility criteria for IVIg/SCIg have similar criteria based on ONLS and MRC sum scores.

3.14 The proposed maximum quantities (4 subcutaneous vials or 4 pre-filled syringes) and maximum repeats (2 repeats for initial; 5 repeats for grandfathering, first and subsequent continuing) provide sufficient coverage for 3 months (initial) or 6 months (grandfathering; continuing) treatment. The Secretariat noted that the draft TGA-PI states that "… Clinical evaluation should be considered 3 to 6 months after treatment initiation to assess the treatment effect and at regular intervals thereafter". However, assessment at 3 months (as proposed in the restriction) is consistent with the ADHERE trial (Stage A), and expert advice from the sponsor's advisory panel indicated that a 3-month duration is sufficient to assess initial response to efgartigimod treatment. The experts noted that the 4-month assessment time point for IVIg was originally used to accommodate busy clinics not able to see the patient within 3 months. The Secretariat considered that maximum quantities and repeats should provide coverage at 3 months for initial and 6 months for grandfathering/continuing (in line with the usual 6-months for chronic diseases), including for patients who transition to fortnightly (Q2W) dosing, and that it may be appropriate for the restrictions to specify that demonstration of response is required within 12 weeks since commencing treatment/initial treatment for first continuing treatment; and every 24 weeks for subsequent continuing treatment.

3.15 The evaluation considered that the risk of efgartigimod use outside the requested restriction in the broader population of CIDP patients who are stable/improving on immunoglobulin therapy was unclear, particularly given the claim that efgartigimod is associated with a lower treatment burden (subcutaneous injection every 1-2 weeks) compared to IVIg (intravenous infusion every 2-6 weeks) and SCIg (subcutaneous infusion every 1-2 weeks).

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

4 Population and disease

4.1 CIDP is a rare autoimmune disease characterised by inflammation around peripheral nerves which damages the myelin sheath leading to impaired function. Key symptoms of the condition include muscle weakness, sensory changes (tingling, numbness, loss of feeling), loss of reflexes, fatigue, and pain. CIDP can have a substantial impact on independence, quality of life, workplace participation and carer burden.

4.2 CIDP can affect people of any age, but the average age of onset is typically around 50 to 60 years old. The disease course is highly variable and can be monophasic,

relapsing/remitting or progressive. Most CIDP cases have a typical presentation with symmetrical weakness and sensory loss (affecting both sides of the body) although other variants exist including motor symptoms only, sensory symptoms only, asymmetrical weakness and sensory loss, symptoms affecting only one focal area, and symptoms primarily affecting hands and feet.

4.3 The estimated prevalence of the disease in the published literature typically ranges from 1 to 10 cases per 100,000 population (pooled prevalence 2.81 cases per 100,000; Broers 2019; Querol 2021; Park 2022). However, the submission noted that data from the NBA indicate that 3,389 patients were accessing immunoglobin treatments for CIDP in Australia in the 2024/2025 financial year. The evaluation noted that this equates to a crude prevalence of approximately 12 cases per 100,000 population based on Australian Bureau of Statistics estimates of the Australian population in March 2025 (3,389 / 27,536,874 × 100,000).

4.4 The EAN/PNS 2021 guidelines recommend that CIDP should be considered in any patient with a progressive symmetric or multifocal polyradiculoneuropathy in whom the clinical course is relapsing and remitting or progresses for more than 8 weeks, especially if there are sensory symptoms, proximal weakness, areflexia without wasting, or preferential loss of vibration or joint position sense. Diagnostic criteria vary by disease subtype but include combinations of clinical features, electrodiagnostic test results (motor and sensory nerves) and other supportive criteria (such as an objective response to treatment IVIg, plasma exchange (PLEX) or corticosteroids).

4.5 The submission acknowledged that the diagnosis of CIDP is challenging and older diagnostic criteria such as the EFNS/PNS 2010 guidelines used in the key clinical trials of efgartigimod and IVIg/SCIg were associated with a high false positive rate (47%; Allen 2015, Allen 2020), particularly in regard to atypical variants. The submission noted that two studies have compared the older EFNS/PNS 2010 guidelines with the current EAN/PNS 2021 guidelines; with one study indicating improved specificity but reduced sensitivity with the new diagnostic criteria (Doneddu 2022), and the other study suggesting that both the previous and current criteria had similar sensitivity and specificity (Rajabally 2022). The high rate of misdiagnosis in clinical practice was also raised as a concern by the sponsor's expert advisory panel and during the MSAC assessment of immunoglobulin for CIDP (MSAC application no. 1564; April 2021) and is discussed in Table 11.

4.6 Efgartigimod is a human IgG1 antibody fragment that binds to the neonatal Fc Receptor (FcRn) and inhibits the recycling of IgG back into circulation. The inhibition of FcRn function is expected to reduce the levels of circulating IgG including pathogenic IgG autoantibodies. The exact mechanism of action for its therapeutic effect in CIDP is currently unknown.

4.7 The submission positioned efgartigimod as a subsequent-line treatment option in patients who are refractory (patients who did not achieve the required response criteria for IVIg/SCIg at 4 months), progressive (patients who initially responded to IVIg/SCIg but no longer meet the requirements for continued treatment) or who are

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intolerant to immunoglobulin therapy. However, the evaluation noted that it is possible that some (or all) patients considered refractory to immunoglobulin therapy may have been misdiagnosed and do not, in fact, have CIDP (see Figure 1 and paragraph 4.5).

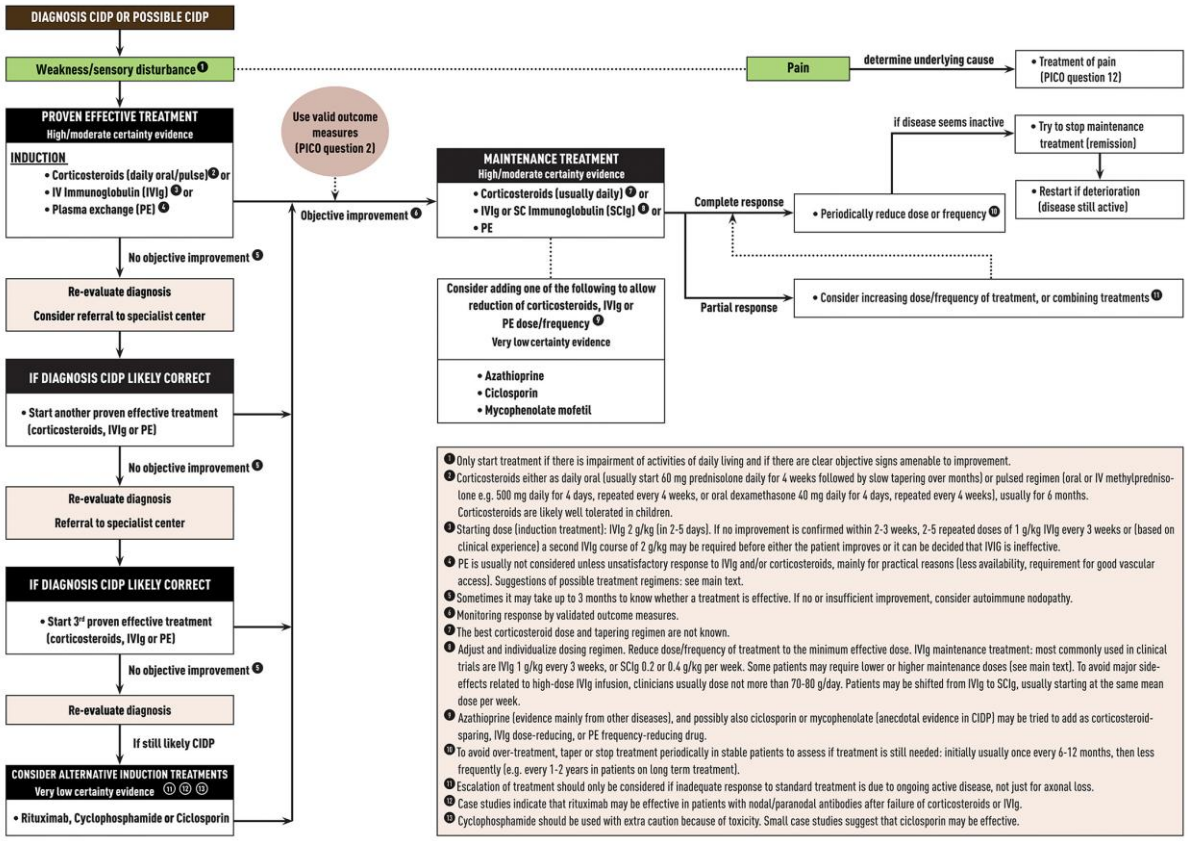
4.8 Efgartigimod is expected to be used as an ongoing therapy for the management of CIDP, and unlike some other therapies (such as corticosteroids and immunoglobulin therapy) there is currently no guidance on treatment weaning or cessation.

4.9 The algorithms presented in the submission did not address the role of corticosteroids, immunosuppressants, rituximab and PLEX either as monotherapy or combination therapy with IVIg/SCIg in the target population.

4.10 The evaluation considered the treatment algorithm from the EAN/PNS CIDP guidelines (van den Bergh 2021; see Figure 1 below) informative in understanding current clinical practice, as it provides guidance on treatment sequencing, use of combination therapy, treatment optimisation, and treatment weaning/cessation. The pre-PBAC response contended that the EAN/PNS algorithm was not relevant as the predominant first line treatment in Australia is immunoglobulin (see also paragraph 6.1).

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Figure 1: EAN/PNS (2021) clinical management algorithm



Source: Flowchart 3 of the Van den Bergh (2021) publication
Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; EAN, European Academy of Neurology; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-Built Overall Disability Scale; IV, intravenous; IVIg, intravenous immunoglobulin; kPA, kilopascal; MRC, Medical Research Council; ONLS, Overall Neuropathy Limitations Scale; PE, plasma exchange; PICO, population, intervention, comparator, outcome framework; PNS, Peripheral Nerve Society; SCIg, subcutaneous immunoglobulin
Note: The guidelines recommend assessment of objective improvement using both a disability measure (≥1-point decrease in INCAT score, ≥4-point increase in I-RODS score) and an impairment measure (≥8-14 kPA increase in grip strength, ≥2-4 increase in MRC score) but notes that the improvement thresholds have not been adequately validated. Australian physicians report using ONLS (≥1-point decrease in score) as a disability measure and MRC as an impairment measure (≥3 increase in MRC score) to assess improvement consistent with NBA eligibility criteria (see Attachments 3 and 4 of the submission).

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

5 Comparator

5.1 The submission nominated both placebo (no active therapy) and IVIg/SCIg as the main comparators.

5.2 The main argument provided to support the nomination of IVIg/SCIg was that these therapies form the backbone of supportive care for CIDP in Australia (based on a survey of Australian neurologists, approximately 80-95% of patients use IVIg/SCIg either as a monotherapy or as part of combination therapy). The evaluation considered that this argument appeared reasonable, noting the potential that some patients not using IVIg/SCIg (e.g. refractory) may have been misdiagnosed, and do not have CIDP (see paragraph 4.7).

5.3 In regard to the specific subgroups identified in the target population, the submission assumed that:

- patients who are refractory (or relapsed though this group was later removed in the PSCR), or intolerant to immunoglobulin therapy would not use IVIg/SCIg treatment (represented by placebo in the submission); while
- patients with 'progressive' disease would continue to use sub-optimal IVIg/SCIg.

Based on these assumptions, the submission calculated that 40.67% of the target population would be using IVIg/SCIg therapy (unadjusted for misdiagnosis rate); although this was adjusted to 50% in the PSCR with the removal of the relapsed population. However, the evaluation considered it was unclear what proportion with a true CIDP diagnosis would be using IVIg/SCIg therapy (see paragraph 5.2).

5.4 Overall, the Sub-Committees considered that the nomination of IVIg/SCIg and placebo as comparators was reasonable. Refer to paragraph 7.7 for PBAC's view.

5.5 The submission did not clearly address the other therapies used in the majority of the target population. The evaluation noted that the proposed place in therapy for efgartigimod appears to align with the current place in therapy for corticosteroids, immunosuppressants, rituximab and PLEX, either as monotherapies or as combination therapy with IVIg/SCIg (EAN/PNS 2021 treatment guidelines). The PSCR argued that the clinical survey results showed that other treatments such as corticosteroids and immunotherapy are used in combination with IVIg/SCIg, rather than as monotherapy. The Sub-Committees noted, as per paragraph 5.3, the submission had assumed that IVIg/SCIg would not be used in approximately half of the target population (i.e. patients who are refractory or intolerant) and thus other therapies (e.g. corticosteroids, immunosuppressants, rituximab) may be a relevant comparator in many patients.

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

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinician discussed the natural history of CIDP, emphasising diagnostic uncertainty due to the absence of a biomarker and a substantial misdiagnosis rate (estimated at 50%). The clinician clarified that in some countries high dose steroids are used first-line to try to induce remission; however, IVIg is the standard of care for first-line treatment of CIDP in Australia as it is effective in the majority of patients, i.e.: ~1/3 recover and ~1/3 can taper to a lower dose); however, some patients remain on lifelong high-dose IVIg and a subset of these patients are refractory and have ongoing active disease despite IVIg. Escalation options such as prednisolone, rituximab, cyclophosphamide and/or PLEX were described as having variable effectiveness and significant tolerability and/or access/logistical limitations, resulting in high treatment burden. The clinician

considered that new therapies (e.g. efgartigimod) are needed for this subgroup with persistent active disease to achieve better disease control.

Consumer inputs

6.2 The PBAC noted and welcomed input from an individual and an organisation via the Office of Health Technology Assessment Consultation Hub. The individual described the substantial burden of CIDP, including fluctuating physical disability, severe fatigue, loss of independence, reduced ability to work, and significant psychosocial and financial impacts. The comments also highlighted the treatment burden associated with regular IVIg infusions, including time commitments, disruptions to work and family life, requirements for monitoring, and anxiety when symptoms recur or treatment response diminishes. They also emphasised the importance of equitable access to new treatments for people with CIDP.

