National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Targeted-release budesonide for treating primary IgA nephropathy (review of TA937)

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Genus Pharmaceuticals Holdings Ltd	NICE recommended TRF-budesonide as an option for treating primary immunoglobulin A nephropathy (IgAN) when there is a risk of rapid disease progression in adults with a urine protein-to-creatinine ratio (UPCR) of 1.5 g/g or more in 2023 (1), however there remains a substantial unmet need for patients with IgAN and UPCR <1.5g/g who currently have no treatment options to address the underlying cause of IgAN and reduce the rate of kidney function loss. This topic is therefore considered important for evaluation. The proposed STA route is appropriate for this topic.	Thank you for your comment. No action required.
	UK Kidney Association (UKKA)	All appropriate	Thank you for your comment. No action required.
	UK Renal Pharmacy Group	The proposed route of single technology appraisal is appropriate in this case.	Thank you for your comment. No action required

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	Novartis Pharmaceuticals UK Limited	NA	No action required.
Wording	Genus Pharmaceuticals Holdings Ltd	No comments. The remit is appropriate for this topic.	Thank you for your comment. No action required.
	UK Kidney Association (UKKA)	Yes	Thank you for your comment. No action required
	UK Renal Pharmacy Group	Yes, there will be a need to consider the increase in the number of patients who will meet the requirements for treatment with the reduced target protein-to-creatinine ratio from 1.5 g/g to 0.8 g/g. The total cost of the drug will therefore increase; however, this should be compared with the number of patients who no longer decline in kidney function requiring haemodialysis.	Thank you for your comment. No action required
	Novartis Pharmaceuticals UK Limited	NA	No action required.
Timing Issues	Genus Pharmaceuticals Holdings Ltd	No timing issues identified.	Thank you for your comment. No action required.
	UK Kidney Association (UKKA)	Relatively urgent as unmet need in this patient population and risk of progression to kidney failure	Thank you for your comment. Comments noted. NICE has scheduled this topic into

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			its work programme. No action required.
	UK Renal Pharmacy Group	Given the target subgroup of patients is people at risk of rapidly progressive IgA nephropathy, the evaluation should be conducted as soon as possible in order to prevent the maximum number of patients' kidney function declining to require dialysis and/or transplantation.	Thank you for your comment. Comments noted. NICE has scheduled this topic into its work programme. No action required.
	Novartis Pharmaceuticals UK Limited	NA	No action required.
Additional comments on the draft remit	Genus Pharmaceuticals Holdings Ltd	Non	Thank you for your comment. No action required.
	UK Kidney Association (UKKA)	NA	No action required.
	UK Renal Pharmacy Group	NA	No action required.
	Novartis Pharmaceuticals UK Limited	NA	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Genus Pharmaceuticals Holdings Ltd	The following revisions are suggested for the background section to improve clarity: 1) Page 1 “A particularly severe form of the disease known as rapidly progressive IgA nephropathy has been reported in a small proportion of people” There are several references to ‘rapidly progressing IgA nephropathy’ throughout the draft scope document however it is not clear how this is being defined by NICE. Could a specific definition of rapidly progressing IgA nephropathy be provided along with an appropriate reference? Please note that draft KDIGO guidelines define patients with IgAN who are at risk of progressive loss of kidney function as those with proteinuria ≥0.5g/day (or equivalent) whilst on or off treatment (2). 2) Page 1 “Between 20% to 40% of people with IgA nephropathy develop kidney failure within 10 to 20 years of diagnosis, leading to end stage kidney disease in around 15% to 50% of people throughout their lifetime” We suggest that this wording is amended to align with data from the IgA nephrology cohort of the UK National Registry of Rare Kidney Diseases (RaDaR; 2023) which states the following: “The majority of patients in the UK progress to ESRD within 10–15 years of diagnosis and almost all patients are at risk of ESRD within their expected lifetime unless an eGFR rate loss ≤1 ml/min per 1.73 m^2 per year can be maintained from diagnosis (3)”. 3) Page 1 “Some people remain at high risk of progression despite optimised supportive care with lifestyle modifications and the maximum tolerated licensed doses of ACE inhibitors or ARBs”	Thank you for your comment and suggested changes. The background section has been updated to reflect the suggested changes.

