National Institute for Health and Care Excellence

Health Technology Evaluation

Efgartigimod with recombinant human hyaluronidase PH20 for treating chronic inflammatory demyelinating polyneuropathy ID6409
Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	argenx	In line with the draft scope, argenx considers Single Technology Appraisal appropriate.	Thank you for your comment.
	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	Seems appropriate.	Thank you for your comment.
	ABN Neuromuscular Advisory Group	Appropriate evaluation and proposed route (single technology appraisal).	Thank you for your comment.
Wording	argenx	In line with the draft scope, the remit appropriately reflects the issues of clinical and cost-effectiveness for the technology undergoing appraisal.	Thank you for your comment.

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	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	Seems appropriate.	Thank you for your comment.
	ABN Neuromuscular Advisory Group	Wording of remit appropriate. We do have some issues with the description of current standard of care for CIDP in the background section, to be discussed later.	Thank you for your comment.
Timing Issues	argenx	A significant unmet need exists in CIDP treatment, with over 30% of patients being refractory to current standard-of-care therapies. While alternative immunosuppressants may be prescribed off-label for these patients, evidence supporting their efficacy is limited, and more than one-third of refractory patients show no response to treatment escalation. Furthermore, existing treatments are associated with significant limitations, including lengthy infusions, severe complications such as thrombosis and acute renal failure, and long-term side effects that can limit sustained treatment. The unmet need has been acknowledged by the MHRA who granted a promising innovative medicine (PIM) designation, which further supports the importance of efgartigimod as an innovative treatment in this indication.	Thank you for your comment. Comments noted. NICE has scheduled this topic into its work programme. No action required.
	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	Not hugely urgent for the NHS, but potentially urgent for people.	Thank you for your comment. Comments noted. NICE has scheduled this topic into its work programme. No action required.

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	ABN Neuromuscular Advisory Group	Thie is a relatively urgent evaluation to the NHS. There is randomised placebo-controlled trial evidence suggesting this therapeutic appears to be as effective as standard of care first line therapy (SOC) in controlling CIDP symptoms in a subset of individuals who have shown previous response to SOC treatment and in treatment naive CIDP. Furthermore, it was well tolerated, with fewer side effects than corticosteroids and IVIg. Importantly, it is deliverable at home by the patient as a rapid push rather than requiring hospital led administration (as is the case for IVIg or PLEX), with potential cost-savings for the NHS when considering resources (staffing/ transportation/ inpatient/daycare hospital beds) required to administer hospital-based treatments. The home care delivery option potentially gives patients greater flexibility and independence, which are important considerations in treatment for a chronic disease, where individuals may have impaired mobility with difficulty accessing hospital-based treatments. Therefore, this new therapy offers an important point of difference from a lifestyle perspective to individuals requiring maintenance immunomodulatory therapy to control CIDP. There is a clinical and socioeconomic argument to support its availability as a therapeutic option in this disease group where the affected demographic is often of working age.	Thank you for your comment. Comments noted. NICE has scheduled this topic into its work programme. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	argenx	*To capture the patient burden and quality of life impact of CIDP, argenx proposes the following amended text:* CIDP is a neurological disorder of myelinated nerves characterised by progressive weakness and impaired sensory function in the arms and legs; this includes the loss of reflexes. The chief symptoms of CIDP are slowly progressive (over at least two months) symmetric weakness of both muscles around the hip and shoulder as well as of the hands and feet (both proximal and distal muscles). Nerve signals become altered causing impairment in motor function and/or abnormal, or loss of, sensation. There are usually some alterations of sensation causing loss of coordination, numbness, tingling or prickling sensations. Other symptoms of CIDP include fatigue, burning, pain, clumsiness, difficulty swallowing and double vision. Weakness, pain, and fatigue contribute to health-related quality of life (HRQoL) impairments in patients with CIDP leading to impacts on psychosocial wellbeing. Overall, studies indicate that patients with CIDP have lower baseline HRQoL measures compared to age- and gender-matched controls, and physical function is especially diminished. *To capture the current understanding and known variability of the treatment pathway, argenx proposes the following amended text:* Insights from a CIDP UK advisory board conducted in May 2024 (N=8 KOLs) highlight IVIg as the first-line treatment option for the majority of patients living with CIDP. In the EAN/PNS guidelines, IVIg, plasma exchange (PLEX) and corticosteroids are considered first-line induction treatments for CIDP;	Thank you for your comment. The background information section of the scope is intended to be very concise. The patient burden and known variability of the treatment pathway have been adequately captured. Scope has been updated with some suggestions.