6.3 The PBAC noted the advice from a health professional working with the Klim Foundation, regarding the likely use of efgartigimod in clinical practice. The organisation advised that the availability of efgartigimod would increase patient choice for those who have an inadequate response or intolerance to current treatments. Further, the availability of an at-home injectable option may reduce reliance on hospital infusion services and improve flexibility for patients and families. The PBAC noted that this advice was consistent with the themes raised in individual consumer input.

Clinical trials

6.4 The submission was based on a phase 2, multi-stage trial of efgartigimod which included a run-in phase in which active treatments were stopped, an enrichment phase where all patients were treated with efgartigimod, a withdrawal phase where efgartigimod responders were randomised to continued efgartigimod treatment or placebo, and an open-label extension phase where all patients received efgartigimod (ADHERE/ADHERE+). The open-label extension phase is currently ongoing with an expected completion date of April 2027 (NCT04280718).

6.5 The submission also presented a Bucher indirect comparison of efgartigimod (ADHERE) versus IVIg/SCIg treatment withdrawal trials (ADVANCE-CIDP, PATH, ICE) using a placebo common reference arm. While the submission focused on treatment withdrawal trials in order to conduct an indirect comparison with the ADHERE trial, there is a substantially larger evidence base using other study designs that supports the use of IVIg/SCIg for the treatment of CIDP (e.g., Bus 2024 and Ramzi 2024 systematic reviews).

6.6 Details of the included studies are provided in Table 2.

Table 2: Studies and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Efgartigimod versus placebo trials		

Trial ID	Protocol title/ Publication title	Publication citation
ARGX-113-1802/1902 (ADHERE/ADHERE+)	Argenx BV (2023). A phase 2 trial to investigate the efficacy, safety, and tolerability of efgartigimod PH20 SC in adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP).	Internal study report.
	Argenx BV (2024). Substudy—Interim analysis 1: Open-label extension of the ARGX-113-1802 trial to investigate the long term safety, tolerability, and efficacy of efgartigimod PH20 SC in patients with chronic inflammatory demyelinating polyneuropathy (CIDP).	Internal study report.
	Argenx BV (2024). Top-line results report, interim analysis 2: open-label extension of the ARGX-113-1802 trial to investigate the long term safety, tolerability, and efficacy of efgartigimod PH20 SC in patients with chronic inflammatory demyelinating polyneuropathy (CIDP).	Internal study report.
	Allen et al (2024). Safety, tolerability, and efficacy of subcutaneous efgartigimod in patients with chronic inflammatory demyelinating polyradiculoneuropathy (ADHERE): a multicentre, randomised-withdrawal, double-blind, placebo-controlled, phase 2 trial.	The Lancet Neurology 23: 1013–1024.
Immunoglobulin versus placebo trials		
NCT02549170 (ADVANCE - CIDP)	Bril et al (2023). Hyaluronidase-facilitated subcutaneous immunoglobulin 10% as maintenance therapy for chronic inflammatory demyelinating polyradiculoneuropathy: The ADVANCE-CIDP 1 randomized controlled trial.	Journal of the Peripheral Nervous System 28: 436-449.
	Pasnoor et al (2025). The results of ADVANCE-CIDP IVIg trial: intravenous immunoglobulin 10% therapy with GAMMAGARD LIQUID/Kiovig for treatment of relapse in chronic inflammatory demyelinating polyradiculoneuropathy.	European Journal of Neurology 32(4): e70110.
	Hadden et al (2025). Long-term safety and tolerability of hyaluronidase-facilitated subcutaneous immunoglobulin 10% as maintenance therapy for chronic inflammatory demyelinating polyradiculoneuropathy: Results from the ADVANCE-CIDP 3 trial.	Journal of the Peripheral Nervous System 29: 441-452.
NCT00220740 (ICE)	Hughes et al (2008). Intravenous immune globulin (10% caprylate-chromatography purified) for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (ICE study): a randomised placebo-controlled trial.	Lancet Neurology 7: 136-144.
	Donofrio et al (2010). Safety and tolerability of immune globulin intravenous in chronic inflammatory demyelinating polyradiculoneuropathy.	Archives of Neurology 67: 1082-1088.
	Merkies et al (2009). Health-related quality-of-life improvements in CIDP with immune globulin IV 10%: The ICE Study.	Neurology 72: 1337-1344.
	Merkies et al (2010). Understanding the consequences of chronic inflammatory demyelinating polyradiculoneuropathy from impairments to activity and participation restrictions and reduced quality of life: The ICE study.	Journal of the Peripheral Nervous System 15: 208-215.
	Keller et al (2019). IVIG efficacy in CIDP patients is not associated with terminal complement inhibition.	Journal of Neuroimmunology 330: 23-27.
NCT01545076 (PATH)	van Schaik et al (2018). Subcutaneous immunoglobulin for maintenance treatment in chronic inflammatory demyelinating polyneuropathy (PATH): a randomised, double-blind, placebo-controlled, phase 3 trial.	Lancet Neurology 17: 35-46.
	Berger et al (2018). IgPro20, the Polyneuropathy and Treatment with Hizentra study (PATH), and the treatment of chronic inflammatory demyelinating polyradiculoneuropathy with subcutaneous IgG.	Immunotherapy 10: 919-933.

Trial ID	Protocol title/ Publication title	Publication citation
	Bril et al (2021). Electrophysiological testing in chronic inflammatory demyelinating polyneuropathy patients treated with subcutaneous immunoglobulin: The Polyneuropathy And Treatment with Hizentra (PATH) study.	Clinical Neurophysiology 132: 226-231.
	Hartung et al (2019). Patient-reported outcomes with subcutaneous immunoglobulin in chronic inflammatory demyelinating polyneuropathy: the PATH study.	European Journal of Neurology 27:196-203.
	Lewis et al (2020). Placebo effect in chronic inflammatory demyelinating polyneuropathy: The PATH study and a systematic review.	Journal of the Peripheral Nervous System 25: 230-237.
	Merkies et al (2022). Analysis of relapse by inflammatory Rasch-built overall disability scale status in the PATH study of subcutaneous immunoglobulin in chronic inflammatory demyelinating polyneuropathy.	Journal of the Peripheral Nervous System 27: 159-165.
	Mielke et al (2019). Restabilization treatment after intravenous immunoglobulin withdrawal in chronic inflammatory demyelinating polyneuropathy: Results from the pre-randomization phase of the Polyneuropathy And Treatment with Hizentra study.	Journal of the Peripheral Nervous System 24: 72-79.

Source: Table 2.2-2, pp76-82 of the submission
Note: Abstracts of studies with full publications are not presented

6.7 The key features of the included trials are summarised in Table 3.

Table 3: Key features of the included trials

Trial ID	Description
Efgartigimod trials	
ADHERE	**Design**: Phase 2, multi-centre (international), multi-stage study with a run-in phase in which active treatments were stopped, an open label phase where all patients were treated with efgartigimod and a withdrawal phase in which efgartigimod responders were randomised to continued efgartigimod treatment or placebo (randomised duration up to 48 weeks). This led to an enriched population in stage B. **Population**: Adult patients with probable or definite CIDP using the EFNS/PNS 2010 criteria with a baseline INCAT score ≥2 who were currently treated with corticosteroids, IVIg/SCIg or no active treatment (N = 342). Patients currently treated with active therapies were required to demonstrate a clinical deterioration in the run-in phase to be eligible for the enrichment phase. Patients in the enrichment phase had to demonstrate a clinical improvement to be eligible for the randomised phase. **Intervention**: Efgartigimod (1,000 mg) co-formulated with vorhyalurindase alfa subcutaneous injection once weekly. Use of concomitant corticosteroids or immunosuppressants was prohibited. **Comparator**: Placebo co-formulated with vorhyalurindase subcutaneous injection. Use of concomitant corticosteroids or immunosuppressants was prohibited. **Primary outcome**: Proportion of patients with confirmed clinical improvement (Stage A open label phase), time to first clinical deterioration (Stage B, randomised phase).
Subcutaneous Ig trials	
ADVANCE-CIDP	**Design**: Phase 3, multi-centre (international), multi-stage study with a randomised treatment phase comparing treatment with SCIg and placebo in previous IVIg users with an IVIg rescue phase for patients with relapse and a SCIg maintenance phase for patients without relapse (randomised duration 6 months). **Population**: Adult patients with probable or definite CIDP using the EFNS/PNS 2010 criteria with a baseline INCAT score 0-7 who had previously responded to IVIg and were receiving a stable dose of 0.4-2.4 g/kg every month (N = 138). Patients with a relapse were eligible for the IVIg rescue phase while patients without relapse were eligible for the SCIg maintenance phase. **Intervention**: Immunoglobulin co-administered with vorhyalurindase alfa subcutaneous infusion once weekly with a stepped titration to match the dose of previous IVIg treatment (average dose 1.1 g/kg every 4.35 weeks). Use of concomitant corticosteroids or immunosuppressants was prohibited. **Comparator**: Placebo co-formulated with vorhyalurindase subcutaneous infusion. Use of concomitant corticosteroids or immunosuppressants was prohibited. **Outcome**: Proportion of patients with clinical deterioration.

Trial ID	Description
PATH	**Design**: Phase 3, multi-centre (international), multi-stage study with a run-in phase in which active treatments were stopped, a stabilisation phase where all patients were treated with IVIg and a withdrawal phase were IVIg responders were randomised to high dose SCIg, low dose SCIg or placebo (randomised duration 24 weeks). **Population**: Adult patients with probable or definite CIDP using the EFNS/PNS 2010 criteria who were currently treated with IVIg at doses ≤1.6 g/kg every 4 weeks (N = 245). **Intervention**: Subcutaneous infusion with high dose (0.4 g/kg) or low dose (0.2 g/kg) immunoglobulin once weekly. Use of concomitant corticosteroids and immunosuppressants (methotrexate, azathioprine, or mycophenolate) was permitted. **Comparator**: Placebo subcutaneous infusion. Use of concomitant corticosteroids and immunosuppressants (methotrexate, azathioprine, or mycophenolate) was permitted. **Outcome**: Proportion of patients with clinical deterioration.
Intravenous Ig trials	
ICE	**Design**: Phase 3, multi-centre (international), multi-stage study with an initial randomised cross-over phase in which patents were randomised to IVIg or placebo (with non-responders crossing over to the alternative treatment) and a subsequent randomisation phase were responders from the initial phase were re-randomised to IVIg or placebo (first randomised duration 24 weeks, second randomised duration 24 weeks). **Population**: Adult patients with diagnosis of CIDP with a baseline INCAT score 2-9 who were currently treated with low-dose corticosteroids or no active treatment (N = 117). Patients who responded to IVIg or placebo in the initial randomised phase were eligible for the second randomisation phase **Intervention**: Intravenous immunoglobulin infusion with a 2 g/kg loading dose and a maintenance dose 1 g/kg every 3 weeks. Use of concomitant low-dose corticosteroids was permitted. **Comparator**: Placebo intravenous infusion. Use of concomitant low-dose corticosteroids was permitted. **Primary outcome**: Proportion of patients with clinical improvement (first randomised phase)

Source: Table 2.4-1, p112; Table 2.4-2, pp115-121 of the submission
Abbreviations: CIDP: chronic inflammatory demyelinating polyneuropathy; EFNS, European Federation of Neurological Societies; INCAT, Inflammatory Neuropathy Cause and Treatment; IVIg, intravenous immunoglobulin; PNS, Peripheral Nerve Society; SCIg, subcutaneous immunoglobulin

6.8 The submission noted that the ADHERE trial was designed in consultation with CIDP experts and used many of the same elements as the PATH trial, which was the basis for the approval of SCIg for patients with CIDP. These elements included:

- A run-in phase where prior therapies (IVIg/SCIg N=165; steroids N = 63; no active treatment N = 94) were discontinued and patients were required to demonstrate clinical deterioration.
- An open-label phase, where patients were required to demonstrate a response to treatment (Stage A).This led to an enriched population in stage B.
- A randomised placebo-controlled withdrawal phase to assess maintenance of response and minimise long-term exposure to placebo (Stage B).
- Flexible durations of the run-in period, Stage A, and Stage B to ensure participants only remained in each stage for as long as necessary to meet the study endpoints.

6.9 The Sub-Committees agreed with published criticisms of the ADHERE trial that have highlighted concerns regarding:

- the diagnostic adjudication process and the potential for inclusion of misdiagnosed patients (diagnostic concordance rate of 52% between trial investigators). The PSCR argued that the 52% concordance rate was based on an analysis that included approximately one third of the screened patients, but an analysis of the complete data set demonstrated higher concordance (75.5%

agreement among all cases and 81.5% among trial participants). The analysis of the complete data set was not provided with the PSCR, and these values could not be verified;

- differential discontinuations between prior therapy groups in Stage A of the ADHERE trial and limited investigation of these differences (prior IVIg/SCIg: 32%; prior corticosteroids: 13%; no active therapy: 9%). The Sub-Committees considered there was insufficient information to determine whether the higher discontinuation rate in patients on prior IVIg/SCIg was linked to the reports of deterioration after switching (refer to paragraphs 6.16, 6.17 and 6.41);
- the lack of a placebo arm in Stage A to assess the magnitude of placebo effects on response (the PSCR outlined that the trial minimised placebo duration due to ethical concerns); and
- incentives to remain in earlier stages of the trial to gain access to open-label efgartigimod in the extension phase (Katz 2025). However, the PSCR contended that it was unlikely that patients would continue in the study without perceivable benefit.

6.10 The evaluation considered that despite the similarities between the ADHERE and PATH trials there were still key differences in diagnostic criteria (the submission claimed that ADHERE used a more rigorous method for case ascertainment), patient characteristics (ADHERE patients appear to have more severe disability at baseline), allowance of concomitant medications (the ADHERE trial prohibited the use of all other CIDP medications), and outcome definitions between trials (the ADHERE trial reported mean values while the PATH trial reported median values) that may preclude a robust indirect comparison of treatments.

