For screen – confidential information redacted

Efgartigimod with recombinant human hyaluronidase PH20 for treating chronic inflammatory demyelinating polyneuropathy

Rare disease committee [19th March 2026]

Chair: Paul Arundel

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Company: Argenx

Efgartigimod with recombinant human hyaluronidase PH20 for treating chronic inflammatory demyelinating polyneuropathy

- ✓ **Background and key issues**
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ❑ Summary

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Key primary issues

Key primary issues for committee discussion		Impact
Decision problem	Population misalignment between company's proposed population and ADHERE	Large
Clinical evidence	ADHERE may have overestimated effectiveness of efgartigimod	Large
	Different outcomes used to assess clinical deterioration and established clinical improvement in ADHERE	Large
	High percentage of people in ADHERE who deteriorated following Ig discontinuation did not improve with efgartigimod	Medium
	Uncertainty in interpreting results of ITCs due to methodological limitations	Large

Abbreviations; ITC, indirect treatment comparison; Ig, immunoglobulin

Large impact

Key primary issues

	Key primary issues for committee discussion	Impact
Cost effectiveness	Health states in the company's model	Unknown
	Choice of model cycle length for first two years	Large
	Uncertainty around use of Ig in clinical practice	Large
	Lack of treatment effectiveness data for people with severe disease	Large
	Uncertainty around the treatment pathway after discontinuing efgartigimod	Large
	Approach to modelling treatment effectiveness in comparator arm	Large
	Approach to modelling discontinuation in comparator arm	Large
	Uncertainty around adverse events	Large
	Approach to modelling caregiver burden	Large

Abbreviations; Ig, immunoglobulin


Large impact

Key secondary issues

Key secondary issues for committee discussion		ICER impact
Clinical & cost effectiveness evidence	Inclusion of biweekly dosing of efgartigimod	Large
Cost effectiveness	Appropriateness of health state utility values	Moderate
	Approach to modelling HRQoL impact of IV administrations	Moderate
	Approach to modelling resource use and costs	Moderate

NICE technical team: Considers these issues are also important and have the potential to substantially impact the cost-effectiveness results, both individually and collectively (as do key primary issues)

Abbreviations; HRQoL, Health-related quality of life; IV, intravenous

Background: Chronic inflammatory demyelinating polyneuropathy

Causes

- Rare condition with different symptoms, a debilitating, acquired immune-mediated neuropathy that causes muscle weakness and sensory disturbances
- Exact causes unknown, but it involves the immune system damaging the myelin sheath of peripheral nerves

Epidemiology

- Estimated prevalence of 1-6 per 100,000 in England, and occurs more frequently in men
- Up to 650 people are diagnosed with CIDP each year in the UK

Diagnosis and classification

- Defined as typical CIDP and atypical CIDP (distal, multifocal, motor, and sensory variants)
- Diagnosis is challenging because of overlapping symptoms and variety in nature of condition

Symptoms and prognosis

- Symptoms depend on the variant. Often include motor and sensory deficits causing problems in walking, upper limbs, numbness and paraesthesia (pins and needles), diminished touch sensation, pain, fatigue & weakness
- Most patients improve or stabilise with available treatments, but some relapse
- Relapse and disease progression impact daily functioning and quality of life as symptoms accumulate over time, but life expectancy is unaffected

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy

Patient perspectives

Submissions from Inflammatory Neuropathies UK and patient experts

Living with CIDP

- Significant impact on all aspects of life for a patient and their family: causing physical, emotional issues, limited sensation, struggle gripping, and social issues
- Patients lose mobility. Some require walking aids, impacting gross & fine motor skills, hands, feet and limbs. Suffer fatigue, depression, brain fogs & pain throughout the body

Current treatments

- Current treatments do not work for all patients → some people receive no treatment due to negative reactions and/or lack of response
- Inconsistent, unequal access to treatment. There is no UK-specific guidance/pathway
- Lack of understanding among clinicians around treatment options
- Current treatments can have unpleasant side effects and may place a burden on families due to the time required for care

Efgartigimod

- Offers choice and hope. Convenient and quick administration at home - will reduce anxiety of going to the hospital, no port injections, and reduced infections, less time in hospital and reduces caregiver time burden and anxiety

"My life now revolves around the 4 weekly IVIg treatment cycle.. feel low and fatigued on the days leading up to treatment and on the days afterwards and I hence avoid arranging any activities during those times"

"Main advantage … is I am able to administer at home. I am diabetic and have no fear of injection myself. However. it is important to note not all patients are able to do this or want to."

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy

Clinical perspectives: Submissions from the Association of Neurologists and Clinical experts

Aim of treatment

- Reverse disability, prevent progression to irreversible neurological deficit, improve function and quality of life, maintain stability, prevent relapse and facilitate independence

Unmet need/current treatment options

- Current treatments require frequent and long hospital visits, blood sampling, long-term side effects, and patients spend time away from family, miss workdays and incur personal costs for travel
- Many patients have contradictions to current treatments, and some treatments fail to achieve a response or achieve only an inadequate response

Efgartigimod: step change as a treatment for CIDP

- Favourable side effect profile, new mechanism/mode and can be self-administered at home - requires less blood monitoring and care giving, with potential cost-savings
- May offer a treatment option for patients with venous access limitations or intolerable SoC side effect profile
- Patients who have had a response or inadequate response to current treatments may respond to efgartigimod, but there is no evidence from the clinical trial
- Not all patients who responded to current treatment will respond to efgartigimod: there is a risk of relapse
- ADHERE demonstrated efgartigimod achieves clinically meaningful improvement at rates comparable to current 1st line treatments

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; SoC, standard of care

Efgartigimod (Vyvgart, Argenx)

Table: technology details

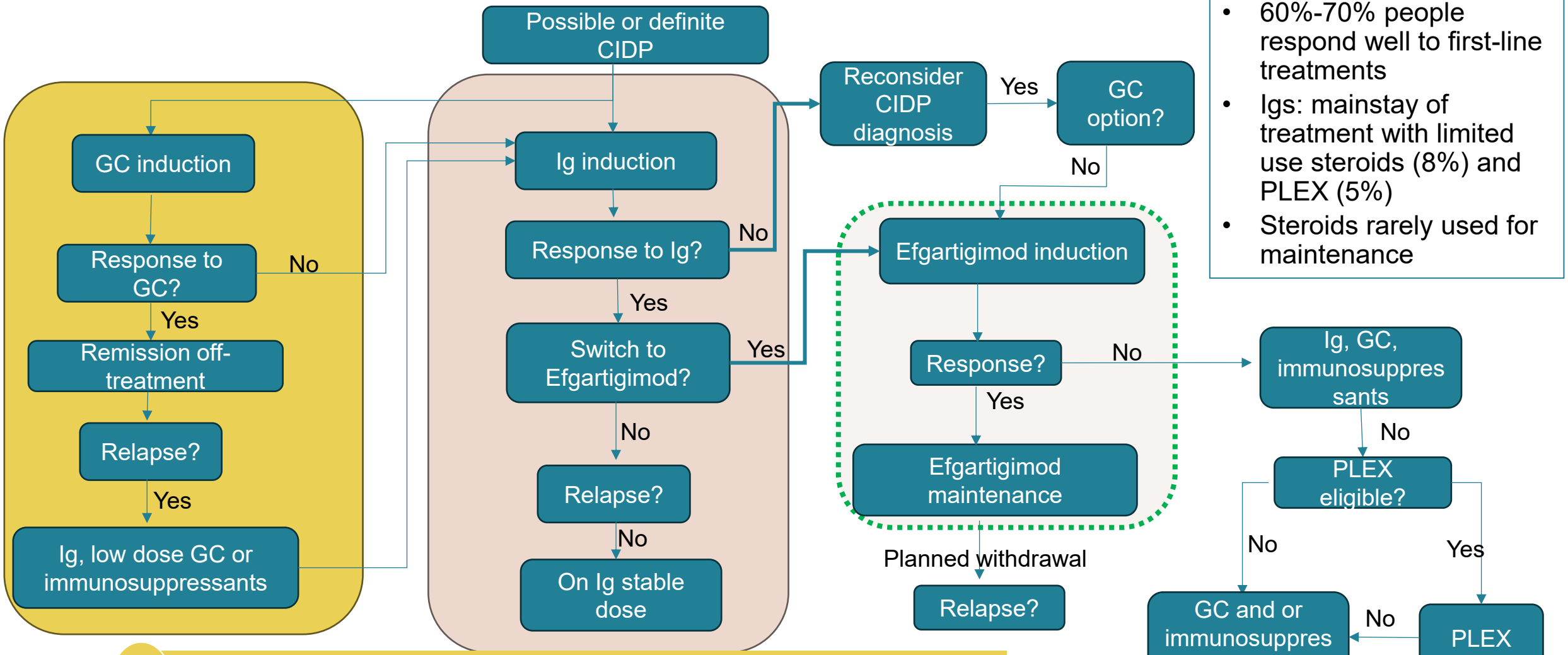
Marketing authorisation	• For the treatment of adult patients with progressive or relapsing active CIDP after prior treatment with corticosteroids or immunoglobulins • Marketing authorisation granted: December 2025
Mechanism of action	• Efgartigimod is a humanised IgG1 Fc fragment that has been engineered with specific modifications to increase its binding affinity for FcRn at both neutral and acidic pH levels • Efgartigimod works by targeting the FcRn system that normally protects IgG antibodies from degradation
Administration	• Pre-filled syringe for subcutaneous administration (can be self-administered at home)
Additional tests	• No specific laboratory tests or diagnostic investigations required by the prescribing information for initiating or maintaining treatment with efgartigimod • Routine clinical monitoring, including vigilance for infection and hypersensitivity reactions
Price	• List price per pre-filled 1000mg in 5ml (200mg/ml): £15,307.47 • List price for 12 months of treatment: [redacted] (assuming [redacted] biweekly dosing) or £798,721.92 (assuming 100% weekly dosing) • Efgartigimod is subject to a simple PAS discount

Abbreviations: CIDP: Chronic inflammatory demyelinating polyneuropathy; Fc: Fragment crystallisable; FcRn: Neonatal Fc receptor; Ig, Immunoglobulin; PAS, patient access scheme; pH, potential of hydrogen

Treatment pathway: CIDP

Company's position

Proposed positioning: people must have received Ig before being eligible for efgartigimod



- 60%-70% people respond well to first-line treatments
- Igs: mainstay of treatment with limited use steroids (8%) and PLEX (5%)
- Steroids rarely used for maintenance

Is the treatment pathway representative of NHS practice?
Where would efgartigimod be used in this pathway?