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		although PLEX is a first-line therapy, it is less often recommended due to practical constraints around administration. These guidelines do not recommend one treatment over the other for typical CIDP, however, recommend IVIg as the first-line induction treatment in motor CIDP based on evidence that deterioration was commonly seen after corticosteroid use in this patient subgroup. Despite inclusion in the European guidelines, corticosteroids are not a preferred first-line treatment option based on the UK-specific insights from the advisory board. Which suggest the majority of patients in the UK are currently being treated with IVIg. Variability exists in the pathway due to the heterogenous clinical presentation of CIDP and lack of differentiation between first-line treatment options in the guidelines. Treatment choice takes into consideration symptom type and severity, disease progression, comorbid conditions, and patient lifestyle, among other factors.	
	Grifols UK	We would recommend modifying the background text related to current treatment to reflect EAN/PNS guidelines and NHS England Clinical Commissioning position *European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force-Second revision. Eur J Neurol. 2021 Nov;28(11):3556-3583. doi: 10.1111/ene.14959. Epub 2021 Jul 30. Erratum in: Eur J Neurol. 2022 Apr;29(4):1288.* *NHS England. Commissioning criteria policy for the use of therapeutic immunoglobulin (Ig) in England, 2024. Available:*	Thank you for your comment. The background information section of the scope is intended to be very concise. The known variability of the treatment pathway has been adequately captured. No change to scope required.

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		https://www.england.nhs.uk/publication/commissioningcriteria-policy-for-the-use-of-therapeutic-immunoglobulin-igin-england-2021/ [Accessed 27 November 2024].	
	Octapharma Limited	The last paragraph (Paragraph 3) has no references. **"IVIg is effective only for a few weeks"** is perhaps not clearly phrased. We suggest referring to the EAN/PNS Guidelines (van den Bergh, P. Y. K., et al. 2021) and adjusting that paragraph accordingly. ***"Access to IVIg and its use is variable"*** We want to understand what is meant by this, considering the UK Clinical Commissioning Policy. The dynamics of the market is changing and over the last few years, IgG supply levels are restored to pre-pandemic levels, and in addition to this, prices are declining meaning access should be better and IgG use should be increased. **Reference**: Clinical Commissioning Policy for the use of therapeutic immunoglobulin (Ig) England (2024)	Thank you for your comments. The reference to "a few weeks" has been changed to "a limited duration". We heard from clinical experts at the scoping workshop that access to IVIg remains regionally variable. No further changes to scope required.
	Takeda	While we appreciate the need to simplify the treatment pathway within the draft scope, we feel as though some complexities and nuances of the CIDP treatment pathway have not been sufficiently captured. We therefore suggest the following amendments be made: • Firstly, we suggest that NICE incorporates the current CIDP treatment guidelines from the European Academy of Neurology (EAN)/Peripheral Nerve Society (PNS) 2021, Lunn at al 2016 and the Clinical Commissioning Policy for the use of therapeutic immunoglobulin (Ig) England (2024), into the background.	Thank you for your comments. The background information section of the scope is intended to be very concise. The treatment pathway has been updated to indicate that people are not necessarily treated with corticosteroids first.

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		• From these guidelines, an important component of CIDP treatment is the distinction between induction and maintenance therapy. We suggest that NICE captures this separation clearly, and clarifies which therapies are used specifically for induction and maintenance treatment. • The draft scope states '*CIDP is usually treated first with corticosteroids*.' And that '*If there is insufficient response to first-line treatment or the individual experiences significant side effects from corticosteroids, people may be offered intravenous immunoglobulin (IVIg)*'. These two statements do not align with the EAN and PNS treatment guidelines 2021. For first line induction therapy, patients are not necessarily treated with corticosteroids first. Patients may receive corticosteroids (such as prednisolone and methylprednisolone) or IVIg therapy. From the guidelines, the decision as to which is commenced first is based on a series of patient-oriented considerations.[1] We suggest that NICE amends the two statements to reflect this. • The draft scope states '*Subcutaneous delivery of immunoglobulin (SCIg) is also available as an alternative to IVIg.'* Although this statement is not incorrect, we suggest, as above, that NICE clearly indicates the difference between induction and maintenance therapy as per the guidelines. For clarification, patients who respond to IVIg induction therapy, may switch over to conventional SCIgs or hyaluronidase facilitated subcutaneous immunoglobulins (fSCIg) as maintenance therapy, which offers the possibility for at home administration and a potential for the reduction of treatment burden. • The draft scope states that methotrexate may be used as an immunosuppressive therapy in conjunction with corticosteroids, IVIg/SCIg	The scope has been updated to highlight that Immunoglobulins are offered either intravenously (IVIg) or subcutaneously (SCIg), with the latter most often used for maintenance treatment. Reference to methotrexate has also

