National Institute for Health and Care Excellence

Health Technology Evaluation

Pegcetacoplan for treating primary complement 3 glomerulopathy and primary immune-complex membranoproliferative glomerulonephritis in people 12 years and over ID6489

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	Swedish Orphan Biovitrum Ltd (Sobi)	Sobi considers the evaluation route (STA) to be appropriate. However, it should be taken into consideration that C3G and IC-MPGN are rare diseases. As acknowledged in the latest NICE health technology evaluations manual, evidence generation is challenging in rare diseases and as a result, the level of evidence for technologies indicated for rare diseases might not be as high as for other technologies.	Thank you for your comment. This topic has been routed as an STA.
	British Association for Paediatric Nephrology	This may be more suited to the Highly Specialised Technology evaluation, in that it is for a very rare disease with small numbers of patients and there are challenges for research and difficulties collecting evidence because of the uniqueness of the disease.	Thank you for your comment. This topic has been routed as an STA.
	National Renal Complement Therapeutics Centre and The	STA is the appropriate route. The company might have opted for HST but would have been borderline for eligibility.	Thank you for your comment. This topic has been routed as an STA.

Section	Stakeholder	Comments [sic]	Action
	UK Kidney Association		
	UK Renal Pharmacy Group	The proposed route of single technology appraisal is appropriate in this case.	Thank you for your comment. This topic has been routed as an STA.
	Kidney Research UK	This is an appropriate topic to evaluate.	Thank you for your comment. This topic has been routed as an STA.
	Clinical expert	I welcome the evaluation of this 1st -in class targeted C3 inhibitor for use in 12+ children for C3GN/IC-MPGN.	Thank you for your comment. This topic has been routed as an STA.
Wording	Swedish Orphan Biovitrum Ltd (Sobi)	Sobi considers that the proposed wording of the draft remit fully reflects the proposed indications.	Thank you for your comment. No change to the scope needed.
	British Association for Paediatric Nephrology	Yes	Thank you for your comment. No change to the scope needed.
	National Renal Complement Therapeutics Centre and The UK Kidney Association	Yes	Thank you for your comment. No change to the scope needed.

Section	Stakeholder	Comments [sic]	Action
	UK Renal Pharmacy Group	The wording regarding the cost effectiveness is largely appropriate. It also should consider the costs of dialysis and transplantation to the NHS that would be saved by slowing the decline in renal function by using this medication. The condition often recurs post transplant, rendering young patients on HD long term, unable to be economically active from early on in life. For example, home HD ~ £25k per patient per year. (£29-33k with transport).	Thank you for your comment. The committee will consider any displacement of future treatment costs when evaluating pegcetacoplan. No change to the scope needed.
	Clinical expert	The wording appropriately encapsulates the issues – would be useful to list the projected costs of annual treatment with pegcetacoplan compared with comparator (frankly ineffective treatments alone – such as ACE/ARB, MMF+/- corticosteroids)/SGLT2i. There is no decent RCT data for these current practices only retrospective case series.	Thank you for your comment. The committee will consider the total costs associated with pegcetacoplan and the total costs associated with current clinical management. No change to the scope needed.
Timing issues	Swedish Orphan Biovitrum Ltd (Sobi)	This appraisal is suitable for prioritisation and expedited process steps where appropriate. There are currently no approved therapies to prevent or reverse disease progression in primary C3G or primary IC-MPGN. Approximately 50% of patients progress to end stage kidney disease (ESKD) within 10 years of diagnosis despite current treatment. These patients will then require renal replacement therapy (dialysis) or a kidney transplant. Up to 80% of patients experience clinical disease recurrence after transplantation with a 76%	Thank you for your comment. This topic has been scheduled into NICE's work programme.

Section	Stakeholder	Comments [sic]	Action
		greater risk of mortality versus other nephropathies. Considering these diseases typically affect adolescents and young adults, the burden of disease is significant. Pegcetacoplan has the potential to address the underlying disease pathophysiology by inhibiting C3 activation, thus preventing glomerular deposition of C3 breakdown products that is present in all patients with C3G and primary IC-MPGN. If licensed, pegcetacoplan will be the first approved therapy to treat primary IC-MPGN (in adults and adolescents) and C3G in adolescents. [redacted]	
	British Association for Paediatric Nephrology	This is relatively urgent – people with C3G and IC-MPGN currently have no NICE approved treatments and are at risk of progression to kidney failure.	Thank you for your comment. This topic has been scheduled into NICE's work programme.
	National Renal Complement Therapeutics Centre and The UK Kidney Association	Urgent – currently no treatments available via NICE.	Thank you for your comment. This topic has been scheduled into NICE's work programme.
	UK Renal Pharmacy Group	Given the target treatment population for this medication is patients with complement 3 gomerulopathy or primary immune-complex membranoproliferative glomerulonrephritis, 50 % of whom will develop ESRD and require dialysis and transplantation in later life, the evaluation should be conducted as soon as possible in order to prevent the maximum number of people progressing to dialysis/transplantation.	Thank you for your comment. This topic has been scheduled into NICE's work programme.

