National Institute for Health and Care Excellence

Health Technology Evaluation

Tixagevimab–cilgavimab for preventing COVID-19 [ID6136]
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	AstraZeneca	AstraZeneca agrees that the timely evaluation of Evusheld is appropriate and that guidance should be issued as soon as possible to support with the protection of high risk patients due to COVID-19. We also agree that the STA route is the most appropriate route for this technology and indication.	Comment noted. No action needed.
	Multiple Sclerosis Trust	Yes, the MS Trust does consider that a single technology appraisal of Evusheld is appropriate.	Comment noted. No action needed.
	Cardiomyopathy UK	We feel that this evaluation route is not appropriate for this specific preventative treatment. Single Technology Appraisals take months to complete for example the recent Mavacamten appraisal we are working on was launched in July 2021 and is due to publish in March 2023. We feel that there should be an expedited process of appropriateness and evaluation. The vaccines and anti-virals against COVID-19 and its variants were approved via a different mechanism and we believe that this preventative technology should be appraised in a similar way.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

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	CLL (Chronic Lymphocytic Leukaemia) Support	This is an important and timely evaluation and a Single TA is appropriate but it needs to be expedited as a matter of extreme urgency. Although post exposure anti viral treatments are available many CLL patients cannot take them because of interactions with their anti leukaemia medication. Many CLL patients, because of their leukaemia and also the treatments they are receiving, do not mount an immune response to vaccinations. Some CLL Patients have received 5 doses with no effect. Despite vaccination and anti-virals, the blood cancer paient group continues to be at higher risk of hospital admission and dying from Covid and requires urgent protection.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Immunodeficiency UK	STA is appropriate but this needs to make rapid progress since we will soon be entering the winter season of respiratory illness.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	National Rheumatoid Arthritis Society (NRAS)	NRAS agrees that this is an appropriate topic for evaluation and that the STA is the right route.	Comment noted. No action needed.
	Evusheld for the UK	We believe, for reasons of urgency, that the usual timescales of the Single Technology Appraisal track are inappropriate. This track may be appropriate for the long-term deployment of tixagevimab–cilgavimab for preventing	Comment noted. Following referral to NICE an appraisal of

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		COVID-19, but it must be in conjunction with an interim authorisation. The context in which we are operating is one of rapid change and we require flexibility to protect our patient body, as we have seen with vaccines and anti-virals.	tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	National Kidney Federation	The usual timescales of the Single Technology Appraisal are inappropriate, this should be through a rapid guideline consultation in the first instance, like other rapid COVID-19 guidelines produced.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Blood Cancer UK	Blood Cancer UK welcomes the evaluation of tixagevimab and cilgavimab (hereby referred to as 'Evusheld') along the single technology appraisal route, while also noting that the appraisal should be conducted with urgency and recommendations generated as soon as possible.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Kidney Research UK	Kidney Research UK welcomes the long-awaited appraisal of tixagevimab-cilgavimab which has had marketing authorisation since March 2022 and is already in use in at least 25 other countries. This treatment is potentially indicated as prophylaxis for those who are unlikely to mount an adequate immune response to COVID-19 vaccination or	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-

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		for whom COVID-19 vaccination is not recommended and could therefore be viewed as having some equivalence with vaccines for those who cannot rely on vaccination to prevent the serious consequences of COVID-19. Vaccinations are not subject to NICE appraisals but instead are evaluated by the JCVI (https://researchbriefings.files.parliament.uk/documents/CBP-9076/CBP-9076.pdf). The Pfizer vaccine received MHRA temporary authorisation on 2 December 2020 and the JCVI recommended its use on 31 December 2020 with the rapid roll-out for the most vulnerable beginning in early January 2021, only 1 month after market authorisation. Whilst this path is not currently open to monoclonal antibodies, the urgency is comparable for those not protected from COVID-19 by vaccination. The NICE process or other approval should be expedited in whatever way possible to recognise the urgency of the need for treatment in this population. Other urgent Covid medications have been given expedited approval routes. We believe tixagevimab–cilgavimab should be afforded the same urgency given the ongoing disproportionate impact of Covid on immunocompromised patients, including significant mortality. This could be addressed by exceptional use authorisation being granted to tixagevimab–cilgavimab while NICE conducts its appraisal. We appreciate this doesn't fall within NICE's remit but wanted to highlight it as a possible way forward. This winter is anticipated to be extremely challenging for the NHS and we believe it is in the best interests of patients and the health system that tixagevimab–cilgavimab is made available as a matter of urgency.	19 has been scheduled into the NICE work programme as a priority. Access to medicines through exceptional authorisation is outside the remit of NICE's Technology Appraisal process.
	Kidney Care UK	It is difficult to overstate the importance of access to effective preventative treatments to people who remain at high risk from Covid-19, despite vaccination (OpenSafely data on ongoing risk, currently in preprint). The STA of Evusheld is therefore extremely welcome. However, given the promising existing data for Evusheld (eg Kertes et al, 2022), we would recommend that the drug is made available to high-risk patients in the UK while the appraisal	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled

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		is being conducted to reduce the risk of hospitalisation and mortality. This would also support people at high risk to resume something more like a normal way of life, which many have been denied for so long. We note the Covid therapeutics were made available for people in the community, before a NICE appraisal, and it is not clear why a similar process was not followed with Evusheld? REF: Kertes, Jennifer, Shirley Shapiro Ben David, Noya Engel-Zohar, Keren Rosen, Beatriz Hemo, Avner Kantor, Limor Adler, Naama Shamir Stein, Miri Mizrahi Reuveni, and Arnon Shahar. 'Association between AZD7442 (Tixagevimab-Cilgavimab) Administration and SARS-CoV-2 Infection, Hospitalization and Mortality'. Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America, 29 July 2022, ciac625.	into the NICE work programme as a priority. Access to medicines through exceptional authorisation is outside the remit of NICE's Technology Appraisal process.
	LUPUS UK	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 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].	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Myeloma UK	We note that this treatment has been allocated to the single technology appraisal process which takes many months to complete, when other COVID treatments have been given expedited approval routes. We believe there is a strong case for this appraisal to be fast tracked given the huge impact which lack of certainty around vaccine effectiveness has on the patient population.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work

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		We recommend that consultees and commentators be informed about expected timelines for this appraisal with a view to speeding up the decision making process. We know that many myeloma patients are continuing to shield to protect themselves from COVID infection, despite receiving the maximum number of vaccinations offered, and that as a result their quality of life is significantly reduced. The authorisation of this technology would help to protect myeloma patients who have not responded well to COVID vaccines and therefore continue to be at risk from COVID infection.	programme as a priority.
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	The evaluation is appropriate but would like to be assured that the STA does not slow down the process of giving access to patients.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Anthony Nolan	Tixagevimab–cilgavimab (Evusheld) is a combination therapy of two neutralizing antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is appropriate for this technology to be evaluated by NICE, using the fastest possible evaluation route. This technology can offer support to patients who have not developed an adequate immune response following vaccination or are considered unsuitable for vaccination.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

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		Without alternative forms of protection, such as prophylactic monoclonal-antibody combination therapies, patients are left unprotected within the community. The status quo poses serious risk factors for most living arrangements; within a family unit, housing of multiple occupancy and single occupancy where the person is self-reliant. Patients are potentially otherwise left at risk to a novel coronavirus, and its latest variants, through any social contact points. This is highly disruptive and distressing to their employment/education, family life and even limited socialising, carrying with it the associated mental health impacts. Results from a Phase III Double-blind, Placebo-controlled Study (PROVENT) of AZD7442 (now Tixagevimab–cilgavimab) have demonstrated that a single dose of AZD7442 had efficacy for the prevention of COVID-19, without evident safety concerns.	
	UK CLL Forum	This is a timely proposal that needs to be fully evaluated and is appropriate. The planned evaluation route of single technology appraisal is also appropriate.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Action for Pulmonary Fibrosis	STA is appropriate but we would urge NICE to launch a rapid appraisal. This population has mostly been shielding in their homes for the last two years. Tixagevimab–cilgavimab is a potential game-changer which could help these people to return to a more 'normal life'. This population currently feels a great sense of injustice when they see people who mount an adequate response to COVID-19 vaccination able to act 'normally. Als, when they look at people in	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled

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		the USA, Isreal, France Italy and many other countries who have been given Tixagevimab–cilgavimab for months.	into the NICE work programme as a priority.
	Polycystic Kidney Disease Charity	We welcome the evaluation of this topic and the single technology appraisal route proposed	Comment noted. No action needed.
	Leukaemia Care	This NICE evaluation of this topic is highly anticipated by the patient communities it could benefit. We therefore strongly welcome the appraisal and believe NICE's consideration of this treatment to be a matter of urgency. Many of the patients who we support are immunocompromised, meaning that for many the vaccines were unable to provide a full protection from severe illness of COVID-19 should they contract the virus. As such, many immunocompromised patients feel trapped, left behind and continue to shield or take additional precautions which negatively affect their quality of life. For many the prospect of having a preventative treatment for COVID-19 would finally allow them to return to a level of normality that they have not been able to since the start of the pandemic. Additionally, there is benefit to the NHS for this treatment to be considered by NICE. Reduced COVID-19 cases in the vulnerable would relieve the operational and cost burden of delivering antiviral treatments in the same quantity and would mean patients are less likely to require hospital care for COVID-19 adverse symptoms. This is especially relevant now given ongoing capacity issues the NHS is facing.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
Wording	AstraZeneca	Yes	No action needed.
	Multiple Sclerosis Trust	Yes, overall. The main issue which has limited NHS implementation of Evusheld is its unknown effectiveness against the prevalent variants of Covid. The dominant variants will continue to change, so it would be appropriate to amend the wording to reflect this concern.	Comment noted. This will be considered during the appraisal.

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	Cardiomyopathy UK	Yes	No action needed.
	CLL (Chronic Lymphocytic Leukaemia) Support	Yes	No action needed.
	Immunodeficiency UK	See points below.	No action needed.
	National Rheumatoid Arthritis Society (NRAS)	Yes	No action needed.
	Evusheld for the UK	Yes	No action needed.
	National Kidney Federation	Yes	No action needed.
	Blood Cancer UK	Yes	No action needed.
	Kidney Research UK	To appraise the clinical and cost effectiveness of tixagevimab and cilgavimab within its marketing authorisation for preventing COVID-19 and adverse outcomes of COVID-19	Comment noted. The remit of the scope is aligned with the marketing authorisation. Adverse outcomes of COVID-19 will be captured in the

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			outcomes included in the economic analysis.
	Kidney Care UK	Yes	No action needed.
	LUPUS UK	Yes	No action needed.
	Myeloma UK	Myeloma UK considers the remit to reflect the issues of clinical and cost effectiveness.	No action needed.
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	There is no mention of the measurement of antibodies or more frequent testing with LFTs required. The cost of treating this patient group – if they get infected currently should include CMDU costs. Effectiveness may need to take into account the likelihood of waves of different variants.	Comment noted. Relevant costs will be included in the economic analysis and costs will be considered from an NHS and Personal Social Services perspective. Comment noted. This will be discussed during the appraisal.
	Anthony Nolan	The remit references the marketing authorisation of Tixagevimab–cilgavimab as a combination therapy. For absolute clarity within the remit itself, it might be helpful to state that its authorisation is for pre-exposure prophylaxis. Also, to state that it is for immunocompromised people who do not possess an adequate immune response to COVID-19.	Comment noted. The remit has been updated to clarify pre-exposure prophylaxis.

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	UK CLL Forum	Yes, the remit includes reference to identified at risk groups. Mortality rates and hospitalisation rates have changed since the PROVENT study was carried out and groups continuing to be at risk currently need to be considered. It isn't clear from the scope what defines an inadequate response to vaccination- is this the presence of an antibody response/titre?	Comment noted. NICE can only make recommendations for tixagevimab–cilgavimab within its marketing authorisation. The definition of the population (those with an inadequate response to vaccination) will be explored throughout the appraisal.
	Action for Pulmonary Fibrosis	No comment	No action needed.
	Polycystic Kidney Disease Charity	Yes	No action needed.
	Leukaemia Care	Yes	No action needed.
Timing issues	AstraZeneca	There is an estimated 1.3 million people in the UK who are immunocompromised and amount an insufficient immune response to COVID-19 vaccination and are therefore at a high risk of adverse clinical outcomes due to COVID-19. Currently, there are no pre-exposure prophylaxis treatments currently commissioned by the NHS despite the MHRA granting a licence for Evusheld since March 2022.[1] There is therefore an urgent need to evaluate the cost-effectiveness of Evusheld to enable for the routine commissioning by the NHS and to enable the protection of patients who are	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work

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		most at risk of severe adverse clinical outcomes due to COVID-19. This urgency was further highlighted by a clinical consensus statement published in July 2022 by over 120 clinicians representing 17 different clinical specialities from across all 4 devolved nations which stated that pre-exposure prophylaxis would have clinical benefit to people who are immunocompromised, and that a protective antibody treatment programme should be delivered as soon as possible.[2] 1. *Medicines and Healthcare products regulatory agency. Evusheld approved to prevent COVID-19 in people whose immune response is poor. https://www.gov.uk/government/news/evusheld-approved-to-prevent-covid-19-in-people-whose-immune-response-is-poor (2022).,.* 2. *All-Party Parliamentary Group on Vulnerable Groups to Pandemics. July 2022. National Clinical Expert Consensus Statement. Coronavirus monoclonal antibodies as a prophylactic therapy against COVID-19 for immunocompromised groups.,.*	programme as a priority.
	Multiple Sclerosis Trust	The MS Trust considers this to be an urgent evaluation as there are currently no preventative options for people who are unable to be treated with the Covid vaccine or who do not mount an adequate antibody response. We know that this is a cause for concern for affected patients. A further peak of Covid infections is anticipated for winter 2022/23 so it would be appropriate to ensure that this appraisal has been completed in a timely manner.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Cardiomyopathy UK	Patients with heart transplants are still having to shield due to the prevalence of COVID19 in society. For this subset of the population and others who have had transplants and are immunosupressed there is an urgency to appraising the use of Tixagevimab–cilgavimab for preventing COVID-19. We	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab

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		believe there is a need for an expedited approach as we are heading into winter, the NHS is already overburdened and vulnerable people who have not been able to develop a immunity to COVID19 have already been shielding for over 2 years. We need to act quickly to give them the quality of life they deserve. Evidence shows that shielding has a negative impact on mental health ((Rettie & Daniels 2022) with those in the clinically vulnerable groups being affected more significantly than those in the general population. The Mental Health Impact of the COVID-19 Pandemic Second Wave on Shielders and their Family Members — the University of Bath's research portal A recent survey of over 550 cardiomyopathy patients showed that 50% of people had struggled to cope emotionally over the last 12 months with 33% reporting loneliness as an issue. A quote from a heart transplant patient “My wife and I go out only if I have to, I wear a mask at all times, I do not go into shops or restaurants or public spaces. I do not use public transport – I am not the only heart transplant patient living this life if you can call it that”.	for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	CLL (Chronic Lymphocytic Leukaemia) Support	It is extremely urgent that this treatment is approved as soon as possible for patients that cannot respond to vaccination. COVID is likely to surge again in the winter and put the NHS under intense pressure, with many of the patients occupying ICU beds being haematology patients who have no immunity to covid despite as many as 5 vaccinations. Access to NHS healthcare is patchy and fragmented for many of the blood cancer patients and this treatment would provide an important safety net.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