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		and plasma exchange (PLEx). This is not aligned with the treatment guidelines, which state that methotrexate is not recommended for patients with CIDP. We suggest that NICE removes methotrexate from the background. Furthermore, for clarification, immunosuppressive drugs are used as second line induction therapy, following failure to respond to any first line induction treatment (corticosteroids, immunoglobulin therapy and PLEx). We suggest the background highlights the distinct stages of treatment clearly as per the guidelines.	been removed. We heard from clinical experts at the scoping workshop that access to IVIg remains regionally variable.
		• The draft scope states that '*Long-term immunosuppressive therapy may be needed to prevent relapse*.' To avoid any inaccurate misinterpretation of this statement, we suggest NICE clarifies that immunosuppressive drugs may be given in conjunction with other maintenance therapies (immunoglobulins, corticosteroids or PLEx); however, immunosuppressive therapy alone is not recommended for long term or maintenance therapy.	The scope has been updated with suggested wording.
		• The draft scope states that '*access to IVIg and its use is variable'*. The clinical commissioning policy for the use of therapeutic immunoglobulin therapy for England (2024) lists CIDP as an indication for the routine commissioning of immunoglobulin therapy. One purpose of this national policy is to ensure equitable access to immunoglobulins for CIDP patients. We therefore suggest that NICE either removes this statement or provides supportive evidence for the existence of varied access to IVIgs.	We heard from clinical experts at the scoping workshop that access to IVIg remains regionally variable. No further changes to the scope are required.
		• The draft scope states that '*IVIg and PLEx are often only effective for a few weeks'*. It is unclear whether this is referring to a single dose of IVIg, or regular IVIg therapy. We request that NICE clarifies this further. The dosing for IVIg has an initial loading dose, and then may require regular	Thank you for your comment.

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		dosing every 3 weeks in accordance with product licence. In a clinical trial setting, ongoing efficacy has been demonstrated whilst on IVIg treatment for at least 48 weeks and while on fSCIg treatment for an average of 33 months. Finally, as explained in the EAN/PNS treatment guidelines 2021, CIDP patients have a diverse range of treatment options with various modes of administration and mechanisms of actions for both induction and maintenance therapy. If patients fail to respond or experience a high burden in terms of adverse events (AEs) or administration, alternative treatments may be used and dosed in multiple combinations or schedules. Furthermore, the development of SCIgs have provided an opportunity for at home maintenance therapy, giving patients an option which can increase independence, flexibility in exact timing and location of treatment and remove the need for venous access. Given this, we suggest that NICE captures the full breadth of treatment options and combinations as described in the guidelines, and specifically notes the impact that SCIg at home maintenance therapy currently has on CIDP patients.	
	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	It would be useful to add comments around the impact of the condition on people and their lives, as well as long term outcomes. CIDP can be a progressive condition, and does have long term impacts on peoples lives, including on ability to work, potential long term disabilities and issues, and on relationships and families. These should be considered as part of quality of life.	Thank you for your comments. The background information section of the scope is intended to be very concise. The patient burden has been adequately captured.

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			No change to scope required.
	ABN Neuromuscular Advisory Group	• Basic description of CIDP and its epidemiology is accurate • The description of SOC does not reflect current UK clinical practice (Kapoor et al., 2024) and EAN/ PNS international guidance (Van der Berg et al.), where corticosteroids, IVIg and PLEX are all considered first-line options for CIDP treatment and chosen on the basis of individual patient characteristics, tolerance and risk profile. While we acknowledge that some Trusts may require evidence of lack of response or significant steroid associated risk prior to the approval of IVIg in CIDP, it is not correct that steroid treatment is first line across the board nationally. NHSE IVIg commissioning guidelines state 'IVIg or PLEX is preferable in patients with motor predominant CIDP or rapidly progressive disease where rapid response is required especially when patients are admitted to hospital.' • Agree that IVIg and PLEX (akin to efgartigimod) are not immunosuppressants. They act in an immunomodulatory fashion and control disease and symptoms through regular maintenance infusions or exchanges usually via the hospital setting. • Agree that SCIg is a homecare delivery option but the infrastructure (nursing support and home care delivery set up) required to support this option is a challenge to the establishment of this service. This is not a widespread option across the UK. Furthermore, the duration of infusion of SCIg is significantly longer than the duration of efgartigimod injection. • In refractory cases that do not respond to first-line treatment options, or where response to first-line treatment is transient and associated with significant fluctuation in level of function, the addition of other immunosuppressive agents to a immunomodulatory therapy (such as	Thank you for your comments. The background information section has been amended to indicate that corticosteroids, IVIg and PLEX are all considered first-line options. Reference to methotrexate has also been removed. No further changes to the scope are required.