Section	Stakeholder	Comments [sic]	Action
		There are currently no specific NICE funded treatments for this condition.	
	Kidney Research UK	Currently there is no approved treatment for either C3 glomerulopathy or immune complex MPGN and the evidence of efficacy for the current standard of care is limited. Despite standard of care in many cases both of these conditions lead to progressive disease and ultimately kidney failure. Therefore there is currently significant unmet need.	Thank you for your comment. This topic has been scheduled into NICE's work programme.
	Clinical expert	I believe this to be an urgent appraisal for a very effective treatment as demonstrated by the VALIANT trial in a rare, devastating condition with a huge unmet need	Thank you for your comment. This topic has been scheduled into NICE's work programme.
Additional comments on the draft remit	British Association for Paediatric Nephrology	It would be worth appraising tolerability given the sub-cutaneous drug delivery route using a specific device	Thank you for your comment. The committee will consider any impacts of subcutaneous treatment in its deliberations. No change to the scope needed.
	Kidney Research UK	In the technology section pegcetacoplan is described as an intravenous treatment stopped this is incorrect subcutaneous.	Thank you for your comment. The scope has been corrected.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Swedish Orphan Biovitrum Ltd (Sobi)	In the “Technology” section it is stated that pegcetacoplan is an intravenous infusion. This is incorrect, pegcetacoplan is administrated via subcutaneous infusion.	Thank you for your comment. The scope has been corrected.
	British Association for Paediatric Nephrology	On page 1, in the first paragraph of the background section, there is a statement “ ‘Primary’ C3 glomerulopathy and IC-MPGN means that the underlying cause of complement dysregulation is not known.1 Secondary C3 glomerulopathy and IC-MPGN can occur due to multiple reasons, including infection, autoimmune conditions, and cancer. This is not accurate. The term ‘primary C3G’ and IC-MPGN’ means that another secondary cause has not been identified (such as infection, cancer etc). The cause of complement dysregulation in Primary C3G/IC-MPGN may indeed be known (such as an anti-complement antibody or a complement gene variant). In the second paragraph of the background, the statement that half of affected people develop kidney failure within 10 years is accurate. However it is worth highlighting that there is a sub-group of patients that progress much more rapidly and it is important to be aware that this is not always a slowly progressive disease. On page 2 (under The technology) Pegcetacoplan is described as an intravenous treatment. This is incorrect. It is a subcutaneous treatment. On page 2 (under The technology) it is stated that Pegcetacoplan has been studied in a randomised controlled trial compared with placebo in people older than 12 years with primary C3 glomerulopathy or primary IC-MPGN. This is incorrect. It has been studied in people 12 years old and older (weighing at least 30kg).	Thank you for your comment. The background section has been updated to reflect: • correct definitions of primary and secondary C3G and IC-MPGN. • progression to kidney failure can be more rapid for some people. • That pegcetacoplan is a subcutaneous treatment. • That the trials for pegcetacoplan had a weight limit.

Section	Consultee/ Commentator	Comments [sic]	Action
	National Renal Complement Therapeutics Centre and The UK Kidney Association	Yes, though reasonable to speculate that incidence of primary IC-MPGN is likely to be comparable to C3G – ie similarly rare.	Thank you for your comment. The scope has been updated to reflect that the incidence of primary IC-MPGN is thought to be similar to C3G.
	UK Renal Pharmacy Group	Yes this information is both accurate and appropriate.	Thank you for your comment. No change to the scope needed.
	Kidney Research UK	The draft remit refers to the treatment of primary C3 glomerulopathy. Later in the background section primary C3 glomerulopathy is defined as a disease where the underlying cause of complement dysregulation is not known. This is potentially incorrect as patients may have a genetic defect in complement regulation leading to the development of C3 glomerulopathy. This would still be defined as primary C3G but in this situation the cause of complement activation is known.	Thank you for your comment. The scope has been updated to reflect the correct definitions of primary and secondary C3G and IC-MPGN.
	Clinical expert	This is accurate and simply worded. It is worth mentioning that eculizumab is not available for the pre-transplant cohort and a word on the relative effectiveness of Eculizumab post-transplant. The recommendations, for what has become a treatment standard (MMF/steroids), are weak in children and borrowed from adult case series	Thank you for your comment.
Population	Swedish Orphan Biovitrum Ltd (Sobi)	The anticipated marketing authorisation is for the treatment of adults and adolescents aged 12 years and older with complement 3 glomerulopathy or primary immune-complex membranoproliferative glomerulonephritis. Sobi recommends aligning the target population accordingly.	Thank you for your comment. The scope has been updated as suggested.

Section	Consultee/ Commentator	Comments [sic]	Action
	British Association for Paediatric Nephrology	This should be “People (of 12 years old and older) with complement* 3 glomerulopathy or primary immune-complex membranoproliferative glomerulonephritis * The term “complement 3” is not used. It is always abbreviated to C3 in this context.	Thank you for your comment. The scope wording has been retained to reflect the anticipated marketing authorisation.
	National Renal Complement Therapeutics Centre and The UK Kidney Association	This is accurate with emphasis on primary forms of C3G and IC-MPGN. One comment is how crucial the company view the distinction between C3G and IC-MPGN. This is specifically relevant if comparing to iptacopan for which trials have been completed in C3G but trials in IC-MPGN are ongoing.	Thank you for your comment. The committee will consider any differences between C3G and IC-MPGN, and whether they require consideration as distinct subgroups. No change to the scope required.
	UK Renal Pharmacy Group	Yes the population is appropriate, although noted that the patient must be diagnosed via biopsy, so this must be made clear in the NICE TA wording.	Thank you for your comment. The scope specifies that use of pegcetacoplan is conditional on the results of renal biopsy and that the economic modelling should include the costs associated with diagnostic testing in people who would not

Section	Consultee/ Commentator	Comments [sic]	Action
			otherwise have been tested. No change to the scope made.
	Kidney Research UK	Yes	Thank you for your comment. No change to the scope required.
	Clinical expert	Yes 12-18+ years, the clinical trials had a 40Kg weight minimum and this is not mentioned here only chronological age.	Thank you for your comment. The scope has been updated to reflect the weight limit in the clinical trial.
Subgroups	Swedish Orphan Biovitrum Ltd (Sobi)	The subgroups suggested in the scope are appropriate.	Thank you for your comment. No change to the scope needed.
	British Association for Paediatric Nephrology	The subgroups suggested are appropriate. We strongly support that the 12-18 year old subgroup should be considered separately, particularly because of the life-long nature of the alternative disease course (end-stage kidney disease, dialysis, transplant). C3G could be further sub-divided into C3 glomerulonephritis and dense deposit disease.	Thank you for your comment. Further subgroups for C3G have been added to the scope.
	National Renal Complement Therapeutics Centre and The	CFHR5 nephropathy and other rare genetic forms of C3G could potentially respond differently to acquired forms [ie due to nephritic factors] however current understanding of disease is insufficient to say if there will be a differential response.	Thank you for your comment. The scope has been updated to include specific genetic subtypes of C3G.