6.11 The evaluation and the Sub-Committees considered that the study design of the other two immunoglobulin trials (ADVANCE-CIDP, ICE) did not appear sufficiently similar to the ADHERE trial to justify their inclusion in an indirect comparison. The PSCR acknowledged that the ICE study was excluded from all meta-analyses in recognition of these differences. However, the PSCR claimed that it was important to include the ADVANCE-CIDP trial as it was the only variable dose immunoglobulin study (PATH was fixed dose), arguing this provides the most clinically relevant treatment comparison (given the range of immunoglobulin doses used by different patients in practice). The PSCR also noted that Canada's Drug Agency (CDA-AMC, formerly CADTH) considered an indirect treatment comparison between the ADHERE, PATH and ADVANCE-CIDP trials in its assessment of efgartigimod for CIDP. However, the Sub-Committees noted that based on this evidence CDA-AMC concluded that '… there may be little to no clinically meaningful difference in efficacy between efgartigimod alfa injection and immunoglobulin among patients with CIDP' (efgartigimod, recommendations and reasons, CDA-AMC January 2026).

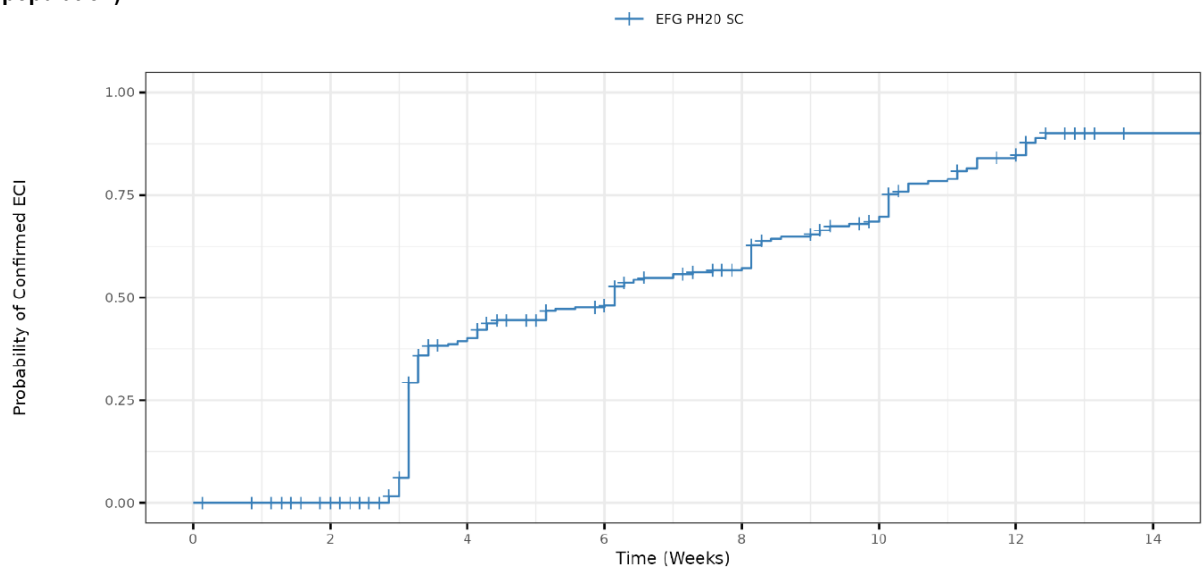
Comparative effectiveness

6.12 After patients ceased all active therapies during the run-in phase and had experienced a further clinical deterioration (≥1-point increase in aINCAT, ≥4-point decrease in I-

RODS, or ≥8-kPa decrease in mean grip strength) if recently treated with corticosteroids or SCIg/IVIg, patients were then treated with efgartigimod in Stage A of the ADHERE trial.

6.13 A Kaplan-Meier plot of the time to initial confirmed clinical improvement with efgartigimod treatment in Stage A of the ADHERE trial is presented in Figure 2.

Figure 2: Kaplan-Meier plot of the time to initial confirmed clinical improvement from Stage A baseline (full study population)



Source: Figure 2.5-3, p197 of the submission

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; ECI, evidence of clinical improvement; EFG PH20 SC, efgartigimod co-formulated with vorhyaluronidase alfa for subcutaneous injection; I-RODS, Inflammatory Rasch-built Overall Disability Scale

Note: For treatment-experienced participants who deteriorated in aINCAT score during the run-in period, a clinical improvement was defined as a ≥1-point decrease in aINCAT score. For treatment-experienced participants who had no change in aINCAT score and deteriorated on I-RODS and/or grip strength during the run-in period a clinical improvement was defined as a ≥1-point decrease in aINCAT score or a ≥4-point increase in I-RODS score (if initial deterioration only demonstrated by I-RODS) or a ≥8 kPa increase in grip strength (if initial deterioration only demonstrated by grip strength) or an improvement in both I-RODS score and grip strength for patients who had initial deterioration in both measures. For treatment-naïve participants a clinical improvement was defined as a ≥1-point decrease in aINCAT score

6.14 Treatment with efgartigimod was associated with a clinical improvement in 214/322 treated patients (66.5%; 95% CI: 61.0, 71.6) with a median time to clinical improvement of 43 days (IQR 22, 71 days).

6.15 Longitudinal analyses of mean disability and impairment scores indicated that efgartigimod treatment responders in Stage A of the ADHERE trial experienced improvements beyond original baseline values.

6.16 There were numerical differences in response rates between subgroups with patients who were previously using IVIg/SCIg having notably lower response rates (58.8%) than patients who were previously using corticosteroids (77.8%) or no active treatment

(72.3%). Subgroup analyses of safety data also suggest that patients with prior IVIg/SCIg had substantially higher rates of serious adverse events rates and adverse events leading to discontinuation compared to the other prior treatment subgroups.

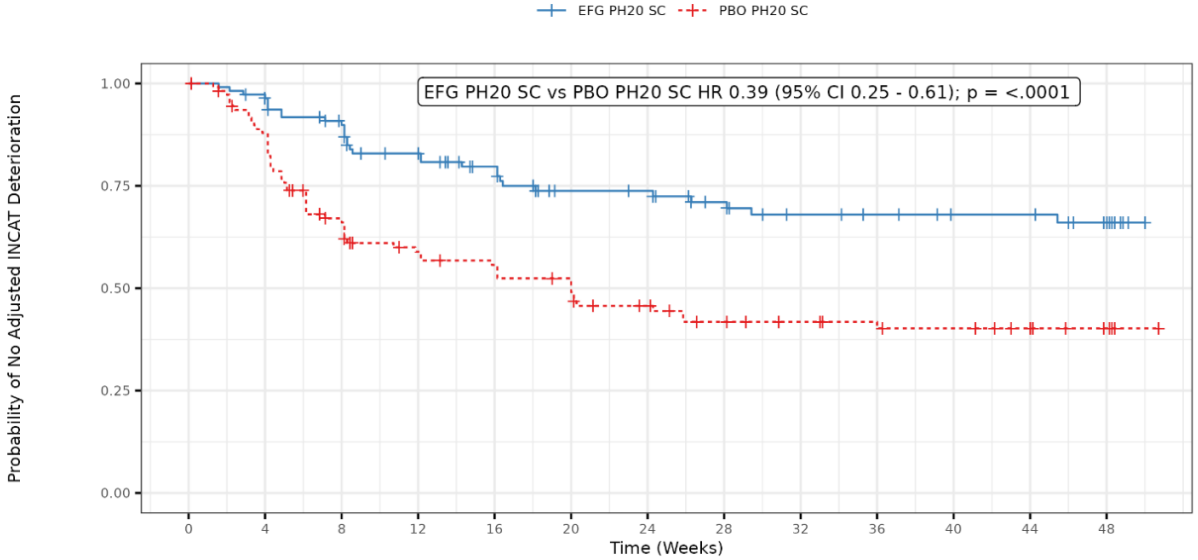
6.17 The submission suggested that patients with prior IVIg/SCIg use may have been more dependent on their prior therapies compared to the other subgroups and therefore were less able to tolerate the requirements of the ADHERE study design, which required patients to discontinue IVIg/SCIg at screening and experience a clinical deterioration in the run-in phase before initiating efgartigimod in Stage A. The PSCR also argued that "selection bias may have contributed to higher responder rates in the corticosteroids group, as typically corticosteroids are used to treat patients with very active CIDP relative to IVIg/SCIg".

6.18 The key publication of the ADHERE trial noted that the optimal approach to transition a patient from IVIg/SCIg therapy to efgartigimod is yet to be determined (Allen 2024). The PSCR stated that a Phase 4 study is underway to assess transitioning patients with CIDP to efgartigimod one week after the last IVIg infusion (see paragraph 6.42).

6.19 Patients who experienced a clinical improvement with efgartigimod treatment in Stage A of the ADHERE trial were then randomised to either efgartigimod or placebo in Stage B of the ADHERE trial (randomised treatment withdrawal design).

6.20 A Kaplan-Meier plot of the time to initial clinical deterioration with efgartigimod or placebo in Stage B of the ADHERE trial (i.e. the population enriched for efgartigimod responders) is presented in Figure 3.

Figure 3: Kaplan-Meier plot of the time to initial clinical deterioration from Stage B baseline (full study population)



Number of participants at risk

EFG PH20 SC	111	107	93	80	68	56	55	48	42	40	36	36	28
PBO PH20 SC	110	94	67	55	51	47	38	31	28	26	24	21	16

Source: Figure 2.5-1, p191 of the submission

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CI, confidence interval; EFG PH20 SC: efgartigimod co-formulated with vorhyaluronidase alfa for subcutaneous injection; HR: Hazard ratio; PBO PH20 SC, placebo co-formulated with vorhyaluronidase for subcutaneous injection

Note: Clinical deterioration was defined as a ≥1-point increase in aINCAT score

Note: The number of randomised participants (n = 221) was higher than that of participants with confirmed clinical improvement (n=214) because there were 13 participants randomised to stage B without confirmed clinical improvements and 6 participants with confirmed clinical improvement who were withdrawn from the study prior to randomisation

6.21 Continued treatment with efgartigimod was associated with a statistically significant reduction in the risk of clinical deterioration events compared to withdrawal of efgartigimod in the placebo arm (HR = 0.39; 95% CI: 0.25, 0.61). The median time to clinical deterioration was 140 days in the placebo arm and was not reached in the efgartigimod arm.

6.22 The trial report noted that the incremental difference between treatment arms was numerically smaller in patients with no active therapy compared to patients who received prior therapy with IVIg/SCIg or corticosteroids. The report claimed that this was due to the lower rate of clinical deterioration events in the placebo arm of this subgroup.

6.23 The mean change in disability measures (aINCAT and I-RODS scores), impairment measures (MRC score and grip strength) and quality of life (EQ-VAS) for the overall population as well as the subgroup with prior IVIg/SCIg use (the subgroup used for the indirect analyses) and the subgroup with prior IVIg/SCIg use who were relapsed or refractory at screening (the subgroup that appears to most closely align with the

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target patient population) during Stage B of the ADHERE trial is summarised in Table 4.

6.24 Table 4 also presents the results for the subgroup of patients who had received prior immunoglobulin and who had a CIDP activity status (CDAS) score of 5B/5C, i.e. those classified as having unstable active disease with relapsing or progressive symptoms despite ongoing therapy (5C) or previous treatment of ≥3 months (5B). The submission argued this subgroup was more consistent with the proposed PBS population of patients with refractory or progressive disease.

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Table 4: Mean change in disability, impairment and quality of life measures over time

	Overall		Prior IVIg/SCIg		Prior IVIg/SCIg and CDAS 5B/5C[a]	
	EFG	PBO	EFG	PBO	EFG	PBO
Change in aINCAT score from Stage B baseline						
N	111	109	48	48	18	21
Mean (SD) change	0.1 (1.08)	0.9 (1.98)	0.1 (1.06)	1.5 (2.32)	0.1 (1.21)	1.9 (2.08)
Mean (95% CI) difference	**-0.8 (-1.2, -0.4)**		**-1.3 (-2.1, -0.6)**		**-1.8 (-2.9, -0.7)**	
Change in I-RODS score from Stage B baseline						
N	111	108	48	47	18	21
Mean (SD) change	0.8 (12.33)	-7.0 (19.10)	3.0 (11.75)	-12.8 (23.15)	3.6 (10.85)	-15.5 (25.94)
Mean (95% CI) difference	**7.8 (3.5, 12.1)**		**15.7 (8.2, 23.3)**		**19.1 (6.4, 31.9)**	
Change in dominant hand grip strength from Stage B baseline						
N	111	109	48	48	18	21
Mean (SD) change	2.1 (13.29)	-8.2 (20.69)	3.4 (14.28)	-13.3 (21.56)	6.1 (15.74)	-16.6 (23.84)
Mean (95% CI) difference	**10.3 (5.6, 14.9)**		**16.7 (9.3, 24.1)**		**22.7 (9.8, 35.7)**	
Change in MRC sum score from Stage B baseline						
N	111	109	48	48	18	21
Mean (SD) change	-0.3 (4.53)	-3.0 (8.95)	-0.8 (4.49)	-5.1 (11.73)	-1.1 (6.05)	-5.8 (9.54)
Mean (95% CI) difference	**2.7 (0.9, 4.6)**		**4.3 (0.7, 7.9)**		4.8 (-0.4, 9.9)	
Change in EQ-VAS score from Stage B baseline						
N	97	90	44	37	17	18
Mean (SD) change	0.5 (17.42)	-10.2 (23.45)	2.3 (14.70)	-14.9 (26.97)	0.7 (15.62)	-19.9 (33.2)
Mean (95% CI) difference	**10.7 (4.7, 16.7)**		**17.2 (7.3, 27.2)**		**20.7 (2.7, 38.6)**	
Change in EQ-5D-5L index score (Australian value set) from Stage B baseline						
N	97	90	44	37	17	18
Mean (SD) change	-0.005 (0.191)	-0.145 (0.352)	-0.024 (0.173)	-0.21 (0.437)	-0.025 (0.19)	-0.265 (0.5)
Mean (95% CI) difference	**0.14 (0.057, 0.223)**		**0.19 (0.034, 0.342)**		**0.24 (-0.022, 0.503)**	

Source: Table 2.5-6, pp194-195; Table 2.5-17, pp212-214 of the submission; Table 2, Attachment 9 of the submission

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment score; CDAS, chronic inflammatory demyelinating polyneuropathy disease activity status; CI, confidence interval; CIDP, chronic inflammatory demyelinating polyneuropathy disease; EFG, efgartigimod; I-RODS, Inflammatory Rasch-Built Overall Disability Scale; IVIg, intravenous immunoglobulin; kPA, kilopascal; MRC, Medical Research Council; NR, not reported; PBO, placebo; SCIg, subcutaneous immunoglobulin; SD, standard deviation

[a] Estimated patient numbers do not align with reported estimates for 5B/5C categories in the larger population with prior immunoglobulin treatment

Note: aINCAT scores are measured on a 0-10 point scale with lower scores indicating less functional impairment

Note: I-RODS scores are transformed to a 0-100 percentile measure with higher scores indicating less disability

Note: Mean grip strength assessed by Martin-Vigorimeter with higher scores indicating more strength (range 0 to 120+ kPA)

Note: MRC scores are measured on a 0-60 point scale with higher scores indicating less functional impairment

Note: EQ-VAS scores are measured on a 0-100 point scale with higher scores indicating better quality of life

Note: EQ-5D-5L index scores (Australian value set) were calculated using the methodology described in the Norman 2023 publication. EQ-5D-5L scores are measured on a 0-1 scale where 0 represents death and 1 represents perfect health, negative scores worse than death are possible

Note: Patients with CDAS 5B/5C are classified has having unstable active disease with relapsing or progressive symptoms despite ongoing therapy (5C) or previous treatment of ≥3 months (5B).