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		The efficacy of tixagevimab–cilgavimab in reducing hospitalization is evidenced by Kertes et al 2022 (92% in a recent real-world Phase Four observational study.	
	Immunodeficiency UK	There is an urgent need to protect those people with primary and secondary immunodeficiency who are unable to mount an adequate COVID-19 vaccine response against COVID-19 infection. A significant proportion of this group may have lung disease or other co-morbidities which compromises their prognosis already. The health needs of this group in terms of alternative protective strategies have been neglected and a significant number of people remain effectively shielding with detrimental consequences to mental health, quality of life and livelihoods. The start of a winter season of potentially high case rates of COVID-19 necessitates swift decision making. Indeed, the time gap between MHRA approval for this technology (March 2022) and the start of this appraisal is both disappointing and lamentable. This is underlined by the fact that many other countries have already made this therapy available to immunocompromised patient groups. While society has slowly shifted back to normal recently, there are currently no preventative measures in place to protect people who are immunocompromised from contracting the virus. People with immunodeficiency have basically been told just to get on with their life. At the same time, recent data from the CO-VAD study indicates that inpatient mortality has remained high (19% for PID, 42.8% for SID) suggesting if you are sick enough to end up in hospital then that is a poor prognostic sign. There is a need for a long-term strategy to safeguard and protect immunocompromised people and making this therapy available is a vital element of that.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

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	National Rheumatoid Arthritis Society (NRAS)	This potential STA is urgent as COVID infections remain high and for certain people who have compromised/suppressed immune systems, this drug could be life-saving.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Evusheld for the UK	This evaluation is of extreme relative urgency and the usual timescales are inappropriate given the rapidly evolving viral situation. We are about to head into a winter covid season in which the immunocompromised will consume much NHS bed space if hospitalized. Given the demonstrated efficacy of tixagevimab–cilgavimab in reducing hospitalization (92% in a recent real-world Phase Four observational study (Kertes et al., 2022) and extremely promising results in France (Nyguen et al., 2022), it is urgent that this therapy be approved in good time for the winter season. We suggest that an emergency interim authorization would be appropriate given the urgency. For more see: ● Kertes, Jennifer, Shirley Shapiro Ben David, Noya Engel-Zohar, Keren Rosen, Beatriz Hemo, Avner Kantor, Limor Adler, Naama Shamir Stein, Miri Mizrahi Reuveni, and Arnon Shahar. 'Association between AZD7442 (Tixagevimab-Cilgavimab) Administration and SARS-CoV-2 Infection, Hospitalization and Mortality'. Clinical Infectious Diseases: An Official	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority. Access to medicines through interim commissioning arrangements is outside the remit of NICE's Technology Appraisal process.

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		Publication of the Infectious Diseases Society of America, 29 July 2022, ciac625. ● Nguyen, Yann, Adrien Flahault, Nathalie Chavarot, Cléa Melenotte, Morgane Cheminant, Paul Deschamps, Nicolas Carlier, et al. 'Pre-Exposure Prophylaxis with Tixagevimab and Cilgavimab (Evusheld©) for COVID-19 among 1112 Severely Immunocompromised Patients'. Clinical Microbiology and Infection: The Official Publication of the European Society of Clinical Microbiology and Infectious Diseases, 1 August 2022, S1198-743X(22)00383-4. There is also evidence to suggest that length of time shielding/in quarantine is associated with poorer mental health (Brooks et al. 2020); rates of mental health in the clinically vulnerable group are already significantly higher than the general population (Rettie & Daniels, 2020; Daniels & Rettie, 2022) Length of time shielding during COVID-19 has been associated with poorer mental health (Daniels & Rettie, 2022), with reported increased rates of mental health difficulties over time when comparing two samples (Rettie & Daniels, 2020; Daniels & Rettie, 2022). These data indicate a more urgent response is required; we should expect to see deterioration in mental health in those shielding equivalent to time spent indoors - there are ethical implications for witholding or delaying potential life-saving treatment, particularly as during this time those clinically vulnerable may contract COVID-19. Brooks, S. K., Webster, R. K., Smith, L. E., Woodland, L., Wessely, S., Greenberg, N., & Rubin, G. J. (2020). The psychological impact of quarantine and how to reduce it: rapid review of the evidence. The lancet, 395(10227), 912-920.	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact will also be captured in the outcomes included in the economic analysis.

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		Rettie, H., & Daniels, J. (2021). Coping and tolerance of uncertainty: Predictors and mediators of mental health during the COVID-19 pandemic. American Psychologist, 76(3), 427. Daniels, J., & Rettie, H. (2022). The Mental Health Impact of the COVID-19 Pandemic Second Wave on Shielders and Their Family Members. International Journal of Environmental Research and Public Health, 19(12), 7333.	
	National Kidney Federation	Very urgent considering the rapid viral changes that are currently happening. Winter is fast approaching with COVID cases likely to escalate considerably, bed space is already at capacity within the NHS, added burden of clinically vulnerable patients taking up bed space should not be added to NHS pressures. Our patients have been constantly telling us that they are suffering with their mental health due to feeling the need to still shield after two years. Therefore delaying the administration of this potential life saving treatment should not happen.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Blood Cancer UK	We strongly recommend that this evaluation is fast-tracked. Evusheld was approved by the MHRA on 17 March 2022 but has yet to be procured and made available to patients. There are currently no prophylactic treatments for Covid-19 available to those who are less likely to mount an adequate immune response from the Covid vaccines. NICE's evaluation of Evusheld and ensuing recommendations are therefore vital to ensuring that those who remain at very high risk are protected. Those with weakened immune systems are more likely to be hospitalised and/or to die from Covid-19. Until prophylaxis is available, those with weakened immune systems must rely on post-exposure treatment and/or shield themselves from public life. Post-exposure treatments must be administered within a very short window of time from symptom onset, which has led to concerns about equity of access, and Paxlovid is contraindicated by a considerable number of treatments	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

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		commonly administered to people with blood cancer. Without a robust post-exposure treatment programme, people with blood cancer require an effective and accessible option for prophylaxis.	
	Kidney Research UK	As described above, this evaluation is extremely urgent and long overdue. Kidney patients, particularly those who are immunosuppressed, either to manage their disease or due to kidney and other solid organ transplants, have been shown to be particularly vulnerable to COVID-19. A cohort study from the OpenSAFELY Collaborative (doi: https://doi.org/10.1101/2021.11.08.21265380) showed that after two vaccinations kidney patients, particularly those on renal replacement therapy and with transplants, along with other immunocompromised individuals, were at increased risk of hospitalisation and death from COVID-19 than the general population. Further new data (August 2022) from the OpenSAFELY Collaborative (doi: https://doi.org/10.1101/2022.07.30.22278161) showed the relative hazard of death due to COVID-19 had increased for kidney transplant patients from 7.37 (relative to the general population) in the first COVID-19 wave to 26 in the third wave (May to December 2021). We know from a plethora of evidence including from the OCTAVE study (doi: 10.1016/S0140-6736(21)02096-1) that kidney transplant recipients have attenuated responses to vaccines and remain at risk daily along with other immunocompromised individuals. The removal of protective behaviours (masks, social distancing, self-isolating etc) for the general public only exacerbates the situation for the immunocompromised who remain at risk of serious consequences from COVID-19 infection and have to lead diminished lives.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Kidney Care UK	It is of extreme urgency that this evaluation is completed as soon as possible. People at highest risk from Covid have been waiting since the treatment was licensed in March 2022 to find out whether it will become available in the UK as it is in over 20 other countries. As highlighted, new OpenSafely data (currently in preprint) shows that while death rates have fallen substantially across many groups, “There was also only a small decrease in death rates	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-

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		between waves in people with kidney disease, haematological malignancies or conditions associated with immunosuppression". Therefore, new protection strategies for these high-risk groups are critical. Since March 2022, Government have said they are evaluating Evusheld, but no further information on progress has been given leading to considerable frustration. After two years of shielding and living very restricted lives, the prospect of a protective treatment is extremely significant and we urge decisions are made without further delay.	19 has been scheduled into the NICE work programme as a priority.
	LUPUS UK	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 provide additional protection and reduce risk of severe illness and hospitalisation.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority. Access to medicines through exceptional authorisation is outside the remit of NICE's Technology Appraisal process.

Section	Stakeholder	Comments [sic]	Action
		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.	
	Myeloma UK	Highly urgent. Many myeloma patients and their families are continuing to shield to protect themselves from COVID infection, despite evidence of good vaccine uptake and effectiveness. This is having a significant impact on their quality of life. From unpublished data (June 2022) we know that 92% of myeloma patients in England have received at least one vaccine dose, 89% have received 2 or more doses, 78% have received 3 or more doses and 47% have received 4 or more doses. While a separate study has shown that 2 doses of COVID-19 vaccine are effective in producing antibodies in over 90% of myeloma patients, we also know that there is a considerable waning of vaccine effectiveness in cancer patients compared to the general population. One study showed that in myeloma patients overall vaccine effectiveness from 2 doses reduced from 77.5% to 63.9% after 3-6 months in myeloma patients.[1] This reinforces the need for additional pharmacological strategies to reduce the risk of COVID-19 to myeloma patients. The scientific rationale for this prophylactic treatment in immunocompromised patients has been collected by the PROVENT study.[2] It showed that tixagevimab–cilgavimab reduced the risk of developing symptomatic COVID-19 by 76.7%, with protection from the virus continuing for at least six months.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

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Section	Stakeholder	Comments [sic]	Action
		A real-world evaluation[3] replicated this result showing that patients who received the prophylactic treatment had lower incidence of SARS-CoV-2 infection, COVID-19 hospitalisation and all-cause mortality. There is also supporting non-clinical trial data that demonstrates the effectiveness of tixagevimab–cilgavimab in immunocompromised patients. One study shows that an increased dose of the prophylactic treatment had neutralising activity against the Omicron variant in blood cancer patients (including 8 with myeloma).[4] Another study demonstrates evidence of prophylaxis benefit, reporting a low rate of COVID-19 infections and severe illnesses in immunocompromised patients treated with tixagevimab–cilgavimab.[5] The lack of certainty about vaccine effectiveness in immunocompromised patients continues to have a significant negative impact on the lives of patients and their family and friends. As we move to winter with pressures on the NHS increasing and concern about any potential new COVID wave it becomes even more imperative to have a strategy in place to keep patients well and minimise burden on the service. A decision on the part to be played by this preventative treatment in the strategy must therefore happen at pace. [1] Lee L, Starkey T, Ionescu M, et al. (2022) Vaccine effectiveness against COVID-19 breakthrough infections in patients with cancer (UKCCEP): a population-based test-negative case-control study. Lancet Oncol. doi:10.1016/S1470-2045(22)00202-9. [2] Levin, M.J. et al. Intramuscular AZD7442 (Tixagevimab-Cilgavimab) for Prevention of Covid-19. N. Engl. J. Med. 386, 2188-2200 (2022). [3] Young-Xu, Y. et al. Tixagevimab/Cilgavimab for Prevention of COVID-19 during the Omicron Surge: Retrospective Analysis of National VA Electronic	

Section	Stakeholder	Comments [sic]	Action
		Data. 2022.05.28.22275716 Preprint at https://doi.org/10.1101/2022.05.28.22275716 (2022) [4] Stuver R, Shah GL et al. Activity of AZD7442 (tixagevimab-cilgavimab) against Omicron SARS-CoV-2 in patients with hematologic malignancies. Cancer Cell. 2022 Jun 13;40(6):590-591. [5] Nguyen Y, Flahault A et al. Pre-exposure prophylaxis with tixagevimab and cilgavimab (Evusheld©) for COVID-19 among 1112 severely immunocompromised patients. Clin Microbiol Infect. 2022 Aug 1:S1198-743X(22)00383-4.	
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	This assessment is regarded as very urgent as it is currently denying access to patients who really need this treatment.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Anthony Nolan	Tixagevimab–cilgavimab received MHRA authorisation to be used before being exposed to the risk of COVID-19 infection in order to prevent disease on 17 March 2022[1]. 148 days later and this technology is still yet to be introduced to clinic. To date, this process has been noticeably slower when compared to other COVID-19 therapeutics that have been fast-tracked to clinic. On 12 August, DHSC issued a statement confirming that the UK Government “will not be procuring any doses at this time”. Without any further fast-tracking within the NICE process, we cannot expect a definitive outcome before April 2023. Given that the World Health	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

Section	Stakeholder	Comments [sic]	Action
		Organisation has forecasted a winter surge in COVID-19 transmission for the European Region in 2022[2], any interim period without access to a pre-exposure prophylaxis puts immunocompromised patients in an intolerable position. It is imperative that NICE and DHSC proactively engage with the pharmaceutical manufacturing company and set a clear and rapid timeline for any further discovery processes and a route to clinic. Immunocompromised patients need timely access to Tixagevimab–cilgavimab, to coincide with the upcoming Autumn booster campaign which is anticipated to begin by the end of September. [1] – MHRA Regulatory approval of Evusheld (tixagevimab/cilgavimab), 17 March 2022 - www.gov.uk/government/publications/regulatory-approval-of-evusheld-tixagevimabcilgavimab [2] – WHO Statement on Europe COVID-19 Strategy, 19 July 2022 - www.who.int/europe/news/item/19-07-2022-rapidly-escalating-covid-19-cases-amid-reduced-virus-surveillance-forecasts-a-challenging-autumn-and-winter-in-the-who-european-region	
	UK CLL Forum	Important to review before the next winter period.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

Section	Stakeholder	Comments [sic]	Action
	Action for Pulmonary Fibrosis	URGENT for reasons given above and because many of the COVID-10 patients currently hospitalised and in intensive care are people who are immune compromised and have a poor vaccine response.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Polycystic Kidney Disease Charity	This is urgent. Many people are continuing to shield and endure the consequences of shielding in fear of getting Covid.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Leukaemia Care	As outlined in our response to the section *"appropriateness of an evaluation and proposed evaluation route",* this evaluation is especially urgent now given ongoing capacity issues the NHS is facing. If the technology was to be approved, it would alleviate some of the burden placed on the NHS including on the antiviral treatment programme.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

Section	Stakeholder	Comments [sic]	Action
Additional comments on the draft remit	Multiple Sclerosis Trust	Several NICE approved treatments for multiple sclerosis are known to blunt the Covid vaccine response: • Sphingosine 1-phosphate receptor modulators (fingolimod, siponimod, ponesimod) • Alemtuzumab treatment within the past 24 months • Anti-CD20 monoclonal antibodies (ocrelizumab, ofatumumab) Furthermore, evidence suggests that people treated with ocrelizumab may be more likely to be hospitalised and need intensive care if they're infected with Covid-19, although the risk appears to be small. People with multiple sclerosis taking these treatments are concerned about exposure to Covid infections and continue to follow a restricted lifestyle in order to maintain social distancing. We are also aware that concerns about a blunted vaccine response is deterring some neurologists from prescribing and some patients from starting treatment with one of these highly effective multiple sclerosis treatments. Multiple sclerosis which is untreated or inadequately treated can lead to long-term disability. There is a significant unmet need for a treatment that provides effective protection from Covid for those who do not respond to the vaccine.	Comment noted. No action needed.
	Cardiomyopathy UK	It is estimated that there are around 250,000 people living with cardiomyopathy in the UK. Around 180 heart transplants are carried out every year of which around 115 (i.e. 64%) will be related to cardiomyopathy.	Comment noted. No action needed.
	Immunodeficiency UK	1. Immunodeficiency UK would like to highlight the case story of a patient with hyper IgM syndrome who contacted us recently (28/7/22) which highlights many of the problems facing people with immunodeficiency who have to live with the threat of COVID-19:	Comment noted. No action needed.