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		regular IVIg or PLEX) can stabilise these fluctuations and improve patient function and reduce dependence on regular maintenance treatments • Cyclophosphamide is very rarely used in refractory cases of CIDP because of toxicity and monitoring requirements. • The EAN/PNS guidelines weakly recommend **against** the use of methotrexate in CIDP (listed in the background as an immunosuppressive drug option) References Kapoor M, Khoo A, Lunn MPT, et al. Pract Neurol Epub ahead of print: [August 2024]. doi:10.1136/pn-2022-003655 Van Der Bergh et al. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force—Second revision. European Journal of NeurologyVolume 28, Issue 11Nov 2021Pagesi-iv, 3541-3874, e86-e96	
Population	argenx	Yes [the population is defined appropriately].	Thank you for your comment.
	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	As well as it can be. Accurate data on prevalence and actual incidence is difficult to obtain, so figures can vary.	Thank you for your comment.
	ABN Neuromuscular Advisory Group	Yes [the population is defined appropriately]. The clinical trial compared efgartigimod to placebo in treatment naïve patients with CIDP (diagnosed according to the PNS/ EAN criteria) AND to patients	Thank you for your comment.

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		with CIDP previously treated with first line SOC (IVIG or steroids or PLEX within the last 6 months) who showed a definite deterioration on treatment withdrawal. This was a two-stage study. In stage A, all patients with active disease were treated open-label with efgartigimod. Only those who showed a meaningful response (according to improvement in CIDP specific outcome measures) where moved to stage B where efgartigimod efficacy was compared to placebo. Therefore, this study was enriched with a subset of CIDP patients that were shown to be efgartigimod responsive.	
Subgroups	argenx	Subgroups based on: • Pre-treatment with IVIg and PLEX • Disease severity based on CDAS (CIDP Disease Activity Status) • Patients with progressive or relapsing active disease after prior treatment with corticosteroids or immunoglobulins	Thank you for your comment. The committee can consider any relevant subgroup if data is presented.
	Octapharma Limited	Consider for both subgroups that the technology is only in cases who are refractory to the recommended first line treatment with several decades of proven efficacy.	Thank you for your comment.
	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	It would be good to indicate if we are also including the various variants of CIDP.	Thank you for your comment.
	ABN Neuromuscular Advisory Group	There is no direct head-to-head evidence that this treatment will be clinically more effective in controlling CIDP than SOC.	Thank you for your comments. Comments noted.

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		However, efgartigimod may be particularly clinically appropriate / cost-effective in: (1) Individuals with impaired mobility, who may require hospital transport or carer support to attend regular daycare /inpatient hospital admissions for IVIg or PLEX (2) Individuals of working age or with other significant responsibilities for whom a self-delivered home treatment option would save considerable time compared to regular hospital visits for maintenance IVIg or PLEX (typically 1-3 days per month in patients with active disease). (3) In patients with significant thrombo-embolic risk profile or previous thrombo-embolic events where the number needed to harm with IVIg treatment is 6.	
Comparators	argenx	*Based on the anticipated position of efgartigimod into the existing care pathway, argenx considers the list of comparators as follows:* • Intravenous Ig (IVIg) • Subcutaneous Ig (SCIg) • Plasma exchange (PLEX) It's important to emphasise that immunoglobulin therapy (IVIg and SCIg) is a key comparator, rather than being positioned as an add-on therapy.	Thank you for your comments. The scope will remain broad and all relevant comparators will be considered by the committee.
	Grifols UK	We consider that the comparators listed do not reflect current standard treatment established by the NHS England clinical commissioning.	Thank you for your comment. The scope will remain broad and all relevant comparators will be considered by the committee.

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	Takeda	Firstly, in accordance with the treatment guidelines, SCIgs are missing from the current comparator list. Furthermore, IVIgs and both conventional and facilitated SCIgs can be given in combination with other treatments, as described in the current draft scope, or alone as standard of care.	Thank you for your comment. The scope will remain broad and all relevant comparators will be considered by the committee. The list of comparators has been updated to include SCIgs.
	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	Yes in the main [all comparators have been included], but to note the Clinical Commissioning Policy states for CIDP that 'Ig should not always be considered 1st line treatment for CIDP, although it may be where steroids are contra-indicated and plasma exchange is not available. Where steroids, Ig and plasma exchange are all available Ig would be considered preferable in patients with motor predominant CIDP, rapidly progressive disease where rapid response is required (particularly patients requiring admission to hospital) or where steroids or plasma exchange are contra indicated. Strong consideration should be given to the early use of steroids or plasma exchange in other circumstances' - Clinical Commissioning Policy for the use of therapeutic immunoglobulin (Ig) England (2024)	Thank you for your comments. Comments noted.
	ABN Neuromuscular Advisory Group	Yes, the comparators listed above are considered standard treatments, although the treatment pathway described differs as described above. For further clarification, SOC for CIDP in the UK is: First line: - Corticosteroids OR IVIg OR PLEX chosen according to individual patient risk profile and availability and continued on the basis of	Thank you for your comments. Comments noted.

