NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Tixagevimab–cilgavimab for preventing COVID-19 ID6136

Stakeholder comment form

Please use this form for submitting your comments on the draft remit, draft scope and provisional list of stakeholders. It is important that you complete and return this form even if you have no comments otherwise we may chase you for a response.

Enter the name of your organisation here: LUPUS UK

Comments on the draft remit and draft scope

The draft remit is the brief for an evaluation. Appendix B contains the draft remit. The draft scope, developed from the draft remit outlines the question that the evaluation would answer.

Please submit your comments on the draft remit and draft scope using the table below. **Please take note of any questions that have been highlighted in the draft scope itself** (usually found at the end of the document).

If you have been asked to comment on documents for more than one evaluation please use a separate comment form for each topic, even if the issues are similar.

Please complete this form and upload it to NICE Docs by **Friday 12 August 2022.** If using NICE docs is not possible please return via email to scopingta@nice.org.uk If you have any questions please contact Michelle Adhemar, Project Manager on 44 (0)20 7045 2239 or at the above email address.

If you do not have any comments to make on the draft remit and draft scope, please state this in the box below.

Comment 1: the draft remit and proposed evaluation route

Section	*Notes*	Your comments
Appropriateness of an evaluation and proposed evaluation route	*NICE welcomes comments on the appropriateness of evaluating this topic and the evaluation route proposed (single technology appraisal, multiple technology appraisal or highly specialised technology evaluation).*	It is urgent that people are able to access tixagevimab–cilgavimab at the earliest opportunity to provide protection against COVID-19 for the clinically extremely vulnerable. The evaluation should not delay access to the treatment for those who need it. Due to the ongoing urgency, if a Single Technology Appraisal is considered the most

Section	*Notes*	Your comments
		appropriate method of evaluation for this treatment, it should have an expedited timeline, similar to the current Multiple Technology Appraisal for COVID-19 therapeutics [ID4038].
Wording	*Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? If not, please suggest alternative wording.*	Yes
Timing Issues	*What is the relative urgency of this evaluation to the NHS?*	This evaluation is exceptionally urgent. The MHRA authorised tixagevimab–cilgavimab on 17/03/2022, yet it remains unavailable for people who remain clinically extremely vulnerable in the UK. There are many people who remain at an increased risk of serious illness from COVID-19 because of their underlying diseases and a lack of protection from vaccines. Despite this, most precautionary measures to limit the spread of infection have been removed, including in many healthcare settings. The number of COVID-19 cases remains very high, resulting in a strong likelihood of those at highest risk being exposed and contracting the virus. This is compounded by the significant problems many immunosuppressed people have experienced in accessing the community delivered post-exposure COVID-19 therapeutics. There have been reports of capacity issues experienced by the COVID-19 Medicines Delivery Units (CMDUs) with many patients facing delays until 6-7 days after testing positive for their assessment. This increases the urgency for a pre-exposure treatment to protect those most at risk. People who are immunosuppressed with underlying conditions are more likely to experience severe COVID-19 disease and require admission to hospital. It is in the interests of these people and the NHS to

Section	*Notes*	Your comments
		provide additional protection and reduce risk of severe illness and hospitalisation. Access to this treatment should not be delayed by this evaluation. Emergency interim authorisation, such as with the post-exposure COVID-19 therapeutics, should be awarded. The UK is approaching autumn/winter which is a time of significant additional pressure on the NHS. As more socialising takes place indoors, airborne viruses such as SARS-CoV-2 spread much more readily. With outdoor contact reduced, those who remain clinically vulnerable to COVID-19 face another period of greater isolation. Any evaluation of this treatment should be expedited to enable access prior to winter 2022/23.
Any additional comments on the draft remit		

Comment 2: the draft scope

Section	*Notes*	Your comments
Background information	*Consider the accuracy and completeness of this information.*	It states that 6 vaccines are authorised in the UK for preventing COVID-19 in adults. However, it should be noted that only 3 of these are currently available (see HERE). The Janssen, Novovax and Valneva vaccines are currently unavailable in the UK. Whilst it is noted that vaccination may be suitable for some people with a history of severe allergic reactions to ingredients in the vaccine, the appraisal should also consider people who are unable to complete their course of vaccination following a serious adverse reaction to a COVID-19 vaccine.
Population	*Is the population defined appropriately?*	The current definition does not adequately reflect the experiences and current circumstances of the people who would be eligible for treatment. Many remain at increased or high risk of severe disease from