Section	Stakeholder	Comments [sic]	Action
		‘Currently on day 18 of a COVID infection that I can’t shift despite 2 courses of Paxlovid. I think I got it travelling to a board meeting. Regret going now, even though the circumstances merited the in- person meeting (we were getting nowhere via zoom). Whole CMDU process has been eye opening - but not in a good way. There really is only one treatment option, Paxlovid - which is not appropriate for immune deficient patients as it relies on the patient’s own immune system to clear the virus and there are so many contraindications. There is no option for combination therapy with a mab. Which is per NERVTAG Dec 21 report recommendations for treating immune deficient patients with anti virals. NERVTAG also said that the strain should be genotyped and carefully monitored. Apparently PSHE is no longer testing variants. There are several other recommendations from the government’s own advisors that have clearly not been implemented based on my experience. Plus, all clinicians I have spoken to over the last 18 days agree that immune deficient patients need a 10 day course not 5, but the CMDU are only allowed to prescribe one course of 5 days of Paxlovid. The CMDU has at no point consulted with my consultant at my hospital. Probably because there are no options to discuss with them. Feels wrong that the people who have been managing my condition for 20+ years are sidelined due to this centralised, tightly controlled process. If Plan B doesn’t work - Plan C is the GSK drug which is unlikely to work. As you know the FDA has removed it from use, but the government seem determined to use up prebought stocks regardless of the science. I was also told by the CMDU that may be my regular immunoglobulin infusion might work. I said that I had had my infusion already and 24 hours later viral load went up significantly and stayed high. He said - “oh well, Paxlovid is the only thing I can give you. Take it or leave it - I suggest you take it.”	

Section	Stakeholder	Comments [sic]	Action
		I have also had to tackle some considerable levels of ignorance via the 111 process just to get referred to the CMDU. One GP said - “so you have high levels of antibody with Hyper IgM? And you have had 5 jabs - you should be ok - just hang in there”. It took 4 phone calls and 24 hours just to get a referral to the CMDU. By which point my symptoms were getting quite serious. Another GP apologised because she had no idea what I was talking about. She had to go and ask a colleague about how to refer to the CMDU. She agreed that this process was ridiculous as it was very clear from my medical file that I was eligible for covid therapeutics, so this was a time-wasting unnecessary step. I have the scary prospect of being stuck with this virus. Or even worse, it hides somewhere latently like in my liver causing chronic damage. My consultant has applied for compassionate use of Evusheld. Fingers crossed. I am trying not to get angry. This has played out exactly as I feared. All the points I have been making to my MP concerning the need for access to Evusheld, for the last 12 months are coming to bear. Let’s hope I get through this. I am symptom free at the moment but still covid positive with 2 days left of the anti virals.’ 2. Comment on ‘Other considerations: impact of different variants of concern of COVID-19 on the clinical evidence of the intervention’. It should be noted that vaccines, were rolled-out without it being known whether they would be effective against future variants. Following the results of the PROVENT study please note the following recent publications showing the effectiveness of the therapy: • Young-Xu, Y. et al. Tixagevimab/Cilgavimab for Prevention of COVID-19 during the Omicron Surge: Retrospective Analysis of National VA	

Section	Stakeholder	Comments [sic]	Action
		Electronic Data. 2022.05.28.22275716 Preprint at https://doi.org/10.1101/2022.05.28.22275716 (2022). • Kertes et al., Association between AZD7442 (tixagevimab-cilgavimab) administration and SARS-CoV-2 infection, hospitalization and mortality | Clinical Infectious Diseases | Oxford Academic (oup.com) Also evidence showing that Evusheld retains activity against BA.4/BA.5 and BA2.75: • Arora, P. et al. Augmented neutralisation resistance of emerging omicron subvariants BA.2.12.1, BA.4, and BA.5. Lancet Infect. Dis. S1473-3099(22)00422–4 (2022) doi:10.1016/S1473-3099(22)00422-4. • Yamasoba, D. et al. Neutralisation sensitivity of SARS-CoV-2 omicron subvariants to therapeutic monoclonal antibodies. Lancet Infect. Dis. 22, 942–943 (2022). • Neutralization sensitivity of Omicron BA.2.75 to therapeutic monoclonal antibodies | bioRxiv. https://www.biorxiv.org/content/10.1101/2022.07.14.500041v1. • Takashita, E. et al. Efficacy of Antibodies and Antiviral Drugs against Omicron BA.2.12.1, BA.4, and BA.5 Subvariants. N. Engl. J. Med. doi 10.1056 (2022). • EMA EPAR confirming neutralisation against major variants of concern evusheld-epar-risk-management-plan_en.pdf (europa.eu)	

Section	Stakeholder	Comments [sic]	Action
	Evusheld for the UK	We re-emphasize that an emergency interim authorization, as with other Covid therapeutics, would be appropriate here to accelerate the timescale, given the urgency. We are unsure, given the urgency of the timescale for the patient groups that we represent, whether the Single Technology Appraisal process is the most appropriate route for an urgently needed therapeutic.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority. Access to medicines through interim commissioning arrangements is outside the remit of NICE's Technology Appraisal process
	National Kidney Federation	Reiterating the need for a rapid guideline to be produced.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.
	Kidney Research UK	Whilst we welcome some progress on this matter, the need for access to this treatment, widely used internationally, is extremely urgent for those patients we represent. We re-iterate that this process needs to be expedited.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab

Section	Stakeholder	Comments [sic]	Action
			for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	AstraZeneca	No comments	No action needed.
	Cardiomyopathy UK	The background information does not include any reference to the MELODY (**M**ass **e**valuation of **l**ateral flow immun**o**assays for the **d**etection of SARS-CoV-2 antibod**y** responses in immunosuppressed people) study where home antibody testing is being applied to improve understanding of responses to COVID-19 vaccination in individuals who are transplanted and receiving immunosuppression. Evidence has shown overall that this group is more likely to have severe infection with increased morbidity and mortality, even following two doses of Covid-19 vaccines, and therefore may remain unprotected from Covid-19. MELODY Study | Faculty of Medicine | Imperial College London The background information has no mention on the impact of shielding by vulnerable people on mental health (see reference to Daniels & Rettie 2022). It is important that this impact is recognised. Other countries are offering this technology and recently published evidence by Nyguen et al 2022 showed a low rate of infections and severe illnesses among immunocompromised patients treated with Tixagevimab–cilgavimab doi:10.1016/j.cmi.2022.07.015.	Comments noted. The scope has been updated to reflect these.

Section	Consultee/ Commentator	Comments [sic]	Action
	CLL (Chronic Lymphocytic Leukaemia) Support	The background information does not give adequate consideration to the impact that long term shielding has had on the blood cancer community. Shielding has continued for many in this group because they are very aware that they have a very impaired response to vaccination and that they are also at high risk of hospitalisation and death if they are infected. The impact of this is not just felt by the blood cancer patients but also all those that they come into contact with, family and friends. Friends and family used to test using lateral flow methods prior to meeting but the expense of these tests means that this is no impossible for many, increasing their isolation and adding to their suffering. The psychological distress of these patients is enormous.	Comment noted. The scope has been updated to reflect this.
	Immunodeficiency UK	The background information is extremely general. Reference should be made to the wealth of information on inadequate vaccination responses in different subgroups of immunocompromised patients. Omissions include: OCTAVE trial data Publications: • Fendler et al., Nat.Rev.Clin. Oncol 2022:19 (6):385-401 • Lee at al., Lancet Oncol 23. 748-757 (2022) • Shields et al., J Clin Immunol 2022 Apr 14;1-12. • Shields et al., Frontiers in Immunology, 02 June 2022 https://doi.org/10.3389/fimmu.2022.912571	Comments noted. The scope has been updated to reflect these.

Section	Consultee/ Commentator	Comments [sic]	Action
		References are needed to the more recent information on the impact of COVID-19 in immunocompromised groups on mortality, hospitalisation and ICU admissions: • QCOVID data (Hippesley-Cox et al., BMJ 374, n2244 (2021) • ICNARC – Reports https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports. There is also no mention of impact of COVID-19 on the mental health of extremely vulnerable groups – see Rettie, H. & Daniels, J. Coping and tolerance of uncertainty: Predictors and mediators of mental health during the COVID-19 pandemic. Am. Psychol. 76, 427–437 (2021).	
	National Rheumatoid Arthritis Society (NRAS)	NRAS agrees with the background information and has nothing further to add	Comment noted. No action needed.
	Evusheld for the UK	It is important that this group are recognised as being psychologically vulnerable due to the long-term effects of shielding because of their clinically vulnerable status (Daniels & Rettie, 2022; Rettie & Daniels, 2020). This has been well documented and provides important context for a NICE evaluation, with precedent in other NICE guidelines. The psychological impact of extensive behavioural measures directed at sustaining life has been pervasive, and should be considered when gaining a fuller understanding of the context of those who are clinically vulnerable. These additional behavioural measures have affected all aspects of life for this patient group, including coping, social interaction, family relationships, health, access to healthcare/medications and work. The impact of this long-	Comment noted. The scope has been updated to reflect this.

Section	Consultee/ Commentator	Comments [sic]	Action
		term quarantine has been most recently reported in The Lancet (Brooks et al. 2020). A significant proportion of this population are experiencing mental health problems to a clinical level, with evidence suggesting that the mental health of those shielding others is also signficantly affected (Daniels & Rettie, 2022). Further data can be provided on this	
	National Kidney Federation	This group should be recognised as being psychologically vulnerable due to the long-term effects of shielding because of their clinically vulnerable status. Due to shielding all aspects of life for this patient group have been severely impacted, including coping, social interaction, family relationships, health, access to healthcare/medications, work and mental health issues.	Comment noted. The scope has been updated to reflect this.
	Long Covid SOS	Information on the extent of morbidity caused by SARSCoV2 should in our view be provided. Significant numbers of people in the UK have suffered considerable morbidity following COVID-19 infection due to Post COVID syndrome/Long Covid: 1.8 million according to the latest ONS release. 369,000 are severely impacted in terms of their ability to function	Comment noted. The scope has been updated to reflect this.
	Blood Cancer UK	While the information is accurate, we recommend including information on patterns in case rates in 2022 to relay the urgency with which this evaluation should be undertaken. New variants of concern have led to spikes in cases approximately every three months, and it is predictable that this pattern will continue throughout autumn and winter. This will have a significant impact on NHS services and workforce, particularly when combined with the predicted number of influenza infections, hospitalisations, and deaths that will occur concurrently.	Comment noted. The scope has been updated to acknowledge the increase in cases caused by COVID-19 variants.

Section	Consultee/ Commentator	Comments [sic]	Action
		Further, it should be noted that Evusheld is already available to patients in 32 countries.	Comment noted. No action needed. The NICE appraisal process provides recommendations for use in the NHS in England.
		Lastly, we recommend including findings from the MELODY study, which assesses antibody response from Covid vaccines in people with weakened immune systems.	Comment noted. The scope has been updated to reflect this.
	Kidney Research UK	OpenSAFELY data (Williamson EJ et al, Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020 Aug;584(7821):430-436. doi: 10.1038/s41586-020-2521-4.) showed that those particularly at risk of death from COVID-19 included those with organ transplants, reduced kidney function or blood cancers. These should be named explicitly in the background section (paragraph 2). It may also be helpful to include in the background an acknowledgement of the psychological impact for those with an increased risk of inadequate response to COVID-19 vaccination. They may, unlike many of the general population, remain vulnerable to COVID-19 and its serious consequences on a daily basis. Whilst the Government now has a policy of 'Living with Covid', this is inappropriate for the vulnerable and many are still living in fear of being infected, to the detriment of their mental health.	Comment noted. The scope has been updated to include information on those at highest risk of hospitalisation or death from COVID-19 after vaccination from an independent UK government advisory group report which covers the groups mentioned.

Section	Consultee/ Commentator	Comments [sic]	Action
	Kidney Care UK	We strongly recommend that the Background section covers the specific impact the pandemic has had and continues to have on high-risk groups unlikely to be protected by the vaccine, in terms of psychological distress, day to day life and economic opportunity. It should include that many within this group are continuing to lead restricted lives due to their ongoing risk from Covid and lack of protection from Covid. The latest ONS data (May 2022) showed 13% of people previously considered CEV reported continuing to follow previous shielding advice and 69% were no longer shielding but were taking extra precautions. Government guidance continues to recommend additional precautions for this group. The Background information should acknowledge that people who may be eligible for Evusheld are living in a very different context than the general population who are more likely to have been able to move on from the pandemic and it's profound effects.	Comment noted. The scope has been updated to reflect this.
	LUPUS UK	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.	Comment noted. The scope has been updated to reflect this. Comment noted. The marketing authorisation for tixagevimab–cilgavimab includes people for whom COVID-19 vaccination is not recommended, so the appraisal will consider this.
	Myeloma UK	Patients with myeloma and other blood cancers are greatly over-represented in COVID-19 deaths. Recent data (published 25 July 2022) shows 217 blood	Comment noted. The marketing authorisation

Section	Consultee/ Commentator	Comments [sic]	Action
		cancer patients died of COVID-19 in the last 3 months, out of a total of 5,192 deaths.[6] It takes the total number of COVID-19 deaths of people with blood cancer during the pandemic to 3,809. In response to this data we need to ensure patients have access to this treatment to prevent COVID-19 infections and further deaths. [6] Office for National Statistics (2022) Pre-existing conditions of people who died due to COVID-19, England and Wales. Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/preexistingconditionsofpeoplewhodiedduetocovid19englandandwales	for tixagevimab–cilgavimab includes people who are unlikely to mount an adequate immune response to COVID-19 vaccination, so the appraisal will consider this.
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	There is no mention in the background of the major groups who cannot raise an immune response. It needs to describe in more detail and accuracy the relevant medical need including patients who are intermittently part of the included patient group – e.g., those awaiting transplants. "Almost 500 000 people in the UK are immunocompromised, including people with blood cancers, those taking immunosuppressive drugs after an organ transplant, or those with conditions such as multiple sclerosis and rheumatoid arthritis. The treatment could offer this group of patients, many of whom are still shielding, protection against covid-19 and help them feel more confident about returning to a normal life." https://www.bmj.com/content/376/bmj.o722 The sentence "Some people also have an increased risk of inadequate response to COVID-19 vaccination" is very light and should perhaps mention people on immunosuppression as this is not specific enough – some of those will raise some response and some hardly at all should this not be	Comment noted. The scope has been updated to reflect this using data from the OCTAVE study and the population identified by an independent UK government advisory group of people at highest risk of hospitalisation and death despite receiving COVID-19 vaccination.