Section	Consultee/ Commentator	Comments [sic]	Action
	UK Kidney Association	Also crescentic forms of C3G were excluded from trials – they form a group with highest unmet need but there is no trial data to inform if or how to treat this group of patients.	
	UK Renal Pharmacy Group	The sub-groups are appropriate and clearly defined.	Thank you for your comment. No change to the scope needed.
	Kidney Research UK	The subgroups are appropriate.	Thank you for your comment. No change to the scope needed.
	MPGN/DDD Support Group	Subgroups that could be considered differently are pre and post transplant cohorts. For post transplant patients showing aggressive signs of disease recurrence and facing an imminent return to dialysis, this technology is likely be a more cost effective treatment than for a pre transplant patient with a slowly progressing disease, one whose disease is managed with MMF and ACE inhibitors.	Thank you for your comment. Kidney transplant is included in the scope as a subgroup of interest.
	Clinical expert	Yes, C3G/IC-MPGN/pre-post transplant I note no eGFR cut-offs (VALIANT trail > 30mls/min/1.73m2 The clinical feeling is that starting early with preserved eGFR is likely to reap the biggest benefits and proteinuria reductions in glomeruli yet to be chronically damaged so the high eGFR and post-transplant recurrences probably likely to benefit the most.	Thank you for your comment. The committee will consider any subgroup analyses based on kidney function presented to it.

Section	Consultee/ Commentator	Comments [sic]	Action
Comparators	Swedish Orphan Biovitrum Ltd (Sobi)	The comparators listed are considered to reflect current standard of care in the NHS, apart from iptacopan which is subject to a NICE evaluation for treating adults with C3G. While iptacopan is still under NICE evaluation, Sobi may consider it an appropriate comparator for the relevant licensed population if it receives NICE approval and the timelines permit. All other relevant comparators have been included, and we propose no changes to the current list.	Thank you for your comment. No change to the scope needed.
	British Association for Paediatric Nephrology	All commonly used comparators are included. In paediatric practice, rapidly progressive disease might be treated with other treatments including IV cyclophosphamide, rituximab and plasma exchange but this is an infrequent scenario. SGLT2 inihibitors are not available to people under the age of 18 years.	Thank you for your comment. The scope has been updated with the comparators suggested.
	National Renal Complement Therapeutics Centre and The UK Kidney Association	Agree. It should be noted that none of the treatments listed in KDIGO are based on robust data.	Thank you for your comment. No change to the scope needed.
	UK Renal Pharmacy Group	The comparators listed are appropriate. Noted that iptacopan is subject to NICE evaluation.	Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	Kidney Research UK	I would not consider angiotensin converting enzyme inhibitors, angiotensin II receptor blockers or SGLT2 inhibitors as comparative as an inclusion criteria for the trial was that patients were on a stable, optimised regime including the above agents. The effect of pegcetacoplan was in addition to these drugs and not in comparison to patients not on these treatments. Iptacopan (subject to NICE evaluation) is considered as a comparator. However, iptacopan is currently being considered for the treatment of C3 glomerulopathy and not immune complex MPGN. The trial design (specifically inclusion criteria) was different for the iptacopan and pegcetacoplan trials so direct comparison of trial outcomes should be performed with caution.	Thank you for your comment. The comparator list has been kept inclusive at this stage to allow committee to consider which are most appropriate to decision making. Caveats have been added to the iptacopan comparator to specify it is only for C3G.
	MPGN/DDD Support Group	The patients who engage with our support group tend to be those patients who suffer with these diseases in their most aggressive form. A common theme is rapid decline into end stage renal failure, dialysis treatment, a transplant, and then a return to dialysis after disease recurrence. Although Eculizumab is approved for use in a limited number of cases, it is not a targeted therapy. The list of comparators does not include dialysis. For patients who experience these diseases in their aggressive forms, the comparators listed are not relevant and do not capture the bigger picture. If a new treatment can stop the decline to end stage renal failure then there are massive savings to be made to the NHS, as the cost of dialysis and transplantation is huge.	Thank you for your comment. Pegcetacoplan is not expected to displace dialysis as treatment for kidney failure, so dialysis has not been included as a comparator. However, the committee will consider any cost-savings associated with delayed/reduced initiation of dialysis.

Section	Consultee/ Commentator	Comments [sic]	Action
	Clinical expert	1. ACE/ARB standard of care 2. MMF+/- corticosteroids 3. SGLT2i yet to fully emerge in paediatrics but limited use off label in practice 4. Some children entered into other trials with Finerenone (Fidelio/FIONA trials)/EPIK sparsentan etc. 5. IPTACOPAN not available to paediatrics <18 years at present 6. Eculizumab	Thank you for your comment. The scope has been amended to better reflect the population who might have iptacopan. Treatments which are not established in NHS practice are not relevant comparators so treatments from other clinical trials have not been included.
Outcomes	Swedish Orphan Biovitrum Ltd (Sobi)	The outcomes listed are considered appropriate to capture the benefits of treatment for these patients.	Thank you for your comment. No change to the scope needed.
	British Association for Paediatric Nephrology	The outcomes listed are appropriate.	Thank you for your comment. No change to the scope needed.
	National Renal Complement Therapeutics Centre and The UK Kidney Association	Yes	Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	UK Renal Pharmacy Group	The outcomes are appropriate.	Thank you for your comment. No change to the scope needed.
	Kidney Research UK	Yes	Thank you for your comment. No change to the scope needed.
	Clinical expert	Yes – all medium-term outcome markers will be surrogates such as 1. eGFR changes – slope eGFR 2. Reductions in proteinuria 3. Time to transplant 4. Composite scores including histological index scores (not done in adolescent trials) 5. Mortality 6. Side effects 7. HrQOL	Thank you for your comment. No change to the scope needed.
Equality	Swedish Orphan Biovitrum Ltd (Sobi)	Sobi does not believe there are equality considerations that are likely to impact the recommendations and their appropriateness. However, the committee should consider whether the longer waiting times faced by Black and Asian people represents a health inequality, as highlighted in the quality impact assessment for iptacopan. This followed comments on the iptacopan draft scope, in which the National Kidney Federation said:	Thank you for your comment. This has been added to the Equality Impact Assessment.