Abbreviations: CIDP: Chronic inflammatory demyelinating polyneuropathy; GC, glucocorticosteroids; Ig, immunoglobulin; IV, intravenous; PLEX, plasma exchange;

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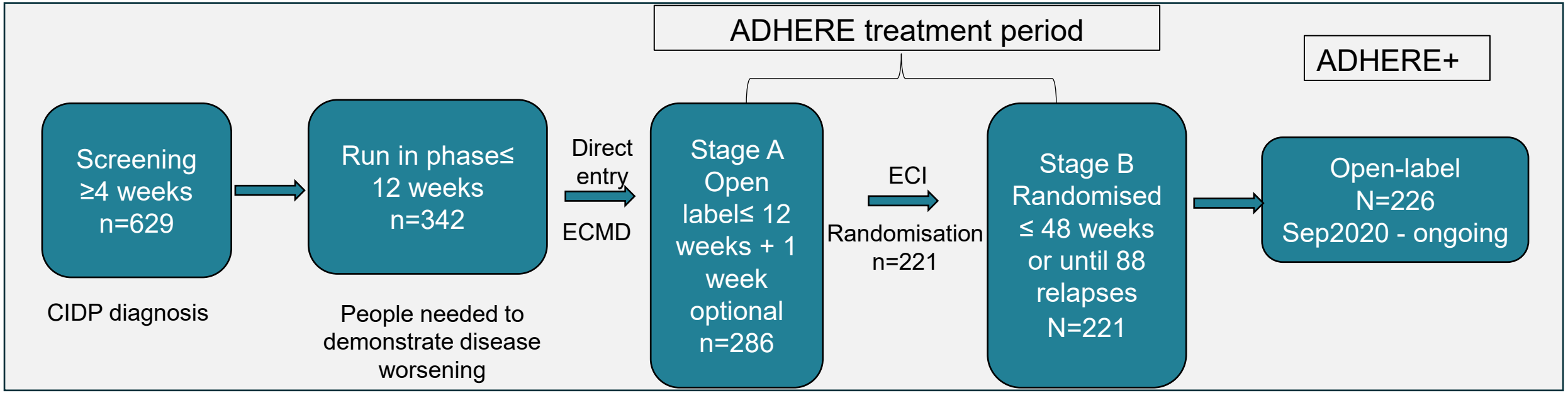
Key clinical trials: ADHERE and ADHERE+



ADHERE

- **Run-in phase**: 28% of screened individuals (179/629) were excluded because they did not have definite or probable CIDP based on EFNS/PNS criteria. CIDP treatment stopped during the 12-week run-in period
- **Stage A**: efgartigimod 1,000 mg once weekly for no longer than 12 weeks, remained in Stage A until ECI confirmed after at least 4 administrations and at 2 consecutive weekly visits
- People who were off treatment and worsening on aINCAT scale within 3 months before screening were allowed to enter stage A without completing the run-in period
- **Stage B**: people who showed ECI randomised (1:1) to continue weekly efgartigimod or placebo up to 48 weeks
- **ADHERE +**: more people were included in ADHERE+ than ADHERE stage B

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIPD; chronic inflammatory demyelinating polyneuropathy; ECI, Evidence of clinical improvement; ECMD, Evidence of clinically meaningful deterioration; EFNS/ PNS, European Federation of Neurological Societies/Peripheral Nerve Society; Ig, immunoglobulin

Company's targeted population

Marketing authorisation: adult patients with progressive or relapsing active CIDP after prior treatment with corticosteroids or Igs

Company's targeted population

- **Proposed population who have had prior, unsatisfactory treatment with Igs: Unsatisfactory was defined as people:**
  - **Have a high burden of Ig treatment:** those who have received at least 6 months of treatment with either IVIg or SCIg, which has a significant impact on their daily life, work, or
  - caregiving responsibilities and who remain symptomatic or
  - require high doses or frequency of Ig to continue to experience the benefits of treatment and avoid variation in symptoms between doses; or
  - **Who are intolerant or refractory to Ig:** who are unable to continue Ig treatment due to comorbidities, adverse events or safety concerns, such as concerns about the risk of developing thromboembolism or heart failure (**Company has informed NICE that it is no longer seeking a recommendation in this population**)

Abbreviations: CIPD; chronic inflammatory demyelinating polyneuropathy; Ig, immunoglobulin

Key issues: Population misalignment

Company

- Selected population best reflected people who are most likely to have efgartigimod in clinical practice
- In the absence of UK-based guidelines, proposed population was validated by clinicians (Structured Expert Elicitation [SEE] report)

EAG

- Consider company's proposed population not clearly represented by the ADHERE population
- ADHERE included people who had treatment with pulsed corticosteroids, corticosteroids and/or IVIg or SCIg **within the previous 6 months**
- 51.2% of people in Stage A and 43.4% in Stage B had prior IVIg, SCIg or corticosteroids, but unclear how many people meet company's high burden criteria, as they did not have full 6 months of IVIg or SCIg treatment
- 29.2% of stage A & 33.9% of stage B = treatment-naïve, who did not meet company's high burden Ig criteria, and also unclear how many of these were intolerant or refractory to Ig and were not identifiable

NICE technical team comments

- In addition to the uncertainty around alignment with clinical trial data, it is important that the company's proposed target population is identifiable in NHS practice, implementable in any potential NICE recommendations and reflected in the company modelled population (in terms of inputs)

Is the company's proposed target population appropriate?

NICE

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; Ig immunoglobulin; IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin; SEE, structured expert elicitation

Key issues: Treatment effectiveness of efgartigimod

Background

- ADHERE methodology may have overestimated efgartigimod treatment: only people with ECI with efgartigimod in stage A progressed to stage B, rather than wider CIDP population including non-responders

Company

- Consider approach is ethically robust as placebo was not used following a period of active deterioration and efficacy demonstrated in a population with confirmed responsiveness
- ADHERE design selected in consultation with regulatory agencies; reflects CIDP heterogeneity - periods of relapse & remission make fixed-duration parallel-group studies less sensitive and ethically challenging

EAG

- Only people achieving ECI (69%: responders) in stage A were randomised to efgartigimod or placebo in stage B
- Excluding people who did not achieve ECI in Stage A may have overestimated treatment effect and underestimated adverse events
- Stage B results confounded by prior treatment, with continued therapy in efgartigimod arm and withdrawal/discontinuation in placebo arm

Does including only responders from stage A overestimate efgartigimod treatment effect?

Abbreviations: CIDP: chronic inflammatory demyelinating polyneuropathy; ECI, Evidence of clinical improvement; Ig, immunoglobulin

Key clinical trials: ADHERE & ADHERE+

Table: Summary of study designs

	ADHERE	ADHERE+
Design	Phase 2, multistage, open-label, randomised-withdrawal, double-blind, placebo-controlled trial	Single-arm, open-label phase 2 extension study with no randomisation
Population	• Adults with definite or probable CIDP, CDAS score ≥2 at screening, and INCAT score ≥2 at first run-in visit or stage A baseline • Participants who received CIDP treatment within 6 months before study entry or who discontinued treatment were required to have evidence of ECMD	Adults who either completed Week-48 of Stage B of ADHERE, deteriorated during Stage B, or were offered participation due to early trial termination
Intervention	Subcutaneous administration of efgartigimod (1,000mg weekly)	
Comparator	Stage A: single arm; stage B: placebo	None
Primary outcome	• Stage A: Percentage of participants with confirmed ECI (responders) • Stage B: Time to first aINCAT deterioration	• Incidence of TEAEs and serious TEAEs • Incidence of clinically significant laboratory abnormalities
Locations	22 countries from Asia-Pacific, Europe, and North America	24 countries from North America, Europe, and Asia

Abbreviations: aINCAT, adjusted inflammatory neuropathy cause and treatment; CIDP, chronic inflammatory demyelinating polyneuropathy; CDAS, CIDP Disease Activity Status; ECI, Evidence of clinical improvement; ECMD, Evidence of clinically meaningful deterioration;TEAE, treatment-emergent adverse event

Key issues: Clinical trial results: ADHERE stage A

Company

- Efgartigimod shown to be clinically effective as 66% (n=214/322, 95% confidence interval [CI]: 61.0-71.6) of people demonstrated evidence of clinical improvement (ECI)

Table: ADHERE Stage A – confirmed ECI responders and non-responders

	Any prior therapy N=322 n (%)	Corticosteroids n=63 n (%)	IVIg or SCIg n=165 n (%)	Off treatment n=94 n (%)
Number of participants with confirmed ECI	214 (66)	49 (78)	97 (59)	68 (72)
95% CI	61.0-71.6	65.5-87.3	50.9-66.4	62.2-81.1
Number of participants without confirmed ECI	108 (34)	14 (22)	68 (41)	26 (28)

EAG

- High % (41%) of people (company's proposed population) having efgartigimod who previously had IVIg or SCIg did not achieve ECI
- Many people may experience poorer outcomes if switching maintenance treatment from Ig to efgartigimod

NICE technical team comments: Concerned that company's model does not fully account for "risk of switching" from Ig to efgartigimod (for people previously responding to Ig) - Clinical input would be useful

Is the high proportion of people who showed clinical deterioration following withdrawal of Ig, but did not achieve ECI with efgartigimod, a concern?

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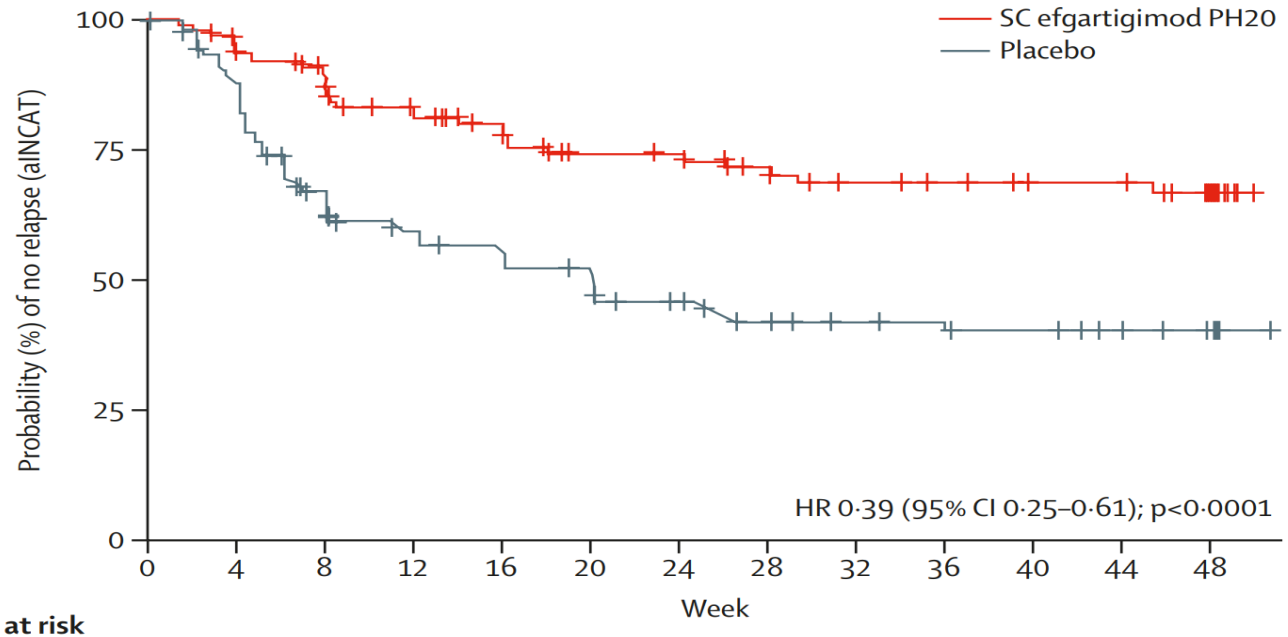
Abbreviations: CI, confidence intervals; ECI, evidence of clinical improvement; IG immunoglobulin; IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin

Secondary efficacy endpoints

Clinical trial results: ADHERE stage B

Figure: Time-to-First aINCAT deterioration compared with stage B baseline



Number at risk (number censored)													
SC efgartigimod PH20	111 (0)	107 (2)	93 (8)	80 (14)	68 (22)	56 (29)	55 (30)	48 (35)	42 (39)	40 (41)	36 (45)	36 (45)	28 (55)
Placebo	110 (0)	94 (3)	67 (8)	55 (12)	51 (13)	47 (14)	38 (17)	31 (21)	28 (24)	26 (26)	24 (27)	21 (31)	16 (35)

Company

- Efgartigimod significantly reduced risk of relapse by 61% at Week 48 vs. placebo
- Rapid separation of KM curves at Week 4, sustained through Week 48