[6] Office for National Statistics (2022) Pre-existing conditions of people who died due to COVID-19, England and Wales. Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/preexistingconditionsofpeoplewhodiedduetocovid19englandandwales

Section	Consultee/ Commentator	Comments [sic]	Action
		considered, if you cannot tell who might not raise a response, you need to protect them all.	
	Anthony Nolan	The background does not adequately describe the position that immunocompromised patients, and specifically those with haematological diseases now find themselves in. Individuals who are immunocompromised are at an increased risk of severe sequelae from coronavirus such as hospitalisation, intensive care unit admission and death[3]. Furthermore, patients with haematological neoplasms who suffer from impaired immunity are at particular risk, with higher morbidity and mortality[4]. With respect to vaccination serving as a primary pharmaceutical intervention for preventing COVID-19, evidence suggests a low seroconversion rate in vaccinated patients with haematological neoplasms compared with healthy controls. It has been demonstrated through OCTAVE trial data, and similar vaccine efficacy studies[5] that allogeneic hematopoietic cell transplantation (allo-HCT) recipients display impaired immune response to SARS-CoV-2 vaccination. Patients within 12 months or less of receiving an allo transplant, or undergoing immunosuppression therapies, had the lowest immune responses to vaccination. For many immunocompromised patients, and in particular HSCT patients, COVID-19 vaccination has a limited to negligible immune effect, and cannot be considered a means of protection from serious illness as a result of a SARS-CoV-2 infection.	Comment noted. The scope has been updated to reflect this.

Section	Consultee/ Commentator	Comments [sic]	Action
		[3] – Coronavirus monoclonal antibodies as a prophylactic therapy against COVID-19 for immunocompromised groups, National Clinical Expert Consensus Statement, APPG on Vulnerable Groups to Pandemics [4] – Mittleman M et al, 2022, Effectiveness of the BNT162b2mRNA COVID-19 vaccine in patients with hematological neoplasms in a nationwide mass vaccination setting – www.sciencedirect.com/science/article/pii/S0006497121017560 [5] – Huang A et al, 2022, Antibody Response to SARS-CoV-2 Vaccination in Patients following Allogeneic Hematopoietic Cell Transplantation, Transplantation and Cellular Therapy – https://doi.org/10.1016/j.jtct.2022.01.019	
	UK CLL Forum	Real world data observational studies are available for at risk populations and the efficacy of this drug in a vaccinated population and since Omicron emerged. These should be considered.	Comment noted. Any clinical effectiveness evidence will be based on all publicly available sources ensuring the data are as up to date as possible.
	Action for Pulmonary Fibrosis	Draft Scope paragraph 2 in 'background section; add pulmonary fibrosis to the list of risk factors for poor COVID-19 vaccine response: (1) Karampitsakos T, Papaioannou O, Dimeas I, Tsiri P, Sotiropoulou V, Tomos I, et al. Reduced immunogenicity of the mRNA vaccine BNT162b2 in. ERJ Open Res. 2022; 8(2): 1-4. Further information: Recent research which shows people with idiopathic pulmonary fibrosis (the most common form of pulmonary fibrosis) are also especially vulnerable to COVID-19 and show poor clinical outcomes (2), high mortality rates (3,4),	Comment noted, the scope has not been updated. The list of risk factors for poor COVID-19 vaccine response in the scope is from the PROVENT study.

Section	Consultee/ Commentator	Comments [sic]	Action
		(2) Naqvi S, Lakhani D, Sohail A, Maurer J, Sofka S, Sarwari A, et al. Patients with idiopathic pulmonary fibrosis have poor clinical outcomes with COVID-19 disease: a propensity matched multicentre research (3) Drake T, Docherty A, Harrison E, Quint J, Adamali H, Agnew S, et al. Outcome of Hospitalization for COVID-19 in Patients with Interstitial Lung Disease: An International Multicenter Study. American Journal of Respiratory and Critical Care Medicine. 2020; 202(12): 1656-1665. (4) Gallay L, Uzunhan Y, Borie R, Lazor R, Rigaud P, Marchand-Adam S, et al. Risk Factors for Mortality after COVID-19 in Patients with Preexisting Interstitial Lung Disease. American Journal of Respiratory and Critical Care Medicine. 2021; 203(2): 245-249.	
	Polycystic Kidney Disease Charity	Should the document mention that this intervention is available in other countries?	Comment noted. No action needed. The NICE appraisal process provides recommendations for use in the NHS in England.
	Leukaemia Care	We would like to see the mention of blood cancers/haematological malignancies (including leukaemia) as reflected in the types of people this technology would help.	Comment noted. The population has been kept broad in line with the marketing authorisation for tixagevimab–cilgavimab.

Section	Consultee/ Commentator	Comments [sic]	Action
Population	AstraZeneca	The definition accurately describes the indicated population. This may be approximated to the "highest-risk clinical subgroups" defined in an independent report commissioned by the Department of Health and Social Care (DHSC) who are eligible for early treatment, and constitutes approximately 1.3 million people in England alone.[3] These patients are currently those who are offered booster vaccinations, and are identified for treatment with an anti-viral or nMAB in the event they develop COVID-19.	Comment noted. No action needed.
	Cardiomyopathy UK	The MELODY methodology proves in one simple fingerpick test if there is a response to vaccine or not. And there are two distinct types of COVID anti-body. That generated by disease, and that generated by vaccine. Could this test be included as part of the criteria for population.	Comment noted. The population has been kept broad in line with the marketing authorisation for tixagevimab–cilgavimab.
	CLL (Chronic Lymphocytic Leukaemia) Support	The marketing authorisation is for groups who are "unlikely" to mount an adequate immune response. It does not ask for this inadequate immune response to be proven in each case. Seropositive antibody results should, therefore, not be required. Others, where the clinician genuinely feels the patient is likely to have an impaired response should be able to access this treatment, so flexibility and clinician discretion is important.	Comment noted. The population has been kept broad in line with the marketing authorisation for tixagevimab–cilgavimab.
	Immunodeficiency UK	The definition is broad and encompassing but see comments below.	Comment noted. No action needed.
	National Rheumatoid	We agree with the definition of the target population which will cover people with a wide range of conditions (our expertise is in the area of RA/AJIA) and	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	Arthritis Society (NRAS)	we cannot speak on behalf of the entire population who might be eligible for Evusheld	
	Evusheld for the UK	The population group can be more specifically defined than it is currently. All patient groups listed in NHS England RAPID-C19. 2022. 'Defining the Highest-Risk Clinical Subgroups upon Community Infection with SARS-CoV-2 When Considering the Use of Neutralising Monoclonal Antibodies (NMABs) and Antiviral Drugs: Independent Advisory Group Report'. GOV.UK. 30 May 2022 should be administered this therapy without the need for an antibody test as they are "unlikely to mount an adequate immune response to COVID-19 vaccination". We note that the scope considers "the impact of vaccination status or SARS-CoV-2 seropositivity on the clinical evidence base of each intervention, generalisability to clinical practice and interaction with other risk factors will be considered in the context of the appraisal." However, the marketing authorisation is for groups who are "unlikely" to mount an adequate immune response, not groups proven to have done so. Seropositive antibody results should, therefore, not be required.	Comment noted. The population has been kept broad in line with the marketing authorisation for tixagevimab–cilgavimab.
	National Kidney Federation	All patient groups listed in NHS England RAPID-C19. 2022. 'Defining the Highest-Risk Clinical Subgroups upon Community Infection with SARS-CoV-2 When Considering the Use of Neutralising Monoclonal Antibodies (NMABs) and Antiviral Drugs: Independent Advisory Group Report'. GOV.UK. 30 May 2022 should be administered this therapy without the need for an antibody test as they are "unlikely to mount an adequate immune response to COVID-19 vaccination"	Comment noted. The population has been kept broad in line with the marketing authorisation for tixagevimab–cilgavimab.
	Long Covid SOS	Do 'people' include children/those under 18? "for whom COVID-19 vaccination is not recommended" is vague we would welcome more clarity, e.g:	Comment noted. The scope is in line with the marketing authorisation

Section	Consultee/ Commentator	Comments [sic]	Action
		- Would this group include people who have suffered health deficits from previous vaccinations - people with Long Covid and also others? Or is this only intended for people who had had 'severe' or life threatening reactions - Would those over the age of 60, or who are obese be eligible as per the PROVENT trial?	for tixagevimab–cilgavimab which states **"**tixagevimab–cilgavimab is indicated for the pre-exposure prophylaxis of COVID-19 in adults who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2 and: • Who are unlikely to mount an adequate immune response to COVID-19 vaccination or • For whom COVID-19 vaccination is not recommended.
	Blood Cancer UK	Yes	No action needed.

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	Kidney Research UK	The population is currently defined in the same terms as the marketing authorisation. This has been more tightly defined by the COVID-19 Therapeutics Clinical Review Panel in their report of May 2022 https://www.gov.uk/government/publications/higher-risk-patients-eligible-for-covid-19-treatments-independent-advisory-group-report/defining-the-highest-risk-clinical-subgroups-upon-community-infection-with-sars-cov-2-when-considering-the-use-of-neutralising-monoclonal-antibodies	Comment noted. NICE will make recommendations for tixagevimab–cilgavimab within its marketing authorisation.
	Kidney Care UK	We recommend the population includes those groups identified as eligible for Covid-19 treatments, due to their ongoing risk of severe complications. This therefore would include people at stage 4 and 5 kidney disease and on dialysis as well as those with transplants.	Comment noted. NICE will make recommendations for tixagevimab–cilgavimab within its marketing authorisation.
	LUPUS UK	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 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.	Comment noted. The population is aligned with the marketing authorisation for tixagevimab–cilgavimab.
	Myeloma UK	There is currently uncertainty in the evidence base which would help to define the population who are unlikely to mount an adequate immune response to COVID-19 vaccination. Two studies have shown that COVID-19 vaccines are effective in producing antibodies in myeloma patients, but there is no data	Comment noted. No action required.

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		that demonstrates the level of protection that myeloma patients get from vaccines. The PREPARE study has shown that 93% of 214 myeloma patients had anti-spike antibodies after their second dose of COVID-19 vaccine.[7] This is markedly increased from the earlier phase of testing for antibodies present in the blood at least 21 days after one dose of COVID-19 vaccine (60%, 17/28). Another study (unpublished) also demonstrated a significant increase in anti-spike antibodies after a second dose of a COVID-19 vaccine, compared to the first dose, in patients with plasma cell disorders (including myeloma). Despite this evidence, more research is required to determine how well patients respond to three or more primary doses of vaccine and importantly, the level of protection myeloma patients get from the vaccine. Therefore, while the population is defined in broad terms, we believe this is the right scope. We are against an approach which would see niche recommendations for smaller populations. We believe that an approval for this patient population is appropriate, supported by clinical guidelines and judgement. [7] Ramasamy K, Sadler R et al. Immune response to COVID-19 vaccination is attenuated by poor disease control and antimyeloma therapy with vaccine driven divergent T-cell response. Br J Haematol. 2022; 197(3): 293-301.	
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	It accurately reflects what is in the UK label though the EMA label is broader.	Comment noted. No action needed.

[7] Ramasamy K, Sadler R et al. Immune response to COVID-19 vaccination is attenuated by poor disease control and antimyeloma therapy with vaccine driven divergent T-cell response. Br J Haematol. 2022; 197(3): 293-301.

Section	Consultee/ Commentator	Comments [sic]	Action
	Anthony Nolan	The population within the draft scope has been defined in the abstract. Without further clarification, this approach may hinder or delay any clinical prioritisation required in the rollout of Tixagevimab–cilgavimab. There remain concerns around the technologies' global supply, as well as localised logistical issues in clinical delivery – the technology is delivered through 2x IM injections and post-injection patient monitoring is advised. These aspects are relevant to population design and clinical delivery capacity. For existing COVID-19 treatments available through NHS England, specific indications have been identified to qualify the clinical high-risk group. This can be helpful in supporting primary care HCPs to identify and approach eligible patients. Should supply constraints form a logistical concern, the approach taken for Evusheld by the Western Australian Department of Health may be a relevant consideration. They have identified 6 groups in priority order (from 'Severe immunocompromised' > 'Any individual (immunocompromised or immunocompetent) where vaccination is medically contraindicated'[6]. Each group carries specific indications and additional risk factors for severe COVID-19 infections. [6] – Drug Guideline- Tixagevimab Plus Cilgavimab (Evusheld®) For Covid-19 Pre-Exposure Prophylaxis, Department of Health, Government of Western Australia - www.healthywa.wa.gov.au/~/media/Corp/Documents/Health-for/Infectiousdisease/COVID19/Treatment/WAGuidelines-for-Use-of-Tixagevimab-plus-cilgavimab-EVUSHELD-for-COVID19-Prophylaxis.pdf	Comment noted. The population is aligned with the marketing authorisation for tixagevimab–cilgavimab. NICE will consider any constraints on implementing its guidance.

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	UK CLL Forum	Yes	No action needed.
	Action for Pulmonary Fibrosis	Yes	No action needed.
	Polycystic Kidney Disease Charity	We think it is	No action needed.
	Leukaemia Care	Yes. Clarity is needed on who will be included in the group not responding to vaccines and, if this is to differ from existing immunocompromised definitions used in other COVID programmes, this must be discussed and clarified now. There are many existing definitions of who needs protection form COVID-19 in other NHS programmes, such as vaccine eligibility programmes and anti-viral treatment eligibility.	Comment noted. The population has been kept broad in line with the marketing authorisation.
Subgroups	AstraZeneca	No, AstraZeneca are not aware of any clinically distinct subgroups in whom the relative cost effectiveness is expected to differ. The scope refers to two subgroups; people who are unlikely to amount an adequate immune response to COVID-19 vaccination, and people for whom COVID-19 vaccination is not recommended. Whilst these populations are specifically mentioned in the wording of the licence granted by the MHRA, the trial population in PROVENT broadly represents both of these populations combined. However, there are no clinical data available from the clinical trial to enable a separate analysis to be conducted for each of these populations. We therefore suggest that these populations are removed from the 'subgroups' section of the scope. Instead, the submission will focus on a population who are at high risk of adverse clinical outcomes due to COVID-19.	Comment noted. The scope has been updated to reflect this.