Section	Consultee/ Commentator	Comments [sic]	Action
		"It should be kept in mind that there are longer waiting time for kidney transplants for black and Asian patients compared to white. A third of people (35%) waiting for a kidney across the UK are from minority ethnic groups but in 2017/18, of those providing their ethnicity when registering on the NHS Organ Donor Register, only 3.3 % were Asian, 1 % were black and 2 % were mixed race. This may need to be factored in when considering who should be treated and when, to ensure all patients have the best chance".	
	British Association for Paediatric Nephrology	Children under the age of 12 years are excluded and thus are discriminated against on the basis of age, which is a protected characteristic. The trial excluded children under 12 years of age and therefore the trial data cannot be applied to this population. Should pegcetacoplan be approved for people of 12 years and older, this will lead to a situation where people over 12 years have access to an effective treatment available but those under 12 years do not.	Thank you for your comment. This has been added to the Equality Impact Assessment.
	National Renal Complement Therapeutics Centre and The UK Kidney Association	Yes	Thank you for your comment.
	UK Renal Pharmacy Group	Disparities in expertise in C3 glomerulopathy and IC-MPGN could lead to a reduction in equity of access for all patients. The numbers of patients in each region will be low, therefore should consider either regional or national MDTs	Thank you for your comment. This has been added to the

Section	Consultee/ Commentator	Comments [sic]	Action
		for approval of the medication to ensure the dug is being used cost effectively and that there is equity of access for all patients regardless of postcode. Access to administration – also need to ensure all centres have access to specialist nursing staff to ensure patients can be taught how to administer medication. Most centres use erythropoietin, therefore have access to homecare services.	Equality Impact Assessment.
	Clinical expert	No Comments seems fine Needed given the benefits seen in so many on the trial with geographical and centre variation into who could enroll	Thank you for your comment.
Other considerations	Swedish Orphan Biovitrum Ltd (Sobi)	Under the current standard of care, patients with C3G and IC-MPGN experience significantly poorer graft survival compared to the overall kidney transplant population and are at a substantially higher risk of second graft loss. Consequently, securing transplants in this disease area is often extremely challenging, and many patients either die waiting or are removed from the waiting list due to deteriorating health. This inequity and difficulty in accessing transplants underscores the urgent need for a disease-modifying therapy. Pegcetacoplan, which has demonstrated the ability to stabilise renal function regardless of transplant status, represents an opportunity to address this unmet medical need. Additionally, it is important to note that unlike pegcetacoplan, current treatment options do not address the underlying cause of disease in these patients. ACE inhibitors and angiotensin II receptor blockers (ARBs) do not target the underlying pathophysiology of C3G or primary IC-MPGN and instead are supportive measures only to help with associated proteinuria and hypertension.	Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Immunosuppressive agents such as corticosteroids and mycophenolate mofetil (MMF) have demonstrated limited effectiveness; do not target the underlying pathophysiology; and are associated with serious side effects, such as osteoporosis, obesity, gastrointestinal bleeding. Eculizumab targets the effector C5 in the complement pathway, which is downstream of C3 and thus appears to be insufficient in preventing complement activation at the C3 level. Most patients experience no response to treatment and high rates of disease progression.	
	Clinical expert	The age range: Most of the presenting paediatric cases are under 12 years with early lesions that stand to gain the most from early intervention – no trial safety data in the < 12s - been campaigning to open a new trial arm for < 12s but there are industry issues and disincentives for this – the appraisal is great news but a huge proportion of children < 12 years stand to lose out when they may benefit the most.	Thank you for your comment. This has been added to the Equality Impact Assessment.
Questions for consultation	Swedish Orphan Biovitrum Ltd (Sobi)	**Question 1: In NHS practice, what are the main differences in how primary C3 glomerulopathy and IC-MPGN are treated?** As there are no licensed therapies that target the pathophysiology of C3G or primary IC-MPGN, current approaches to treatment are the same for both conditions - that is, supportive treatment with ACE inhibitors/angiotensin II receptor antagonists, SGLT-2 inhibitors and immunosuppression. However, the pathophysiology of these two conditions may be different. C3G is triggered by abnormalities in the complement alternative pathway resulting in dominant C3 deposition in the glomerulus. Although C3 deposition also occurs in primary IC-MPGN, it is not dominant, with presence of other	Thank you for your comments and responses to the questions.

Section	Consultee/ Commentator	Comments [sic]	Action
		immune complexes activated by the complement classical pathway. Considering the different pathophysiological mechanisms involved, future treatment for C3G and primary IC-MPGN should be with licensed therapies (where available) with demonstrated efficacy and safety in each individual condition. **Question 2: Are all relevant comparators included?** All relevant comparators are included **Question 3: Would pegcetacoplan be used alongside or instead of ACE inhibitors, ARBs, corticosteroids, mycophenolate mofetil, and SGLT inhibitors?** Pegcetacoplan would be used alongside ACE inhibitors or ARBs and SGLT-2 inhibitors. Pegcetacoplan could also be used alongside corticosteroids and mycophenolate mofetil (MMF). However, considering the lack of evidence and extensive side-effect profiles of these immunosuppressive agents, we do not envisage these treatments being used with pegcetacoplan in most patients. **Question 4: Would budenoside or sparsentan ever be used as treatment for C3 glomerulopathy or IC-MPGN and if so, would they be considered a comparator or a concomitant treatment** Budesonide or sparsentan are not licensed for C3G or primary IC-MPGN and neither treatment would be considered a comparator or a concomitant treatment. C3G and IC-MPGN disease pathogenesis is centred on the complement cascade. There is no published evidence that budenoside (which targets IgA	Thank you for your comments and responses to the questions.