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		Please see comment above in point 1) regarding the definition of high risk of progression throughout the draft scope. We would suggest amending the wording to align with the definition of patients at risk of progressive kidney function loss to align with the draft KDIGO guideline: “Some people are at risk of progressive loss of kidney function” 4) Page 1 “Second-line treatments are offered to people with more than 1 gram of proteinurea per day”. Draft KDIGO guidelines and other expert commentaries state that the goal of treatment for patients with IgAN who are at risk of progressive loss of kidney function (defined as proteinurea ≥0.5 g/day) should be to simultaneously prevent/reduce IgA immune complex formation and immune complex mediated glomerular injury and manage the consequences of existing IgAN-induced nephron loss (2, 4). The population in the anticipated licensed indication will include patients with [redacted]. The approach to treatment for the population of relevance to the scope should therefore include addressing the underlying immunological cause of IgAN as well as managing the consequences of CKD development (2, 4), and therefore such treatments would be considered as a simultaneous approach to treatment for this population rather than a second-line intervention. We believe that it is important to clarify the need to both address the underlying immunological cause of IgAN as well as managing the consequences of CKD, as this dual approach to managing the disease informs which treatments should be considered as part of standard of care and which are true comparators for TRF-budesonide. We suggest that the wording is updated to “People with more than 1 gram of proteinuria per day are offered treatments to prevent or reduce IgA complex formation and immune	

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		complex mediated glomerular injury and manage the consequences of existing IgAN-induced nephron loss (2, 4).”	
	UK Kidney Association (UKKA)	All accurate and complete	Thank you for your comment. No action required.
	UK Renal Pharmacy Group	Yes this information is both accurate and appropriate.	Thank you for your comment. No action required.
	Novartis Pharmaceuticals UK Limited	NA	No action required.
Population	Genus Pharmaceuticals Holdings Ltd	The population is defined appropriately.	Thank you for your comment. No action required.
	UK Kidney Association (UKKA)	Yes	Thank you for your comment. No action required.
	UK Renal Pharmacy Group	Yes, noted that protein-to-creatinine ration target has been reduced from > 1.5 g/g to > 0.8 g/g.	Thank you for your comment. No action required.

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	Novartis Pharmaceuticals UK Limited	NA	Thank you for your comment. No action required.
Subgroups	Genus Pharmaceuticals Holdings Ltd	The specified subgroup “people at risk of rapidly progressive IgA nephropathy” is not defined. Could a definition of this population please be provided? NICE have already recommended TRF-budesonide as an option for treating primary IgAN when there is a risk of rapid disease progression in adults with a urine protein-to-creatinine ratio of 1.5 g/g or more in TA937 (1). No other subgroups are considered relevant for this submission.	Thank you for your comment. The scope has been updated with to define the subgroup as per the population in TA937.
	UK Kidney Association (UKKA)	NA	No action required.
	UK Renal Pharmacy Group	The subgroup is appropriate but can be difficult to define ‘rapidly progressive’, therefore it should be reiterated that this treatment should be discussed with an expert local MDT prior to initiating.	Thank you for your comment. No action required.
	Novartis Pharmaceuticals UK Limited	NA	No action required.
Comparators	Genus Pharmaceuticals Holdings Ltd	The appropriate comparator for this submission is established clinical management without targeted-release budesonide, such as ACE inhibitors and ARBs at the maximum tolerated licensed doses, diuretics and dietary and lifestyle modification. The following treatments are not considered to be relevant comparators:	Thank you for your comment. The comparators listed in the scope has been updated to individually optimised standard care without targeted-

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		• Glucocorticoids: As stated in the background section of the draft scope (page 1), during the development of TA937, clinical experts explained that the use of glucocorticoids is rare or limited in UK clinical practice because of safety issues associated with their systemic use (1) • SGLT-2 inhibitors: as highlighted by clinicians in the development of TA937, and in KDGIO 2024 guidelines, SGLT-2 inhibitors are given to reduce kidney function loss and to address the cardiovascular risk associated with the condition, and may be used as part of SoC. SGLT-2 inhibitors do not represent an alternative to TRF-budesonide as they do not address the underlying immunological cause of IgAN (1, 2) • MMF: the committee concluded in TA937 that MMF is rarely used in UK clinical practice due to a lack of evidence and is not part of standard of care (1) • Cyclophosphamide is only recommended for people with rapidly deteriorating renal function (2); cyclophosphamide was excluded from the final scope of TA937 for this reason (5) Sparsentan is a dual endothelin-1 and angiotensin II receptor blocker. Sparsentan can be used to treat the generic response to IgAN induced nephron loss and it has been suggested by clinical experts that sparsentan may be an alternative to RASi (4). Sparsentan does not address the underlying immunological cause of IgAN and is therefore not an appropriate comparator for TRF-budesonide.	release budesonide. The company can propose to exclude comparators in its evidence submission. The most appropriate comparator will be discussed by the appraisal committee.
	UK Kidney Association (UKKA)	Yes	Thank you for your comment. No action required.
	UK Renal Pharmacy Group	The evidence from the NefIgArd study included patients who were on the maximally tolerated doses of ACE inhibitors and ARBs. I have not seen	Thank you for your comment. The