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	Cardiomyopathy UK	Heart and other transplant patients are highly vulnerable as are other organ transplant patients. A finger prick antibody test could be applied to this subgroup.	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.
	CLL (Chronic Lymphocytic Leukaemia) Support	Yes, appropriate but clinical discression would be advisable in individual cases and should be allowed.	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.
	Immunodeficiency UK	Yes. The therapy is essential for those patients with primary antibody failure who will not recover B cell function due to having a primary immunodeficiency and proven secondary immunodeficiency, especially antibody failure. Prophylactic monoclonal antibody therapy will prevent serious infection in these very vulnerable patients. Prevention of infection is preferable to treating COVID infection itself, since most of these patients may have lung disease compromising their prognosis already. Criteria for patient selection is given in this publication APPG on Vulnerable Groups to Pandemics 'National Clinical Expert Consensus Statement 'Coronavirus monoclonal antibodies as a prophylactic therapy against COVID-19 for immunocompromised groups' https://bit.ly/3bpE6oO	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.
	National Rheumatoid	In the RA population there are groups of patients on specific treatment regimens who are more likely to require this drug than others with RA to prevent more serious disease/hospitalisation/worse should they get COVID.	Comment noted. Subgroups have been updated to include

Section	Consultee/ Commentator	Comments [sic]	Action
	Arthritis Society (NRAS)		those at highest risk of adverse COVID-19 outcomes.
	Evusheld for the UK	There should be scope for additional discretionary inclusion on the advice of individual clinicians where there is a genuine belief that the patient is "unlikely" to have mounted an adequate vaccine response.. It may be wise to conduct further subgroup analyses on those who are already defined as being at high risk (as described by NICE in the background); and those from the differing clinical groups who may not benefit from intervention, e.g. those with organ transplants vs. COPD for example.	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.
	Long Covid SOS	Unclear at present which subgroups are included as the criteria is the same We would recommend that those affected by Post Covid Syndrome/Long Covid who have had a significant worsening of symptoms after a previous vaccine should be considered for this intervention. Additionally, there is a subgroup of people (numbers not established) who have developed Long Covid symptoms after vaccination without a Covid-19 infection. Subsequent vaccination for both of these groups could put people at risk of worsening health status Additionally, many have developed Long Covid after a breakthrough infection post vaccination, suggesting they may not have been adequately protected by vaccination	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes. The population includes those for whom COVID-19 vaccination is not recommended.
	Blood Cancer UK	Subgroups within the population where Evusheld is expected to be more clinically and cost effective are among those who are currently eligible for post-exposure Covid-19 treatments. These recommendations were also generated for use with prophylaxis. Within the blood cancer cohort, those with T-cell cancers not undergoing treatment should also be included, as their ability to mount an adequate T-cell response is severely impaired as a result	Comment noted. Subgroups have been updated to include those at highest risk of

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		of their condition, leaving them at high risk of developing severe disease. To aid in developing an eligibility list, we suggest that NICE seeks evidence-based advice on whether serology testing would be an appropriate mechanism for identification of eligible patient cohorts. Within the blood cancer cohort, Evusheld will likely be more clinically and cost-effective in (1) those with evidence of clinically significant immune system failure (such as recurrent infections), (2) those whose treatment type and schedule are likely to cause or are causing clinically significant immune system failure, and (3) those for whom infection with Covid-19 would disrupt life-prolonging treatment (e.g., blood cancer patients receiving or about to receive induction therapy). The evaluation should also consider the stark disparity in mortality rates from Covid-19, along ethnic and socioeconomic lines. The evaluation must consider not only which groups are at highest risk from Covid due to disease type (e.g., blood cancer) and treatment type and schedule (e.g., CAR-T therapy), but also non-clinical factors which contribute greatly to patient outcomes (e.g., ethnicity and deprivation level, as referenced in the 'Background' section). Evusheld will likely be most cost effective for those groups who are at disproportionate risk of dying from Covid-19. For instance, in January and February 2022 the age-standardised mortality rate from Covid in men of Bangladeshi origin was 483.2, while the same rate in men of white British origin was 182.3.	adverse COVID-19 outcomes.
	Kidney Research UK	The current sub-groups suggested seem to be a wider group than the population, potentially including children and those infected with COVID-19, and therefore inappropriate and not in line with the marketing authorisation. Subgroups could include specifically those at particular risk of death from COVID-19 despite vaccination. This would include kidney transplant patients, other solid organ transplant patients, those with reduced kidney function, blood cancer patients, those with auto-immune conditions and those on immunosuppressant medications. This group of patients are the subject of the MELODY study, due to report soon.	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.

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		(https://www.imperial.ac.uk/medicine/research-and-impact/groups/melody-study/)	
	Kidney Care UK	No comment	No action needed.
	LUPUS UK	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 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	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.

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		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.	
	Myeloma UK	The scope defines both the population and subgroups equally so we are unsure what further groups would be offered the treatment.	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.
	Faculty of Pharmaceutical Medicine	Some subgroups will raise some response and some hardly at all should this not be considered as if you cannot tell who might not raise a response you need to protect them all. Those on high dose immunosuppressive	Comment noted. Subgroups have been updated to include

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	(endorsed by Royal College of Physicians)	chemotherapy or those severely immunosuppressed for underlying disease should have high priority. Others on immunosuppressants or with diseases that may supress response could have antibody assessments (but this is likely to be more expensive than simply treating them). Also, some patients may need shorter term cover if they are only intermittently part of the group.	those at highest risk of adverse COVID-19 outcomes.
	Anthony Nolan	Refer to Population comment above. Identifying priority subgroups, beginning with 'Severe immunocompromised' would be helpful on a clinical effectiveness basis. However, all patients covered by the draft scope population should be granted timely access to Tixagevimab–cilgavimab.	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.
	Crohn's & Colitis UK	We recommend that the subgroups are defined based upon government guidance: COVID-19: guidance for people whose immune system means they are at higher risk - GOV.UK (www.gov.uk)	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.
	UK CLL Forum	How will poor vaccination response be defined? No antibody response or low titre response?	Comment noted. Subgroups have been updated to include those at highest risk of adverse COVID-19 outcomes.
	Action for Pulmonary Fibrosis	Transplant patients are on high doses of immune suppression and are especially vulnerable.	Comment noted. Subgroups have been updated to include those at highest risk of

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			adverse COVID-19 outcomes.
	Leukaemia Care	Yes, subgroups are appropriate.	Comment noted. No action needed.
Comparators	AstraZeneca	Yes – there are no pre-exposure prophylaxis treatments available and therefore the wording in the scope is appropriate.	Comment noted. No action needed.
	Cardiomyopathy UK	Unaware of any comparators at present	Comment noted. No action needed.
	CLL (Chronic Lymphocytic Leukaemia) Support	Vaccination is not a suitable comparator, because this population do not respond well and are largely unprotected.All control comparators should be included so that there is the widest scope of evidence. Many of these will be from RCT trials which will provide the highest quality evidence.	Comment noted. No action needed.
	Immunodeficiency UK	Yes	No action needed.
	National Rheumatoid Arthritis Society (NRAS)	Yes, there are none which relate to COVID	Comment noted. No action needed.
	Evusheld for the UK	Vaccines might be comparators, although the point is that this population do not respond well to such therapies. We presume that 'no prophylaxis' includes placebo as per the published studies. However, it may be beneficial to state that all control comparators will	Comment noted. No action needed. "No prophylaxis" in the scope means that currently, there are no available prophylactic

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		be included so that the widest scope of evidence is included; these will naturally fall into RCT trials which provide the highest quality evidence.	options available for people who are unlikely to mount an adequate immune response to COVID-19 vaccination or for whom COVID-19 vaccination is not recommended.
	Blood Cancer UK	Yes	No action needed.
	Kidney Research UK	Comparators should be as wide as possible to allow the maximum number of studies to be included. This may include use of placebo and comparison with vaccination. It is important that the level of clinical effectiveness for tixagevimab-cilgavimab is not required to be above that for current vaccine programmes, given that vaccination is still encouraged despite the level of breakthrough infections of the Omicron variant in people vaccinated. Comparators should consider only prophylaxis and not post-infection treatment.	Comment noted. No action needed. The comparator for tixagevimab–cilgavimab is currently no prophylaxis.
	Kidney Care UK	Many people at highest risk have led extremely restricted lives during the pandemic as a preventative measure. In earlier waves people classed as CEV followed government guidance to shield and some also continue to restrict social, employment and leisure activities (see ONS data, May 2022). These restrictions reduce risk from Covid - although observational data, OpenSafely found mortality rates in Wave 1 were 71.1 per 1000 person years in people on dialysis (not advised to shield initially and then unable to shield due to hospital visits) and 19.48 in people with kidney transplants (generally	Comment noted. The outcomes included in the economic analysis will aim to capture all health outcomes.

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		more able to shield). In Wave 3 (when behaviour is likely more similar) mortality in those groups were 11.72 and 14.1 respectively. However, restrictive behaviour comes at a heavy price in terms of quality of life, employment opportunities and mental and physical health. We recommend NICE consider how to incorporate within their assessment the behavioural measures adopted by higher risk people when there are no other preventative interventions available.	
	LUPUS UK	Yes, this is complete and accurate.	No action needed.
	Myeloma UK	Yes	No action needed.
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	The relevant comparisons are between no prophylaxis (i.e. unvaccinated subjects), SARS CoV2 vaccinated subjects and those that received pre-exposure prophylaxis with Evusheld with the outcomes being rate of infections, hospitalisations and deaths from Covid-19 and all cause mortality over a time period which matches 6 and 12 months post receipt of Evusheld. An additional comparison could be made which takes into account receipt of antiviral treatment for infection/covid illness.	Comment noted. No action needed.
	Anthony Nolan	The draft scope is correct to state that there are no other available prophylaxis pharmaceutical candidates, in which to make a comparative analysis. • Vaccination cannot be considered a comparator for this population, not when the vast majority will fail in mounting an adequate immune response. • Sotrovimab, a neutralising monoclonal antibody (nMAb) is not a prophylactic comparator but can be administered intravenously to non-	Comment noted. No action needed.

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		hospitalised patients with mild-to-moderate disease and at least one risk factor for disease progression. • Given allo-transplant patients can be severely immunocompromised and possess multiple risk factors, it should not be considered acceptable that their single line of defence is available only once they are symptomatic. Timely access to these treatments is also a concern. In real-world practice, the only viable alternative to preventing COVID-19 infections is Nonpharmaceutical Interventions (NPIs). Limiting and managing social contact is not always within the scope of the patient alone, and requires significant psychological resilience to maintain an adequate distance from others who may be infectious.	
	UK CLL Forum	Yes	No action needed.
	Action for Pulmonary Fibrosis	No comment	No action needed.
	Polycystic Kidney Disease Charity	Yes	No action needed.
	Leukaemia Care	We would like to see “shielding” considered as a comparator of prophylaxis treatment. This is not the case for all patients, but it is the case for some who do not see any alternative to shielding until prophylaxis treatment is available to them. This has a significant toll on patient’s mental health and quality of life if this situation applies to them, so deserves adequate consideration by NICE.	Comment noted. No action needed. The comparator for tixagevimab–cilgavimab is currently no prophylaxis, which will include the

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			psychological and quality of life impact for people who receive no prophylaxis.
Outcomes	AstraZeneca	Yes	No action needed.
	Cardiomyopathy UK	The outcomes listed are all medical and do not consider the psychological impact of shielding for long periods of time. The QALY score is useful for defining extension of life but doesn't address the burden of the condition on daily activities. Living with a heart transplant is exacerbated by being immunocompromised and vulnerable to infection with SARS-Co-V2. This has a significant affect on daily quality of life. There needs an QoL measure included to pick up improved mental health.	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact will also be captured in the outcomes included in the economic analysis.
	CLL (Chronic Lymphocytic Leukaemia) Support	The mental health aspects of this treatment have not been recognised in this scope. Clinically Extremely Vulnerable (CEV) patients and those who are still shielding as per NHS guidance have been very adversely affected psychologically by their vulnerability and isolation from normal society. e.g. Rettie & Daniels, 2020; Daniels & Rettie, 2022) with 40% reporting clinical levels of health related anxiety. This is significantly higher than those in non-vulnerable groups which was reported as <5%. In addition, the knowledge that there is an effective prophylactic treatment and the withholding of that treatment from those whose lives are at risk is a significant psychological burden and distress to the patient.	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact will also be captured in the outcomes included in the economic analysis.

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		The cost to NHS services of the psychological distress and poor mental health should be considered in the economic analysis.	
	Immunodeficiency UK	These should be extended to include • Psychological benefits - improved mental health and relief of strong feelings of anxiousness and isolation and increased confidence to reduce shielding – a recent poll (June 2022) found that 30% of people affected by primary immunodeficiency had little or no confidence in going out or leaving the house and were effectively still shielding • Improvement in health as people who are immunocompromised feel more comfortable in accessing care – noting that NHS England ceased to enforce the mandatory use of face coverings in hospitals and GP practices, based on guidance from the UK Health Security Agency • Reduced clinical demand overall – GPs, A&E, hospitalisations, ICU costs • Reduced call on CMDU services and use of anti-virals • Reduced cases of chronic coronavirus infections and consequent health costs • Prevention of new pathogenic escape variants due to inability of the immunocompromised to clear COVID-19 infection, even after treatment with anti-viral therapies -see the patient case study above. Other benefits of access would include: • Helping people to re-enter their workplace and carry out normal activities of daily family life and social interaction • Reduce the fear of getting infection from family members or in work-related environment following lifting of all restrictions • Socio/economic benefits as people can contribute more fully as members of society • Demonstration that the health system is supporting all members of society going forward in the living with COVID-19 plan.	Comment noted. Anxiety and depression have been added as outcomes in the scope. The suggested outcomes will also be captured in the outcomes already included in the economic analysis.

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		These benefits are consistent with the NICE interpretation of quality of life: 'Quality of life It is often measured in terms of the person's ability to carry out the activities of daily life, and freedom from pain and mental disturbance.' There should also be consideration of the psychological impact of not having access to this therapy when it is available to immunocompromised groups in other countries see - Rettie, H. & Daniels, J. Coping and tolerance of uncertainty: Predictors and mediators of mental health during the COVID-19 pandemic. Am. Psychol. 76, 427–437 (2021). This is especially harmful since there is no alterative therapeutic prevent strategy for people with primary and secondary immunodeficiency who have not been able to benefit from vaccination.	
	National Rheumatoid Arthritis Society (NRAS)	Yes we believe so	No action needed.
	Evusheld for the UK	A body of research indicates that the mental health and psychological wellbeing of those who have been Clinically Extremely Vulnerable (CEV) and of those who are still shielding (due to following guidance to take additional precautions and known vulnerability) has been adversely affected (e.g. Rettie & Daniels, 2020; Daniels & Rettie, 2022) with 40% reporting clinical levels of health related anxiety. This is significantly higher than those in non-vulnerable groups (<5%). It is also noted that withholding treatment from those whose lives are at risk is ethically and morally questionable, and will bear a significant psychological burden to the patient. None of the outcomes measured here includes the psychological impact of shielding, or withholding treatment, including HRQoL; this is a fairly insensitive measure of psychological distress.	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact will also be captured in the outcomes included in the economic analysis.

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		The long-term cost of mental health problems in those with health problems is well documented (Kings Fund, 2012). This aspect might be measured using a brief psychological measure such as the combined GAD-7 PHQ-9, or the DASS. The cost savings of reducing the (already established) mental health impact will be significant and should be taken into account in the economic analysis for cost-benefit analysis.	
	Long Covid SOS	"symptoms of post-COVID-19 syndrome" – will this outcome measure include severity of symptoms? Or just the presence of any symptom?	Comment noted. Severity and presence of symptoms will be captured in the outcomes included in the economic analysis.
	Blood Cancer UK	Health related quality of life (HRQoL) will play a significant role in this appraisal, as Evusheld will be a vital tool in protecting the immunocompromised as they manage the risks from Covid that arise from going about everyday life. We urge the committee to factor the socioeconomic and mental health aspects of HRQoL into its analysis as a top priority, and to enable patient support organisations to provide evidence of the potential impact of Evusheld on HRQoL. To provide a brief view of the scale of this issue, we conducted a survey of our members. It must be noted that due to the mechanism of participant recruitment, this is a self-selected sample. The following findings may therefore underestimate the scale of this issue, as the survey was unlikely to capture the experiences of those most at risk: 1) Almost a quarter of people with blood cancer are so concerned about Covid that they are only leaving home for essential trips;	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact will also be captured in the outcomes included in the economic analysis.