Section	Consultee/ Commentator	Comments [sic]	Action
		production and is indicated for treating primary immunoglobulin A nephrology (IgAN)) would be effective, and therefore would be considered off-label. Sparsentan is also indicated for treating primary IgAN. **Question 5: Would there be any other concomitant treatments that should be accounted for in the modelling?** There are no other treatments expected to be included. **Question 6: Does diagnosis of C3 glomerulopathy or IC-MPGN in order to be eligible for pegcetacoplan require biopsy or other diagnostic testing in people that would otherwise not have been tested?** Yes, a renal biopsy is required to confirm a diagnosis. **Question 7: Where do you consider pegcetacoplan will fit into the existing care pathway for C3 glomerulopathy and IC-MPGN?** We expect that pegcetacoplan would be used in adults at least 18 years of age and adolescents (aged 12-17 years) with C3G or primary IC-MPGN (with or without a previous kidney transplant) who are at risk of progressing to kidney failure despite treatment with current standard of care. This would include patients with a uPCR of at least 1 g/g. We expect pegcetaoplan to be used alongside ACE inhibitors/ARBs. Considering the lack of evidence and substantial side-effect profiles with immunosuppression (corticosteroids and MMF) we expect pegcetacoplan to come before these agents in the care pathway. As eculizumab (currently only an option in post-transplant patients) has limited evidence, is not licensed, and works downstream of C3 in the complement system, we do not expect it to have a major role in the care pathway if pegcetacoplan is licensed and reimbursed for C3G and primary IC-MPGN.	Thank you for your comments and responses to the questions.

Section	Consultee/ Commentator	Comments [sic]	Action
		Question 8: Would the existing care pathway differ between people aged between 12 and 18 years and people over 18 years? If so, how? We do not anticipate that pegcetacoplan would integrate differently into the current care pathway for individuals aged 12 to 17 years compared to those aged 18 years and older. **Question 9: Please select from the following, will pegcetacoplan 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):** Pegcetacoplan will be prescribed in secondary care with routine follow-up in secondary care. **Question 10: For comparators please detail if the setting for prescribing and routine follow-up differs from the intervention.** The setting for all comparators is anticipated to be the same for both prescribing and routine follow-up. **Question 11: Are the subgroups listed appropriate?** Yes **Question 12: Are the outcomes listed appropriate? Are there any further outcomes which should be considered?**	Thank you for your comments and responses to the questions.

Section	Consultee/ Commentator	Comments [sic]	Action
		The outcomes are appropriate - there are no further outcomes to be included. **Question 13: Would pegcetacoplan be a candidate for managed access?** Sobi proposes that pegcetacoplan is not a candidate for managed access, given the robust body of evidence from completed and ongoing clinical studies that supports this appraisal. VALIANT (NCT05067127) evaluates the efficacy and safety of pegcetacoplan versus placebo in 124 patients aged ≥12 years with C3G or primary IC-MPGN, with 52 weeks data available. Patients who complete VALIANT (52 weeks) are eligible to enter the VALE extension trial (NCT05809531), which will provide long-term safety and efficacy data for pegcetacoplan in C3G and primary IC-MPGN. An estimated 100 patients aged ≥12 years who completed VALIANT and achieved clinical benefit will continue to receive twice-weekly doses of pegcetacoplan for a minimum of approximately 2.5 years. **Question 14: Do you consider that the use of pegcetacoplan 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.** Yes, the physical limitations, emotional distress, disruption to work or school, and the strain on caregivers associated with chronic progressive diseases such as C3G and primary IC-MPGN impose a substantial burden on patients'	Thank you for your comments and responses to the questions.

Section	Consultee/ Commentator	Comments [sic]	Action
		quality of life. These impacts are not fully captured within traditional QALY measures. Both diseases are associated with significant healthcare resource utilisation, including frequent healthcare provider visits, biopsies, laboratory testing, hospitalisations, and the costs of managing chronic kidney disease and kidney failure. Additionally, patients often face indirect costs, such as loss of productivity and inability to work. Children face even greater challenges, including developmental delays that can affect academic performance, self-esteem, and overall quality of life. These challenges also have a profound and detrimental impact on the quality of life of their caregivers. Pegcetacoplan is expected to improve the quality of life for both patients and caregivers by positively influencing emotional, physical, and social functioning. These improvements are anticipated to translate into economic benefits through increased productivity and a reduced caregiver burden. Sobi will clearly highlight, within its submission, data demonstrating health-related benefits that are not fully captured by the QALY calculation.	Thank you for your comments and responses to the questions.
	British Association for Paediatric Nephrology	i) In NHS practice, what are the main differences in how primary C3 glomerulopathy and IC-MPGN are treated? The main difference would be that IC-MPGN patients would undergo evaluation for a secondary cause and treatment may be directed to the underlying cause (e.g. chronic infection).	Thank you for your comments and responses to the questions.