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		COVID-19 infection whilst society has removed most precautionary measures to reduce the spread of the virus, including in many healthcare settings. There are many people who have been shielding since March 2020, limiting contact with people outside their household and potentially isolating from family who cannot shield with them. The health impacts of shielding during the first year of the pandemic have been well documented. These will likely be more pronounced in those continuing to take the additional precautions.
Subgroups	*Are there groups within the population that should be considered separately? For example, are there subgroups in which the technology is expected to be more clinically or cost effective? If subgroups have been suggested in the scope, are these appropriate?*	The first sub-group is very vague in its description. What parameters will be used to determine likelihood of mounting an immune response and what will be considered an 'adequate' response? Will this subgroup include all patient groups identified as belonging to the 'Highest-Risk Clinical Subgroups' from the Independent Advisory Group Report published on 30/05/2022? (**HERE**) The above subgroup includes people who have received anti-CD20 monoclonal antibody therapy (such as rituximab) in the last 12-months. It should be considered whether the time since last treatment should be increased. The B-cell depleting effects of these therapies can be significantly longer than 12-months and if this was used as an eligibility criterion it could leave some people at high risk from COVID-19. Will there be some form of spike-protein antibody test for people to determine whether they are more likely to benefit from the treatment? If there are concerns regarding the cost and available quantity of the treatment, it could help the NHS to prioritise those people with the weakest vaccine responses who are at highest risk. The current subgroup specifies that, to be eligible, the patient must be 'unlikely' to mount an adequate immune response; it does not specify that they have been proven to have

Section	*Notes*	Your comments
		an inadequate immune response. Evidence from clinical trials indicates that some immunosuppressive and biologic therapies are more likely to prevent someone from mounting an adequate response than others. B-cell depleting therapies such as rituximab appear to have one of the worst effects on vaccine immune response (**HERE**). There is clinical evidence of patients having no measurable vaccine response after three doses when treated with other immunosuppressive drugs too, including mycophenolate mofetil (**HERE**). There is also variance in immune response based on treatment protocol. An example is the inconsistent advice for people treated with methotrexate to pause their treatment around vaccination. The VROOM clinical trial showed that those who paused methotrexate after vaccination had more than twice as much antibody against spike-protein at four and twelve weeks after the vaccination compared to those who continued treatment (**HERE**). The timing of other treatments around vaccine doses will also impact how likely someone is to have mounted an adequate response. With regards to the subgroup of people for whom COVID-19 vaccination is not recommended, will this only include people with a known serious allergy to an ingredient in the vaccines? It is important that it also includes people who have experienced a serious adverse reaction to a COVID-19 vaccine dose and therefore are unable to complete their recommended course and get adequate protection.
Comparators	*Are the comparators listed considered to be the standard treatments currently used in the NHS with which the technology should be compared? Have all relevant comparators been included?*	Yes, this is complete and accurate.
Outcomes	*Are the outcomes listed appropriate? Will these*	It is unclear what will be considered under 'health-related quality of life'. An important

Section	*Notes*	Your comments
	outcome measures capture the most important health related benefits (and harms) of the technology?	outcome to consider is psychological impact of having some protection against COVID-19 for some people who may have been shielding since March 2020. These individuals have forgone social activities, travel and, in some cases, lived separately from family. As such, a comparison of many aspects of quality of life before and after the treatment is needed to measure potential improvements. The evaluation should consider the costs of post-exposure COVID-19 therapeutics if tixagevimab–cilgavimab is not administered. The population for this treatment will largely be eligible for community-delivered COVID-19 therapeutics such as sotrovimab if they contract the virus. Would these post-exposure treatments be required in someone successfully treated with tixagevimab–cilgavimab?
Equality	*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 draft remit and scope may need changing in order to meet these aims. In particular, please tell us if the draft remit and scope:* • *could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/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*	The method of delivering this treatment should be carefully considered, with patient choice/preference at the centre of any decisions. Many people eligible for this treatment may have been mostly shielding or taking additional precautions to minimise contact with people from outside their household since March 2020. This may result in significant anxiety about accessing the treatment in any busy community space, such as a vaccine centre. It should also be considered that some people from this clinically vulnerable group will have significant health and mobility problems caused by their underlying disease. It may be necessary for the treatment to be administered by a community nurse in these instances. Any roll-out of this treatment should be well-publicised, involving clinicians, patient organisations and community groups. Extra care should be taken to ensure that people from ethnic minority groups and those who are socially and economically disadvantaged have appropriately targeted campaigns to