6.25 Withdrawal of efgartigimod in the placebo arm was associated with a statistically significant worsening of mean aINCAT and I-RODS scores compared to patients who continued treatment with efgartigimod. The difference in change from baseline between treatment arms met the nominated threshold for a minimal clinically important difference (MCID) in I-RODS score (≥4-point increase) but not aINCAT score (≥1-point reduction) in the overall population. During the extension study, all patients received efgartigimod treatment with mean disability scores remaining relatively stable over time.

6.26 Withdrawal of efgartigimod in the placebo arm was associated with a statistically significant worsening of mean grip strength and MRC score compared to patients who continued treatment with efgartigimod. The difference in change from baseline between treatment arms met the nominated threshold for a MCID in grip strength (≥8 kPA improvement) but not MRC score (≥4-point change) in the overall population. During the extension study, all patients received efgartigimod treatment with mean impairment scores remaining relatively stable over time.

6.27 Withdrawal of efgartigimod in the placebo arm was associated with a statistically significant worsening of mean EQ-VAS and EQ-5D-5L index (Australian value set) scores compared to patients who continued treatment with efgartigimod in the overall population. During the extension study, all patients received efgartigimod treatment with mean EQ-VAS scores remaining relatively stable over time.

6.28 The submission claimed that the subgroup analyses demonstrated that treatment with efgartigimod is likely to have larger benefits in patients with prior IVIg/SCIg use and unstable active disease (CDAS score of 5B/5C) compared to the overall study population. The evaluation considered that the results of the subgroup analyses should be interpreted with caution due to the small sample sizes and wide confidence intervals around most estimates. The pre-PBAC response provided the results of tests for interaction and claimed the analyses demonstrated that efgartigimod is equally effective in the relapsed and refractory population (CDAS 5B and 5C) and the stable/improving/non-refractory complement (CDAS 2 to 5A).

6.29 An indirect comparison of the time to clinical deterioration with efgartigimod and IVIg/SCIg is summarised in Table 5.

Table 5: Results of the indirect comparison of the time to clinical deterioration with efgartigimod and IVIg/SCIg

Trial	Efgartigimod n/N (%)	Placebo n/N (%)	IVIg/SCIg n/N (%)	Treatment difference HR (95% CI)
ADHERE (Stage B – prior IVIg/SCIg subgroup)	14/48 (29.2%)	28/48 (58.3%)	-	**0.30 (0.15, 0.57)**
ADVANCE-CIDP (SCIg variable dose)	-	22/70 (31.4%)	6/62 (9.7%)	**0.28 (0.12, 0.70)**
PATH (SCIg low dose)	-	36/57 (63.2%)	22/57 (38.6%)	**0.49 (0.29, 0.84)**
PATH (SCIg high dose)	-	36/57 (63.2%)	19/58 (32.8%)	**0.38 (0.22, 0.67)**
ICE (IVIg recommended dose)	-	45%	13%	**0.19 (0.05, 0.70)**
Meta-analyses of Ig studies				
Meta-analysis of ADVANCE-CIDP, PATH low dose and ICE (I^2 = 22%)				**0.37 (0.22, 0.63)**
Meta-analysis of ADVANCE-CIDP, PATH high dose and ICE (I^2 = 0%)				**0.33 (0.21, 0.51)**
Meta-analysis of ADVANCE-CIDP and PATH low dose (I^2 = 5%)				**0.42 (0.26, 0.68)**
Meta-analysis of ADVANCE-CIDP and PATH high dose (I^2 = 0%)				**0.35 (0.22, 0.56)**
Indirect comparison of efgartigimod vs Ig				
Indirect comparison of ADHERE with ADVANCE-CIDP, PATH low dose and ICE				0.81 (0.35, 1.89)
Indirect comparison of ADHERE with ADVANCE-CIDP, PATH high dose and ICE				0.91 (0.41, 2.01)
Indirect comparison of ADHERE with ADVANCE-CIDP and PATH low dose				0.70 (0.31, 1.58)
Indirect comparison of ADHERE with ADVANCE-CIDP and PATH high dose				0.85 (0.38, 1.90)

Source: Table 2.5-3, p189; Table 2.5-7, pp195-196; Table 2.6-1, p262; Table 2.6-2, p263 of the submission
Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CI, confidence interval; HR, hazard ratio; IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin
Note: Clinical deterioration was defined as a ≥1-point increase in aINCAT score

6.30 The indirect analyses indicate that there were no statistically significant differences in the time to clinical deterioration after withdrawal of efgartigimod treatment in the placebo arm of the ADHERE trial compared to withdrawal of immunoglobulin treatment in the placebo arm of the comparator trials.

6.31 The indirect analyses also indicated that withdrawal of efgartigimod treatment in the placebo arm of the ADHERE trial was associated with a larger deterioration in mean aINCAT, I-RODS, grip strength, MRC and EQ-VAS scores compared to withdrawal of immunoglobulin treatment in the placebo arm of the comparator trials. The differences between treatment arms were statistically significant for the some of the comparisons.

Comparative harms

6.32 An overall summary of the adverse events with efgartigimod treatment in Stage A of the ADHERE trial is presented in Table 6.

Table 6: Summary of adverse events in Stage A of the ADHERE trial

	Overall		Prior IVIg/SCIg		Prior steroids		No active treatment	
	n/N (%)	Event rate	n/N (%)	Event rate	n/N (%)	Event rate	n/N (%)	Event rate
Stage A (efgartigimod enrichment phase)								
Any adverse event	204/322 (63.4%)	1,343.1	110/165 (66.7%)	1,359.8	40/63 (63.5%)	1441.8	54/94 (57.4%)	1,260.2
Treatment-related adverse event	101/322 (31.4%)	554.3	53/165 (32.1%)	501.7	23/63 (36.5%)	681.8	25/94 (26.6%)	557.9
Procedure-related adverse event	33/322 (10.2%)	140.7	19/165 (11.5%)	105.6	4/63 (6.3%)	67.1	10/94 (10.6%)	236.3
Serious adverse event	21/322 (6.5%)	51.2	18/165 (10.9%)	92.4	1/63 (1.6%)	11.2	2/94 (2.1%)	13.1
Adverse events leading to treatment discontinuation	22/322 (6.8%)	46.9	20/165 (12.1%)	88.0	2/63 (3.2%)	22.4	0/94 (0.0%)	0
Adverse events leading to treatment interruption	11/322 (3.4%)	32.0	5/165 (3.0%)	35.2	2/63 (3.2%)	22.4	4/94 (4.3%)	32.8
Deaths	2/322 (0.6%)	4.3	2/165 (1.2%)	8.8	0/63 (0.0%)	0	0/94 (0.0%)	0
Infections and infestations	44/322 (13.7%)	121.5	24/165 (14.5%)	140.8	7/63 (11.1%)	100.6	13/94 (13.8%)	105.0
Localised injection site reactions	62/322 (19.3%)	264.3	35/165 (21.2%)	268.4	13/63 (20.6%)	223.5	14/94 (14.9%)	282.2

Source: Table 2.5-24, p244 of the submission

Abbreviations: CI, confidence interval; IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin

Note: Event rates calculated based on total number of events divided by total years of patient exposure expressed as an event rate per 100 patient years of follow-up

6.33 The most frequently reported adverse events (>5% of patients) in Stage A were injection site erythema, CIDP deterioration and headache, with the majority of adverse events being mild to moderate in severity. Treatment-related events followed a similar pattern with the most commonly reported events being injection site reactions, CIDP deterioration, headache, abnormal investigations, and infections. Serious adverse events were primarily related to CIDP deterioration and infection.

6.34 Patients with prior IVIg/SCIg use had substantially higher rates of serious adverse events and adverse events leading to discontinuation compared to other patient groups in Stage A of the ADHERE trial. The evaluation considered it was unclear which specific adverse events were driving the higher rates of serious adverse events and adverse events leading to discontinuation in the prior IVIg/SCIg subgroup.

6.35 The PSCR presented a comparison of the most frequent adverse events by prior therapy (Table 7), across all adverse events regardless of adverse event severity/whether it led to discontinuation. As such, it did not adequately address concerns regarding the nature of events driving the higher rates of serious adverse events and adverse events leading to discontinuation in the prior IVIg/SCIg group compared to other populations.

Table 7: ADHERE Stage A Individual AEs reported in ≥5% patients in any prior treatment arm

	Ig prior treated (n=165, PYFU=22.72)			CS prior treated (n=63, PYFU=8.95)			Treatment naïve (n=94, PYFU=15.24)		
	n (%)	m	ER[a]	n (%)	m	ER[a]	n (%)	m	ER[a]
Injection site erythema	19 (11.5)	24	105.6	7 (11.1)	8	89.4	7 (7.4)	21	137.8
CIDP	17 (10.3)	19	83.6	0	-	-	0	-	-
Headache	10 (6.1)	16	70.4	0	-	-	6 (6.4)	12	78.8
URTI	4 (2.4)	4	17.6	4 (6.3)	5	55.9	3 (3.2)	3	19.7

Source: Table 1 of the PSCR (p3), derived from CSR Table 14.3.1.4.a.
N = number of participants with event; m = number of events. PYFU = person year of follow-up
[a] Event rate (ER) was calculated as the number of events × 100/PYFU (person year of follow-up). PYFU was calculated as the sum of the follow-up times in Stage A of all participants, expressed in years.

6.36 An overall summary of the adverse events reported with efgartigimod and placebo treatment in Stage B of the ADHERE trial is presented in Table 8.

Table 8: Overall summary of adverse events in Stage B of the ADHERE trial

Events	Efgartigimod (N = 111)		Placebo (N = 110)	
	Incidence n/N (%)	Events, n (rate/100 pt-yrs)	Incidence n/N (%)	Events, n (rate/100 pt-yrs)
Any adverse event	71 (64.0)	197 (348)	62 (56.4)	215 (511)
Treatment-related adverse event	27 (24.3)	61 (108)	22 (20.0)	65 (154)
Procedure-related adverse event	8 (7.2)	12 (21)	3 (2.7)	5 (12)
Serious adverse event	6 (5.4)	8 (14)	6 (5.5)	8 (19)
Adverse events leading to treatment discontinuation	3 (2.7)	3 (5)	1 (0.9)	1 (2)
Adverse events leading to treatment interruption	18 (16.2)	23 (41)	21 (19.1)	25 (59)
Deaths	0 (0.0)	0 (0)	1 (0.9)	1 (2)
Adverse events of special interest				
Infections and infestations	35 (31.5)	43 (76)	37 (33.6)	53 (126)
Localised injection site reactions	16 (14.4)	22 (39)	7 (6.4)	9 (21)

Source: Table 2.5-26, pp246-247 of the submission

6.37 The pattern of adverse events reported during the treatment withdrawal stage (Stage B) was broadly consistent with the enrichment phase (Stage A), although the reported adverse event rates were substantially lower during the former stage. The incidence of several adverse event reported outcomes were numerically higher in patients randomised to continued efgartigimod treatment compared to in patients randomised to withdrawal of efgartigimod in the placebo arm.

6.38 The interim analysis of the ADHERE+ extension study (February 2024 cut-off; 58-week mean duration of exposure) did not identify any additional safety concerns associated with efgartigimod treatment.

6.39 The submission provided additional data on potential safety concerns with efgartigimod based on a Periodic Benefit Risk Evaluation Report (June 2024 to December 2024). The report included use of efgartigimod as both an intravenous infusion and subcutaneous injection for a range of indications including generalised myasthenia gravis, CIDP, primary immune thrombocytopenia, bullous pemphigoid, idiopathic inflammatory myopathy, lupus nephritis, primary membranous nephropathy, primary Sjögren's syndrome, thyroid eye disease, ocular myasthenia gravis, and in kidney transplant recipients with antibody-mediated rejection.

6.40 No new safety concerns were identified in the report. The only important identified risk of efgartigimod is hypersensitivity reactions and infusion-related reactions. Important potential risks include serious infections and malignancies. Missing information includes use during pregnancy and lactation, use with live/attenuated vaccines, use with monoclonal antibodies, use in renal impairment, long-term safety of efgartigimod treatment and use in immunocompromised patients.

6.41 The submission identified a retrospective observational case series of 9 patients with CIDP from a single treatment centre in the United States (Levine 2025[3]). Patients in the study directly transitioned from IVIg to efgartigimod subcutaneous injection without having a treatment break. The study authors noted that 4 patients experienced a severe relapse with incomplete recovery after switching to efgartigimod (requiring rescue therapy with IVIg, PLEX and/or corticosteroids) while the remaining 5 patients did not notably improve or worsen with efgartigimod treatment. The submission noted that the 4 patients with severe relapse were responsive to IVIg therapy with lower baseline INCAT scores (1 or 2) than the requested restriction, and therefore would not be eligible for efgartigimod treatment.