EAG

- Similar effect for people who had prior:
  - IVIg or SCIg (HR 0.30 [95% CI: 0.15 to 0.57]
  - corticosteroid (HR 0.29 [95% CI: 0.11 to 0.81])
- Off treatment subgroup: HR 0.72 [95% CI: 0.34 to 1.53]
- Agreed results indicate reduced relapses for efgartigimod compared with placebo
- Consider relapse rates underestimated in both arms due to exclusion of I-RODS or MGS as indicators of relapse (see issue)

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CI, confidence intervals; HR, hazard ratio; I-RODS, Inflammatory Rasch-built Overall Disability Scale; MGS, mean grip strength; KM, Kaplan-Meier; SC subcutaneous

Key issues: Different outcomes used to assess clinical deterioration and ECI in ADHERE

Background

- Company used aINCAT, I-RODS and MGS in run-in and stage A, while only aINCAT for stage B for ECI
- EAG considers using aINCAT in stage B may have underestimated number of people who had relapsed

Company

- Agree with EAG that the number of people who relapsed may been underestimated but consider this would be similar for both arms due to consistency in visit schedules & definition of relapse
- In stage B, aINCAT was assessed as a primary endpoint whereas I-RODS and MGS were secondary endpoints, showing consistent results with those reported for relapse

EAG: Some people may not have been considered to have relapsed if they showed decline in I-RODS or MGS, but not in aINCAT: may not affect both arms equally, given magnitude of benefit of efgartigimod vs placebo. ITCs also used only aINCAT as an outcome (see ITC issue)

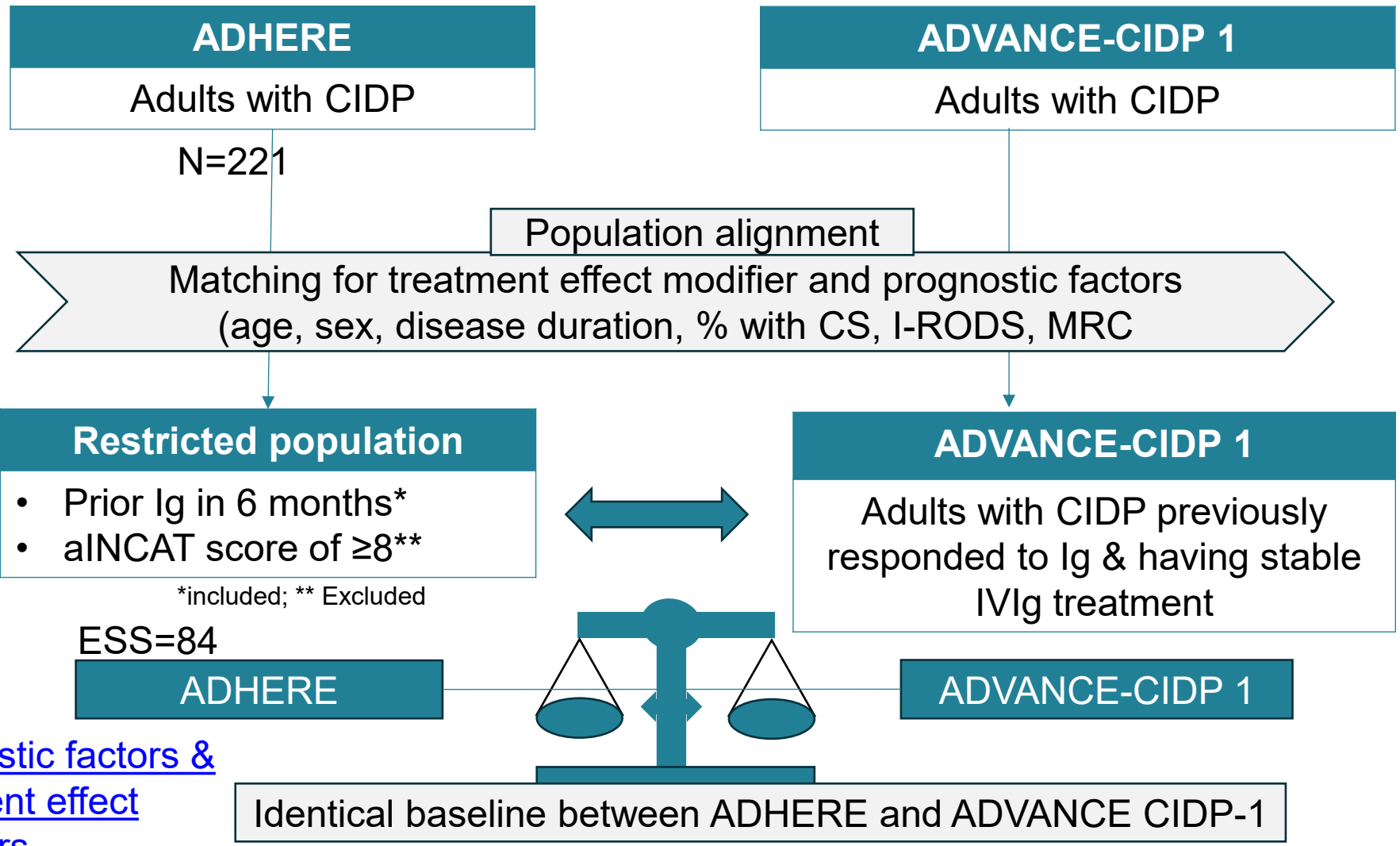
- Clinical opinion to EAG: aINCAT, I-RODS and MGS used in combination rather than relying on one
- Both EAG's experts and results from company advisory board highlighted that some clinicians prefer to use I-RODS due to concerns over aINCAT lacking sensitivity in assessing disease burden & treatment response

Clinical experts: NHSE Immunoglobulin treatment guidelines recommend clinical monitoring in CIDP with at least 3 disease-specific clinical outcome measures

Which outcomes are used to measure ECI in clinical practice?
Does use of only aINCAT in stage B underestimate or overestimate efgartigimod response?

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; ECI, Evidence of clinical improvement; I-RODS, Inflammatory Rasch-built Overall Disability Scale; ITC, indirect treatment comparison; MGS, mean grip strength

Indirect treatment comparison: Methodology 1/3



Company: No head-to-head trial comparing efgartigimod with Igs - did an anchored MAIC

- Conducted 2 SLRs. Identified 5 trials reporting relevant comparator and outcome (aINCAT)
- Considered only ADVANCE-CIDP 1 was suitable for comparison against ADHERE Stage B and excluded ADVANCE-CIDP-1 (Epoch 2), PATH PIMPA & Katzberg 2013

Prognostic factors & treatment effect modifiers

Weighted/reweighted baseline characteristics

Abbreviations: INCAT, Inflammatory Neuropathy Cause and Treatment, CIDP, Chronic inflammatory demyelinating polyneuropathy; CS, corticosteroids; ESS, effective sample size; I-RODS, Rasch-built Overall Disability Scale; Ig, immunoglobulins; ITC, indirect treatment comparison; MGS, mean grip strength; MRC, Medical Research Council

Indirect treatment comparison: methodology 2/3

EAG

- Concerned about relevance of ADVANCE-CIDP-1 population to company's proposed population, differences in trial design, placebo response, and limited reporting of TEM in ADVANCE-CIDP-1
- Consider comparison with PATH and ICE had fewer concerns about trial design than comparisons between ADVANCE-CIDP-1 and ADHERE but:
    - PATH did not report mean change in aINCAT and
    - ICE extension had smaller numbers, and most baseline characteristics needed for MAIC adjustments were not available for extension phase
- Lack of clear differentiation b/w prognostic factors and treatment effect modifiers, and the number of TEMs identified could not be adjusted for:
    - such as typical or atypical CIDP in each trial, and after weighting adjustment, the change from baseline in aINCAT was greater in placebo arm of ADHERE than ADVANCE-CIDP-1
- Company restriction of aINCAT score of ≥8 excluded people who may have represented some of company's proposed population
- Differences in trial designs & limited adjustment of treatment effect modifiers → likely to have affected response to treatment
- Company provided STC ADHERE and ADVANCE-CIDP-1 to validate anchored MAIC on EAG's request
- Although STC matched MAIC results, the unmeasured prognostic factors and TEMs in ADVANCE-CIDP-1 raises concern about heterogeneity b/w trials and bias

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; INCAT, Inflammatory Neuropathy Cause and Treatment; CIDP, chronic inflammatory demyelinating polyneuropathy; Ig, Immunoglobulin; MAIC, Matching-adjusted indirect comparison; STC, simulated treatment comparison; TEMs, treatment effect modifiers

Indirect treatment comparison: results 3/3

Table: ITC results for change from baseline in aINCAT

Comparator trial	Comparator treatment	Follow-up time	Difference in means (95% CI)*	P value
ADVANCE-CIDP-1 (n=132)	SCIg	32 weeks	-0.88 (-1.72 to -0.04)	0.040
ICE (n=57)	IVIg	24 weeks	-0.53 (-1.53 to 0.47)	0.297
PATH (n=113)	SCIg (low dose)	25 weeks	-1.13 (-2.05 to -0.21)	0.015
PATH (n=114)	SCIg (high dose)	25 weeks	-0.58 (-1.45 to 0.29)	0.194

EAG

* Values below 0 favours efgartigimod

- ITC results suggest differences between trials not clinically meaningful (improvement of ≥1 point): results highly uncertain due to differences in placebo arm between ADHERE and ADVANCE-CIDP1
- Effect estimates favoured efgartigimod over SCIg and IVIg from ICE and PATH: but were highly uncertain due to differences between treatment effect modifiers and lack of reporting of baseline characteristics
- Consider ITC results highly uncertain as it was unclear how trial populations were relevant to company's proposed population, and some factors that could influence results were not reported

NICE technical team comments:

- A scenario assuming equal efficacy between efgartigimod and Ig may be informative (given lack of data in proposed population, high uncertainty in ITC results and comments in clinical expert submissions)

- How robust are the company's indirect treatment comparisons (ITCs)?
- Does ITC evidence show that efgartigimod is clinically more effective than Ig?

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Abbreviations: CI, confidence intervals; CIDP, Chronic Inflammatory Demyelinating Polyneuropathy; ITC, indirect treatment comparison; IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin; MAIC, Matching-adjusted indirect comparison; STC, stimulated treatment comparison

Statistical advantage

Numerical advantage

Efgartigimod with recombinant human hyaluronidase PH20 for treating chronic inflammatory demyelinating polyneuropathy