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		recorded evidence of response according to CIDP specific outcome measures. - 60-70% of patients with CIDP will respond well to one of the three first line options - In those who do not respond, switching to another first line option results in meaningful response in up to 80% (Cocito et al 2010) Second line: - In those who show suboptimal or transient response to any of the first line options, the addition of an immunosuppressive steroid or immunoglobulin sparing agent is indicated - But reappraisal of the diagnostic security is essential (EFNS/ PNS criteria) Third line / refractory disease: - This is very rare in CIDP and thorough re-evaluation of the case and consideration of a second opinion is sensible - Treatment options are limited but might include cyclophosphamide Reference: Cocito, D et al (2010), A nationwide retrospective analysis on the effect of immune therapies in patients with chronic inflammatory demyelinating polyradiculoneuropathy. European Journal of Neurology, 17: 289-294. https://doi.org/10.1111/j.1468-1331.2009.02802.x	
Outcomes	argenx	The draft scope appropriately reflects the outcomes of interest for this appraisal.	Thank you for your comment.
	Grifols UK	The outcomes listed are broadly appropriate. However, to best capture health benefits and harms the following outcome should be considered as clinically important:	Thank you for your comment. The outcomes list is not

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		• Discontinuation rates and reasons for discontinuation	exhaustive, and the committee will consider all relevant outcome data.
	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	Generally yes [the outcomes listed are appropriate], as long as 'disease progression' takes into consideration rate of relapse, and length of time before relapse	Thank you for your comment.
	ABN Neuromuscular Advisory Group	We suggest the use of CIDP-specific clinical outcome measures and minimally clinically important differences in the recording of treatment response. These listed in current NHSE IVIg commissioning guidelines and include: - MRC score - INCAT sensory sum score - ONLS - Hand dynamometry - Inflammatory RODS score - 10-m walk (in seconds) - Up and go 10m walk (in seconds) Berg Balance scale Other validated disability score From a cost-effectiveness perspective (considering the points of difference of this therapy) it may be sensible consider: - Inpatient or day care bed utilisation (for maintenance IVIg or PLEX: 1-3 days per month on average)	Thank you for your comments. The outcomes listed in the scope are broad and generally will not include specific outcome measures. No change to scope required.

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		- Cost of IVIg or PLEX blood products, other consumables, hospital inpatient/daycare staffing - Hospital transport costs - Individual transport costs and time - Loss of employment - Cost of running SCIg homecare delivery service/ staffing support	
Equality	argenx	The draft remit and scope have been reviewed against equality considerations, and no aspects have been identified that could lead to unlawful discrimination or differential access for groups with protected characteristics. While it is recognised that there is a disproportionate male gender distribution in the prevalence of this condition, this reflects the natural epidemiology of the disease rather than any discriminatory aspect of the proposed scope or technology evaluation process. No additional evidence gathering is considered necessary for equality impact assessment, as the proposed scope already enables comprehensive consideration of the relevant patient populations and their characteristics.	Thank you for your comments. Comments noted.
	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	Not within the current scope.	Thank you for your comment.
	ABN Neuromuscular Advisory Group	No particular concerns.	Thank you for your comment.

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Questions for consultation	argenx	**What is the existing treatment pathway for CIDP?** Insights from a CIDP UK advisory board conducted in May 2024 highlight IVIg as the first-line treatment option for the majority of patients living with CIDP. In the EAN/PNS guidelines, IVIg, PLEX and corticosteroids are considered first-line induction treatments for CIDP; although PLEX is a first-line therapy, it is less often recommended due to practical constraints around administration. These guidelines do not recommend one treatment over the other for typical CIDP, however, recommend IVIg as the first-line treatment in motor CIDP based on evidence that deterioration was commonly seen after corticosteroid use in this patient subgroup. Second-line options include immunosuppressive medications (such as azathioprine, methotrexate, or rituximab). Variability can exist in the pathway due to no differentiation between first-line treatment options. As part of the evidence-generation activities for this appraisal, argenx is carrying out a market research questionnaire with clinicians to determine establish UK treatment pathway. https://niceuk.sharepoint.com/sites/Cancer_Topics/Shared%20Documents/ID6474%20cabozantinib/13%20-%20Committee/ACM1/cPAS%20part2/ID6474%20Cabozantinib%20part%202%20slides%20for%20PMB%20%5bCPAS,%20CON%5d.pptx?web=1 **Where do you consider efgartigimod with recombinant human hyaluronidase PH20 will fit into the existing care pathway for CIDP?** It is expected that efgartigimod will be used in patients diagnosed with CIDP who are previously treated with IVIg and/or PLEX therapy. The positioning in the existing care pathway will be supported by the ongoing market research questionnaire with UK clinicians.	Thank you for your comments. Comments noted.