6.42 During the evaluation, it was noted that the FDA had been evaluating the need for regulatory action due to the risk of severe CIDP worsening in patients treated with efgartigimod (January - March 2025, Potential Signals of Serious Risks/New Safety Information Identified by the FDA Adverse Event Reporting System). The pre-PBAC response stated that [redacted] signalled the potential worsening of CIDP symptoms after initiating treatment with efgartigimod and resulted in updates to the US PI. The pre-PBAC response reiterated that a Phase 4 study was underway to evaluate the optimal approach for transitioning patients with CIDP to efgartigimod following cessation of immunoglobulin, but, as noted in paragraph 0, the sponsor [redacted].

Benefits/harms

6.43 A comparison of the benefits and harms of efgartigimod compared to placebo was not conducted due to the complex, multi-stage design of the ADHERE trial with placebo used only during the randomised treatment-withdrawal period.

6.44 A comparison of the benefits and harms of efgartigimod compared to IVIg/SCIg was not conducted as the indirect analyses were not considered reliable given differences in study design, patient characteristics, circumstances of use and outcome definitions between trials.

Clinical claim

6.45 The submission described efgartigimod as superior in terms of efficacy and non-inferior in terms of safety compared to placebo. The evaluation and the Sub-

[3] Levine T. Early deterioration of CIDP following transition from IGIG to FcRn inhibitor treatment. J Neurol Sci. 2025 an 15:468:123313. doi: 10.1016/j.jns.2024.123313

Committees considered that this claim was reasonable in regard to efficacy, but was not adequately supported in terms of safety.

6.46 The PBAC considered that the claim of superior comparative effectiveness compared to placebo was reasonable.

6.47 The PBAC considered that the claim of non-inferior comparative safety compared to placebo was inconsistent with the data presented.

6.48 The submission described efgartigimod as superior in terms of efficacy and non-inferior in terms of safety compared to IVIg/SCIg. The evaluation and the Sub-Committees considered that this claim was not adequately supported.

6.49 The ADHERE trial used a multi-stage study design in order to demonstrate the efficacy of efgartigimod treatment for CIDP, however the evaluation and the Sub-Committees noted that the complexity of the study design also limited the generalisability of results to clinical practice. As discussed in paragraph 6.9, published criticisms of the ADHERE trial have highlighted concerns regarding the diagnostic adjudication process and the potential for inclusion of misdiagnosed patients, differential discontinuations between prior therapy groups in Stage A of the trial and limited investigation of these differences (prior IVIg/SCIg: 32%; prior corticosteroids: 13%; no active therapy: 9%), the lack of a placebo arm in Stage A to assess the magnitude of placebo effects on response, as well as incentives to remain in earlier stages of the trial to gain access to open-label efgartigimod in the extension phase (Katz 2025).

6.50 The proposed PBS population comprised patients who are unable to take or not responding to immunoglobulin, while the ADHERE trial included patients irrespective of their response to prior therapy. The Sub-Committees considered this added uncertainty as to the applicability of the trial results. The PSCR argued that the subgroup of patients most consistent with the proposed PBS population (i.e. those with prior IVIg/SCIg use and unstable active disease) demonstrated a larger benefit than the full study population; however, the evaluation and the Sub-Committee's considered this was a small subgroup and the confidence intervals were wide.

6.51 As discussed in paragraph 6.10, the key publication of the ADHERE trial noted that the optimal approach to transition a patient from IVIg/SCIg therapy to efgartigimod is yet to be determined, as this population had substantially higher adverse event rates and discontinuations compared to other study groups in the trial. Observational data also indicates that the direct transition from IVIg to efgartigimod subcutaneous injection (without having a treatment break) may be associated with a risk of severe relapse with incomplete recovery (Levine 2025).

6.52 The evaluation and the Sub-Committees considered that the indirect comparison of efgartigimod and IVIg/SCIg was largely uninformative given differences in study design, patient characteristics, circumstances of use and outcome definitions.

6.53 The PBAC considered that the claim of superior comparative effectiveness compared to IVIg/SCIg was not adequately supported by the data.

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6.54 The PBAC, noting that no comparative data were presented, considered that the claim non-inferior comparative safety compared to IVIg/SCIg was not supported.

Economic analysis

6.55 The submission presented a cost analysis of efgartigimod subcutaneous injection compared to IVIg. The cost analysis included drug, administration and monitoring costs over a 2-year timeframe, as well as a price premium for efgartigimod based on the claim of superior efficacy in the target population, reduced treatment burden to patients, and re-allocation of limited health system resources. The submission stated that the use of a cost-analysis approach was a pragmatic decision to expedite the PBS listing of efgartigimod for CIDP by avoiding the complexity associated with a cost-effectiveness model. The submission claimed that the PBAC has previously accepted a similar approach in its considerations of complement inhibitors (ravulizumab, zilucoplan) and FcRN blockers (efgartigimod, rozanolixizumab) for myasthenia gravis.

6.56 The evaluation and the Sub-Committees considered that the approach may not be appropriate, as it was unclear whether efgartigimod was superior to IVIg/SCIg in the target population and it was difficult to determine whether efgartigimod would be cost effective with the requested price premium. Further, the submission did not assess the cost effectiveness versus placebo (one of the nominated comparators) or non-immunoglobulin therapies (see paragraph 5.5).

6.57 The results of the cost analysis of efgartigimod compared to IVIg over a two-year time horizon are summarised in Table 9. The cost analysis was conducted at the AEMP level for efgartigimod.

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Table 9: Cost analysis of efgartigimod compared to IVIg over a two-year time horizon

Variable	Value	Source
Cost of IVIg		
Total IVIg dispensed over 2 years per patient	[redacted] g	Based on the recommended loading dose in the Privigen PI (2 g/kg administered in divided doses over 2-5 days) and an estimated maintenance dose based on high dose treatment regimens reported for IVIg refractory patients by Australian physicians (1.54 g/kg every 3 weeks). Estimates per patient were calculated based on the average weight of patients accessing IVIg for CIDP under the NBA in 2024/2025 (83.64 kg).
Cost of dispensed IVIg	$[redacted]	Based on linear extrapolation of the reported cost per gram of IVIg dispensed under the NBA from 2019 to 2025 to estimate a projected cost per gram in 2026-2027 (increased from $[redacted] to $[redacted] per gram, an increase of [redacted]%).
Total IVIg administration days over 2 years per patient	54	Based on the assumption that the loading dose would be administered over 3.5 days (midpoint of dosing recommended in Privigen PI) and the assumption that maintenance doses would be administered over 1.5 days (midpoint of maintenance dosing recommended in Privigen PI) once every 3 weeks.
Cost of IVIg administrations	$[redacted]	Based on hospital costs for non-admitted minor medical procedures (Item 10.13) using the 2025-2026 NWAU calculator ($[redacted] per day).
Cost of vascular access for IVIg over 2 years per patient	$325	In the first 6 months of treatment, it was assumed that 90% of patients would have peripheral vascular access with no additional cost, 1% would require a PICC line and 9% would require a port-a-cath. After the initial 6 months of treatment it was assumed that 80% of patients would have peripheral vascular access with no additional cost, 1% would require a PICC line and 19% would require a port-a-cath. Cost of a PICC line: $183.00 for the device (10.09.02, TX035; 2020 National Protheses List) + $265.30 medical fee (MBS 13318; central vein catheterisation by open exposure, in a patient under 12 years of age) + $558 day surgery/operating theatre cost (Item 10.03; minor surgical procedure using 2025-2026 NWAU calculator). Cost of a port-a-cath: $267.00 for the device (10.09.03, TX054; 2020 National Protheses List) + $265.30 medical fee (MBS 13318; central vein catheterisation by open exposure, in a patient under 12 years of age) + $558 day surgery/operating theatre cost (Item 10.03; minor surgical procedure using 2025-2026 NWAU calculator).
Cost of monitoring over 2 years per patient	$402	Based on the assumption that IVIg use would require full blood counts (MBS 65070; $17.35) and liver and kidney function testing (MBS 66512; $17.70) every 6 months and a once-off cost for neuromuscular electrodiagnosis conduction studies (MBS 11018; $261.30)
Total cost of IVIg	$[redacted]	Calculation: $[redacted] + $[redacted] + $325 + $402
Cost of efgartigimod		
Total cost of efgartigimod (without premium)	$[redacted]	Same as total cost of IVIg.
Costs of additional specialist visits for injection training	$358	Based on the assumption that patients will require 4 specialists visits (MBS 116; $89.40) before being adequately trained to self-administer efgartigimod subcutaneous injections. Assumed all patients will self-administer all subsequent injections
Direct medicine costs of efgartigimod over 2 years (without premium)	$[redacted]	Calculation: $[redacted] - $358
Premium over 2 years	$[redacted]	Assumed a [redacted]% premium for efgartigimod due to superior efficacy in the target population, reduced treatment burden to patients and re-allocation of limited health system resources.
Direct medicine cost of efgartigimod over 2 years (with premium)	$[redacted]	Calculation: $[redacted] + $[redacted]

Variable	Value	Source
Number of injections over 2 years per patient	[redacted][a]	Based on the assumption that all patients would use weekly dosing for the first [redacted] weeks and then [redacted]% would switch to fortnightly dosing while the remainder continue with once weekly dosing. Doses were also adjusted for treatment adherence reported in the ADHERE+ extension study (98.46%) [0.9846 ([redacted]+([redacted] × [redacted])+([redacted] × [redacted]))].
AEMP per injection (with premium)	$[redacted][b]	Calculation: $[redacted] / [redacted]
DPMQ per 4 injections (with premium)	$[redacted]	Based on July 2026 PBS fees and mark-ups. [($[redacted] × 4) + $[redacted] (wholesaler mark-up) + $[redacted] (administration and handling fee) + $[redacted] (dispensing fee)]

Source: Table 3.8-1, p316 of the submission

Abbreviations: IVIg, IVIg, intravenous immunoglobulin; MBS, Medicare Benefits Schedule; NBA, National Blood Authority; NWAU, National Weighted Activity Unit; PICC, peripherally inserted central catheter

[a] Pre-PBAC response proposed that the [redacted] Along with a 95% compliance assumption (reduced from 98.46% in the submission), this reduced the average number of doses per patient to [redacted] doses.

b Pre-PBAC response proposed an AEMP of $[redacted] per injection. This AEMP maintained the sponsor's proposed direct medicine cost of efgartigimod over 2 years of $[redacted], including the [redacted]% price premium.

6.58 Based on the cost analysis, the submission estimated an annual cost of $[redacted] ($[redacted] / 2) for efgartigimod subcutaneous injections with a proposed AEMP per injection of $[redacted] and a proposed DPMQ per 4 injections of $[redacted].

6.59 The pre-PBAC response proposed [redacted] and a change to [redacted].

6.60 The submission estimated immunoglobulin dosing based on a sponsor-commissioned survey of 10 Australian neurologists who manage patients with CIDP. The estimate used in the submission was based on IVIg use in treatment refractory patients using high dose treatment regimens (weighted average maintenance dose: 1.54 g/kg every 3 weeks). The evaluation and the Sub-Committees considered that the submission did not adequately justify using this estimate given a mix of refractory, progressive and intolerant patients are expected to use efgartigimod. In particular, estimated IVIg doses based on patients with 'progressive' disease (patients switching from first-line to second-line or second-line to third-line treatments) from the physician survey were substantially lower (approximately 0.7 g/kg every 3 weeks) than the estimates for patients with treatment refractory disease (1.54 g/kg every 3 weeks).

6.61 Further, the submission and PSCR assumed that only half of the target population would otherwise use immunoglobulin therapy (i.e. those with 'progressive' disease) while the remaining patients with 'refractory disease' or 'intolerance' would not use immunoglobulin therapies. The PSCR argued that the cost of high dose IVIg/SCIg could be used as a proxy for the cost of health resources used in other patients in the target population who were unable to use IVIg/SCIg. However, the Sub-Committees considered this was not justified given the submission had not presented a cost-effectiveness analysis.

6.62 The average annual IVIg/SCIg dose across all CIDP patients accessing treatment under the NBA was 605 g in 2024/2025. This equates to a maintenance dose of approximately 0.4 g/kg every 3 weeks. However, the evaluation noted that this estimate would include patients who are responsive to IVIg/SCIg, and the Sub-

Committees considered that this average maintenance dose (0.4 g/kg every 3 weeks) likely underestimated the dose in the requested population of patients not adequately responding to immunoglobulin.

6.63 The Sub-Committees noted that the IVIg PI recommends 1.0 g/kg every three week for maintenance dosing (which represents a middle dosing value across sub-populations including progressive and refractory), therefore considered that assuming a 1.0 g/kg maintenance dose, resulting in an average 2,983 g dose, would likely be more appropriate.

6.64 While the PSCR reiterated that evidence exists that dose escalation can lead to improved responses to immunoglobulin therapy, the Sub-Committees considered that a maintenance dose of 1.0 g/kg every 3 weeks appropriately reflects the broad range of immunoglobulin dosing used across the proposed PBS population of patients who are progressive, refractory or intolerant to immunoglobulin.

6.65 The cost per gram for immunoglobulin was based on NBA cost data extrapolated to 2026/2027 on the basis that the earliest expected PBS listing date for efgartigimod would be in the latter half of 2026. This increased the immunoglobulin cost per gram from $[redacted] in 2024-25 to $[redacted] in 2026-27, an increase of [redacted]%. The Sub-Committees noted that the use of projected costs for immunoglobulin was not consistent with the PBAC Guidelines which state that future costs should be valued at current prices (i.e. $[redacted] per gram). The Sub-Committees noted that this decreased the AEMP by [redacted]% (refer to Table 10).

6.66 The submission estimated administration costs for IVIg based on hospital costs for non-admitted minor medical procedures (Item 10.13) using the 2025-2026 National Weighted Activity Unit (NWAU) calculator ($762 per day). However, the Manual of Resource Items and Their Associated Unit Costs v5.0 (2016) states that the relevant MBS Schedule fee is the most suitable resource for determining the economic cost. The cost per infusion for IVIg could be mapped to MBS Item 14245 (immunomodulating agent, administration of, by intravenous infusion for at least 2 hours duration; fee: $111.60). The PSCR argued that the MBS item costs are an underestimate given IVIg requires prolonged, resource-intensive hospital-based infusions.