Section	*Notes*	Your comments
	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.*	avoid inequitable uptake of the treatment.
Other considerations	*Suggestions for additional issues to be covered by the evaluation are welcome.*	It should be carefully considered how the treatment should be offered and how eligible patients will be identified. There are inconsistencies in patient records held by primary care and secondary care. Many immunosuppressant treatments are prescribed by secondary care, meaning that GPs may not have up-to-date records for the patients on their register. This has been observed during the issuing of shielding guidance and priority vaccine invitations during the pandemic. Immunosuppressed patients have experienced significant challenges in accessing previous vaccine rollouts from primary care, particularly the third primary dose rollout in autumn 2021. Many patients did not receive invitations despite being eligible and were frequently met with disbelief and dismissal when they requested the dose from their GP. For a successful rollout, there should be an opportunity for patients to self-refer for tixagevimab–cilgavimab and then be screened by clinicians. The government has stated on several occasions that the provision of tixagevimab–cilgavimab was delayed due to a lack of evidence about the efficacy of the treatment against emerging variants of SARS-CoV-2. Subsequent clinical studies have found reasonable levels of protection in the BA.4 and BA.5 Omicron variants which are currently dominant. There have been significantly higher levels of scrutiny over the

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		efficacy of tixagevimab–cilgavimab than the COVID-19 vaccines and post-exposure therapeutics for this patient group. Even a relatively low level of protection could be better than having no protection for those who are clinically extremely vulnerable. Any recommendation for the treatment will need to consider re-dosing. Tixagevimab–cilgavimab is administered every six months after the initial dose. Accurate record keeping will be needed so that patients are invited for repeat doses at the appropriate time.
Questions for consultation	*Please answer any of the questions for consultation if not covered in the above sections.*	***Where do you consider tixagevimab–cilgavimab will fit into the pathway for preventing COVID-19?*** People who are eligible for tixagevimab–cilgavimab should be identified and invited for the treatment urgently. As a preventative prophylactic, it should be administered to eligible people at the earliest opportunity to provide protection before exposure to SARS-CoV-2. Eligibility for the treatment should be regardless of vaccination status or spike-protein antibody seropositivity. ***Do you consider that the use of tixagevimab–cilgavimab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?*** The QALY calculation is unlikely to capture the full social benefit of providing someone with protection from COVID-19 and enabling them to have fewer risks from participating in society again. These effects will not only be felt by the patient but also their family, friends, employer and work colleagues. There are significant health costs associated with shielding from COVID-19, but there are also significant economic costs for the patient and wider society.

Section	*Notes*	Your comments
Any additional comments on the draft scope None.		

Comment 3: provisional stakeholder list

The provisional stakeholder list (Appendix C) is a list of organisations that we have identified as being appropriate to participate in this evaluation. If you have any comments on this list, please submit them in the box below.

NICE is committed to promoting equality and eliminating unlawful discrimination. Please let us know if we have missed any important organisations from the list, and which organisations we should include that have a particular focus on relevant equality issues.

If you do not have any comments to make on the provisional stakeholder list of consultees and commentators, please cross this box: ☒

Comments on the provisional stakeholder list

Comment 4: regulatory issues (to be completed by the company that markets the technology)

Section	*Notes*	Your comments
Remit	*Does the wording of the remit reflect the current or proposed marketing authorisation? If not, please suggest alternative wording.*	
Current or proposed marketing authorisation	*What are the current indications for the technology?*	
	What are the planned indications for the technology?	
	FOR EACH PLANNED INDICATION:	
	Which regulatory process are you following?	

Section	*Notes*	Your comments
	What is the target date (mm/yyyy) for regulatory submission?	
	What is the anticipated date (mm/yyyy) of CHMP positive opinion (if applicable)?	
	What is the anticipated date (mm/yyyy) of EU regulatory approval?	
	What is the anticipated date (mm/yyyy) of UK regulatory approval if different to Europe?	
	What is the anticipated date (mm/yyyy) of UK launch?	
	Please indicate whether the information you provide concerning the proposed marketing authorisation is in the public domain and if not when it can be released. All commercial in confidence information must be highlighted and underlined.	
Economic model software	*NICE accepts executable economic models using standard software, that is, Excel, DATA, R or WinBUGs. Please indicate which software will be used. If you plan to submit a model in a non-standard package, NICE, in association with the EAG, will investigate whether the requested software is acceptable, and establish if you need to provide NICE and the EAG with temporary licences for the non – standard software for the duration of the evaluation. NICE reserves the right to reject economic models in*	

Section	*Notes*	Your comments
	non-standard software	

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