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		How often are intravenous immunoglobulin or plasma exchange used for CIDP? If used, in which populations are they used and for how long (short-term v chronic longer-term use)? From a UK clinician advisory board, it was established that the majority of UK patients with CIDP are being treated with IVIg. Whereas some advisors treat with steroids or with both steroids and IVIg. For patients who do not respond to IVIg, advisors may consider use of PLEX or immunosuppressive medications. Further quantification of the existing care pathway is being explored as part of the UK market research survey. **Please select from the following, will efgartigimod with recombinant human hyaluronidase PH20 be:** A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): Option C - Prescribed in secondary care with routine follow-up in secondary care. **For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** It is expected that prescribing and routine follow-up will not differ for comparators and subsequent treatments. Initial prescribing and routine follow-up for IVIg, SCIg and PLEX are managed in secondary care through specialist neurology centres and non-specialist hospitals, given the	

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		complexity of diagnosis, need for careful monitoring, and administration requirements. While some maintenance therapy may be administered at home (such as SCIg), ongoing assessment and treatment modifications would necessitate regular specialist oversight in these hospital centres. **Would efgartigimod with recombinant human hyaluronidase PH20 be a candidate for managed access?** Yes, recognising that CIDP is a rare disease and that there is a paucity of data available in this population for some comparators. **Do you consider that the use of efgartigimod with recombinant human hyaluronidase PH20 can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** Not applicable. **NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:** • **could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which efgartigimod with recombinant human hyaluronidase PH20 will be licensed;**	

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		• **could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;** • **could have any adverse impact on people with a particular disability or disabilities.** **Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.** As above - The draft remit and scope have been reviewed against equality considerations, and no aspects have been identified that could lead to unlawful discrimination or differential access for groups with protected characteristics. While it is recognised that there is a disproportionate male gender distribution in the prevalence of this condition, this reflects the natural epidemiology of the disease rather than any discriminatory aspect of the proposed scope or technology evaluation process. No additional evidence gathering is considered necessary for equality impact assessment, as the proposed scope already enables comprehensive consideration of the relevant patient populations and their characteristics.	
	Octapharma Limited	• <u>What is the existing treatment pathway for CIDP?</u> The current treatment pathway for CIDP typically includes a combination of immunomodulatory therapies aimed at reducing inflammation and improving nerve function. First-line treatments include: • Corticosteroids • Intravenous immunoglobulin (IVIg)	Thank you for your comments. Comments noted.

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		• Plasma exchange (PLEX) Immunosuppressive agents such as azathioprine, methotrexate, or mycophenolate mofetil may be used in cases where first line treatments do not provide adequate control. **Reference**: van den Bergh, P. Y. K., et al. (2021). *European Academy of Neurology/Peripheral Nerve Society Guideline on the diagnosis and treatment of chronic inflammatory demyelinating polyneuropathy*. *European Journal of Neurology*, 28(5), 1379-1392. [DOI:10.1111/ene.14859] As CIDP is a chronic disease long-term, treatment is necessary in most patients. *If the first-line treatment is effective, continuation should be considered until the maximum benefit has been achieved (strong recommendation) and then the dose should be reduced, or the interval increased to find the lowest effective maintenance dose (Good Practice Point). SCIg and IVIg can both be considered as maintenance treatment in IVIg-responsive patients with active disease (strong recommendation).* • <u>Where do you consider efgartigimod with recombinant human hyaluronidase PH20 will fit into the existing care pathway for CIDP?</u> Only in cases who are refractory to the recommended first line treatment with several decades of proven efficacy. For the moment Efgartigimod is not included in the EAN/PNS recommendations as more real-world experience is needed to determine where efgartigimod fits into the recommended pathway. In the beginning it will	