Section	Consultee/ Commentator	Comments [sic]	Action
		2) Over one third are avoiding meeting people unless they must, and are staying away from indoor places such as restaurants and shops. An evaluation of Evusheld's impact and cost effectiveness should take into account the significant impact of long-term shielding on mental health for this patient group.	
	Kidney Research UK	The outcome measures are appropriate. When considering health-related quality of life, due consideration should be given to psychosocial impact for immunocompromised and vulnerable individuals of living in a society where there are few measures in place to prevent the transmission of COVID-19. Many are still shielding, or at the very least, are living more cautiously than the rest of the population. This has led to loss of work, social isolation, exclusion from family activities and lack of physical exercise which contribute to impoverished physical and mental wellbeing. These have been well-documented in the media, such as a story in the Financial Times featuring a kidney transplant patient (https://www.ft.com/content/fe03bc3b-a381-462d-b373-87dabde0a9ab) We understand that NICE can adopt a wider perspective in its economic evaluation for a technology appraisal where given direction by the DHSC. https://www.bmj.com/content/371/bmj.m4491/rr-0 We consider this would be an appropriate topic in which the societal benefits of a return to a full life for the immunocompromised should form part of the evaluation. When assessing the efficacy of treatment, it is important to note that infection rates (and therefore hospitalisation and mortality rates) can be affected by behaviours to promote safety as well as by prophylactic treatment, so that the population being studied may show lower rates of infection than would be the case if they resumed normal lives where no steps to prevent infection with	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact will also be captured in the outcomes included in the economic analysis. Comment noted. NICE health technology evaluations: the manual states that "In exceptional circumstances for medicines, when requested by the Department of Health

Section	Consultee/ Commentator	Comments [sic]	Action
		Covid were taken. Hospitalisation and mortality rates may also be affected by post-infection antiviral treatments.	and Social Care in the remit for the evaluation, the scope will list requirements for adopting a broader perspective on costs". This has not been requested and therefore costs will be considered from an NHS and Personal Social Services perspective.
	Kidney Care UK	It is important that the assessment considers i) **any reduction in anxiety and psychological distress among patients able to access preventative treatment.** Many people who remain at high risk from Covid continue to experience considerable anxiety due to their vulnerability, which may be assuaged by access to an effective preventative treatment. This paper assesses the effect of vaccination on mental wellbeing. Kidney Care UK found 68% of kidney patients who responded to our survey (March 2021) reported wanting help to manage their worries during the pandemic. ii) **wider benefits such as restarting day to day activities, enhanced employment opportunities, enhanced social and family interaction.** Many people who remain at high risk from Covid are living restricted lives (and 13% still define themselves as 'shielding (ONS data)). Patients indicate they may feel more confident about re-joining previous activities, seeing family and friends, and going back out to work should they be able to access a protective treatment. We believe it is imperative to consider the benefits of living a more normal life.	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact and impact on daily activities will also be captured in the outcomes already included in the economic analysis.

Section	Consultee/ Commentator	Comments [sic]	Action
		Neither of these outcomes will be adequately captured within the assessment HRQoL.	
	LUPUS UK	It is unclear what will be considered under 'health-related quality of life'. An important 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.	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact and impact on daily activities will also be captured in the outcomes already included in the economic analysis.
		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?	Comment noted. Costs will be considered from an NHS and Personal Social Services perspective. The availability of routinely commissioned subsequent treatment technologies will be taken into account.

Section	Consultee/ Commentator	Comments [sic]	Action
	Myeloma UK	Yes	No action needed.
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	Should exacerbation of underlying disease be included here as all these patients are being treated for a different primary diagnosis? Should there also be a patient reported outcome perceived from some of the patient surveys? E.g., less home delivered health care as they can go out to the surgery or collateral on carers. In addition, reduction of isolation stresses and mental health issues should be considered.	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact and impact of the underlying disease will also be captured in the outcomes already included in the economic analysis.
	Anthony Nolan	For transplant patients undergoing active treatment or are considered to be in acute recovery – any adverse effects or disruption to their anticipated treatment pathway, as a result of a SARS-CoV-2 infection – should be recorded as an outcome measure.	Comment noted. Time to return to normal activities post COVID-19 has been added as an outcome in the scope.
	UK CLL Forum	Yes	Comment noted
	Action for Pulmonary Fibrosis	Yes but does 'health related quality of life' include the positive impacts on mental health of being able to adopt a more normal life with Tixagevimab–cilgavimab.?	Comment noted. Anxiety and depression have been added as outcomes in the scope. The psychological impact will also be

Section	Consultee/ Commentator	Comments [sic]	Action
			captured in the outcomes already included in the economic analysis.
	Polycystic Kidney Disease Charity	Could 'worsening of existing health condition(s) beyond expectation' be considered as an outcome?	Comment noted. Worsening of existing health condition will be captured in the outcomes already included in the economic analysis.
	Leukaemia Care	Under 'health-related quality of life', we would like to see this extended to the impact on a patient's ability to work, conduct everyday activities and on their mental health etc.	Comment noted. The impact on daily activities will be captured in the outcomes already included in the economic analysis
Equality	AstraZeneca	Evusheld is expected to be used in routine clinical practice to offer a prophylaxis therapeutic to patients at the highest risk of adverse clinical outcomes due to COVID-19. This population is likely to be equivalent to those documented in an independent report commissioned by the DHSC which identified patient groups, as defined by their underlying health conditions, who are deemed to be at the highest risk of adverse clinical outcomes due to COVID-19.[3] These patients predominately comprise of those who are immunocompromised and therefore amount an insufficient response to COVID-19 vaccination. Therefore, this population represent a group of	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.

Section	Consultee/ Commentator	Comments [sic]	Action
		patients in whom are expected to confer the greatest value of a prophylactic therapeutic. The submission will therefore target this population. As these patients have already been identified by the DHSC and the NHS as needing to be offered treatment with anti-viral or neutralising monoclonal antibody therapeutics upon a positive COVID-19 test, AstraZeneca believes there is a need to support a similar population of patients with a prophylaxis therapeutic. 3. *UK Government. Defining the highest-risk clinical subgroups upon community infection with SARS-CoV-2 when considering the use of neutralising monoclonal antibodies (nMABs) and antiviral drugs: independent advisory group report.* *https://www.gov.uk/government/publications/higher-risk-patients-eligible-for-covid-19-treatments-independent-advisory-group-report/defining-the-highest-risk-clinical-subgroups-upon-community-infection-with-sars-cov-2-when-considering-the-use-of-neutralising-monoclonal-antibodies (2022),.*	
	Cardiomyopathy UK	There is much evidence that some groups of society are more prone to infection and severe reactions to infection with SARS-Co-V2. If this subgroup has also had a heart transplant they will be more significantly affected. These subgroups should be identified and there may be a need for an awareness campaign to identify these groups needs against the general population.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal
	CLL (Chronic Lymphocytic Leukaemia) Support	Those eligible are also more likely to experience mobility difficulties or be homed in health and social care settings (learning disability, older people, mental health) treatment must be accessible for all groups. Ensuring that all necessary clinicians are aware of the published guidance is also important to ensure equal access.	Comment noted. The committee will consider how the recommendation requires consideration

Section	Consultee/ Commentator	Comments [sic]	Action
		Patients who would benefit from this technology would be identified through the same mechanism that targeted them for additional vaccinations All patient groups listed in NHS England RAPID-C19. 2022. 'Defining the Highest-Risk Clinical Subgroups upon Community Infection with SARS-CoV-2 When Considering the Use of Neutralising Monoclonal Antibodies (NMABs) and Antiviral Drugs: Independent Advisory Group Report'. GOV.UK. 30 May 2022 should be administered this therapy.	of equalities issues during the appraisal
	Immunodeficiency UK	The protect strategy through vaccination is not working for some people with primary and secondary immunodeficiency, who as a group fall under the Equality Act 2010 and have protected characteristics. The delay in access to this therapy has meant that their quality of life has been severely compromised when it need not have been. The availability of antiviral drugs to treat Covid is a poor substitute for preventive treatment of these groups, given the narrow window in which treatment must be commenced and the difficulty in practice of obtaining them quickly via a CMDU. Some antivirals cannot be given to these patients due to the long list of contraindications. Furthermore, different standards seem to have been applied to the making this preventive Mab treatment available compared to the availability of other vaccines/antivirals/monoclonal antibodies. This, in itself, could amount to indirect discrimination.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.
	National Rheumatoid Arthritis Society (NRAS)	You have listed clearly the health inequality data available regarding the characteristics of people for whom worse/worst outcomes from COVID are strongly associated. Such people who also meet the 'population' criteria should be identified as having additional risk factors and prioritised for Evusheld if/where deemed appropriate by their Dr./clinical team.	Comment noted. The committee will consider how the recommendation requires consideration

Section	Consultee/ Commentator	Comments [sic]	Action
		Should this drug receive a positive STA, we think that particular efforts will need to be made to raise awareness of its existence within certain high-risk populations who may remain unaware of it, particularly where mental health &/or learning difficulties/language/cultural barriers to receiving best care exist.	of equalities issues during the appraisal
	Evusheld for the UK	Evidently many of those who will be most affected will be those covered under the equality act due to long-term health problems and disabilities. These groups are known to be most physically and psychologically vulnerable over the pandemic, and it is important that charities and patient representatives are involved in the decision making process so the impact can be fully considered. It is also more likely that those with long-term health problems and/or multiple morbidities will also be more likely to be experiencing socioeconomic deprivation. Thus this should be considered if the prophylactic is distributed outside of a trial (e.g. travel to treatment centres presenting additional costs to those immunocompromised should not lead to economic disadvantage to those most vulnerable, for reasons beyond their control). Those eligible are also more likely to experience mobility difficulties, or be homed in health and social care settings (learning disability, older people, mental health) treatment must be accessible for all groups. It is important that any roll out of this medication is well publicised among both patient groups and clinicians. Those from BAME background and immunocompromised are likely to be at higher risk, more likely to be from low socioeconomic background, and less likely to be engaged with health services when these aspects are present. Therefore it is vital that a roll out also targets those from under-represented groups to achieve equity of care.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal
	Blood Cancer UK	Please refer to the above comment in the 'Subgroups' section for an outline of how measures of cost effectiveness should consider disparity in risk from Covid-19, including due to both clinical and non-clinical factors.	Comment noted. The committee will consider how the

Section	Consultee/ Commentator	Comments [sic]	Action
		Relevant evidence includes (1) data on mortality and hospitalisation from Covid-19 disaggregated by ethnicity and deprivation level, (2) NHSE Covid-19 vaccine uptake data among the immunosuppressed, disaggregated by ethnicity and deprivation, and (3) data on the percentage of eligible patients who are treated for Covid-19, after testing positive and being referred to a Covid-19 Medicines Delivery Unit (CMDU), disaggregated by ethnicity and deprivation level. In each dataset, deprivation and ethnicity are strong indicators of whether a patient will die from Covid-19. Those living in the most deprived areas, for instance, are least likely to easily access vaccines, least likely to be given Covid treatment despite their eligibility and testing positive, and most likely to die from Covid. Secondly, cost per QALY is an imperfect unit of measurement in this instance and should be adjusted accordingly. A significant number of those who are unlikely to mount an adequate response to vaccines are, for instance, living with cancer or undergoing cancer treatment. Evusheld would undoubtedly improve and extend QALYs, not least by helping this patient group to mitigate the risks pervasive in their everyday lives. That said, the cost per QALY will be unreasonably higher for this group than if this treatment were available to healthy patients, because cancer patients are more likely to have a lower baseline quality of life when evaluating it using this scale of measurement. Using the cost per QALY measurement would therefore underestimate the benefit this treatment would have. The threshold of what is considered cost effective based upon cost per QALY should therefore be lowered in this instance, to account for this special circumstance and to adjust for what constitutes a 'healthy life' for those who are disabled, such as cancer patients, and particularly for those who are at highest risk due to clinical factors.	recommendation requires consideration of equalities issues during the appraisal
	Kidney Research UK	Many immunocompromised individuals are suffering from a substantial and long-term inability to carry out their normal day to day activities, such as going	Comment noted. The committee will consider how the

Section	Consultee/ Commentator	Comments [sic]	Action
		out shopping, meeting with family and friends, using public transport and going to work. As a matter of equality, it is imperative that the provision of prophylactic treatment is provided for this group of people, as it has been provided for the general population through vaccination. To leave the most vulnerable members of society unprotected from COVID-19 whilst prioritising a rapid roll-out of vaccine to protect healthy individuals is indefensible.	recommendation requires consideration of equalities issues during the appraisal
	Kidney Care UK	We know that many people within the highest risk groups (who would generally fall within equality legislation) feel unable to fully participate in society because of their ongoing risk from Covid. This poses the risk of restricted access to employment, fewer opportunities to maintain physical health, and a detrimental impact on mental health. It is important that the NICE appraisal is able to capture the benefits of being able to access an effective preventative treatment and therefore being able to more fully participate in society. By doing so, it will better promote equality between those at continuing high risk and the rest of the population. NICE should consider barriers to accessing treatment which may impact more on certain population groups, such as requirements to travel to hospital to receive Evusheld. This may be a barrier for people from lower socio-economic groups who cannot afford transport. To date, the routes to vaccines (particularly 3rd primary doses and subsequent boosters) and treatments have been heavily web based, which may create digital exclusion. Furthermore, many people with kidney disease have reported unnecessary complications within the system, with multiple phonecalls to different parts of the NHS and patients having to explain why they are eligible for a particular vaccine or treatment. This risks certain groups less able to advocate for themselves being excluded. We recommend a rollout of Evusheld is as streamlined and patient friendly as possible.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal

Section	Consultee/ Commentator	Comments [sic]	Action
	LUPUS UK	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 avoid inequitable uptake of the treatment.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal
	Myeloma UK	No comments	No action needed.
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	The population who needs access to this treatment are often handicapped in many other ways. The survey could fail to measure other compromises in housebound shielding for example elderly carers of an immunocompromised spouse, or the other issues measured in patient surveys.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal
	Anthony Nolan	**Psychological impact** Without an available prophylactic such as Tixagevimab–cilgavimab (Evusheld), many stem cell transplant patients are left with little alternative	Comment noted. The committee will consider how the

Section	Consultee/ Commentator	Comments [sic]	Action
		but continue adopting NPIs and shield themselves from their families and communities. Many have done this for some time now and take no pleasure whatsoever in contemplating a future where this continues. Anthony Nolan has surveyed transplant patients throughout the pandemic, including a specific study focused on minority ethnic patients. Our findings have been consistent in demonstrating an increase in anxiety and low wellbeing when having to shield and take additional social precautions. The psychological impact of shielding has been recorded across multiple disease areas[7,8]. Symptoms of anxiety, depression, and significant stress are recorded in all these groups. As the wider population returns to a form of normalcy, a sense of loneliness and abandonment risks compounding these factors to a greater degree. **Patients from a minority ethnic background** It has been observed that vaccine hesitancy is greater amongst minority ethnic communities. The UK Government commissioned a study on factors influencing COVID-19 vaccine update among minority ethnic groups which shows that Black African and Black Caribbean people are less likely to be vaccinated (50%) compared to White people (70%)[9]. Annecotedly, this same hesitancy has been shared by stem cell transplant patients and other haematological patients from the same backgrounds. It remains a risk that a minority of patients will continue to be hesitant around new technologies, especially those that have been recently introduced and which are administered intravenously. **Age and frailty**	recommendation requires consideration of equalities issues during the appraisal

Section	Consultee/ Commentator	Comments [sic]	Action
		Patients aged over 60 years are noted to have additional risk factors for severe COVID-19, according to Western Australian Department of Health. Analysis of England population-level data also indicates that mortality rates for patients aged over 70 were significantly higher than the rest of the population. These risk factors continue for transplant patients of the same age, especially those additionally immunocompromised. **Clinical Delivery of COVID-19 therapeutics** How Tixagevimab–cilgavimab will be clinically delivered will carry its own inequities. The starkest of issues can be seen between urban and rural patients, given that this technology requires 2x IM injections. What's more, a report on antiviral and nMABs delivery shows that for haematological diseases and stem cell transplant recipients, only 58% of those eligible for Sotrovimab received their IV. This is significantly lower than for solid organ transplant recipients at 72%. • A plan is required for its safe delivery as quickly as possible. Choosing to use the CMDU network has implications, with many attending patients being infectious. • Relying on primary care would require Information training required for patients, GPs, doctors and pharmacists and communities. This would be to ensure they have the information about Evusheld available for them. • Primary care pressures would also need to be factored in, including whether the rollout can be completed alongside the wider autumn immunisation programme.	