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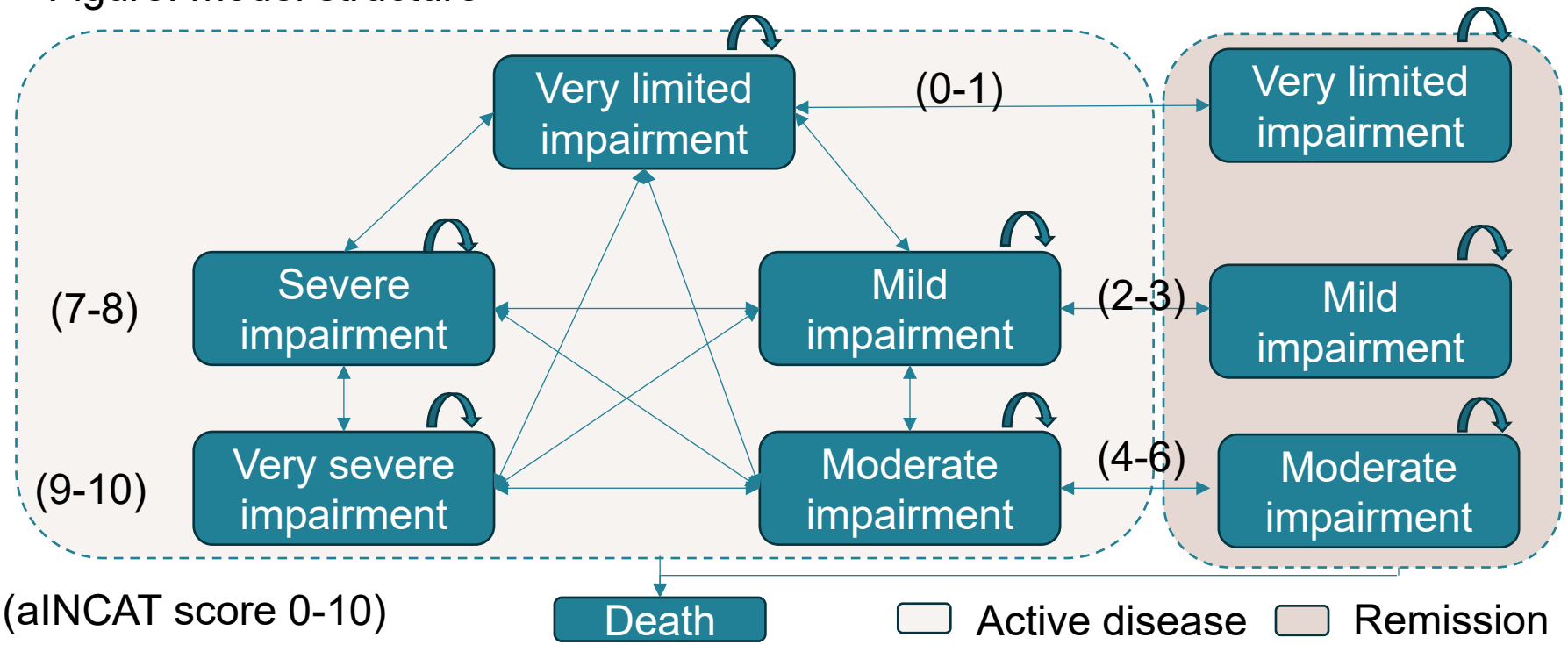
Company's model overview 1/3

EAG: broadly agreed with company's model structure

Figure: model structure



Affects QALYs by:

- Reducing disease severity, + HRQoL impact of IV treatment
- Reducing impact on caregivers' quality of life

Affects costs by:

- Higher total costs than current treatments
- Subcutaneous self-administration at home
- Reducing monitoring, mobility, hospitalisation and professional caregiving costs

- HS defined by aggregating aINCAT score (5 categories) and whether people have active disease or in remission
- People can move b/w active disease states based on transition probabilities specific to treatment received
- People can move b/w active disease & remission HS at same rate for very mild, mild and moderate impairment, & independently of treatment received (NICE technical team: assumptions around remission are uncertain, see slide)
- At baseline, all people start in active disease: for Ig maintenance and Ig-intolerant cohorts, distribution informed by ADHERE run in phase; for Ig-refractory cohort, distribution informed by ADHERE stage A

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP, chronic inflammatory demyelinating polyneuropathy; HRQoL, Health-related quality of life; HS, health states; Ig, Immunoglobulin; IV, intravenous; QALY, Quality-adjusted life year

Definitions of health states

Company's model overview 2/3

Table: Baseline distribution in the model

Health state	Distribution at baseline: Ig maintenance and Ig-intolerant	Distribution at baseline: Ig-refractory
Very limited impairment	0.0%	0.0%
Mild impairment	42.1%	27.4%
Moderate impairment	51.8%	58.5%
Severe impairment	5.5%	9.8%
Very severe impairment	0.6%	4.3%

Company

- Used data from baseline of ADHERE run-in phase for Ig maintenance and Ig-intolerant cohorts, but used data from baseline of ADHERE Stage A for Ig-refractory cohort

EAG

- Preferred to inform baseline distribution for Ig maintenance using baseline data from run-in period of ADHERE for all treatments: a more consistent approach
- For Ig-intolerant & Ig-refractory, used run-in data from stage A of ADHERE (scenario analysis)

NICE technical team comments

- While baseline distributions are based on trial data, there may be uncertainty in how closely the distributions in the model reflect the company's target population

Are the baseline distributions in the model appropriate?

Abbreviations: Ig, immunoglobulin

Company's model overview: remission 3/3

Table: Input values for parameters included in remission and relapse probability calculations

Parameter	Input value	Source
Proportion of people on a stable dose of Ig at any given time	60.8%	Koay et al. 2025
Proportion of people on a stable dose, who were willing and eligible to undergo a dependency test	45.2%	SEE with UK clinical experts
Proportion of people who successfully discontinued Ig after a dependency test and remain clinically stable for the following 6 months	31.0%	SEE with UK clinical experts
Proportion of people, among those in remission at 6 months, who would not remain in remission for an additional 12 months	20.6%	SEE with UK clinical experts

EAG: broadly agree with company's modelling of remission and relapse

- People having efgartigimod modelled to potentially enter remission after being on maintenance treatment for at least 1 year, people having Ig modelled to potentially enter remission health states from baseline
- % of people on a stable Ig dose was based on Koay et al (1 centre in UK),12/45 people on a stable dose of Ig were willing and eligible for a dependency test, 8/12 remained stable off treatment for at least 12 months

NICE technical team comments

- Assumptions around remission highly impacts on costs. Inputs on % of people who are considered for temporary withdrawal of treatment and how long they may withdraw treatment for are based on limited data (including clinical expert input). ADHERE did not report % of people who temporarily withdrew treatment

Is inclusion of remission health states, with temporary treatment withdrawal, appropriate?
If so, how robust are the inputs informing these health states?

Abbreviations: Ig, immunoglobulin; HS, health states; SEE, structured expert elicitation

Key issues: Choice of cycle length for first-two years

Background

- Company preferred a 6-month cycle length for entire time horizon, while EAG preferred a 3-month cycle length for 1st two years from baseline but thereafter a 6-month cycle length

Company

- 6-month cycle length aligns with standard interval for assessing dose adjustments for Ig, and a 6-month timeframe should be short enough to capture fluctuations in aINCAT score
- 3-month cycle length results in less robust transition probabilities due to fewer data points, and it was not possible to model transitions to remission states from baseline in comparator arm
- People are normally seen by clinicians on a 6-monthly basis, so consider a 6-month cycle was appropriate

EAG

- Clinical opinion to EAG: a 6-month cycle length not sufficient to capture granularity of rapid changes in disease severity after starting a new treatment
- 6-month cycle incompatible with ADHERE → leading to misalignment b/w model & time of observation
- Disagree that it was not possible to model the transition to remission state from baseline in comparator
- People are seen 6-monthly basis when they are stable on treatment, but seen regularly if they are undergoing a rapid change: so a 3-month cycle is more appropriate
- Preferred to rescale 6-month probabilities avoiding issues with company's 3-month probabilities

Is a 3-month or a 6-month cycle length more appropriate to use in the model?

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment, Ig, immunoglobulin

Key issues: Use of Ig in clinical practice

Background

- EAG consider company's assumption of Ig dosages & brand are uncertain

Company

- Used UK chart review interim analysis (n=69; 4 NHS sites) study to inform split b/w IVIg and SCIg (94.9% and 5.13%)
- Sourced proportion of people on each dosage of Ig from the company's SEE

NICE technical team comments

- Ig is a high-cost treatment – important that assumptions/methods regarding frequency of Ig dose are robust/accurate

Is the company's or EAG approach more appropriate? What is the most appropriate Ig dosing frequency and dosing levels?

Abbreviations: CIDP: Chronic inflammatory demyelinating polyneuropathy; Ig, immunoglobulin; IV, intravenous; PLEX, plasma exchange; SC, subcutaneous; SEE, structured expert elicitation

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Ig dose data: SEE

Ig dose data: chart review

EAG

- Split b/w IVIg and SCIg informed from Immunoglobulin Database Annual Report and % from final data cut analysis more appropriate (76.7% and 23.3%)
- Company's chart review data on distribution across Ig brands based on a small sample size showed a discrepancy in split b/w IVIg and SCIg
- While for dosage, company's chart review data estimates a lower frequency and administrations of both IVIg and SCIg compared to SEE report
- Consider chart review study small but reflective of NHS data

Table: Distribution of people across Ig products

Ig product	Proportion (interim analysis): company preferred	Proportion (final analysis): EAG preferred
Privigen (IVIg)	51.28%	[redacted]
Gamunex (IVIg)	38.46%	[redacted]
Hizentra (SCIg)	5.13%	[redacted]
Flebogamma (IVIg)	5.13%	[redacted]

Key issues: Lack of treatment effectiveness data for severe disease

Background

- Lack of data from ADHERE and ADHERE+ on severe & very severe impairment states to inform model

Company

- Used combined ADHERE & ADHERE+, aINCAT data for efgartigimod responders to derive transition probabilities for up to 144 weeks
- Only used first 96 weeks because data beyond this point limited, with fewer than 10 people
- Transition probabilities derived for 24-week time periods (~6 months, in line with model cycles)

Table: people in each health state

State	Weeks			
	0-24	24-48	48-72	72-96
Very limited	[redacted]	[redacted]	[redacted]	[redacted]
Mild	[redacted]	[redacted]	[redacted]	[redacted]
Moderate	[redacted]	[redacted]	[redacted]	[redacted]
Severe	[redacted]	[redacted]	[redacted]	[redacted]
Very severe impairment	[redacted]	[redacted]	[redacted]	[redacted]

EAG

- Low number of data points informing 24-week transition probabilities
- No data to inform transitions out of very severe & very limited data to inform severe impairment health states
- Preferred to assume all people in severe and very severe impairment health states remain in these health states indefinitely, regardless of whether they are having efgartigimod or comparator

Is there sufficient evidence to reliably model the severe disease health states?
Is the company's or EAG's approach preferred?

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment

Key issues: Treatment pathway after discontinuing efgartigimod

Background
- Uncertainty around subsequent treatments people have after discontinuing efgartigimod

Company
- Used SEE to inform people having subsequent treatment after efgartigimod
- Modelled separate pathways for Ig maintenance and Ig intolerant/refractory
- Discontinuation of efgartigimod was only modelled for first 18 months of treatment
- Provided scenarios with % of people recommencing Ig ranging from 0% to 100% (Ig maintenance)

EAG
- Suggest proportion returning to Ig treatment after efgartigimod is implausibly low
- Clinical opinion to EAG → most would recommence Ig after efgartigimod
- Noted disagreement b/w clinical experts in SEE report; inputs settled on as a compromise b/w clinical experts
- For Ig maintenance, PLEX or corticosteroids are used as rescue therapies, many return to treatment with Ig in long-term after symptoms have stabilised

Table: % people receiving each subsequent treatments

Subsequent treatment	Proportion (first line)
Ig	31.0%
PLEX	14.5%
Corticosteroids	49.9%
Immunosuppressants	4.6%

NICE technical team comments
- Assumptions about treatment pathway in both model arms highly impactful on cost-effectiveness results

What proportion of people have each subsequent treatment after discontinuation of efgartigimod?