6.67 The Sub-Committees noted that for generalised myasthenia gravis (gMG), the PBAC had recommended "a premium to account for the administration benefits associated with the newer therapies compared with IVIg, noting the extensive administration requirements associated with IVIg, with an infusion time of around 2 to 4 hours and up to 8 hours, which have resource implications and a direct impact on patients and carers" (paragraph 8.24, efgartigimod Public Summary Document [PSD], March 2025 PBAC meeting). In November 2025, the PBAC noted that quantifying the administration costs of IVIg based on NWAU costings "could equate to approximately [redacted]% of the total drug costs for gMG. Consequently, the PBAC considered that it would not be unreasonable for the newer gMG therapies to have up to a [redacted]% premium over the drug costs of IVIg. The PBAC recognised that [redacted]% was not a 'small' premium but

considered that it would still be acceptably cost-effective in view of the broader patient and carer benefits associated with the reduced administration burden of the newer therapies" (paragraph 5.3, Medicines for generalised myasthenia gravis, November 2025 PBAC meeting). The [redacted]% premium was applied instead of any administration costs. Refer to paragraph 6.72.

6.68 The submission assumed all patients would use weekly efgartigimod dosing until Week [redacted], and then assumed that [redacted]% of patients would switch to fortnightly efgartigimod dosing based on a sub-study of less frequent efgartigimod dosing during the ADHERE+ extension phase. Limited follow-up data were available; however, the evaluation and the Sub-Committees noted that a Kaplan-Meier plot of the time to clinical deterioration suggests a relatively high probability of clinical deterioration with less frequent dosing and considered that the proportion of patients able to maintain disease control with fortnightly dosing over the longer term was unclear. The Sub-Committees considered that it may be appropriate to assume lower rates of fortnightly dosing given the relatively high probability of clinical deterioration.

6.69 The submission proposed a [redacted]% premium for efgartigimod based on the clinical claim of superior efficacy compared to IVIg/SCIg in the target population of patients who are progressive, refractory and/or intolerant to immunoglobulin products (equivalent to a cost per patient of $[redacted] over the two year time horizon). The submission also claimed that efgartigimod, which is administered as a subcutaneous injection every 1-2 weeks, would have a lower treatment burden than immunoglobulin products which are typically administered as an intravenous infusion every 2-6 weeks or as a subcutaneous infusion every 1-2 weeks. Additionally, the submission claimed that efgartigimod would allow a reallocation of limited health system resources (access to infusion centre chairs, less reliance on imported immunoglobulin products). While the submission provided a general argument for a price premium, the submission did not provide any justification for the proposed size of the premium. The Sub-Committees considered that a [redacted]% price premium was inappropriately high given the limited evidence of superiority and the absence of a cost-effectiveness analysis in the submission (refer to paragraph 6.72), and in the context of the large cost impact (i.e. the [redacted]% premium increased the cost per patient by $[redacted] over two years).

6.70 During the evaluation, multivariate sensitivity analyses were conducted to assess the impact of changes to immunoglobulin dosing, efgartigimod dosing, and the price premium for efgartigimod (shown in Table 10). The analyses conducted during evaluation were based on drug costs only (due to the additional complexity associated with quantifying non-drug costs, which have a limited impact on the economic analysis) and used the current cost of immunoglobulin subsidised for CIDP under the NBA. However, the non-drug costs were included in the additional multivariate sensitivity analyses conducted during preparation of the ESC Advice (unless otherwise stated).

Table 10: Multivariate sensitivity analyses of the cost analysis approach

Analyses (2-year time horizon)	Efgartigimod AEMP (% change in AEMP from base case)			
	[redacted]% premium	[redacted]% premium	[redacted]% premium	No premium
Assume [redacted]% of patients will switch to fortnightly efgartigimod dosing				
IVIg maintenance dose: [redacted] g [base case; high doses; refractory patients; survey] [a]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg maintenance dose: 3,377 g [all doses; refractory patients; survey] [b]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg maintenance dose: 2,983 g [IVIg product information] [c]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg maintenance dose: 2,195 g [all doses; third-line patients; survey] [d]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg dose: 1,210 g [2024-2025 NBA data for CIDP patients] [e]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
Assume [redacted]% of patients will switch to fortnightly efgartigimod dosing				
IVIg maintenance dose: [redacted] g [base case; high doses; refractory patients; survey] [a]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg maintenance dose: 3,377 g [all doses; refractory patients; survey] [b]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg maintenance dose: 2,983 g [IVIg product information] [c]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg maintenance dose: 2,195 g [all doses; third-line patients; survey] [d]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg dose: 1,210 g [2024-2025 NBA data for CIDP patients] [e]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
Assume all patients use weekly efgartigimod dosing				
IVIg maintenance dose: [redacted] g [base case; high doses; refractory patients; survey] [a]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg maintenance dose: 3,377 g [all doses; refractory patients; survey] [b]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg maintenance dose: 2,983 g [IVIg product information] [c]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg maintenance dose: 2,195 g [all doses; third-line patients; survey] [d]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
IVIg dose: 1,210 g [2024-2025 NBA data for CIDP patients] [e]	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)	$[redacted] (-[redacted]%)
Sensitivity analyses using submission base case as starting point (i.e. submission's projected Ig costs and administration and monitoring costs in the base case)				
Submission base case vial price (AEMP)	$[redacted]			
A. Most recent Ig price	$[redacted] (-[redacted]%)			
B. IVIg maintenance dose: 2,983 g (1 g/kg every 3 weeks per product information	$[redacted] (-[redacted]%)			
C. No premium (given administration costs are already based on NWAU)	$[redacted] (-[redacted]%)			
D. Premium of [redacted]% applied to IVIg drug costs AND no admin costs included	$[redacted] (-[redacted]%)			
E. [redacted]% switch to fortnightly efgartigimod dosing	$[redacted] (-[redacted]%)			
Multivariate sensitivity analyses - **All include A + B (Most recent Ig price + IVIg maintenance dose: 1 g/kg every 3 weeks)**				
A + B + C (no premium)	$[redacted] (-[redacted]%)			
A + B + D ([redacted]% premium AND no admin costs)	$[redacted] (-[redacted]%)			
A + B + C + E (no premium AND [redacted]% switch to fortnightly efgartigimod dosing)	$[redacted] (-[redacted]%)			

Analyses (2-year time horizon)	Efgartigimod AEMP (% change in AEMP from base case)
A + B + D + E ([redacted]% premium AND no admin costs AND [redacted]% switch to fortnightly efgartigimod dosing)	$[redacted] (-[redacted]%)
A + B + no administration costs + [redacted]% premium [f]	$[redacted] (-[redacted]%) i.e. same as A + B + C [f]
Pre-PBAC revised base case:	
[redacted]	$[redacted] ([redacted]%) after the [redacted]

Source: Constructed during the evaluation based on the Attachment 16 cost analysis Excel workbook
Abbreviations: AEMP, approved ex-manufacturer price; CIDP; chronic inflammatory demyelinating polyneuropathy; IVIg, intravenous immunoglobulin; NBA, National Blood Authority
[a] [redacted] g maintenance dose (1.54 g/kg every 3 weeks) based on high dose IVIg dosing regimens in refractory patients from Australian physician survey.
[b] 3,377 g maintenance dose (1.14 g/kg every 3 weeks) based on all reported IVIg dosing regimens in refractory patients from Australian physician survey (excluding doses in excess of NBA limits).
[c] 2,983 g maintenance dose (1 g/kg every 3 weeks) based on initial recommended dose in Privigen product information.
[d] 2,195 g maintenance dose (0.72 g/kg every 3 weeks) based on all reported IVIg dosing regimens for third-line treatment from Australian physician survey (excluding doses in excess of NBA limits).
[e] 1,210 g dose based on the average grams dispensed per patient per year with CIDP under the NBA in 2024-2025 (605 g × 2).
[f] At a dose of 1 g/kg every 3 weeks (and the most recent Ig price), the following two scenarios result in an equivalent AEMP: (i) NWAU-based administration costs with no premium; (b) a premium of [redacted]% with no administration costs.

6.71 The proposed price for efgartigimod was highly sensitive to the different combinations of immunoglobulin dosing and efgartigimod price premium.

6.72 The Sub-Committees considered that:

- IVIg doses were overestimated in the submission, and a maintenance dose of around 1.0 g/kg every 3 weeks may better reflect clinical practice in the relevant population (refer to paragraph 6.63);
- efgartigimod costs should reflect a lower uptake of fortnightly dosing;
- immunoglobulin costs should be based on the most recent cost at the time of PBAC consideration; and
- the requested [redacted]% price premium was inappropriately high given limited evidence of superiority and the absence of a cost-effectiveness analysis in the submission. The Sub-Committees considered that a smaller price premium may be appropriate to account for the reduced administration costs of IVIg (and, to a lesser extent, SCIg) and the broader patient and carer benefits associated with the reduced administration burden of efgartigimod. The Sub-Committees noted that for gMG the premium ([redacted]%) was applied instead of administration costs, and was an amount equivalent to the IVIg administration costs based on NWAU costings. However, the Sub-Committees considered it was unclear whether a [redacted]% premium (applied to IVIg drug costs) would be appropriate for CIDP given higher IVIg doses were applied in the cost-analysis compared with gMG. In the sensitivity analysis with IVIg maintenance dosing of 1 g/kg every 3 weeks, the NWAU-based administration costs would equate to a premium of [redacted]%, i.e. lower than the [redacted]% premium applied in gMG due to the substantially lower IVIg dose recommended by the PBAC in the cost-comparison for gMG (i.e. 541 g per year in gMG versus 1,481 g per year[4] in

[4] Based on a dose of 2,983 g over two years

this multivariate sensitivity analysis for CIDP). While the Sub-Committees acknowledged that the PBAC's preferred approach is to use the proxy MBS Schedule fee, the premium would also be intended to account for the broader patient and carer benefits associated with the reduced administration burden of efgartigimod (refer to paragraphs 6.65 and 6.67).

Drug cost/patient (at the price proposed in the submission)

6.73 The cost analysis estimated a cost for efgartigimod of $[redacted] over 2 years, based on the proposed DPMQ for 4 injections of $[redacted]; assuming weekly dosing for all patients until Week [redacted], followed by weekly dosing for [redacted]% of patients and fortnightly dosing for [redacted]% of patients ([redacted] doses over 2 years); and adjusted by a relative dose intensity of 98.5%. Treatment persistence was not included in the cost analysis.

6.74 The budget impact analysis estimated a cost for efgartigimod of $[redacted] over 2 years for the 71% of patients meeting the response criteria at 12 weeks, based on the proposed DPMQ for 4 injections of $[redacted]; assuming weekly dosing for all patients until Week [redacted], followed by weekly dosing for [redacted]% of patients and fortnightly dosing for [redacted]% of patients ([redacted] doses over 2 years); and assuming a relative dose intensity of 100%. Subsequent annual costs are $[redacted] per continuing patient. Continuing patients have an annual efgartigimod treatment discontinuation rate of 10%.

6.75 The budget impact analysis estimated a cost for efgartigimod of $[redacted] for the 29% of patients not meeting the response criteria at 12 weeks, based on the proposed DPMQ for 4 injections of $[redacted]; and assuming weekly dosing (12 doses over 3 months); assuming a relative dose intensity of 100%.

Estimated PBS usage & financial implications

6.76 The submission used an epidemiological approach to estimate the utilisation and financial impacts of listing efgartigimod as a treatment for CIDP patients who are progressive, relapsing, refractory and/or intolerant to immunoglobulin products. The PSCR proposed withdrawing the group of relapsing patients from the proposed PBS population, and acknowledged the forward estimates would need to be adjusted, but did not present an updated budget impact model. The Pre-PBAC response included revised financial estimates (see paragraph 6.83 and Table 13), taking into account Sub-Committee recommendations. The key inputs used to derive the financial implications are presented in Table 11.

Table 11: Key inputs for financial estimates

Data	Value	Source	Comment
Prevalent CIDP patients prior to 2026	3,184 Pre-PBAC response: 2,752	Based on 3,389 patients using IVIg/SCIg for CIDP under the NBA in 2024/2025.	Currently the estimated number of patients accessing IVIg/SCIg for CIDP under the NBA (equivalent to 12 cases per 100,000 population) exceeds expected values from published epidemiology studies (1-10 cases per 100,000 population; pooled prevalence 2.81 cases per 100,000).

Data	Value	Source	Comment
		Adjusted to account for 19% of patients being misdiagnosed, as reported in the sponsor-commissioned survey of Australian neurologists. Adjusted to 30% in Pre-PBAC response. The estimate was also adjusted to account for 16% of patients not actively using IVIg/SCIg, but who have used treatment in the past, as reported in survey of Australian neurologists. Calculation in submission: 3,389 × (1 - 0.19) × (1.16)	The Sub-Committees noted that: • population studies using confirmed diagnosis (EFNS/PNS criteria, Park 2022)) report the true prevalence of CIDP in Australia as ~ 5.0–5.7 per 100,000, which suggests there are currently ~ 1,300–1,500 patients. • the pooled prevalence rate of 2.81 per 100,000 (95% CI: 1.58–4.39; I^2 = 99.1%) was reported in Broers 2019 that included an Australian study which reported prevalence from 1996. • IVIg use currently exceeds epidemiological expectations for CIDP in Australia. the misdiagnosis rate in clinical practice is highly uncertain. The sponsor's advisory panel and the published literature suggests that up to 50% of cases may be misdiagnosed, particularly for atypical presentations (Allen 2015, Allen 2020). The Sub-Committees considered: • it may be appropriate to apply different misdiagnosis rates to the different groups of patients. • the misdiagnosis rate is likely higher than 19%. An estimate of 30% would be reasonable. The 16% inflation factor applied for patients not currently on Ig treatment (can include patients achieving disease remission) was insufficient to account for the high proportion of the target population not receiving treatment with IVIg/SCIg (826 patients; 59.3% [the complement of the proportion of patients who would otherwise have used IVIg/SCIg – estimated as 40.7% by the submission, see below] of the target prevalent population who are relapsing, refractory or intolerant). The Sub-Committees considered: • the number of patients no longer receiving treatment would include patients in disease remission. • the inflation factor (16%) may be reasonable, with some sensitivity analysis to support decision making, as there was no better data to confirm this. Overall, the Sub-Committees considered the prevalence of CIDP was uncertain and likely overestimated.