Section	Consultee/ Commentator	Comments [sic]	Action
		• BMT clinicians could give the IM injections to their own patients rather than a general care centre. • At a trust level, there will be a need for sufficient resource to allow delivery in secondary care and beyond. All delivery models should be led by the prioritisation of immunocompromised sub-groups, as per the approach in Western Australia. This will ensure a rapid rollout to those with the greatest clinical benefit. [7] – Spurr L et al, 2022, Psychosocial impact of the COVID-19 pandemic and shielding in adults and children with early-onset neuromuscular and neurological disorders and their families: a mixed-methods study, BMJ Open - https://bmjopen.bmj.com/content/12/3/e055430.info [8] – Westcott K, 2021, The impact of COVID-19 shielding on the wellbeing, mental health and treatment adherence of adults with cystic fibrosis, Future Healthcare Journal - www.ncbi.nlm.nih.gov/pmc/articles/PMC8004337/ [9] – BAME vaccination hesitancy, NHSE/I, 2021 - www.england.nhs.uk/south-east/wp-content/uploads/sites/45/2021/05/BAME-vaccination-hesitancy-A4.pdf [10] – Changes in COVID-19-related mortality across key demographic and clinical subgroups: an observational cohort study using the OpenSAFELY platform on 18 million adults in England - https://doi.org/10.1101/2022.07.30.22278161 [11] – Antivirals and nMABs for non-hospitalised COVID-19 patients: coverage report, 2022 - https://reports.opensafely.org/reports/antivirals-and-nmabs-for-non-hospitalised-covid-19-patients-coverage-report/	

Section	Consultee/ Commentator	Comments [sic]	Action
	Action for Pulmonary Fibrosis	No comment	No action needed
	Polycystic Kidney Disease Charity	No comment	No action needed
	Leukaemia Care	N/A	No action needed
Other considerations	AstraZeneca	None	No action needed
	Cardiomyopathy UK	None	No action needed.
	National Rheumatoid Arthritis Society (NRAS)	There is a strong case for arguing for access to the drug for people, especially those who have failed to mount antibody responses to the vaccines. In rheumatology, this is most likely to be people on rituximab or abatacept. It is not going to be for everyone in our beneficiary population. Also, there are some important caveats according to NRAS medical advisors : • The drug may increase the risk of cardiac events (especially in people with pre-existing cardiac risks) • The drug has not been evaluated in people with autoimmune diseases In summary, we are in favour of proceeding down this path for a well-defined high-risk population. What we at NRAS (without Medical Advisor input) are not sure about is whether people with ILD or other forms of lung disease in	Comment noted. NICE can only make recommendations for tixagevimab–cilgavimab within its marketing authorisation.

Section	Consultee/ Commentator	Comments [sic]	Action
		addition to their RA who are on drugs other than RTX or ABC would also fall into the high-risk RA population.	
	Blood Cancer UK	While Appendix B includes that "The impact of vaccination status or SARS-CoV-2 seropositivity" will be considered, it should be noted that seronegativity does not preclude the presence of a T-cell response to the Covid vaccines.	Comment noted. No action needed.
	LUPUS UK	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 efficacy of tixagevimab–cilgavimab than the COVID-19 vaccines and post-exposure therapeutics for	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		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.	
	Myeloma UK	No other considerations	No action needed.
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	The impact of no access to prophylaxis (due to no response to vaccines) on carers and other family members.	Comment noted. The scope identifies the main measures of outcomes that are relevant to estimating clinical effectiveness. That is, they measure health benefits and adverse effects that are important to patients and their carers
	Anthony Nolan	• There are a significant number of Long-COVID datasets that demonstrate an increase sequele on cardiac, neurological etc. Together they evidence that Long-COVID is indeed a real side-effect that poses serious impacts on long term health and we do not want transplant patients to acquire this and for it to disrupt their recovery.	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		• There should be a consideration for a monitoring programme such as that used for flu, to assess the ongoing risk factors for immunocompromised patients. This will help to ensure patients are protected in the long term. • Specific to stem cell transplant patients – routinely we do not re-vaccinate until several months after transplant. During this period, they are highly immunosuppressed and need prophylactic protection to fill that stop gap before vaccination. • Transplant patients also respond better to vaccinations after first resolving any Graft vs Host Disease issues (GvHD). Stem cell transplant population – to ensure surety of supply of Tixagevimab–cilgavimab, NICE/NHSE should engage the British Society of Blood and Marrow Transplantation and Cellular Therapies (BSBMTCT) in assessing the latest transplant population data, and who forms the priority sub-groups.	
	Action for Pulmonary Fibrosis	The 'health related quality of life'outcome should include the positive impacts on mental health of patients being able to adopt a more normal life with Tixagevimab–cilgavimab.?	Comment noted. The psychological impact will be captured in the outcomes included in the economic analysis
Questions for consultation	AstraZeneca	**How many people in England would be eligible for treatment with tixagevimab–cilgavimab? How would these people be identified in practice?** The NHS RAPID C-19 supported report '*Defining the highest-risk clinical sub-groups upon community infection with SARS-CoV-2 when considering the use of neutralising monoclonal antibodies (nMABs) and antiviral drugs'* was published in May 2022. The report was commissioned at the request of the	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Deputy Chief Medical Officer and outlines specific sub-groups who may be eligible for treatment and/or prophylaxis of COVID-19.[3] Whilst the report doesn't specifically outline which sub-groups would be eligible for prophylaxis, it does state that "…prophylaxis is usually reserved for use where the consequences of infection for a person or group of people is likely to be severe, either because of particular susceptibility of the people, or the inherent nature of the infection. This is because the balance of risk to benefit for prophylaxis is different to treatment" In England, the size of the eligible at-risk treatment cohort is estimated to be approximately 1.3 million. These patients are currently those who are offered booster vaccinations, and are identified for treatment with an anti-viral or nMAB in the event they develop COVID-19. Whilst the report identifies 1.3 million at-risk patients, the inherent risk may differ between groups of patients. We believe that these patients could be proactively identified and contacted in the same way that they were for vaccination or to advise of their eligibility for treatment upon community infection. Opportunistic "non-digital" identification and treatment is feasible and likely for both initial and repeat dosing Extremely high-risk vulnerable patients have regular engagements with Secondary Care specialist consultants (outpatient and in-patient appointments). There has been significant interest in tixagevimab-cilgavimab through both clinicians, academics, patients and patient groups; and there is likely to be a cohort of highly engaged, informed individuals who would proactively seek out treatment **Where do you consider tixagevimab–cilgavimab will fit into the pathway for preventing COVID-19?**	

Section	Consultee/ Commentator	Comments [sic]	Action
		Extremely high-risk vulnerable patients would benefit from pre-exposure prophylaxis as an adjunct to the current vaccination program as important additional preventative measure against developing symptomatic and severe COVID-19. Patients would be proactively identified via WebView and dosed every 6 months; tracked via blueteq. They could receive treatment at primary care, alongside secondary care, or at a vaccination centre. **Would tixagevimab–cilgavimab be used in both primary and secondary care settings? If so, about what proportion of use would you expect in each setting?** Patients who are likely to be eligible for treatment with a pre-exposure prophylaxis will likely be severely immunocompromised. We are also aware that 13% of this high-risk population are continuing to shield, and a further 68% whilst no longer shielding, are taking extra precautions.[4] We therefore believe that it may be most appropriate for patients to receive their prophylaxis treatment in secondary care during their routine clinical appointments. However, we understand this may not always be feasible, and may delay the deployment of this important therapeutic, and therefore believe that deployment could be facilitated in primary care, or in vaccination centres, so long as extra precautions are taken to minimise risks to the patient. **Would tixagevimab–cilgavimab be used at vaccination centres?** See comment above **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?**	Comment noted. No action needed. Comment noted. No action needed. Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Whilst included in the QALY calculation, it is important to consider the QoL decrement associated with the fear and anxiety of COVID-19; particularly in this high-risk population. Whilst there is no longer a recommendation to shield, a large population (81%) of those who are at high risk of adverse clinical outcomes due to COVID-19 are continuing either shield (13%), or are taking extra precautions (68%) when engaging with society.[4] Sixty-eight percent also advised that they would welcome a prophylaxis treatment, and we therefore believe that this will lead to improvements in their QoL. This is not too dis-similar to the approach adopted in TA769.[5] In addition, a large number of these high-risk, immunocompromised individuals will have carers, and therefore a carer disutility is likely. However, due to a paucity of published data, it's difficult to estimate this. Nonetheless, all QALYs will be considered, included the anxiety QoL decrement and carer perspective. 3. *UK Government. Defining the highest-risk clinical subgroups upon community infection with SARS-CoV-2 when considering the use of neutralising monoclonal antibodies (nMABs) and antiviral drugs: independent advisory group report. https://www.gov.uk/government/publications/higher-risk-patients-eligible-for-covid-19-treatments-independent-advisory-group-report/defining-the-highest-risk-clinical-subgroups-upon-community-infection-with-sars-cov-2-when-considering-the-use-of-neutralising-monoclonal-antibodies (2022),.* 4. *Office for National Statistics. Coronavirus and treatments for people at highest risk in England - experimental statistics. May 2022.* 5. *National Institute for Health and Care Excellence. NICE TA769: Palforzia for treating peanut allergy in children and young people. (2022).,.*	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	Cardiomyopathy UK	None	No action needed.
	Immunodeficiency UK	Many of the questions for consultation have been answered in the publication National Clinical Expert Consensus Statement 'Coronavirus monoclonal antibodies as a prophylactic therapy against COVID-19 for immunocompromised groups https://bit.ly/3bpE6oO. We urge NICE to consult this document which has been produced through the input of 17 medical specialities. Immunodeficiency UK cannot stress enough the absolute need for comprehensive clinical assessment and judgement for decision making for access to this therapy by treating clinicians. Treating clinicians are the people that know their patients best. They are specialists in the underlying health condition and have access to all relevant clinical details. Decision making solely by a CMDU would effectively cut off condition specific specialist input. We understand from patient and clinician experience that CMDU guidance is currently impeding and restricting access to longer doses of anti-virals vitally needed to help ensure clearance of COVID-19 infections in people with primary and secondary immunodeficiency.	Comment noted. No action needed.
	National Rheumatoid Arthritis Society (NRAS)	In regard to rheumatology: Hospital Trusts/Rheumatology teams should be able to identify patients on RTX and Abatacept. Would anticipate that this drug would be used in a secondary care setting, not primary care.	Comment noted. No action needed.
	Long Covid SOS	**How many people in England would be eligible for treatment with tixagevimab–cilgavimab? How would these people be identified in practice?** Please see comments to Population/Subgroups section	Comment noted. No action needed.

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		Where do you consider tixagevimab–cilgavimab will fit into the pathway for preventing COVID19? Currently the only way to prevent COVID-19 is to avoid infection with SARSCoV2. It is unclear from the literature whether this technology is more efficient at preventing infection and transmission compared to current available vaccines, although effectiveness against Omicron variants especially BA.4/5 appears to be reduced. The pathway to preventing COVID-19 should include adequate ventilation and mask wearing where possible, with this intervention offered to those who are exposed and not able to be protected by appropriate measures https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/coronavirus-disease-covid-19-ventilation-and-air-conditioning	Comment noted. No action needed.
		Would tixagevimab–cilgavimab be used in both primary and secondary care settings? If so, about what proportion of use would you expect in each setting? We would expect this to be managed in secondary care settings or via central hubs which identify those who require it/are at risk in a similar way to those who quality for antivirals in acute covid infection.	Comment noted. No action needed.
		Would tixagevimab–cilgavimab be used at vaccination centres? We would not recommend this due to the risk of anaphylaxis and other side effects. Also, uncertain how eligibility would be established	Comment noted. No action needed.
		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? This intervention would benefit those with Long Covid who have previously had an adverse reaction to a Covid vaccine causing symptoms to significantly deteriorate, or a return of symptoms after a previous resolution, and this should be taken into account in QALY	Comment noted. No action needed.

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		calculations. Reinfection can also negatively impact people with Long Covid therefore avoidance of infection is important Additionally, as some of those at risk for other reasons might currently have Long Covid. It would be useful to know if receiving this intervention improves their health, as this might signal a potential future health benefit. **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits** Several papers have been published demonstrating that Covid vaccination has a mixed impact on those with Long Covid. This study found that for 18% their symptoms deteriorated: https://www.mdpi.com/2076-393X/10/5/652 NB many studies (e.g. ONS) report on the average change in symptoms or the odds of experiencing Long Covid symptoms after vaccination. Data usually shows a positive trend overall but a significant minority are nevertheless negatively impacted by the vaccine	Comment noted. No action needed.
	Blood Cancer UK	Eligibility should include those who remain at highest risk from Covid-19, for whom pharmaceutical interventions such as vaccination aren't adequately effective. Further, groups who are least likely to receive treatment after contracting Covid-19 and have the highest mortality rates (based on clinical and non-clinical factors) should be prioritised. Identifying those at highest risk can be done by first identifying those groups least likely to mount an effective immune response to the Covid vaccines (e.g., people with immunosuppression as a result of a chronic condition, such as blood cancer, and/or as a result of medication or treatment). This has already been conducted with clinical input to produce the eligibility list for post-exposure and prophylactic Covid treatment, although it unduly excludes people with T-cell cancers not undergoing cancer treatment.	Comment noted. No action needed.