Section	Consultee/ Commentator	Comments [sic]	Action
		Once secondary causes are excluded, IC-MPGN and C3G are treated in the same way in NHS practice. ii) Would pegcetacoplan be used alongside or instead of ACE inhibitors, ARBs, corticosteroids, mycophenolate mofetil, and SGLT inhibitors? The clinical trials have not addressed the question of the place of pegcetacoplan in the clinical pathway for patients. If pegcetacoplan is approved, it is likely that it will be used alongside ACEi and ARB, which have benefits regardless of the cause of proteinuria. It is likely that clinicians will commence pegcetacoplan for existing patients in order to reduce/stop their existing immunosuppression (usually steroids +/- mycophenolate mofetil - MMF). In newly presenting patients with mild to moderate disease, it is possible that pegcetacoplan could replace steroids/MMF completely. In patients with newly presenting severe disease, it is likely that steroids may be used initially in order to reduce severe inflammation. However it is likely that this would be of short duration only (e.g. < 3 months) and that MMF may not be needed in most patients who are treated with pegcetacoplan. iii) Would budenoside or sparsentan ever be used as treatment for C3 glomerulopathy or IC-MPGN and if so, would they be considered a comparator or a concomitant treatment? In paediatric patients, it is unlikely that budesonide would be used as a treatment for C3G. In paediatric patients, a few patients who are intolerant of ACEi/ARB might receive sparsentan but this is unlikely.	Thank you for your comments and responses to the questions.

Section	Consultee/ Commentator	Comments [sic]	Action
		iv) Would there be any other concomitant treatments that should be accounted for in the modelling? A proportion of paediatric patients reach ESKD from IC-MPGN/C3G. They would then receive lifelong kidney replacement thearpy, in the form of dialysis or kidney transplantation. This should be accounted for. v) Does diagnosis of C3 glomerulopathy or IC-MPGN in order to be eligible for pegcetacoplan require biopsy or other diagnostic testing in people that would otherwise not have been tested? In people under 18 years old, it is not anticipated that an available treatment such as pegcetacoplan will result in higher number of patients undergoing kidney biopsy. This is because all people under 18 years with significant proteinuria and without an alternative known cause would undergo kidney biopsy. vii) Where do you consider pegcetacoplan will fit into the existing care pathway for C3 glomerulopathy and IC-MPGN? In patients with mild proteinuria, we envisage that treatment with ACEi/ARB may be sufficient. However for patients with significant proteinuria despite ACEi/ARB (or who do not tolerate ACEi/ARB) we envisage that pegcetacoplan would be used next in the pathway, before other immunosuppression (unless severe disease in which case concomitant with short-term steroids as per ii) above). Patients with acute inflammatory changes on biopsy, with reduced eGFR but without heavy proteinuria would likely benefit from pegcetacoplan early in the pathway (before ACEi/ARB) in	Pegcetacoplan is not expected to displace dialysis as treatment for kidney failure. However, the committee will consider any cost-savings associated with delayed/reduced initiation of dialysis.

Section	Consultee/ Commentator	Comments [sic]	Action
		order to reverse kidney threatening disease. See answer ii) above for more detail on how pegcetacoplan may be used alongside existing treatments. viii) Would the existing care pathway differ between people aged between 12 and 18 years and people over 18 years? If so, how? The existing care pathway differs between 12 to 17 year olds and over 18 year olds. 12-17 year olds are assessed, diagnosed and treated in tertiary care, with subsequent shared care with secondary care in some cases. Over 18 year olds are assessed, diagnosed and treated in secondary care, with subsequent shared care with primary care in some cases. ix) Please select from the following, will pegcetacoplan 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):** Detailed answer to ix) (option D - other) It is likely that prescribing of pegcetacoplan would be within secondary care (adults) or tertiary care (paediatrics), with oversight/shared care from a highly specialised service. Benefits of centralised oversight would include equitable access to accurate diagnostics in order to initiate treatment, and expedited learning regarding the best real-world use of pegcetacoplan. For example understanding which particular diagnostic/monitoring biomarkers correlate with response to treatment, where pegcetacoplan fits into the overall treatment pathway	Thank you for your comment. No change to the scope needed. .

Section	Consultee/ Commentator	Comments [sic]	Action
		(including other available approved therapies), when treatment can be discontinued and adverse effect surveillance. x) For comparators please detail if the setting for prescribing and routine follow-up differs from the intervention. Adults: current treatments are typically initiated in secondary care, with routine follow up in secondary care. Prescribing may be undertaken by primary care under supervision – practice varies. 12-17 years: current treatments are typically initiated in tertiary care, with routine follow up in shared care between tertiary and secondary care. Some prescribing may be undertaken by primary care under supervision – practice varies. xi) Would pegcetacoplan be a candidate for managed access? Yes. It will be important to consider how requests for access to treatment for children under 12 years old will be considered and how data regarding this use would be collated and reviewed. xii) Do you consider that the use of pegcetacoplan can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? End-stage kidney disease (ESKD) has a massive impact on non-health outcomes such as ability to work. The wider impact of a child/adolescent developing ESKD – e.g. on parental employment and mental health, impact on siblings (mental health) and future employment also should be considered.	Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		If pegcetacoplan can stop/delay development of ESKD, these are significant benefits which should be explored. xiii) Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. For children, PedQL can be used to capture quality of life data that includes School functioning. Stories from patients and families with lived experience should be included in the outcome assessment to capture these unmeasured potential benefits. Some references are included below: The significance of relationships and dynamics in families with a child with end-stage kidney disease: A qualitative study - PubMed (nih.gov) Experiences of parents who have children with chronic kidney disease: a systematic review of qualitative studies - PubMed (nih.gov)	
	National Renal Complement Therapeutics Centre and The UK Kidney Association	In terms of C3G vs IC-MPGN – the distinction of the two diagnoses as suggested in background is subject to limitations of immunostaining of the kidney biopsy. Practically a key difference is emphasis on excluding secondary causes [larger list if IC-MPGN]. Otherwise treatment of IC-MPGN is comparable to that of C3G with key exception that phase 3 trials of iptacopan in C3G have completed [and awaiting NICE] whereas phase 3 trials of iptacopan in IC-MPGN are ongoing.	Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		It is plausible that pegcetacoplan is used alongside ACEi/ARB/SGLT2/Steroids/MMF especially in prevalent patients who are on some or all but have had unsatisfactory clinical response. In more recently diagnosed patients, useful to consider whether pegcetacoplan should be used first-line. Budesonide [modified release] (Kinnpeygo) specifically targets IgA production in IgAN and not relevant to C3G or IC-MPGN. A role of Sparsentan as a DEARA in C3G or IC-MPGN would be an extrapolation of existing data in IGAN and FSGS. It would not be targeting the main pathogenesis of disease [alternative pathway dysregulation]. Non-specific findings of proteinuria and abnormal creatinine signify a broad differential of kidney disorders. A biopsy rules in C3G / IC-MPGN and excludes other disorders such as IGAN. Detecting evidence of complement dysregulation, complement activation or specific abnormalities associated with complement dysregulation might strongly suggest C3G or IC-MPGN but these tests can be difficult to obtain and interpret with screening for complement abnormalities done mostly at the National Renal Complement Therapeutics Centre. Pegcetacoplan would be used early in the pathway following diagnosis of C3G. It is likely that ACE or ARB will have been commenced as part of non-specific general proteinuria management. I see it replacing MMF and steroids for the treatment of ‘moderate’ disease [ie proteinuria over ~1g a day].	