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		most probably bring the most benefit to autoAb positive patients as well as to patients refractory to the well-established first line treatments. Given its mechanism of action, efgartigimod may be especially effective for autoantibody-positive patients, but its potential benefits in autoantibody-negative patients should not be ruled out without further evidence. Clinical or real-world data will be crucial in determining whether it should be restricted to autoantibody-positive patients or made available to a broader CIDP population. **References**: • Zanjani, M., et al. (2023). *Efgartigimod in chronic inflammatory demyelinating polyneuropathy: results from a phase 3 clinical trial*. *Lancet Neurology*, 22(5), 397-405. [DOI: 10.1016/S1474-4422(23)00025-1] • Dalakas, M. C. (2021). *Efgartigimod: A novel treatment for autoimmune diseases*. *The Lancet Neurology*, 20(5), 341-344. [DOI: 10.1016/S1474-4422(21)00057-3] • How often are intravenous immunoglobulin or plasma exchange used for CIDP? If used, in which populations are they used and for how long (short-term v chronic longer-term use)? IVIg is often used for induction and maintenance treatment of all patients with CIDP. If a treatment naïve patient shows good improvement on IVIg, long term treatment should be considered until maximum benefit is reached, then dose should be reduced, or interval increased (see recommendation above). PLEx is less often used mainly due to administrative reasons but also because IVIg is generally better tolerated.	

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		• Please select from the following, will efgartigimod with recombinant human hyaluronidase PH20 be: C. Prescribed in secondary care with routine follow-up in secondary care. Given that efgartigimod with recombinant human hyaluronidase PH20 is a novel treatment still requiring specialist oversight for administration and monitoring, it is likely to be prescribed in secondary care settings (e.g., neurology departments or specialist clinics). Routine follow-up, including monitoring of adverse events, efficacy, and potential adjustments to the treatment regimen, is expected to occur in secondary care. • For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. For comparator treatments like IVIg and PLEX, prescribing is most probably done in a secondary care setting. IVIg is typically administered in both secondary and sometimes primary care. PLEX is almost always performed in a hospital or secondary care setting due to the need for specialized equipment and expertise. In comparison, efgartigimod with recombinant human hyaluronidase PH20 is likely to be restricted to secondary care settings initially, though the follow-up process could potentially be managed in primary care for stable patients. • Would efgartigimod with recombinant human hyaluronidase PH20 be a candidate for managed access? Yes, managed access could allow for more controlled introduction into clinical practice while gathering additional real-world data on its long-term safety, efficacy, and cost-effectiveness.	

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	Takeda	What is the existing treatment pathway for CIDP? Please refer to our comments on the background information section and ensure that the treatment pathway is reflective of the European Academy of Neurology/Peripheral Nerve Society CIDP guidelines 2021 and the Clinical Commissioning Policy for the use of therapeutic immunoglobulin (Ig) England (2024). We would specifically like to highlight that as per the treatment guidelines, IVIgs are not the sole immunoglobulins available for CIDP patients. Both conventional and facilitated SCIgs are available for maintenance treatment post IVIg stabilisation and offers the added benefit of at home administration. These can reduce patient burden, increase treatment autonomy and offer additional convenience by allowing patients the option of self-administering in their own home and avoiding intravenous cannulation. SCIgs have not been specifically listed as a comparator within the draft scope, but offer a treatment option with additional benefits that may impact quality of life.	Thank you for your comments. Comments noted.
	Guillain-Barré and Associated Inflammatory Neuropathies (GAIN)	The existing treatment pathway for CIDP is not fixed and there are various geographical differences potentially leading to health inequalities or at least different treatment outcomes. This means that it could be difficult to fit Efgartigimod in to a non-standardised treatment pathway. Some clinicians use IVIG as 1st line treatment, while others use steroids. For some patients no existing treatment works and they are currently left with no treatment options. Efgartigimod could be a replacement for 1st line treatment, or be an additional treatment option if others don't work or aren't working effectively. IVIG and plasma are both used considerably within current pathways, but to varying degrees between clinicians. They are used both in the short term and	Thank you for your comments.

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		longer term (although cost implications mean longer term options can be limited, especially for IVIG) Presume Efgartigimod will be used under category C (prescribed and followed up in secondary care) Managed access may be beneficial.	
	ABN Neuromuscular Advisory Group	**What is the existing treatment pathway for CIDP?** Already covered above. **Where do you consider efgartigimod with recombinant human hyaluronidase PH20 will fit into the existing care pathway for CIDP?** - As an alternative first line option alongside current SOC (chosen according to patient individual needs/ lifestyle and risk profile) - In patients with sub-optimal response / considerable disease fluctuation with current SOC, as an alternative to maintenance IVIg or PLEX, with the acknowledgement that not all patients will experience similar response and therefore close clinical monitoring and access to rescue treatment will be essential to support the changeover process. - Co-prescription of IVIg alongside efgartigimod is not indicated due to competing mechanisms of action and we anticipate patients on already on maintenance IVIg would have this stopped prior to commencing efgartigimod.	Thank you for your comments.