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		Evusheld should be made available to those eligible primarily via the secondary care route (e.g., their specialist teams and consultants). Evusheld should be deployed through specialist teams as they have a comprehensive and long-term view of the patient's condition, history, treatment type and schedule, and immune system. For this reason, it should not be delivered in the primary care setting, as primary care providers often do not know whether their patients are eligible for interventions such as additional Covid vaccine doses or post-exposure Covid treatments. It is arguable that eligible patients would encounter similar issues if attempting to access Evusheld via primary care. Evusheld should not be deployed via existing Covid-19 services such as Covid Medicines Delivery Units (CMDUs), as these are already struggling to cope with demand and leave at-risk patients without treatment, treating only around one quarter or less of eligible Covid-positive patients. However, if CMDUs had adequate capacity to administer Evusheld, they could do so under the direction of the patient's specialist team. Further, making Evusheld available through the secondary care route would reduce inequity in access to the treatment, reducing the risk of racial and socioeconomic disparity already seen in vaccine uptake (which are largely available only through external centres and pharmacies) and in delivery of post-exposure treatment (which are also available through external CMDUs). Those groups with low uptake in these areas are more likely to have higher uptake if a treatment is delivered via the secondary care route. Their specialist team would be responsible for discussing Evusheld with their patient and working through any concerns or hesitations the patient may have. Finally, safeguards must be created to ensure that patients who are eligible for Evusheld but are not undergoing treatment or do not regularly see their secondary care team for other reasons have equitable access. This includes those on 'watch and wait' or those who completed their cancer treatment course several months prior. Clear procedures must be in place for patients	

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		who are unduly refused treatment with Evusheld to advocate for themselves and access the treatment, if they are eligible. This is particularly important for the blood cancer cohort, who are largely immunosuppressed as a result of their condition, rather than solely due to their cancer treatment. They are more likely than other cohorts, therefore, to be at highest risk from Covid while not undergoing active cancer treatment. Whichever process is established for the delivery of Evusheld, it must be ensured that it is equitably accessible.	
	Kidney Research UK	**1. How many people would be eligible for treatment and how would these people be identified in practice?** It has been estimated that there are 500,000 immunocompromised individuals in the UK who could benefit from prophylactic monoclonal antibody treatment. (https://www.bmj.com/content/376/bmj.o722) Kidney and other solid organ transplant patients can be identified from the NHS Blood and Transplant Registry and those with autoimmune diseases or blood cancer may be identified by the National Disease Registration Service. Many of these individuals have already been identified as needing a third primary vaccine dose or Spring Booster. **2. Where do you consider tixagevimab–cilgavimab will fit into the pathway for preventing COVID-19?** Tixabevimab-cilgavimab needs to be made available to the groups already identified as soon as possible to provide the kind of protection which is already available to the general population through vaccination.	Comment noted. No action needed. Comment noted. No action needed.

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		3. Would tixagevimab–cilgavimab be used in both primary and secondary care settings? The deployment should be made as simple as possible to prevent the confusion which arose with third primary doses of vaccine and who was responsible for delivering that. Ideally it could be delivered through the existing Covid Medicines Delivery Units (CMDUs). Due to potential side effects at the time of injection, and the combination of using two products, this should be carried out by experienced staff in a secondary care setting.	Comment noted. No action needed.
		4. Would tixagevimab–cilgavimab be used at vaccination centres? Due to the site of injection and the need for privacy, this should not be delivered at vaccination centres. It would more appropriately be delivered at existing CMDUs	Comment noted. No action needed.
		5. 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? Many immunocompromised have been shielding or leading restricted lives for the past two and a half years, with no end in sight. The mental health issues associated with isolation have been well documented, and these have been prolonged for this group of people, well beyond the terms of lockdown for the general population. In addition, they can see others getting back to normal life – face to face work meetings, friends meeting in the pub or at the cinema, family parties, foreign holidays - and feel let down and forgotten, which compounds the depression and isolation. In addition, they tend to lead more sedentary lives, working from home, not using public transport, not going to the supermarket and carrying bags of shopping home. Over time this leads to a loss of physical fitness and stamina and a lack of variety of physical activity. This will impact on cardiovascular	Comment noted. The psychological impact will be captured in the outcomes included in the economic analysis

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		and bone health, already an issue for many of these individuals due to their underlying conditions. The use of tixagevimab-cilgavimab to protect against COVID-19 would enable these individuals to reclaim their lost lives, regain their fitness and once more become productive members of society. **5. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** Qualitative studies and systematic reviews on social isolation and sedentary behaviour Individual patient stories in the mainstream media eg https://www.frontiersin.org/articles/10.3389/fpsyg.2020.02201/full Knight RL et al. Moving Forward: Understanding Correlates of Physical Activity and Sedentary Behaviour during COVID-19-An Integrative Review and Socioecological Approach. Int J Environ Res Public Health. 2021 Oct 17;18(20):10910. doi: 10.3390/ijerph182010910. PMID: 34682653; PMCID: PMC8535281.	Comment noted. No action needed.
	Kidney Care UK	*Would tixagevimab–cilgavimab be used in both primary and secondary care settings? If so, about what proportion of use would you expect in each setting?* *Would tixagevimab–cilgavimab be used at vaccination centres?* Its important that we learn from the vaccine rollout about maximising accessibility. Many people will find it easier/would prefer to access the drug at	Comment noted. No action needed.

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		a local site, such as their GP or vaccination centre or pharmacy. We are also hearing more concern about travel costs to hospital appointments leading to decisions to cancel. However, some patients may want to have a discussion about risks and benefits with their kidney specialist before making a decision about the treatment. We do not have data on the likely split. Kidney Care UK received a huge number of calls from people who were experiencing significant stress when trying to access the third primary vaccine dose. Limited understanding of the correct process and eligibility criteria among GPs, hospital specialists, 119 and vaccination sites was a key problem. There have also been problems in the Spring Booster rollout and access to the antivirals, again related to difficulties in accessing correct information as well as lack of understanding about eligibility in some NHS staff. It's important any rollout of Evusheld learns from this and ensures communication across all teams is clear and comprehensive, and the responsibility of each part of the system is clear. OpenSafely data on vaccine rollout and use of antivirals in the community shows lower usage among certain groups, including Asian, Black and Mixed ethnic groups and lower socio-economic groups. An Evusheld rollout must be designed to avoid unequal access across different groups. *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?* See comment above regarding impact on anxiety, day to day activities/social interaction and confidence to enter back into employment.	
	LUPUS UK	***Where do you consider tixagevimab–cilgavimab will fit into the pathway for preventing COVID-19?***	Comment noted. No action needed.

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		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.	Comment noted. No action needed.
	Myeloma UK	*How many people in England would be eligible for treatment with tixagevimab–cilgavimab? How would these people be identified in practice?* There are over 20,000 patients living with myeloma in England.[8] Clearly there are a much larger number who have been identified as clinically extremely vulnerable, with 561,630 people in England identified as severely immunosuppressed in March 2022.[9] As previously stated there remain clinical uncertainties about which patients mount an immune response and further, what level of protection immune response, particularly antibodies provide. Further work and clinical input are needed to ascertain the best way to identify those most at risk based on the data we have.	Comment noted. No action needed.

[8] Cancer Prevalence UK Data Tables (2015) National Cancer Registration and Analysis Service. Available at: http://www.ncin.org.uk/about_ncin/segmentation
[9] COVID-19 vaccinations of severely immunosuppressed individuals (March 2022) NHS England. Available at: https://www.england.nhs.uk/statistics/statistical-work-areas/covid-19-vaccinations/

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		To identify myeloma patients that have not mounted an adequate immune response to COVID-19 vaccination would require data collection of laboratory ascertained absent (or low) SARS-CoV-2 spike protein antibody response following vaccination. *Where do you consider tixagevimab–cilgavimab will fit into the pathway for preventing COVID-19?* If approved for use, this will be the first treatment available to prevent COVID-19 infection. The National Clinical Expert Consensus Statement[10] outlines the strong emerging evidence that this treatment would be an effective strategy for immunocompromised individuals. We believe that this evidence supports the treatment to be part of the clinician's toolkit, in addition to vaccinations, to provide patients with the highest possible level of protection from COVID-19 infection. *Would tixagevimab–cilgavimab be used in both primary and secondary care settings? If so, about what proportion of use would you expect in each setting?* We support the National Clinical Expert Consensus Statement[10] that states clinical care should be designed to maximise uptake of tixagevimab–cilgavimab amongst eligible immunocompromised individuals whilst simultaneously making effective use of healthcare resources. We therefore expect the treatment to be used in both settings depending on which is most accessible for the individual patient. It is important that precautions are in place to ensure there is minimal risk of SARS-CoV-2 transmission from individuals with a known infection to those receiving prophylactic antibody therapy.	Comment noted. No action needed. Comment noted. No action needed.

[10] Lee LYW, Agrawal S et al. (2022) National Clinical Expert Consensus Statement: Coronovirus monoclonal antibodies as a prophylactic therapy against COVID-19 for immunocompromised groups. Available at: https://getevusheld.uk/assets/downloads/consensusstatement.pdf

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		Would tixagevimab–cilgavimab be used at vaccination centres? Yes, it is also an option to consider using the technology at vaccination centres. This would increase accessibility and reduce pressures in both primary and secondary care settings to deliver it. It is important to implement precautions in these centres to minimise the risk of SARS-CoV-2 transmission between individuals. *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?* No. [9] COVID-19 vaccinations of severely immunosuppressed individuals (March 2022) NHS England. Available at: https://www.england.nhs.uk/statistics/statistical-work-areas/covid-19-vaccinations/ [10] Lee LYW, Agrawal S et al. (2022) National Clinical Expert Consensus Statement: Coronovirus monoclonal antibodies as a prophylactic therapy against COVID-19 for immunocompromised groups. Available at: https://getevusheld.uk/assets/downloads/consensusstatement.pdf	Comment noted. No action needed. Comment noted. No action needed.
	Faculty of Pharmaceutical Medicine (endorsed by Royal College of Physicians)	Should the population be extended to some of the clinical trial population beyond immunocompromised patients. For example, those for whom vaccination may not be effective. (Such as those who are clinically obese) A key consideration is that patients should be able to access treatment through the primary care setting.	Comment noted. NICE can only make recommendations for tixagevimab–cilgavimab within its marketing authorisation.

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	Anthony Nolan	**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?** • It is not clear how the QUALY includes the varied long-term risks of a COVID-19 infection such ss heart, renal, liver etc. as well as Long COVID. It is important to measure the psychosocial and wellbeing effects of Tixagevimab–cilgavimab. Patients would be able to undertake some social interactions and would be able to stop shielding – which has a direct health-related benefit.	NICE health technology evaluations: the manual states health effects should be expressed in quality-adjusted life years. The manual also states that economic modelling should be long enough to reflect all important differences in costs or outcomes between the technologies being compared so relevant short and long term risks should be captured.
Additional comments on the draft scope	AstraZeneca	Note that the APPG on Vulnerable Groups to Pandemics published a clinical expert consensus statement in July 2022 in which it highlighted the urgent need to make prophylaxis treatments available as soon as possible to provide an immunity boost to vulnerable patients.[2] This reference should be added to the Related National Policy section. 2. *All-Party Parliamentary Group on Vulnerable Groups to Pandemics. July 2022. National Clinical Expert Consensus Statement. Coronavirus monoclonal antibodies as a prophylactic therapy against COVID-19 for immunocompromised groups.,.*	Comment noted.
	CLL (Chronic Lymphocytic	Our only additional comment would be to emphasis the urgency of this appraisal for this small group of clinically extremely vulnerable people so that the impact of covid19 on their mental health is reduced and they can return to	Comment noted. No action needed.

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	Leukaemia) Support	mainstream society as soon as possible. This will also have important benefits for their wider family, friends and carers. There is strong clinical support for Evusheld across a range of medical specialities from the evidence already available which includes the impact on mental health.	
	Evusheld for the UK	**1. How would these people be identified in practice?** Through the same mechanisms as those identified as eligible for additional vaccinations i.e. those who are immunocompromised/CEV. We reiterate that all patient groups listed in NHS England RAPID-C19. 2022. 'Defining the Highest-Risk Clinical Subgroups upon Community Infection with SARS-CoV-2 When Considering the Use of Neutralising Monoclonal Antibodies (NMABs) and Antiviral Drugs: Independent Advisory Group Report'. GOV.UK. 30 May 2022 should be administered this therapy. **2. Where do you consider tixagevimab–cilgavimab will fit into the pathway for preventing COVID-19?** As a prophylactic, this should initially be rolled out to all those meeting the criteria, regardless of vaccination status or seropositivity results. Further research is needed to support the degree of utility the vaccination has in context of the prophylactic; i.e. evidence is needed to consider whether prophylactic-only should be recommended, or whether vaccination should continue in those groups who are less responsive to the vaccine. This will influence where on the pathway this falls, however, unequivocally this should be available to all who meet the specific criteria as early as possible.	Comment noted. No action needed. Comment noted. No action needed.

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		3. 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? Yes. Unequivocally mental health, when patients are able to a normal functioning level, engaging in enjoyable activities, socialising and returning to work. The socio-economic benefits of a currently isolated social group returning to the wider world – and to work – should also be taken into account. **4. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** Three papers explore this with those who are identified as clinically vulnerable. ● Brooks, S. K., Webster, R. K., Smith, L. E., Woodland, L., Wessely, S., Greenberg, N., & Rubin, G. J. (2020). The psychological impact of quarantine and how to reduce it: rapid review of the evidence. The lancet, 395(10227), 912-920. ● Daniels, J., & Rettie, H. (2022). The Mental Health Impact of the COVID-19 Pandemic Second Wave on Shielders and Their Family Members. International Journal of Environmental Research and Public Health, 19(12), 7333. ● Rettie, H., & Daniels, J. (2020). Coping and tolerance of uncertainty: Predictors and mediators of mental health during the COVID-19 pandemic. American Psychologist, 76(3), 427.	Comment noted. An NHS and Personal Social Services perspective will be taken. The psychological impact will also be captured in the outcomes included in the economic analysis. Comment noted. No action needed.

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		These are published in respected journals with n=>720 in each paper; there are also other smaller scale studies which speak to the same issues. **5. NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:** **• could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which tixagevimab–cilgavimab is 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.** Yes, as described above, there are natural barriers to treatment for those who are more severely disabled, older, disengaged from the healthcare system or from deprived backgrounds. Particular consideration of equity of access should be given to those who are in health and social care settings, e.g. those with learning disabilities, older peoples homes, and those harder to reach such as those with more significant mental health problems, all of whom we know from the research are likely to have poorer compliance and health-related behaviours. **Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.**	Comment noted. No action needed.

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		Gathering data on the uptake of the vaccinations in these specific hard-to-reach groups may be useful; gathering qualitative data/survey data from charities and patient groups on these issues; secondary data analysis of Genera Practice Data for Planning and Research (GPDPR) datasets.	Comment noted. No action needed.
	Long Covid SOS	We would be interested to know if there is any data on whether this intervention has an impact on Long Covid symptoms or trajectory, or whether people who have been given this have gone on to develop Long Covid after a breakthrough infection, or symptoms similar to Long Covid without a Covid-19 infection	Comment noted. No action needed.
	Blood Cancer UK	There is a wealth of evidence demonstrating that Covid infections in people with weakened immune systems are more likely to generate new variants, due to both the nature of their immune systems and the relatively longer length of infection. There is, therefore, a broader public health question around minimising the risk of new variants that must be considered when evaluating the effectiveness of Evusheld.	Comment noted. No action needed.
	Kidney Care UK	We have now heard that this consultation will not lead to draft guidance until April 2023 although at the time of writing the NICE website does not say that. This timeline is extremely disappointing and kidney patients have told us that they are heartbroken and angry as they had hoped that guidance would come out in time for winter 2022.	Comment noted. Following referral to NICE an appraisal of tixagevimab–cilgavimab for preventing COVID-19 has been scheduled into the NICE work programme as a priority.

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

Anaphylaxis UK
Heart UK
Positively UK
Downs Syndrome UK