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		evidence comparing those on targeted-release budesonide with those on SGLT1 inhibitors, however we know from the DAPA-CKD study and EMPA-KIDNEY, that a large percentage of patients had IgA nephropathy and therefore that the SGLT2 inhibitors are effective at reducing proteinurea in these patients. Lowering the protein-to-creatinine ratio would allow for patients to be on maximally tolerated doses of ACE inhibitors/ARBs plus that of SGLT2 inhibitors and still be eligible for target-release budesonide to maximise their treatment and prevent decline in kidney function onto dialysis. Sparsentan NICE TA is still pending but should be included as the PROTECT trial has been published. No other comparators needed.	comparators listed in the scope has been updated individually optimised standard care without targeted-release budesonide. The company can propose to exclude comparators in its evidence submission. The most appropriate comparator will be discussed by the appraisal committee.
	Novartis Pharmaceuticals UK Limited	Cyclophosphamide and mycophenolate mofetil (MMF) do not represent UK standard of care for the treatment of IgA nephropathy and should be removed as comparators. According to the KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases, cyclophosphamide is not recommended in IgA nephropathy, unless in the setting of rapidly progressive disease. MMF is not recommended by the KDIGO 2021 guideline except for in Chinese patients; in non-Chinese patients there is insufficient evidence to support its use (Practice Point 2.3.1.5). The final scope of the initial NICE appraisal of targeted-release budesonide for treating IgA nephropathy [TA937] included neither of these treatments as comparators.	Thank you for your comment. The comparators listed has been amended to remove cyclophosphamide and mycophenolate mofetil (MMF). The company can propose to exclude comparators in its evidence submission. The most appropriate comparator will be discussed by the appraisal committee

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Outcomes	Genus Pharmaceuticals Holdings Ltd	Disease progression to dialysis/transplant and mortality have not been investigated in the TRF-budesonide clinical trial programme and are therefore not appropriate outcomes for this appraisal. All other outcomes listed in the draft scope are appropriate.	Thank you for your comment. The outcomes have been kept broad to allow committee to consider the relevant outcomes.
	UK Kidney Association (UKKA)	Yes	Thank you for your comment. No action required.
	UK Renal Pharmacy Group	The outcome measures are appropriate.	Thank you for your comment. No action required.
	Novartis Pharmaceuticals UK Limited	NA	Thank you for your comment. No action required.
Equality	Genus Pharmaceuticals Holdings Ltd	No comments.	Thank you for your comment. Comment noted. No action required.
	UK Kidney Association (UKKA)	Do not feel any changes are needed	Thank you for your comment. No action required.

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	UK Renal Pharmacy Group	ICB commissioning could lead to discrepancies between time to implementation and blueteq criteria between ICBs. Guidance for ICBs on criteria to include in the blueteq to be as simple as possible and using regional networks can reduce disparity.	Thank you for your comment. No action required.
	Novartis Pharmaceuticals UK Limited	NA	
Other considerations	Genus Pharmaceuticals Holdings Ltd	Page 2: The technology – could Targeted-release budesonide (Kinpeygo, Britannia Pharmaceuticals) please be updated to targeted-release budesonide (Kinpeygo, Genus Pharmaceuticals Holdings Ltd)	Thank you for your comment. The scope has been amended with the suggested wording.
	UK Kidney Association (UKKA)	NA	No action required.
	UK Renal Pharmacy Group	NA	No action required.
	Novartis Pharmaceuticals UK Limited	NA	No action required.
Questions for consultation	Genus Pharmaceuticals Holdings Ltd	NA	No action required.
	UK Kidney Association (UKKA)	Where do you consider targeted-release budesonide will fit into the existing care pathway for primary IgA nephropathy? C For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.	Thank you for your comments. No action required.

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		No difference Would targeted-release budesonide be a candidate for managed access? Yes Do you consider that the use of targeted-release budesonide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? No	
	UK Renal Pharmacy Group	Where do you consider target-release budesonide will fit into the existing care pathway for primary IgA nephropathy? C. Prescribed in secondary care with routine follow up in secondary care. High cost and highly specialist area of prescribing. Would targeted-release budesonide be a candidate for managed access? No Do you consider that the use of targeted-release budesonide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? I am not an expert in health economics but it should be considered whether the increased number of patients eligible for treatment will reduce the decline in kidney function dialysis and therefore save the system.	Thank you for your comments. No action required.
	Novartis Pharmaceuticals UK Limited	NA	No action required.

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Additional comments on the draft scope	Genus Pharmaceuticals Holdings Ltd	NA	No action required.
	UK Kidney Association (UKKA)	NA	No action required.
	UK Renal Pharmacy Group	NA	No action required.
	Novartis Pharmaceuticals UK Limited	NA	No action required.

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

Kidney Care UK