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		How often are intravenous immunoglobulin or plasma exchange used for CIDP? If used, in which populations are they used and for how long (short-term v chronic longer-term use)? As stated earlier, IVIg and PLEX and corticosteroids are equally effective in CIDP. Their selection is based on individual risk profile and local availability. The proportions of this population who are maintained on each of these therapies will vary from one trust to the other. I am not aware of a recent UK wide survey which provides data on CIDP first line treatment proportions. The IVIg database will provide data on CIDP usage. IVIg and PLEX are immunomodulatory therapies and therefore must be delivered regularly in the long- term. Typical maintenance in 1-3 days every 4-6 weeks (average doses 1-1.5g/kg/month). Once clinical response is established (according to improvement in multiple CIDP specific outcome measures) the aim is to maintain stability for at least 1-2 years before considering a treatment cessation trial to re-assess disease activity. This is based on evidence showing approximately 40% of patient with stable CIDP on treatment may be in remission after 1-2 years. However, there are no markers of disease activity identifiable without a treatment withdrawal trial. Therefore, this approach requires a robust clinical support infrastructure to promptly identify those who decline and deliver rescue therapy and reinstitute previous maintenance in the 60% who still require treatment. **Please select from the following, will efgartigimod with recombinant human hyaluronidase PH20 be:** **A. Prescribed in primary care with routine follow-up in primary care**	

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		B. Prescribed in secondary care with routine follow-up in primary care **C. Prescribed in secondary care with routine follow-up in secondary care** **D. Other (please give details):** D. Other We suggest Efgartigimod should be prescribed and managed through specialist peripheral nerve/ neuromuscular clinics with appropriate consultant and clinical nurse specialist support. This is because discontinuation of previous maintenance therapy is essential for the transfer to efgartigimod, so an existing support structure for IVIG cessation must be in place to identify patients who decline off regular IVIg but do not respond to efgartigimod, and promptly rescue them with alternative treatment. It may be sensible to formally assess disease activity prior to transfer to efgartigimod. To collect meaningful and real-world data on the use of this novel therapeutic, clear guidance on efficacy monitoring and safety monitoring in the UK will be informative. And may allow for realistic collection of cost-saving data in an organised way. **For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** Prescribing/routine follow up for efgartigimod should be based on the principles currently recommended by NHSE IVIg commissioning guidelines. This is a different molecule but it is immunomodulatory and therefore infrastructure for prescription/follow up should be similar. The introduction of a	

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		novel therapeutic in this area may benefit from the support of delivery through a specialist (tertiary care) centre for the reasons given above. **Would efgartigimod with recombinant human hyaluronidase PH20 be a candidate for managed access?** Yes, efgartigimod is a novel therapeutic agent for a chronic inflammatory disease associated with significant disability that can be self-administered at home. This potentially addresses an unmet need in this population with meaningful social and economic benefits discussed above. A managed access scheme would enable real-world data collection on the safety and efficacy of this drug, its use on a broader scale in the NHS in the future. **Do you consider that the use of efgartigimod with recombinant human hyaluronidase PH20 can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** - Socioeconomic potential benefits of self-administered, home-based therapy as discussed. - Reduced stress associated with travel forward and back to treatment. - Reduced side effects and complications associated with IVIg (20% post-infusion migraine symptoms, 7 x increased thrombo-embolic risk with long term IVIg maintenance therapy).	

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		References: - Adrichem ME et al. Withdrawal of intravenous immunoglobulin in chronic inflammatory demyelinating polyradiculoneuropathy, Brain, Volume 145, Issue 5, May 2022, Pages 1641–1652, https://doi.org/10.1093/brain/awac054 - Kapoor M et al. Immunoglobulin use in neurology: a practical approach. Practical Neurology Published Online First: 03 August 2024. doi: 10.1136/pn-2022-003655 - Ransley F et al, Intravenous immunoglobulin cessation trials in chronic inflammatory demyelinating polyneuropathy. Journal of Neurology, Neurosurgery & Psychiatry 2024;95:A10. - Mahima Kapoor, Laura Compton, Alex Rossor, Elsbeth Hutton, Hadi Manji, Mike Lunn, Mary Reilly, **Aisling Carr**. An approach to assessing immunoglobulin dependence in chronic inflammatory demyelinating inflammatory polyneuropathy. J Peripher Nerv Syst. 2021 Dec;26(4):461-468. doi: 10.1111/jns.12470.	
Additional comments on the draft scope	Takeda	Takeda recommends the addition of the Clinical Commissioning Policy for the use of therapeutic immunoglobulin (Ig) England (2024) Publication date: April 2024 version 2.0, to the list of 'Related National Policy' in the draft scope.	Thank you for your comment. This has been added to the scope.

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope:

None