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Supplementary slide

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; Ig, immunoglobulin; PLEX, plasma exchange; SEE, structured expert elicitation

Key issues: Modelling comparator treatment effectiveness 1/2

Background

- Uncertainty around methodology used by company to derive transition probabilities for comparators

Company

- Derived transition probabilities for comparator by combining data for efgartigimod with outcomes of company's ITC comparing efgartigimod and Ig based on ADHERE and ADVANCE-CIDP-1
- Based on ITC results, assumed 88% people had 1 greater improvement in aINCAT if treated with efgartigimod as compared with Ig, while rest had same response to efgartigimod and Ig
- People in ADHERE having efgartigimod suggested similar mean changes in aINCAT in Stage B for different aINCAT scores at baseline
- Assumed people did not move b/w aINCAT categories after 2 years from baseline because they would be on stable treatment

Table: Mean CfB in aINCAT over Stage B of ADHERE

aINCAT score at Stage B baseline	Mean aINCAT CfB over Stage B: efgartigimod arm	Mean aINCAT CfB over Stage B: placebo arm
0-1	[redacted]	[redacted]
2-3	[redacted]	[redacted]
4-6	[redacted]	[redacted]
7-8	[redacted]	[redacted]

Abbreviations: CIDP: Chronic inflammatory demyelinating polyneuropathy ;aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CfB, change from baseline; ITC, indirect treatment comparison

Key issues: Modelling comparator treatment effectiveness 2/2

EAG

- ITCs are not an appropriate source for model inputs: methodology is uncertain & assumptions are flawed
- To derive transition probabilities for comparator, the company assumed difference in CfB is the same, regardless of aINCAT score at baseline: clinically implausible
- Considerable difference between aINCAT CfB by aINCAT scores at baseline for efgartigimod and placebo
- Company approach inappropriate because people enter model in Ig maintenance already stable on treatment, it was assumed their disease stays broadly the same over time, so modelling early changes and then long-term stability would not be consistent
- EAG assumed that people having comparator treatments from baseline would remain in same aINCAT categories for entire duration of model time horizon

Which approach for comparator treatment effectiveness is the most appropriate?

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CfB, change from baseline; ITC, indirect treatment comparison

Key issues: Modelling comparator discontinuation

Background

- EAG consider assuming people can discontinue Ig in 1st few cycles while on maintenance but would not discontinue comparator while on maintenance not logically coherent

Company

- Included probability of discontinuation from baseline to 6 months, and for 6 to 18 months for people having Ig
- Used ICE study and PATH studies for 1st 6 months to inform the probability of discontinuation from baseline to 6 months, and for 6 to 18 months from PATH (open-label)

EAG

- Company's approach to modelling Ig discontinuation not appropriate: assumed people will be on a stable treatment at baseline, and that people will not discontinue treatment after 18 months on treatment
- Consider it is more appropriate to exclude treatment discontinuation for people having Ig

Is the company's or EAG's approach more appropriate for comparator discontinuation?

Abbreviations: Ig, immunoglobulin

Per-cycle Ig discontinuation

Key issues: Modelling adverse events

Background

- Very few data informing frequency, costs, and HRQoL impact of AEs treatments included in model

Company

- Used duration of AEs from TA706 (ozanimod for treating relapsing–remitting multiple sclerosis)
- If duration of an AE not available from TA706, assumed average duration of 21.6 days based on TA706 (arthralgia and pain, back pain, headache, influenza, infusion/injection site reaction, upper respiratory tract infection and depression)
- Efgartigimod associated with low incidence of serious AEs while PLEX associated with a high incidence

EAG comments

- Substantial uncertainty in data informing AEs → definitions not consistent across treatments, mainly due to how data were reported for comparators and different criteria
- Duration of AEs based on average of all AEs is not reflective of how long event lasts
  - e.g. duration of 21.6 days was assumed for dizziness compared to a duration of one day for influenza
- AEs reported for treatments are mild or moderate, most treated by GP and NHS staff are trained and use sterile techniques to deliver IV treatment and PLEX, so complications to IV treatment are rare
- Therefore, preferred to remove AEs and complications related to IV administration in its base case

Whose approach of modelling AEs, the company or the EAG, is more appropriate?

Abbreviations: AE, adverse events; aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP, chronic inflammatory demyelinating polyneuropathy; HRQoL, Health-related quality of life; IV, intravenous; PLEX, plasma exchange

Key issues: Modelling caregiver burden 1/2

Background

- Company included caregiver QoL in its model: due to a lack of evidence on disutilities, company parametrised caregiver disutility using disutilities measured for caregivers of people with multiple sclerosis (MS)
- Used disutilities from TA533 (ocrelizumab for treating relapsing-remitting MS), informed by Gani et al 2008, based on EDSS categories

Company

- Discussed approach with 6 clinical experts who agreed motor disability from CIDP is comparable to MS and requirement of care giving likely to be similar
- Mapping from aINCAT scores to EDSS was also validated with clinical experts

EAG

- Consider disutilities, mapping & number of caregivers applied used for each health state not appropriate → limited validation of approach with clinician and no validation with caregivers
- Mapping aINCAT (7-8) scores to EDSS (7.5-9.5) overrepresents functional impairment, as people with EDSS 7.5-9.5 are restricted to a wheelchair or bed
- Disutilities from Gani et al. 2008 not validated by caregivers and were based on assumptions
- Consider EQ-5D-5L data for 21 UK-based caregivers of people with CIDP in a cross-sectional survey of burden collected by the company are more robust
- Preferred utility decrements for caregivers, weighted by % of people requiring a caregiver (maximum 1)

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP, chronic inflammatory demyelinating polyneuropathy; EDSS, expanded disability status scale; EQ-5D-5L, EuroQol 5-Dimension 5-Level

Key issues: Modelling caregiver burden 2/2

Table: Proportion of people requiring caregivers by aINCAT score, from UK Adelphi dataset

aINCAT category	Proportion of people requiring a caregiver	EAG-preferred disutilities	Company preferred disutilities
0-1 (very limited impairment)	2.8%	-0.000339	0.000
2-3 (mild impairment)	14.8%	-0.001791	-0.0025
4-6 (moderate impairment)	51.8%	-0.006268	-0.0275
7-8 (severe impairment)	70.0%	-0.00847	-0.2500
9-10 (very severe impairment	100%	-0.0121	-0.2500

Patient experts

- Care is often given by spouses and partners, and can also impact parents and children
- Most carers provide informal care, and amount of care is linked to severity of condition, which impacts on carer's own physical and emotional health, as well as on several social factors
- Carers feel tiredness, ill health, mental health impact, impact on employment, and changes to social life

- Which approach to model caregiver burden is more appropriate?
- Should caregiver burden be included in the economic model or considered qualitatively in decision-making?

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment

Key issues: Switching from weekly to bi-weekly dose 1/2

Background

- Uncertainty around switching from weekly dose to biweekly based on ADHERE+ after 24 week

Company

- People who had stable disease entered the dosing substudy (ADHERE +) could have a biweekly dose after 24 weeks, if stable from the last 2 scheduled visits (12 weeks)
- Baseline characteristics of substudy (ADHERE+) similar to stage A and overall ADHERE population
- Assumed [redacted] remained stable on biweekly dosing indefinitely after 6 months from baseline

EAG

- Clinical opinion to EAG: people are unlikely to switch to a less frequent dose if the disease is responding; some specific subgroups may choose to switch
- High % ([redacted]) of people in ADHERE+ substudy deteriorated at week 24 on biweekly dosing, out of which [redacted] restabilised on weekly dosing, [redacted] having restabilised by first post- weekly baseline visit (week 6)
- [redacted] who were stable on weekly dose did not return to stable levels following the switch to biweekly dosing
- EAG scenario analysis assuming 100% weekly dosing results in a large increase in the ICER

NICE technical team comments:

- Assumptions around % having weekly vs. bi-weekly substantially impacts costs of efgartigimod – important that assumptions on this issue are generalisable to company's target population (high current burden of Ig)
- No reduction in dosing made over the model time horizon for Ig treatment (clinical input may be valuable)

Abbreviations: ICER, Incremental cost-effectiveness ratio

Key issues: Switching from weekly to bi-weekly dose 2/2

ADHERE+: Kaplan–Meier analysis of time to clinical deterioration during biweekly dosing

ADHERE+:Kaplan–Meier time to restabilisation on weekly dosing after clinical deterioration during biweekly

- Would people switch from weekly to biweekly efgartigimod dosing in clinical practice?
- If so, what % should be assumed to have biweekly dosing, and for how long?

Key issues: Health state utility values

Background
- Uncertainty around utilities used in the economic model

Company
- Used HRQoL (EQ-5D-5L) data collected in ADHERE and pooled utilities from stage A & B to maximise data:
  - Weekly Stage A: baseline up to 12 weeks
  - Every 4 weeks (stage B): baseline up to 48 weeks
- Used mixed-effect model to estimate HSUVs from mapped EQ-5D-3L data

EAG
- Values for very severe health state lacks face validity: average EQ-5D-5L domain scores were not low enough to have negative utilities (EAG assume 0 for very severe)
- Observations low at each time point. In 2 domains, scores spanned both lower + upper ranges: very uncertain
- Mixed-effect model overly simplistic: additional covariates should have been explored (age, sex, treatment & other)
- Multiple imputation should have been used for missing data to address high attrition

NICE technical team comments:
- Values for all health states, except very mild, appear low: face validity concerns (IV disutility applied also)
- High decrements between states: relatively small assumed efficacy changes = large impacts

Table: Responses collected at baseline to Week 48

STAGE	Baseline	Week			
		12	24	36	48
A	315	16	-	-	-
B	195	137	90	67	51

Table: Health state utility values in the model

Health state	Mean (SE) utility
Very limited impairment	0.851 (0.024)
Mild impairment	0.630 (0.013)
Moderate impairment	0.426 (0.012)
Severe impairment	0.084 (0.025)
Very severe impairment	-0.216 (0.046)

NICE Are the health state utility values appropriate?

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; EDSS, expanded disability status scale; EQ-5D-3:L, EuroQol 5-Dimension 3-Level; HSUV, health-state utility values

Key issues: Modelling HR-QoL impact of IV administrations

Background

- Disutilities related to intravenous (IV) administration, may have been overestimated

Table: IV administration disutility per cycle

Disutilities	Utility decrement	Source
IV administration	-0.022	Jørgensen 2017
Hospital setting	-0.011	
Number of admin / cycle	-0.006	
IV admin route / hour	-0.009	Matza. 2013

Company

- Used linear regression model fitted to data from Jorgensen et al. 2017 to derive disutility associated with IV admin, in-hospital admin & number of administrations/ cycle
- Used Matza et al. 2013 to inform disutility for increasing length of infusion
- Applied total disutility per cycle associated with IVIg administration = -0.114 and -0.218 for PLEX
- Provided scenarios using alternative estimates

EAG

- Disutilities may have been double-counted and overestimated impact of IV administration
- Clinical opinion to EAG, people feel reassured having treatment in hospital & it has little impact on their HR-QoL
- Agreed vein depletion could be an issue associated with frequent IV administration in some people, so preferred to exclude all utility decrements associated with IV administration, with the exception of baseline utility decrement (-0.021 and -0.022 for IVIg and PLEX, respectively)
- Coefficient associated with baseline IV administration was only statistically significant term in company's regression model

Which approach to model disutilities related to IV administration is more appropriate?