Data	Value	Source	Comment
Incident CIDP patients each year from 2026	135 Pre-PBAC response: 100	Based on the cumulative annual rate of growth in CIDP patients accessing IVIg/SCIg under the NBA between 2021/2022 and 2024/2025 (4.24%). This estimate was applied to the adjusted prevalent population to estimate the new incident population in each year. Calculation: 3,184 × 0.0424	The Sub-Committees noted that the method applied by the submission included new patients starting therapy as well as existing patients stopping therapy. The Sub-Committees noted Broers 2019 reported a pooled crude incidence rate for the total population of 0.33 per 100,000 person-years, equivalent to approximately 90 new cases per year. The estimate of incident cases in the submission of 135 per year was approximately 50% higher than published incidence estimates. However, the Sub-Committees acknowledged that the Australian study included in Broers 2019 reported incidence from 1986 to 1995 and acknowledged this may underestimate the current incidence. The Sub-Committees considered there are likely to be between 90 and 100 new patients per year.

Data	Value	Source	Comment
Patients who are progressive, relapsing, refractory and/or intolerant	43.7% PSCR: 35.64% (= (17% + 22% ~~+ (16% × 63.4%)~~ + 5%) × (1-19%))	Based on the estimated proportion of patients meeting each qualifying criterion and adjusted for misdiagnosis. Refractory: the proportion of patients using 1L therapy who have no response or a duration of response <4 months (17%) reported in the sponsor-commissioned survey. Progressive: the proportion of patients using 1L therapy or second-line therapy who switch to a subsequent-line therapy (22%) reported in the sponsor-commissioned survey. The PSCR proposed the removal of relapsing patients from the forward estimates, to match the proposed PBS restriction. Intolerant: the proportion of CIDP patients with a contraindication to IVIg/SCIg (5%) estimated by the sponsor's advisory panel Misdiagnosis: the proportion of immunoglobulin users with suspected CIDP who would be subsequently diagnosed with another condition (19%) reported in the sponsor-commissioned survey.	The calculation was poorly justified and the assumption that the proportion of patients with an inadequate response is independent of the proportion of patients using subsequent-line therapy was not reasonable. The sponsor's advisory panel indicated that approximately 5-10% of patients would be intolerant and 5% would be contraindicated to immunoglobulin therapy. However, the experts noted intolerance can develop later and therefore there may be overlap with the nominated 'progressive' population. The application of the same misdiagnosis rate to all identified populations was inconsistent with expert advice from the sponsor's advisory panel which suggested that approximately 50% of IVIg/SCIg non-responders may be misdiagnosed cases. The Sub-Committees agreed that the misdiagnosis rate is likely to be higher in non-responders and that the application of one misdiagnosis rate overestimates patients. When physicians were directly asked about IVIg use rather than lines of therapy, the responses from the survey indicated that 24% of CIDP patients would have an inadequate response or intolerance to immunoglobulin therapy. The sponsor's advisory panel indicated that approximately 30% of patients do not respond to IVIg. The panel also noted that 10-15% of patients would have a contraindication or intolerance although it is unclear whether this estimate overlaps with the 30% non-responder value. The Sub-Committees considered the estimate of 35.6% included in the PSCR may be reasonable.
Efgartigimod uptake rate in eligible prevalent patients	Yr 1: [redacted]% Yr 2: [redacted]% Yr 3: [redacted]% Yr 4: [redacted]% Yr 5: [redacted]% Yr 6: [redacted]% Pre-PBAC response: [redacted]%	Based on the assumption that [redacted] eligible prevalent patients ([redacted]%) would trial efgartigimod in the first 5 years of availability, with higher uptake in the earlier years.	The Sub-Committees considered that: • while high uptake is possible, particularly if early initiators report positive experiences, there are uncertainties including safety concerns relating to switching currently under FDA review. • different overall uptake rates across prevalent and incident patients did not seem justified.

Data	Value	Source	Comment
Efgartigimod uptake rate in incident eligible patients	[redacted]% Pre-PBAC response: [redacted]%	Assumption.	Equalised to [redacted]% in Pre-PBAC response.
Patients who meet response criteria with efgartigimod treatment at 3 months	71% Pre-PBAC response: 66.5%	Based on the proportion of the overall ADHERE population that completed Stage A of the study without premature treatment discontinuation. Adjusted in Pre-PBAC response to reflect ADHERE 12 week results.	The Sub-Committees considered that the approach taken in the submission was not an appropriate method to inform treatment response rates at 12 weeks. Data from the overall population suggest that 66.5% of patients had a confirmed improvement with efgartigimod treatment at 12 weeks in the ADHERE trial. This was adjusted in the pre-PBAC response. There were differences in response rates between subgroups, with patients who were previously using IVIg/SCIg having lower response rates (58.8%) than patients who were previously using corticosteroids (77.8%) or no active treatment (72.3%).
Annual efgartigimod discontinuation rate	10%	Assumption.	This assumption was inadequately justified and uncertain, but the Sub-Committees considered it may be a reasonable assumption.
Efgartigimod treatment adherence	100% Pre-PBAC response: 95%	Assumption. The submission claimed that this assumption is consistent with data from Stage A of the ADHERE trial (maximum of 12 weeks treatment) which indicated that median 'compliance' was 100%.	May not be representative of clinical practice. The Sub-Committees considered it would be more appropriate to apply 95%. This was adjusted in the pre-PBAC response.
Distribution of efgartigimod dosing	Weekly: [redacted]% Fortnightly: [redacted]%	Estimated based on a sub-study of less frequent efgartigimod dosing during the ADHERE+ extension phase. At the time of the interim data cut-off, [redacted]% of patients had switched back to once-weekly dosing, [redacted]% were continuing with once every 2 weeks dosing and [redacted]% had switched to once every 3 weeks dosing.	Limited follow-up data were available at the interim data cut-off. However, a Kaplan-Meier plot of the time to clinical deterioration suggests a relatively high probability of clinical deterioration with less frequent dosing and the proportion of patients able to maintain disease control with fortnightly dosing over the longer term is unclear. The Sub-Committees considered this assumption was uncertain, but noted there were no better data to estimate dosing distribution. The Sub-Committees noted sensitivity analyses in the economics based on [redacted]% uptake of fortnightly dosing.
Specialist visits for efgartigimod administration training	4 per initiating patient	Assumption. Based on the draft efgartigimod PI which recommends a minimum of 4 training visits before patients can self-administer.	The Sub-Committees commented that clinician experience with other SC therapies suggested it would be reasonable that a large majority of patients would transition to self-administration, and considered this assumption to be reasonable.

Data	Value	Source	Comment
Patients who would otherwise have used IVIg/SCIg	40.67% Pre-PBAC response: 50%	The submission's calculation was based on the proportion of CIDP patients with 'progressive' disease (22%) relative to the target population as a proportion of the CIDP population (54.1%; unadjusted for misdiagnosis).	Based on this calculation only a minority of the target population were actively treated with IVIg/SCIg (prevalent: 566 patients; incident: 24 patients) while the majority are untreated (prevalent: 826 patients; incident: 35 patients) which was inconsistent with eligible population estimates. The Sub-Committees noted that relapsed patients should be removed from this calculation (22%/54.1% should be updated to 22%/44% = 50%, which was adopted in the pre-PBAC response). Even with this correction, this calculation remained inconsistent with the submission's approach to estimating patient numbers which only adjusted IVIg/SCIg patient numbers by 16% to account for patients who are not actively using IVIg/SCIg.
IVIg dosing regimen	2 g/kg loading dose and 1.54 g/kg maintenance dose every 3 weeks	Based on a sponsor-commissioned survey of 10 Australian neurologists who manage patients with CIDP. The estimate used in the submission was based on IVIg use in treatment refractory patients using high dose treatment regimens (≥1 g/kg per administration). Average patient weight (83.64 kg) was estimated based on patients accessing IVIg/SCIg under the NBA for CIDP in 2024/2025.	The definition of 'progressive' disease used to define patients using IVIg/SCIg treatment in the budget impact estimates (patients switching to subsequent lines of therapy, with no IVIg/SCIg dosing requirements) was inconsistent with the definition used for 'treatment refractory' in the dosing estimates (patients refractory to available CIDP treatments who are using high dose IVIg/SCIg treatment regimens). Estimated maintenance dosing of IVIg/SCIg reported in the survey for the second- (0.69 g/kg) and third-line (0.72 g/kg) settings are substantially lower than estimated in the submission. The average annual IVIg/SCIg dose across all CIDP patients accessing treatment under the NBA in 2024/2025 was 605 g. This equates to a maintenance dose of approximately 0.4 g/kg every 3 weeks. However, it should be noted that this estimate would include patients who are responsive to IVIg/SCIg. The Sub-Committees considered that the IVIg dosing regimen was likely overestimated. As noted in paragraphs 6.59 to 6.63, the Sub-Committees noted that the IVIg product information recommends 1.0 g/kg for maintenance dosing (which represents a middle dosing value across sub-populations including progressive and refractory) would be more appropriate.

Data	Value	Source	Comment
Blood count tests (in patients otherwise treated with IVIg/SCIg)	2 per patient per year $13.88 per test	Number of tests per year were assumed. The submission claimed that this was consistent with the economic analysis presented in the MSAC assessment of immunoglobulin for chronic inflammatory demyelinating polyneuropathy (MSAC application no. 1564; April 2021). Blood count: 80% of MBS item 65070; Kidney/liver function tests: 80% of MBS item 66512 (≥5 biomarker tests); Neuromuscular electrodiagnosis: 80% of MBS item 11018.	The inclusion of blood counts as well kidney/liver function tests appears reasonable. The Sub-Committees considered that the inclusion of neuromuscular testing was not appropriate. The assumption was based on a superseded version of the MSAC review (November 2019) which included this test for assessment of treatment response. This test was not included in the later version of the MSAC immunoglobulin review which appears consistent with current NBA restrictions which assess treatment response based on clinical criteria.
Kidney/liver function tests (in patients otherwise treated with IVIg/SCIg)	2 per patient Given the substantial expenditure estimated in the submission, the PBAC considered it important that the most appropriate patient population be clearly defined. $14.16 per test		
Neuromuscular electrodiagnostic tests (in patients otherwise treated with IVIg/SCIg)	1 per patient $209.04 per test		
Efgartigimod cost per script	$[redacted]	Proposed effective AEMP with July 2026 PBS fees and mark-ups	-
Cost of IVIg	$[redacted] per gram	Based on NBA data on IVIg/SCIg use for CIDP and gMG between 2019 and 2025. The cost per gram for the 2026-2027 financial year was extrapolated using a linear function on the basis that the earliest expected PBS listing date for efgartigimod would be in the latter half of 2026.	The Sub-Committees agreed with the evaluation that the use of projected costs for immunoglobulins was not consistent with the PBAC Guidelines, which state that future costs should be valued at current prices. The most appropriate cost to use (at the time of PBAC consideration) would be $[redacted] per gram supplied under the NBA for CIDP in the 2024-2025 financial year.

Data	Value	Source	Comment
Patient copayment	$7.05 per script	Weighted average distribution of patients across beneficiary categories for all PBS listed therapies (2023/2024 PBS expenditure report). Copayment thresholds based on proposed copayment thresholds for January 2026.	-

Source: Section 4.2, pp 322-324 of the submission
Abbreviations: 1L, first-line; DPMQ, dispensed price for maximum quantity; IVIg, intravenous immunoglobulin; MBS, Medicare Benefits Schedule; MSAC, Medical Services Advisory Committee; NBA, National Blood Authority; PBAC, Pharmaceutical Benefits Advisory Committee; PBS, Pharmaceutical Benefits Scheme; SCIg, subcutaneous immunoglobulin

6.77 The estimated number of treated patients, scripts dispensed and net cost to government associated with listing efgartigimod for the treatment of CIDP patients who have previously failed treatment with IVIg/SCIg (being progressive, refractory and/or intolerant to immunoglobulin products) is summarised in Table 12.

Table 12: Net cost to government of listing efgartigimod for CIDP (as estimated in the submission and PSCR)

	Year 1 (2026)	Year 2 (2027)	Year 3 (2028)	Year 4 (2029)	Year 5 (2030)	Year 6 (2031)
Submission						
Patients treated with efgartigimod	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Total efgartigimod scripts	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost to NBA	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]
Cost to MBS	-$[redacted][4]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]
Net cost to government	**$[redacted][2]**	**$[redacted][2]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][3]**	**$[redacted][2]**
PSCR revised estimates (updated to remove relapsed patients)						
Patients treated with efgartigimod	[redacted][8]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Total efgartigimod scripts	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost to NBA	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]
Cost to MBS	-$[redacted][4]	-$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]	$[redacted][5]
Net cost to government	**$[redacted][2]**	**$[redacted][2]**	**$[redacted][2]**	**$[redacted][2]**	**$[redacted][2]**	**$[redacted][2]**

Source: Table 4.3-1, p328; Table 4.8-1, p340 of the submission
Abbreviations: MBS, Medicare Benefits Schedule; NBA, National Blood Authority; PBS, Pharmaceutical Benefits Scheme; RPBS, Repatriation Pharmaceutical Benefits Scheme.
The redacted values correspond to the following ranges:
[1] *500 to < 5,000*
[2] *$100 million to < $200 million*
[3] *$200 million to < $300 million*
[4] *net cost saving*
[5] *$0 to < $10 million*

6.78 The PSCR estimated that the net cost to the PBS/RPBS of listing efgartigimod for CIDP patients who have previously failed treatment with IVIg/SCIg (being progressive, refractory and/or intolerant to immunoglobulin products with relapsing patients

removed) would be [redacted] in Year 1, increasing to [redacted] in Year 3, before declining to [redacted] in Year 6. The cumulative net cost was > $1 billion over the first 6 years of listing.

6.79 The estimated cost savings to the NBA associated with reduced immunoglobulin utilisation was $500 million to < $600 million of the first 6 years of listing.

6.80 The estimated changes to the MBS associated with increased specialist visits for efgartigimod administration training sessions and decreased pathology testing due to reduced immunoglobin use were minimal. However, the submission claimed that efgartigimod is likely to be associated with substantially decreased costs to state hospital systems due to the reduced need for IVIg administrations and vascular access.