Section	Consultee/ Commentator	Comments [sic]	Action
		The disease is comparable in patients aged 12-17 and those aged over 18. Adolescent patients would present to paediatric centres and diagnosed by a paediatric nephrologist in a tertiary centre whereas adult patients would present to adult centres, and diagnosed aby an adult nephrologist that may work in tertiary or secondary care. Consideration of secondary causes of either C3G or IC-MPGN requires greater scrunity the older the patient – especially for monoclonal gammopathy that may require expert pathology review to ensure that light chain restriction has been reliably excluded. Recommendations for comparator treatments [aside from iptacopan] would be made in secondary care and followed up in secondary care. Some treatments eg ACEi or SGLT2i could be prescribed in primary care and others such as MMF would be prescribed in secondary care. However, referrals are often made to expert centres for advice regarding diagnosis from which comparator treatments might currently be given. Iptacopan is undergoing NICE appraisal. I would expect pegcetacoplan to be prescribed in secondary care but recommendation and ongoing support would be led in a tertiary care or C3G / IC-MPGN expert centre setting. This helps resolve any diagnostic uncertainty and help evaluate treatment response. Pegcetacoplan would be a candidate for managed access. Patients would need to be supported in terms of understanding infection risk to meningococci and other encapsulated organisms. Support with injections required, especially for adolescents. Children under 12 remain excluded from	