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Abbreviations: HR-QoL, Health-related quality of life; IV, Intravenous; PLEX, Plasma exchange

Key issues: Modelling resource use and costs 1/2

Background

- EAG concerned assumptions used by company for modelling disease monitoring, mobility aids and hospitalisation are not aligned with NHS practice
- Proportion of people who would get funded professional care likely to be overestimated

Company

- Assumed 16% people having Ig would require funded transportation, but not for people having efgartigimod
- SCIg is administered in hospital over multiple days, and some will have IVIg in an inpatient setting
- GP consultation for 1 hour and proportion of people needing a wheelchair and risk of hospitalisation (active disease) taken from Adelphi study (from 5 EU countries including UK, Japan and USA)
- Used data corresponding to INCAT scores of 7-10 for severe and very severe health states
- Assumed professional care costs incurred for people with moderate, severe and very severe impairment based on Adelphi dataset (n=804, people from UK, France, Germany, Italy, Spain, USA and Japan)
- Company did a UK-based patient survey of people with CIDP on the level of care they have

Health state	% requiring professional care	No. of hours of professional care	Total cost per model cycle
Moderate impairment	9.0%	21.3	£1,449.20
Severe impairment	80.0%	45.0	£27,215.00
Very severe impairment	80.0%	45.0	£27,215.00

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Abbreviations: CIDP: Chronic inflammatory demyelinating polyneuropathy; INCAT, Inflammatory Neuropathy Cause and Treatment; IVIg, IVIg, intravenous immunoglobulin

Key issues: Modelling resource use and costs 2/2

EAG

- Transportation costs reasonable, but should be applied for both treatment arms
- 1 hour GP appointment not justified: BMA recommends a 15-minute consultation, so EAG used the cost of a GP appointment based on a 10-minute consultation (PSSRU)
- EAG's experts suggested model underestimated % with very severe impairment requiring a motorised wheelchair, separate data (INCAT 9-10) showed a higher need for mobility aid compared with severe impairment (INCAT 7-8)
- PSSRU is more appropriate to inform per the cost of an ICU bed rather than NHS reference costs
- Clinical opinion to EAG suggested that very few people with CIDP require professional care. In company's survey:
  - only 6.3% (n=4/63) of people required both types of care, and 12.7% (n=8/63) received formal care
- In UK Adelphi study, only 1 person had a professional caregiver, and company's survey of caregivers suggests 0% of people receive formal care from a professional healthcare provider
- Company's surveys suggest low usage of formal care and that if professional care was required, it would likely be for people with very severe disease who are confined to a wheelchair (~5 hours/day)
- Applying professional care to all moderate and severe HS likely overestimated need, and there was no available data on what % are confined to a wheelchair and who would have an NHS continuing healthcare package
- Preferred approach: exclude professional caregiver costs from its base case

Is the company's or EAG'S approach to model resource use and costs more appropriate?

Abbreviations: BMA, British Medical Association; CIDP; Chronic inflammatory demyelinating polyneuropathy INCAT, Inflammatory Neuropathy Cause and Treatment; HS, health states; IVIg, intravenous immunoglobulin; PSSRU, Personal Social Services Research Unit

Health state costs in model

Efgartigimod with recombinant human hyaluronidase PH20 for treating chronic inflammatory demyelinating polyneuropathy

- ❑ **Background and key issues**
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ✓ Other considerations
- ❑ Summary

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Equality considerations & Severity weighting

Inflammatory Neuropathies UK

- Many people with CIDP are considered disabled, so impact on disability, especially in terms of access to a treatment that may reduce disability, should be considered
- Most people with CIDP are generally older, so age may be a factor to consider in any decision making

Company

- Due to religion or belief, some people avoid blood products, i.e., IVIg made from donated human plasma, so some people may decline this option
- The severity modifier was considered not to be applicable

Are there any relevant equality issues that should be considered in decision making?

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; IVIg, intravenous immunoglobulin

Uncaptured benefits

Company

- Several benefits of efgartigimod in CIDP were not fully captured in QALY calculation including:
  - improved disease control and reduced treatment burden
  - greater workforce and community participation
  - reduced work absence due to sickness
  - fewer hours of informal care required
  - reduced treatment and service burden
  - NHS system resilience and supply security by reducing need for plasma-derived treatments

EAG

- Several benefits already captured in model for e.g., disease control and treatment burden, disutilities associated with IV treatment, and informal carer
- Company assumed use of IV treatments will reduce with the introduction of efgartigimod: 95% people in the company base were stable on IVIg, who are unlikely to switch to efgartigimod

Are there any uncaptured benefits that should be taken into account in decision making?

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; IVIg, intravenous immunoglobulin

Managed access

Company:

- **No managed access proposal made**: ADHERE+ anticipated completion April 2027 will provide additional information on long-term outcomes, duration of response and safety but will not generate comparative data vs. IVIg therapies

Criteria for a managed access recommendation

The committee can make a recommendation with managed access if:

- the technology cannot be recommended for use because the evidence is too uncertain
- the technology has the **plausible potential** to be cost effective at the **currently agreed price**
- new evidence that could **sufficiently support the case for recommendation** is expected from ongoing or planned clinical trials, or could be collected from people having the technology in clinical practice
- data could feasibly be collected within a reasonable timeframe (up to a **maximum of 5 years**) without **undue burden**.

Abbreviations: IVIg, intravenous immunoglobulin

Efgartigimod with recombinant human hyaluronidase PH20 for treating chronic inflammatory demyelinating polyneuropathy

- ❑ **Background and key issues**
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ✓ Summary

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Key issues for committee discussion

Key issues for committee discussion	
Decision problem	Is the company's proposed target population appropriate? Does including only responders from stage A overestimate the efgartigimod treatment effect?
Clinical effectiveness	Is the high proportion of people who showed clinical deterioration following the withdrawal of Ig, but did not achieve ECI with efgartigimod, a concern?
	Which outcomes are used to measure ECI in clinical practice? Does the use of only aINCAT in stage B underestimate or overestimate efgartigimod response?
	How robust are the company's indirect treatment comparisons (ITCs)? Does the evidence show that efgartigimod is clinically more effective than Ig?

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; ECI, Evidence of clinical improvement; Ig, , immunoglobulin; ITC, indirect treatment comparison

Key issues for committee discussion

	Key issues for committee discussion
Cost effectiveness	Are baseline distributions in the model appropriate? Are there uncertainties in how remission health states are informed in the model?
	Is a 3-month or a 6-month cycle length is more appropriate to use in the model?
	Is the company's or EAG approach more appropriate to inform use of Ig more appropriate?
	Is there sufficient evidence to reliably model the severe disease health states? Is the company's or EAG's approach preferred?
	What proportion of people have each subsequent treatment after discontinuation of efgartigimod?
	Which approach for comparator treatment effectiveness is the most appropriate? Is the company's or EAG's approach more appropriate for comparator discontinuation?
	Whose approach of modelling AEs, the company or the EAG, is more appropriate?
	Whose approach to model carer burden more appropriate? Should caregiver be included in the economic model or considered qualitatively in decision-making?
	Would people switch from weekly to biweekly efgartigimod dosing in clinical practice? If so, what % should be assumed to have biweekly dosing, and for how long?
	Are the health state utility values appropriate?
	Whose approach to model disutilities related to IV administration more appropriate?
	Is the company's or EAG's approach to model resource use and costs more appropriate?

Abbreviations: AE, adverse events; Ig, immunoglobulin; IV, intravenous

Summary of company and EAG base case assumptions 1/3

Assumptions in company and EAG base cases

	Assumption	Company base case	EAG base case
Model cycle	Apply 3-month cycle length for first two years	No (6 months for entire time horizon)	Yes
Patient characteristics	Proportion of corticosteroids in alternative treatment basket	CS: 77% (SE report)	CS: 52% (UK Centres Chart Review)
	Proportion of people on PLEX who then return to Ig	0%	90%
	Distribution people b/w treatments for first subsequent treatment after efgartigimod	31%	95%
	Source for proportion of patients on each Ig dose	SEE	UK centres Chart Review
	Baseline distribution across health states for Ig-refractory and Ig-intolerant cohorts	Baseline distribution from Stage A for Ig-refractory, baseline distribution from run-in for Ig-intolerant	Baseline of ADHERE run-in phase for all cohorts
Treatment effectiveness	Approach to severe and very severe impairment health states	Include transitions for Severe and Very Severe health states	Severe and Very Severe remain in same health state
	Approach to extrapolate comparator efficacy	No movement b/w health states after 24 months	No movement b/w health states from baseline

Abbreviations: CS, corticosteroids; Ig, immunoglobulin; IV, intravenous; PLEX, plasma exchange; : SEE, structured expert elicitation

Summary of company and EAG base case assumptions 2/3

Assumptions in company and EAG base cases

	Assumption	Company base case	EAG base case
Treatment effectiveness	Disease worsening after relapse	No	Yes
Discontinuation	Duration over which Ig discontinuations applied	Up to 18 months	No unplanned discontinuations
Adverse events	AEs included for all treatments (including IV access)	Included	Excluded
HSUV	Approach to parametrising HSUVs	Mixed model	Utility in Very Severe HS = 0
	IV administration disutilities	Jørgensen et al. and Matza et al.	Jørgensen et al. and considering only the coefficient for route of administration

Abbreviations: AEs, adverse events; HS, health states; HSUV, health states utility values; Ig, immunoglobulin; IV, intravenous; ITC, indirect treatment comparison; PLEX, plasma exchange; SC, subcutaneous: SEE, structured expert elicitation

Summary of company and EAG base case assumptions 3/3

Assumptions in company and EAG base case

	Assumption	Company base case	EAG base case
Admin/ drug costs	IVIg/SCIg split	UK Chart Review Study	Immunoglobulin Database Annual Report
	Transport costs	Ig arm	Ig and efgartigimod arms
	Administration cost for SCIg	Based on infusion duration and number of days for administration	Set equal to efgartigimod
	SCIg treatment is administered once per week in hospital	No	Yes
	IVIg administered in hospital is administered in outpatient setting	No	Yes
HCRU costs	1. GP consultation, 2. % requiring a wheelchair 3. Cost of ICU	1. 1 hour GP appointment 2. Adelphi study 3. £2,276	1. 10 min GP appointment 2. Aldephi study disaggregated by aINCAT 3. PSSRU:£1,907
Carer burden	HRQoL burden on informal caregivers and costs for professional caregivers	Included	Professional care costs not included HRQoL from informal care included
	Source for patient requirements for caregivers	Gani et al 2008	Adelphi UK and max 1 caregiver
	Source of carer utility decrement	Gani et al 2008	Company caregiver survey

Abbreviations: aINCAT, adjusted inflammatory neuropathy cause and treatment; AEs, adverse events; ICU, intensive care unit; HRQoL; health-related quality of life; Ig, immunoglobulin; IVIg, intravenous immunoglobulin; PSSRU, Personal Social Services Research Unit; SCIg; subcutaneous immunoglobulin

Cost-effectiveness results

All ICERs are reported in PART 2 slides due to confidential prices

Company base case
Ig maintenance: Dominant
Ig-intolerant/refractory: above £200,000/QALY

EAG base case
Ig maintenance: above £500,000/QALY
Ig-intolerant/refractory: above £3,000,000/QALY (vs basket treatment)

Abbreviations: IG, immunoglobulin; QALY, quality-adjusted life years

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Efgartigimod with recombinant human hyaluronidase PH20 for treating chronic inflammatory demyelinating polyneuropathy [ID 6409]

Supplementary appendix

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Decision problem

Table: Decision problem

	Final scope	Decision problem addressed	EAG comment
Population	People with CIDP	Adults with CIDP after prior unsatisfactory treatment with immunoglobulin (IVIg or SCIg)	Population identifiable in clinical practice but concerns about lack of alignment b/w company's definition and ADHERE
Intervention	Efgartigimod with recombinant human hyaluronidase PH20		
Comparator	• corticosteroids • Igs (IVIg or SCIg) • Plasma exchange (PLEX) • immunosuppressive therapies	• corticosteroids • Igs (IVIg or SCIg) • plasma exchange (PLEX) • immunosuppressive therapies	• Appropriate (Ig main comparator for most people & basket treatments for Ig intolerant or refractory) • But was not possible to identify which people in ADHERE were Ig intolerant or refractory
Outcomes	• Physical function change from baseline • Disease progression • Hospitalisations • Adverse effects of treatment • HRQoL		
Subgroups	NA	• People who have a high burden of Ig treatment • People who are intolerant to Ig and people who are refractory to Ig	• ADHERE inclusion criteria was not restricted people with high burden of Ig • ADHERE did not include patients who were intolerant or refractory to Ig

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; HQRoL, health-related quality of life; Ig, immunoglobulin; IVIg, intravenous immunoglobulin; PLEX, plasma exchange; SCIg, subcutaneous immunoglobulin