6.81 The estimated net cost to the government of listing efgartigimod for CIDP was $100 million to < $200 million in Year 1, increasing to $100 million to < $200 million in Year 3, before declining to $100 million to < $200 million in Year 6. The cumulative net cost was $900 million to < $1 billion over the first 6 years of listing. For context, the current cost to the NBA of all IVIg use for CIDP was $211.1 million in 2024-2025.

6.82 The evaluation considered that the estimated net cost to government presented in the submission was highly uncertain due to the following reasons:

- Logical inconsistencies in the calculation of patient numbers resulted in implausible estimates, such as the estimated number of untreated patients in the target population exceeding the estimated number of untreated patients in the total CIDP population.
- The estimated proportion of patients failing IVIg (43.7%; who are progressive, relapsing, refractory and/or intolerant to IVIg/SCIg) was derived from multiple data sources and is likely to be an overestimate. Based on a sponsor-commissioned survey of Australian neurologists, 24% of CIDP patients would have an inadequate response or intolerance to immunoglobulin therapy. The sponsor's advisory panel indicated that approximately 30% of patients do not respond to IVIg.
- The estimation of treatment response rates at Week 12 based on the proportion of patients who discontinued treatment prematurely during Stage A of the ADHERE trial (71%) was inappropriate. Data from the overall trial population suggest that 66.5% of patients had a confirmed improvement with efgartigimod treatment at 12 weeks. However, there were numerical differences in response rates between subgroups with patients who were previously using IVIg/SCIg having lower response rates (58.8%) than patients who were previously using corticosteroids (77.8%) or no active treatment (72.3%).
- The assumed annual discontinuation rate for efgartigimod used in the submission was not adequately justified and the utilisation estimates do not appear to account for the potential for patients to have multiple courses of efgartigimod treatment.
- The assumption that the incident and prevalent pools of patients are mutually exclusive and stable over time was not adequately justified (e.g. the prevalent pool should decrease over time if there are no additional incident patients entering the

pool to offset losses, and the model does not include any mechanism to allow accrual of untreated incident patients over time).

- The estimated number of dispensed efgartigimod scripts was dependent on the estimated use of once weekly ([redacted]%) and once fortnightly ([redacted]%) dosing of efgartigimod. The dosing frequency estimates were based on a small sub-study conducted during the ADHERE+ open-label extension phase with limited follow-up. Overall, the proportion of patients able to maintain disease control with fortnightly dosing over the longer term is unclear.
- The estimated maintenance IVIg dose used in the submission was based on physician estimates for patients who are treatment refractory to IVIg/SCIg and was further limited to doses at or above the recommended maintenance dose. In contrast, the utilisation estimates for 'progressive disease' were based on physician estimates of patients who are progressive despite first-line/second-line therapy with no specific IVIg/SCIg dose requirements. The use of the estimated maintenance dose in the broader population who are progressive on first line therapy resulted in very high utilisation estimates.
- The estimated cost per gram of IVIg was inappropriately based on extrapolated estimates for the 2026-2027 financial year. The most appropriate cost to use (at the time of PBAC consideration) would be $[redacted] per gram dispensed under the NBA for CIDP in the 2024-2025 financial year.

6.83 The pre-PBAC response included updated financial estimates, as outlined in Table 11. These changes reduced the estimated cost to the PBS/RPBS to > $1 billion over the first 6 years of listing, and the net cost to government to $600 million to < $700 million over the first 6 years of listing (see Table 13).

Table 13: Pre-PBAC response updated Net cost to government for listing efgartigimod for CIDP

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Patients treated with EFG	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Total EFG scripts	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Cost to PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
	–	–	–	–	–	–
Total cost to PBS/RPBS	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**	**$[redacted]**
Savings to NBA & Infusion centres	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]
Change to MBS	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]
Net cost to government	**$[redacted][5]**	**$[redacted][6]**	**$[redacted][7]**	**$[redacted][7]**	**$[redacted][7]**	**$[redacted][7]**

Source: Pre-PBAC response, table PCR.2

EFG, efgartigimod; MBS, Medicare benefits schedule; NBA, national blood authority; Q3W, every 3 weeks

The redacted values correspond to the following ranges:

[1] *< 500*

[2] *500 to < 5,000*

[3] *5,000 to < 10,0004*

[4] *net cost saving*

[5] *$40 million to < $50 million*

[6] *$90 million to < $100 million*

[7] *$100 million to < $200 million*

Quality Use of Medicines

6.84 The submission stated that the sponsor intends to establish a national patient support program which will ensure that treatment is initiated and maintained in accordance with the proposed restriction and clinical evidence, and to minimise risks of inappropriate or unsafe use.

6.85 The program will provide education for patients and carers on treatment objectives, administration requirements and potential adverse effects. Prescribers and their care teams will also receive program information and resources to support correct patient selection and adherence to the restriction.

6.86 The Sub-Committees noted that Australia is in the top three users per capita of IVIg, and commented that a large amount of IVIg is potentially being wasted in Australia. The PBAC also noted that the dosing of IVIg should be based on ideal body weight.

Financial Management – Risk Sharing Arrangements

6.87 The submission proposed a risk sharing arrangement consisting of an expenditure cap based on the presented utilisation estimates with a [redacted]% rebate for all use beyond these estimates. The submission claimed that the [redacted]% rebate [redacted].

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

7 PBAC Outcome

7.1 The PBAC did not recommend efgartigimod alfa (herein referred to as efgartigimod) for the treatment of patients with active chronic inflammatory demyelinating polyneuropathy (CIDP) who have progressive or refractory symptoms despite immunoglobulin treatment or who are intolerant to immunoglobulin products. The PBAC noted that there was a high unmet need for new treatment options for these patients. However, the PBAC considered that it was unclear whether the place in therapy proposed in the submission would target the most appropriate patient population, given the requirement to be refractory to immunoglobulin potentially enriched the population with patients misdiagnosed with CIDP. The PBAC also noted the publication from Levine 2025 and the concerns raised by the FDA relating to reports of worsening of CIDP symptoms after initiating treatment with efgartigimod following treatment with immunoglobulin. The PBAC considered that there was insufficient evidence to support the clinical claims of non-inferior safety compared to placebo and superior efficacy and non-inferior safety compared to immunoglobulin. Overall, the PBAC considered that the proposed price was very high (approximately $[redacted] per year for a responding patient) and the resulting estimated cost to the PBS/RPBS was substantial (estimated at > $1 billion over the first 6 years of listing in the pre-PBAC response).

7.2 The PBAC considered that the primary reason for this outcome was uncertainty regarding the proposed place in therapy.

7.3 The PBAC considered that there was a high unmet need for new treatment options for patients with active CIDP. The PBAC acknowledged the consumer input which supported the submission and highlighted the treatment burden associated with regular intravenous immunoglobulin (IVIg) infusions.

7.4 The PBAC noted that the proposed restrictions attempted to target patients with the highest unmet clinical need. The PBAC noted that the submission proposed efgartigimod be used in patients who have progressive or refractory symptoms despite immunoglobulin treatment. However, the PBAC noted that response to treatment (particularly immunoglobulin) was part of the European Academy of Neurology (EAN)/Peripheral Nerve Society (PNS) diagnostic guidelines for CIDP. Noting that the diagnosis of CIDP is challenging and that the rate of misdiagnosis was high in clinical practice (see paragraph 4.5), the PBAC was concerned that the submission's proposed place in therapy, i.e. patients who are not responding to immunoglobulin treatment, assumed that all these patients had CIDP. This would result in a large proportion of patients (potentially around 30% of patients) who may have been misdiagnosed with CIDP receiving efgartigimod.

7.5 The PBAC considered that the restrictions in any future resubmission would need to be revised to target an appropriate place in therapy and advised the issues outlined in Section 3 should be addressed.

7.6 The PBAC was also concerned that there was insufficient evidence to inform how patients should be safely transitioned from immunoglobulin therapy to efgartigimod. The PBAC noted that patients transitioning from prior immunoglobulin therapy had notably lower response rates (58.8%) compared to those who previously received corticosteroids (77.8%) or no active treatment (72.3%) and experienced substantially higher rates of serious adverse events (10.9%), and adverse events leading to treatment discontinuation (12.1%), compared with other patient groups in Stage A of the ADHERE (see Table 6). The PBAC considered that the optimal approach to transitioning patients from immunoglobulin to efgartigimod remains uncertain, and noted emerging safety signals, including observational data from Levine 2025, suggesting that direct transition without a treatment break may be associated with severe disease relapse with incomplete recovery (see paragraphs 6.18 and 6.41). The PBAC noted that [redacted] (see paragraph 6.42). The PBAC also noted that the PSCR and pre-PBAC response stated that a phase 4 study was underway to evaluate the optimal approach for transitioning patients from IVIg to efgartigimod. The PBAC was concerned that patients with progressive CIDP despite treatment with immunoglobulin (i.e. a key population targeted in the submission) would be at risk of disease worsening if they transitioned to efgartigimod.

7.7 The PBAC noted that the submission nominated placebo (i.e. no active therapy) and IVIg/subcutaneous immunoglobulin (SCIg) (i.e. immunoglobulin) as comparators. The PBAC considered that best supportive care (including corticosteroids, immunosuppressants and rituximab), rather than placebo, may be the most appropriate comparator for patients with CIDP who were refractory or intolerant to

immunoglobulin. As noted above however, a proportion of patients who do not respond to immunoglobulin may have been misdiagnosed with CIDP and would potentially receive suboptimal treatment. For patients who had progressive disease despite immunoglobulin therapy, the PBAC considered that at least a portion would continue to receive suboptimal IVIg/SCIg.

7.8 The PBAC noted that the key trial, ADHERE, was a phase 2, multi-stage study with a complex design (paragraph 6.9). The PBAC noted several methodological concerns with ADHERE, including uncertainty around diagnostic accuracy and misdiagnosis, higher and poorly explained discontinuation rates among patients previously on IVIg/SCIg, the absence of a placebo arm in Stage A, and potential incentives created by access to open-label treatment. The PBAC also considered that the treatment sequencing evaluated in ADHERE did not reflect Australian clinical practice, particularly with respect to prior corticosteroids and noted that the ADHERE trial included patients irrespective of their response to prior therapy, including immunoglobulins (see paragraphs 6.49 to 6.52). In addition, the PBAC noted that the higher discontinuation rate of patients previously treated with immunoglobulin in Stage A may also have limited the applicability of the Stage B results to the population requested in the submission (while the PBAC acknowledged the results of the subgroup of patients with CDAS of 5B/5C who had received prior immunoglobulin, the Committee also noted the small sample sizes and wide confidence intervals of these subgroups).

7.9 The PBAC noted that in Stage B of the ADHERE trial, continued treatment with efgartigimod was associated with a statistically significant reduction in the risk of clinical deterioration events compared to withdrawal of efgartigimod in the placebo arm (HR = 0.39; 95% CI; 0.25, 0.61). Patients who continued treatment with efgartigimod also had reduced declines in mean adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) and Inflammatory Rasch-Built Overall Disability Scale (I-RODS) scores and mean grip strength. Based on these results, the PBAC considered that efgartigimod was superior compared to placebo in terms of effectiveness, noting that the minimal clinically important differences were not met for all outcomes and the uncertainties with the trial design.

7.10 The PBAC noted that the submission claimed that efgartigimod was non-inferior compared to placebo in terms of safety; however, the PBAC noted that the incidence of several safety outcomes were numerically higher in patients who continued efgartigimod compared to those who discontinued treatment (i.e. the placebo arm in Stage B, see Table 8). Overall, the PBAC considered that the claim of non-inferior safety versus placebo was inadequately supported by the data presented.

7.11 For the comparison with immunoglobulin, the submission presented indirect treatment comparisons comparing efgartigimod (ADHERE) with IVIg/SCIg (ADVANCE-CIDP, PATH, ICE treatment withdrawal trials). The PBAC noted that there were key differences between the trials in terms of design, patient characteristics, circumstances of use and outcome definitions which meant the comparisons were

largely uninformative (see paragraphs 6.10 and 6.11). Thus, the PBAC considered that the claim of superior comparative effectiveness of efgartigimod compared with immunoglobulin was not supported by the available evidence.

7.12 The PBAC, noting that the submission did not present any comparative data, considered that the claim that efgartigimod was non-inferior in terms of safety compared to IVIg/SCIg was not supported.

7.13 The PBAC considered that it was unclear if the economic evaluation and financial estimates presented in the submission were relevant as these were underpinned by the proposed clinical positioning and clinical claims which were not accepted. In general terms, for the population in whom immunoglobulin is an appropriate comparator, the PBAC agreed with the advice of the Sub-Committees outlined in paragraph 6.72.

7.14 The PBAC noted that, at the price requested in the submission, the cost per continuing patient would be approximately $[redacted] per year with the submission estimating a cost to the PBS/RPBS of > $1 billion over the first 6 years of listing to treat approximately 500 to < 5,000 patients per year (revised to > $1 billion over six years to treat approximately 500 to < 5,000 patients per year in the pre-PBAC response).

7.15 The PBAC considered a resubmission for efgartigimod should address the proposed place in therapy for efgartigimod (noting: the potential for misdiagnosis; the reports of worsening of CIDP symptoms when transitioning from immunoglobulin; clinical uncertainties arising from the trial design; and the substantial expenditure estimated in the submission). The PBAC advised that the clinical evidence, economic approach, utilisation and financial estimates and restrictions would require reassessment. The resubmission may be lodged at any future standard due date for PBAC submissions using the standard re-entry pathway.

7.16 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:
Not recommended

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

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9 Sponsor's Comment

Given the PBAC's acknowledgement of the high unmet need in this patient population, argenx is disappointed with the decision not to recommend efgartigimod alfa (Vyvgart®) for the treatment of CIDP. argenx thanks consumers for their input highlighting the significant patient and carer burden, as well as the need for new treatment options in CIDP. The company remains committed to working with the PBAC to ensure the clinical value of efgartigimod in CIDP is fully recognised, and to providing CIDP patients with sustainable access to innovative treatments that help them live healthier and more productive lives, while also reducing the demand on Australia's constrained immunoglobulin supply.

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