Section	Consultee/ Commentator	Comments [sic]	Action
		trials but disease is this cohort can be as devastating. There is an urgent need to ensure that these younger patients get access to effective drugs. The data to inform NICE will be from phase 2 [DISCOVERY] phase 2 [NOBLE], phase 3 [VALIANT] and compassionate use experience, noting that experience of pegcetacoplan in England included patients enrolled into NOBLE and VALIANT.	
	UK Renal Pharmacy Group	In NHS practice, what are the main differences in how primary C3 glomerulopathy and IC-MPGN are treated? Both conditions are treated very similarly with ACE/ARBs, steroids and mycophenolate. Primary and secondary diseases are sometimes treated differently, for example secondary disease will be treated according to the underlying condition driving it, such as lupus. Are all relevant comparators included? Would pegcetacoplan be used alongside or instead of ACE inhibitors, ARBs, corticosteroids, mycophenolate mofetil, and SGLT inhibitors? Yes. Used alongside all of the above drugs as per the Valiant Study. Eculizumab is for patients with recurring disease post-transplant only and is very rarely used. Would budesonide or sparsentan ever be used as treatment for C3 glomerulopathy or IC-MPGN and if so, would they be considered a comparator or a concomitant treatment? Budesonide – no because the mechanism of action would not be effective against C3 GN or IC-MPGN.	Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Sparsentan – there is potential for this to be considered in the future as sparsentan also has strong evidence for reducing proteinuria, however this will require a separate study. Multiple medication options would be positive as it may allow a degree of patient choice.	Thank you for your comment. No change to the scope needed.
		Would there be any other concomitant treatments that should be accounted for in the modelling? No	Thank you for your comment. No change to the scope needed.
		Does diagnosis of C3 glomerulopathy or IC-MPGN in order to be eligible for pegcetacoplan require biopsy or other diagnostic testing in people that would otherwise not have been tested? Patients should already have had a biopsy in order to be diagnosed with C3 GN or IC-MPGN. A repeat biopsy would not be necessary for drug approval.	Thank you for your comment. No change to the scope needed.
		Where do you consider pegcetacoplan will fit into the existing care pathway for C3 glomerulopathy and IC-MPGN? Standard of care medication should be optimised first, i.e. ACE/ARBs and SGLT2 inhibitors, unless the disease is rapidly progressing, in which case pegcetacoplan may need to be initiated more quickly. This would require an expert MDT decision to define rapidly progressing disease and therefore speed of initiation.	Thank you for your comment. No change to the scope needed.
		Would the existing care pathway differ between people aged between 12 and 18 years and people over 18 years? If so, how? Children sometime present with more aggressive disease, therefore more likely to have immunosuppressant therapy. SGLT2 inhibitors are not licensed	Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		in children so may not have been initiated. Would require an expert MDT decision for indication of pegcetacoplan. Please select from the following, will pegcetacoplan 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): For comparators please detail if the setting for prescribing and routine follow-up differs from the intervention. There would be an increase in workload for prescribers, pharmacists and homecare services involved in the GN MDT and prescribing/supplying pegcetacoplan. Need to consider cold chain and fridge space for patients. Would pegcetacoplan be a candidate for managed access? Yes Do you consider that the use of pegcetacoplan can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? This is a disease of young adults, therefore impacts ability to work and look after young families, which may not be included in the calculations. 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:	Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		• could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which pegcetacoplan will be licensed; • 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. See full results of the Valiant trials once published in order to asses the cost effectiveness. Survey to determine GN services nationally to ensure adequate regional MDT services are available to be set up if appropriate.	Thank you for your comment. No change to the scope needed.
	Kidney Research UK	C3 glomerulopathy and immune complex MPGN are managed in a similar way with antiproteinuric therapy, blood pressure control and immunosuppression (usually corticosteroids and MMF). With the exception of aggressive post transplant recurrence complement inhibition is not currently used in the UK.	Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Pegcetacplan would be used alongside standard treatments of proteinuria kidney disease including ACE inhibition, ARBs and SGLT2 inhibitors. Oral budesonide is used for the treatment of IgA nephropathy and would not normally be considered for the treatment of C3 glomerulopathy or immune complex MPGN. There are no other treatments that require consideration. The diagnosis of C3 glomerulopathy or IC m.p. GN is made by biopsy. It is expected that all patients eligible for pegcetacoplan treatment will have undergone kidney biopsy (either transplant or native). To confirm eligibility testing to exclude causes of secondary disease will be required including infection, malignancy monoclonal gammopathy and systemic autoimmune disease. Other tests can be performed to assess the degree of complement activity including soluble C5-9 levels and evidence of C3 degradation. It will also be possible to perform tests to identify the cause of complement dysregulation including genetic screening and testing for the presence of autoantibodies (nephrotic factors and anti-FH autoantibodies. These tests would not be required to prescribe pegcetaplan but can be useful in determining the cause of disease and potentially the duration of treatment required. Pegcetacoplan should be considered as first-line treatment in patients with primary C3 glomerulopathy or immune complex MPGN where there is evidence of ongoing glomerular injury. The care pathway would be similar in adolescence and adults.	Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Treatment will be prescribed in secondary care with follow-up in secondary care. Consideration should be given to whether there needs to be specialist oversight of diagnosis and prescribing. The setting for prescribing and routine follow-up will be similar. The subgroups and outcomes listed in the scope are appropriate. Pegcetacoplan would be a candidate for a managed access programme. The main advantage will be the prevention of end-stage kidney disease which occurs in a substantial proportion (approximately 50% 10 years) patients with C3 glomerulopathy and immune complex MPGN. Data will be available from the phase 3 clinical trials. There was also data from the UK renal rare disease registry which documents the natural history of these diseases without complement inhibition. This state also occludes analysis of the importance in proteinuria in predicting long term outcome which was the primary endpoint of the phase 3 clinical trial.	Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed.
	Clinical expert	1. No practical differences in how C3G/IC-MPGN are diagnosed/treated they can be considered two points along the same disease spectrum 2. Relevant comparators seem fine 3. Budesonide – No Sparsentan Yes – some are enrolled in EPIK trial	Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		4. Yes – biopsy is required at outset but frequent biopsy not required in children just to assess Rx response this can be done with surrogate markers/serum C3/Complement products/eGFR and proteinuria 5. Given the rarity of the diagnosis, the known long term ineffectiveness of just anti-proteinuria therapies, I would position pegcetacoplan as first line with other supporting adjuncts to come in to 'mop up' residual proteinuria. 6. In the adult services, more investigation to rule out secondary C3G/Ic-MPGN would need to be done first and have those factors treated/removed 7. PEGCETACOPLAN would be prescribed and monitored in 2nd Care (Answer C) 8. Discussed further outcomes above 9. YES – Peg could be for managed access by the Newcastle C3G/aHUS service as for Eculiz 10. HRQOL data - no formal data collected on this to date but the reduction in CKD progression can infer some important QOL improvements and could be measured	
	Clinical expert	**In NHS practice, what are the main differences in how primary C3 glomerulopathy and IC-MPGN are treated?** No real difference – care is quite individualised with general immunosuppression, often with little success. **Are all relevant comparators included? Would pegcetacoplan be used alongside or instead of ACE inhibitors, ARBs, corticosteroids, mycophenolate mofetil, and SGLT inhibitors?**	Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Used alongside initially **Would budenoside or sparsentan ever be used as treatment for C3 glomerulopathy or IC-MPGN and if so, would they be considered a comparator or a concomitant treatment?** Not common practice at the moment **Does diagnosis of C3 glomerulopathy or IC-MPGN in order to be eligible for pegcetacoplan require biopsy or other diagnostic testing in people that would otherwise not have been tested?** Biopsy essential **Where do you consider pegcetacoplan will fit into the existing care pathway for C3 glomerulopathy and IC-MPGN?** Treatment in those with persistent heavy proteinuria (to be defined) and declining kidney function not controlled on ACE and corticosteroids. **Would the existing care pathway differ between people aged between 12 and 18 years and people over 18 years? If so, how?** I don't believe so **Please select from the following, will pegcetacoplan 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**	Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed. Thank you for your comment. No change to the scope needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		C. Prescribed in secondary care with routine follow-up in secondary care **D. Other (please give details):** Best given in tertiary care centres – specialist nephrology services **Are the subgroups listed appropriate?** Yes appropriate **Are the outcomes listed appropriate? Are there any further outcomes which should be considered?** Further outcomes – annual corticosteroid burden? **Would pegcetacoplan be a candidate for managed access?** Yes **Do you consider that the use of pegcetacoplan 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.** A well designed open-label RCT with crossover. This showed clear and unambiguous reduction in Proteinuria within 1 year. Awaiting further data on long-term outcomes. Shown to be safe in repeated trials.	Thank you for your comment. No change to the scope needed. Thank you for your comment. Adverse effects of corticosteroids will be captured under the 'adverse effects of treatment outcome'. No change to the scope needed. Thank you for your comment. No change to the scope needed.

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

- Novartis