ADHERE baseline characteristics

Table: Baseline characteristics for intervention and comparator

Characteristic		ADHERE		Placebo n=110	ADHERE + N=228
		Stage A n=322	Stage B n=111		
Mean age (years)		54.0 (13.92)	54.5 (13.18)	51.3 (14.47)	53.2 (14.1)
Male, n (%)		208 (65%)	73 (66%)	69 (63%)	142 (62.3)
Time since diagnosis (mean), years		4.9 (6.09)	3.7 (4.40)	3.8 (4.68)	4.9 (5.6)
Typical CIDP diagnosis		268 (83%)	97 (87%)	95 (86%)	199 (87.3)
CIDP treatment within the past 6 months	Corticosteroids	63 (20%)	24 (22%)	23 (21%)	51 (22.4)
	Immunoglobulins (IV or SC)	165 (51%)	48 (43%)	48 (44%)	104 (45.6)
	Off treatment	94 (29%)	39 (35%)	39 (36%)	73 (32.0)
Total INCAT score		4.6 (1.67)	3.1 (1.51)	3.3 (1.57)	4.5 (1.6)
CDAS	2	6 (2%)	1 (1%)	0	-
	3	96 (30%)	28 (25%)	29 (26%)	-
	4	23 (7%)	8 (7%)	5 (5%)	-
	5	197 (61%)	74 (67%)	76 (69%)	-

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; CDAS, CIDP Disease Activity Status; CIDP, chronic inflammatory demyelinating polyneuropathy; IV, intravenous; INCAT, inflammatory neuropathy cause and treatment; SC, subcutaneous

ADHERE stage A results: secondary efficacy results

Secondary endpoints	Efgartigimod (N=322)
aINCAT n= [redacted], mean (SD)	-0.9 (1.71)
I-RODS score, n= [redacted] mean (SD)	7.7 (15.48)
MGS (dominant hand), kPa, n= [redacted] mean (SD)	12.3 (18.68)
MGS (non-dominant hand), kPa, n=[redacted], mean (SD)	11.2 (21.12)
MRC sum score (SD)	[redacted]
TUG test score (SD)	[redacted]
EQ-5D-5L VAS, n=[redacted]	10.7 (S: 22.3)

- Efgartigimod improved aINCAT score, MGS, I-RODS score and mean scores EQ-5D-5L-VAS
- Lower aINCAT scores represent better outcomes while higher MGS and I-RODS scores represent improvements in function

NICE

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; EQ-5D-5L, EuroQol 5-Dimension 3-Level, I-RODS, Inflammatory Rasch-built Overall Disability Scale; MGS, Mean grip strength; SD standard deviation; VAS, visual analogue scale

ADHERE stage B results: secondary efficacy results

Secondary endpoints	Efgartigimod, n (%)	Placebo, n (%)	HR/OR (95% CI)	Nominal p-value
Time to CIDP progression*	40 (36)	57 (52)	HR 0.54 (0.35-0.81)	0.0034
Improved functional level*	50 (45)	40 (36)	OR 1.44 (0.81-2.57)	0.23
aINCAT score***	0.1 (0.1)	0.9 (0.19)	-	-
I-RODS score***	0.8 (1.17)	-7.0 (1.84)	-	-
MGS (dominant hand), kPa***	2.1 (1.26)	-8.2 (1.98)	-	-
MGS (non-dominant hand), kPa***	2.0 (1.64)	-6.9 (2.04)	-	-
MRC sum score***	-0.3 (0.43)	-3.0 (0.86)	-	-
TUG test, seconds***	0.8 (0.36)	1.9 (0.60)	-	-
EQ-5D-5L VAS***	0.5 (17.4)	-10.2 (23.5)	-	-

*Time to first I-RODS deterioration ≥4 points; ** I-RODS improvement of ≥4 points from Stage B baseline;*** Mean (SE) change from Stage B baseline to last assessment

- Efgartigimod arm of Stage B generally maintained or showed improvements across the secondary endpoints while placebo arm deteriorated
- Lower aINCAT scores represent better outcomes while higher MGS and I-RODS scores represent improvements in function

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Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP; Chronic inflammatory demyelinating polyneuropathy; CI, confidence intervals; EQ-5D-5L, EuroQol 5-Dimension 3-Level, HR, hazard ratio; I-RODS, Inflammatory Rasch-built Overall Disability Scale; MRC, Medical Research Council; SE, standard error; SD standard deviation; TUG, Timed up and Go

Prognostic factors and treatment effect modifiers

Table: Prognostic factors and treatment effect modifiers identified by the company's clinical experts for comparison with advance-CIDP-1

Prognostic factors and/or treatment effect modifiers adjusted for in the ITC analysis	Prognostic factors and/or treatment effect modifiers that were not adjusted for in the ITC analysis
• Age • Sex • Disease duration / time from diagnosis • % prior treatment with corticosteroids • I-RODS • MRC sum score	• CIDP type (typical vs atypical) • Symmetrical vs asymmetrical symptoms • CIDP Disease Activity Status score • % prior treatment with Ig • % treatment naïve • MGS

Abbreviations: CIDP, Chronic inflammatory demyelinating polyneuropathy; I-RODS, Inflammatory Rasch-built Overall Disability Scale; Ig, immunoglobulin, ITC, indirect treatment comparison; MGS, mean grip strength

ADHERE & ADVANCE-CIDP-1 before and after population weighting adjustments

Baseline characteristics	ADVANCE-CIDP-1	ADHERE Stage B	
		Unweighted*	Weighted†
Number/ESS	132	[redacted]	[redacted]
% female	43.9	[redacted]	[redacted]
Mean age (years)	54.4	[redacted]	[redacted]
Mean disease duration (years)	4.10	[redacted]	[redacted]
Mean aINCAT score	3.00	[redacted]	[redacted]
Mean I-RODS score	58.2	[redacted]	[redacted]
Mean MRC Sum Score	55.3	[redacted]	[redacted]
% receiving corticosteroids as prior treatment	10.6	[redacted]	[redacted]

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP; Chronic inflammatory demyelinating polyneuropathy; ESS, effective sample size; I-RODS, Inflammatory Rasch-built Overall Disability Scale; MRC, Medical Research Council

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Main slide

How company incorporated evidence into model

Table: Model inputs

Input	Assumption and evidence source
Structure and time horizon	• Markov model time-varying transition probabilities • Lifetime (45 years)
Baseline characteristics	• Aligned with patient characteristics at screening for ADHERE
Cycle length	• 6 months (See key issue)
Intervention efficacy	• ADHERE and ADHERE+
Comparator efficacy	• Indirect treatment comparison (baseline characteristics including age, weight and sex were aligned with patient characteristics at screening for ADHERE)
Utilities	• ADHERE
Costs	• PSSRU 2023 and PSSRU 2015 • NHS National Cost Collection 2023/24
Resource use	• BNF • NHS pay award prices workbook 2025/26 • NHS 2023/24 National Cost Collection • Unit Costs of Health and Social Care 2024
Perspective	• NHS and PSS

Abbreviations: BNF, British National Formulary; PSSRU, Personal Social Services Research Unit

Definitions of model health states

Table: Definitions of model health states

Health state	aINCAT score
Very limited impairment, active disease	0-1
Very limited impairment, remission	
Mild impairment, active disease	2-3
Mild impairment, remission	
Moderate impairment, active disease	4-6
Moderate impairment, remission	
Severe impairment, active disease	7-8
Very severe impairment, active disease	9-10

Abbreviations: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment

Functional impairment definitions associated with each level of the aINCAT score

Table: Functional impairment associated with each level of the aINCAT disability score

aINCAT disability score	Arm component	Leg component
Level 0	No upper limb problems	Walking not affected
Level 1	Symptoms, in one or both arms, not affecting the ability to perform ADLs	Walking affected, but walks independently outdoors
Level 2	Symptoms, in one arm or both arms, affecting but not preventing any ADLs1	Usually uses unilateral support to walk outdoors
Level 3	Symptoms, in one arm or both arms, preventing one or two ADLs1	Usually uses bilateral support to walk outdoors
Level 4	Symptoms, in one arm or both arms, preventing three or all ADLs1	Usually uses wheelchair to travel outdoors, but able to stand and walk a few steps with help
Level 5	Inability to use either arm for any purposeful movement	Restricted to wheelchair, unable to stand and walk a few steps with help

1. Doing all zips and buttons; washing or brushing hair; using a knife and fork together; handling small coins

Abbreviations: ADL: Activity of daily living: aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment

Ig dose data: SEE

Table: Ig dose data – SEE

Dose	Proportion on dose %	Average time between treatment cycles (weeks)	Average no. of Ig cycles per 6-month period
IVIg (N=66)			
<0.50 g/kg	0.17%	3.63	7.19
0.50 – 0.99 g/kg	15.51%	3.79	6.88
1.00 – 1.99 g/kg	60.30%	4.08	6.39
2.00 g/kg	24.03%	4.11	6.35
SCIg (N=16)			
0.50 – 0.99 g/kg	15.67%	1.0	26.09
1.00 – 1.99 g/kg	84.33%	1.0	26.09

Abbreviations: Ig, immunoglobulin; IV, intravenous immunoglobulin; SC, subcutaneous immunoglobulin

Main slide

Ig dose data: company chart review study

Table: Ig dose data – company chart review study

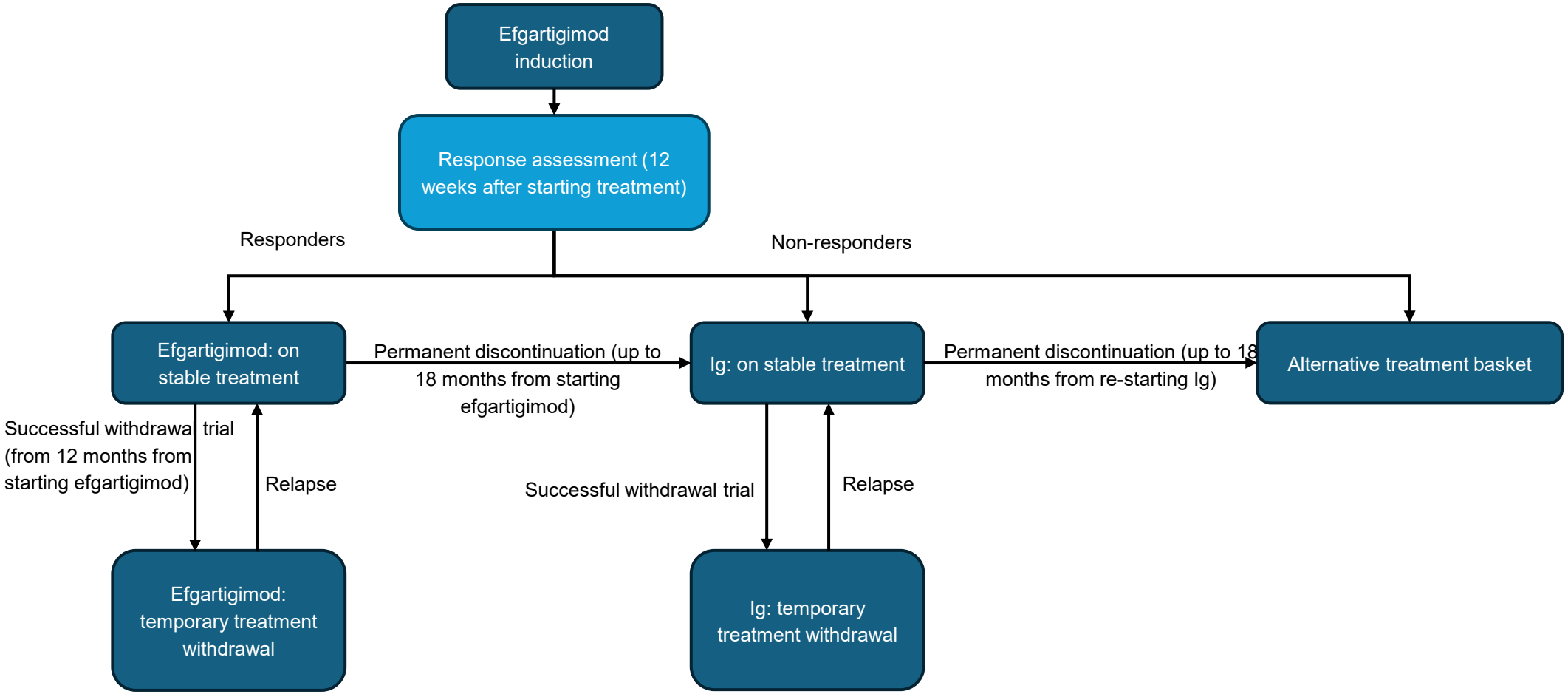
Dose	Number of patients	Proportion on dose %	Average time between treatment cycles (weeks)	Average no. of Ig cycles per 6-month period
IVIg (N=66)				
<0.50 g/kg	[redacted]	[redacted]	[redacted]	[redacted]
0.50 – 0.99 g/kg	[redacted]	[redacted]	[redacted]	[redacted]
1.00 – 1.99 g/kg	[redacted]	[redacted]	[redacted]	[redacted]
2.00 g/kg	[redacted]	[redacted]	[redacted]	[redacted]
SCIg (N=16)				
<0.50 g/kg	[redacted]	[redacted]	[redacted]	[redacted]
0.50 – 0.99 g/kg	[redacted]	[redacted]	[redacted]	[redacted]
1.00 – 1.99 g/kg	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: Ig, immunoglobulin; IV, intravenous immunoglobulin; SC, subcutaneous immunoglobulin

Main slide

Treatment pathway for efgartigimod arm + Ig maintenance

Figure: Company's treatment pathway for the efgartigimod arm

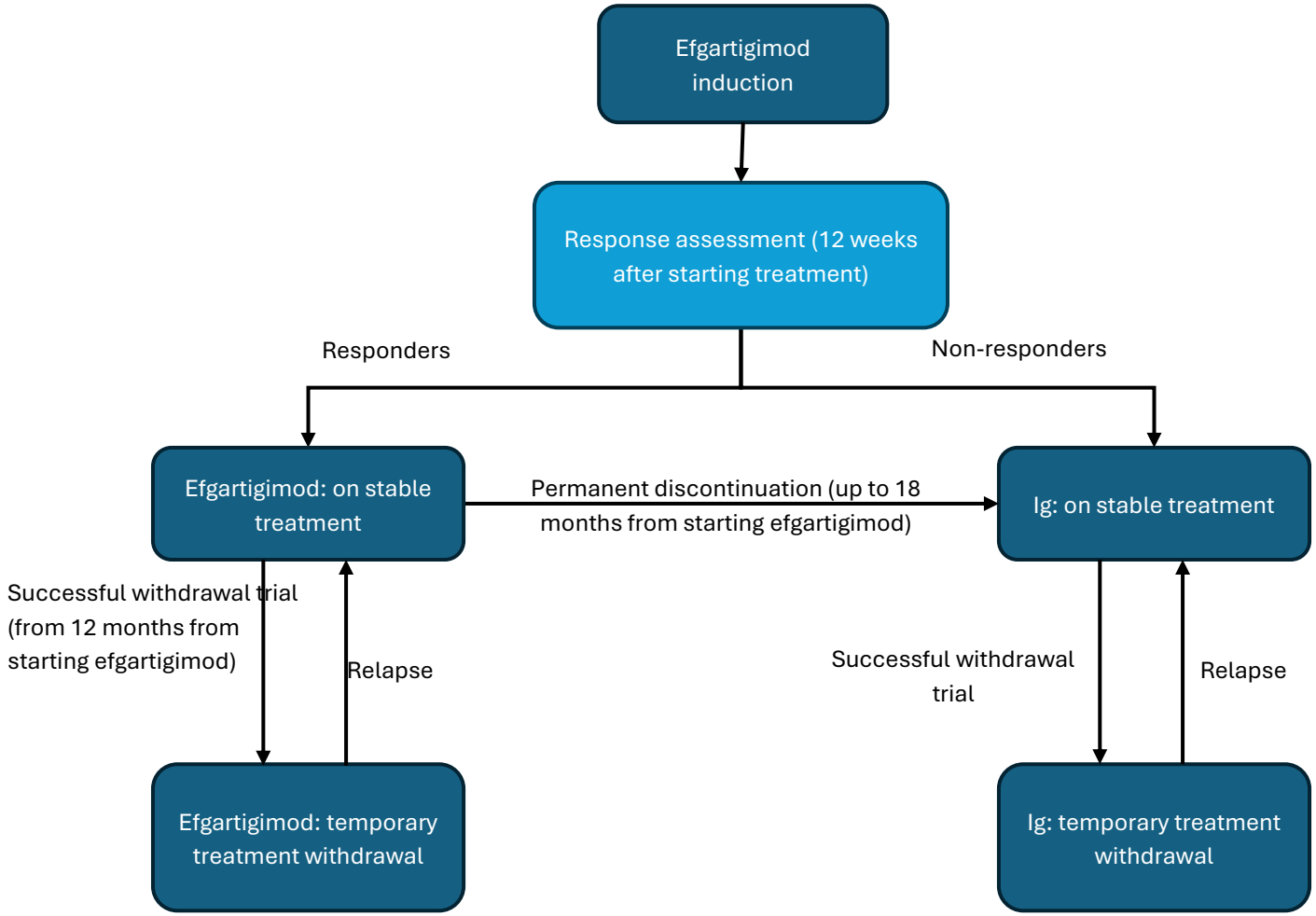


Abbreviations: Ig, immunoglobulin

Main slide

Treatment pathway for efgartigimod arm

Figure: EAG's treatment pathway for the efgartigimod arm



Abbreviations: Ig, immunoglobulin

Main slide

Treatment pathway for comparator arm

Figure: Company treatment pathway, comparator arm

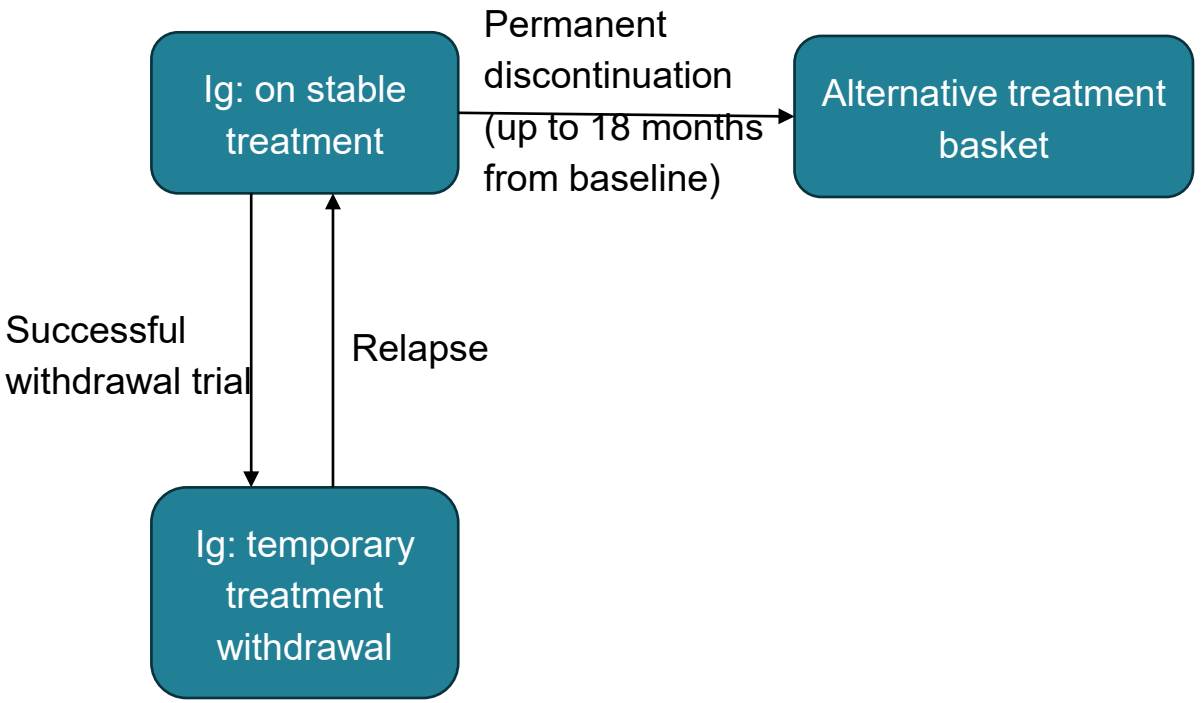
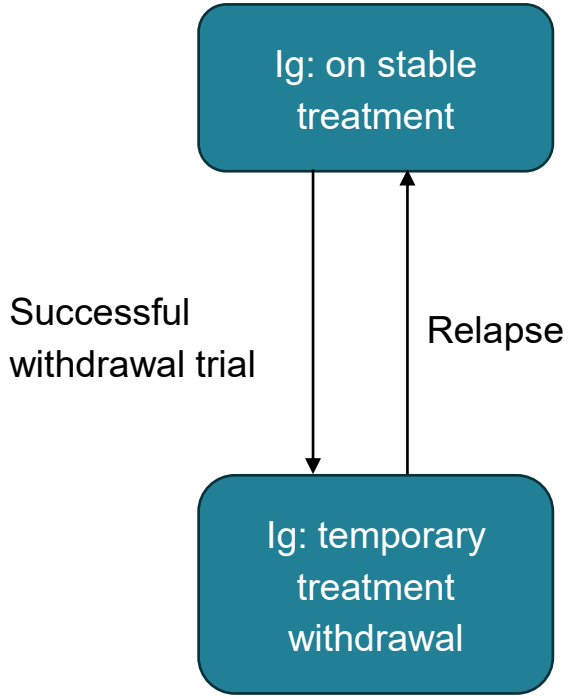


Figure: EAG's treatment pathway, comparator arm



Abbreviations: Ig, immunoglobulin

Main slide

Per-cycle permanent discontinuation probabilities for Ig

Table: Per-cycle permanent discontinuation probabilities for Ig treatment

Time from baseline	Per-cycle discontinuation (6 months)	Per-cycle discontinuation (3 months)	Source
0-6 months	7.49%	3.82%	Pooled data ICE and PATH
6-18 months	3.36%	1.69%	PATH open-label

Abbreviations: Ig, immunoglobulin

Key issues: Modelling resource use and costs

Table: Proportion of people requiring mobility aids by severity

Health state	Proportion requiring a manual wheelchair	Proportion requiring a motorised wheelchair
Moderate impairment (INCAT 4-6)	[redacted]	[redacted]
Severe impairment (INCAT 7-8)	[redacted]	[redacted]
Very severe impairment (INCAT 9-10)	[redacted]	[redacted]

Abbreviations: INCAT, Inflammatory Neuropathy Cause and Treatment

Main slide

Key issues: Modelling resource use and costs

Table: Health state costs in the company model

Health state	Six-month health state costs (without professional caregiver costs)	Six-month health state costs (with professional caregiver costs, company assumptions*)
Very limited	£1,063.96	£1,063.96
Mild	£1,110.49	£1,110.49
Moderate	£1,255.83	£2,705.03
Severe	£1,914.06	£29,129.11
Very Severe	£2,500.03	£29,715.08

* EAG scenario analysis was also conducted in which professional caregiver costs are applied for the very severe health state only, assuming 35 hours of professional care per week. In this case, all costs are unaffected, with the exception of the very severe health state, which has a six-monthly cost of £23,667.29