# Single Technology Appraisal
# Tixagevimab–cilgavimab for preventing COVID-19 [ID6136]
# Patient Organisation Submission

Thank you for agreeing to give us your organisation's views on this technology and its possible use in the NHS.

You can provide a unique perspective on conditions and their treatment that is not typically available from other sources.

To help you give your views, please use this questionnaire with our guide for patient submissions.

You do not have to answer every question – they are prompts to guide you. The text boxes will expand as you type. [Please note that declarations of interests relevant to this topic are compulsory].

**Information on completing this submission**

- Please do not embed documents (such as a PDF) in a submission because this may lead to the information being mislaid or make the submission unreadable
- We are committed to meeting the requirements of copyright legislation. If you intend to include **journal articles** in your submission you must have copyright clearance for these articles. We can accept journal articles in NICE Docs.
- Your response should not be longer than 10 pages.

## About you

| | |
|---|---|
| **1.Your name** | **Professor Martin Paul Eve** |
| **2. Name of organisation** | Evusheld for the UK |
| **3. Job title or position** | Patient Campaign Coordinator |
| **4a. Brief description of the organisation (including who funds it). How many members does it have?** | Evusheld for the UK is a patient-led campaigning group working for the availability of prophylactic monoclonal antibody therapies to prevent Covid in the immunocompromised in the United Kingdom.<br><br>We accept no funding from anyone or any organisation and work entirely on a voluntary basis.<br><br>We represent a patient body of approximately 500,000 people. We have an active group membership on Facebook of just under 2,000 members and a similar number on Twitter. |
| **4b. Has the organisation received any funding from the company bringing the treatment to NICE for evaluation or any of the comparator treatment companies in the last 12 months? [Relevant companies are listed in the appraisal stakeholder list.]** | No. We have not received any funding from anywhere. |
| **4c. Do you have any direct or indirect links with, or funding from, the tobacco industry?** | No. |

| | |
|---|---|
| **5. How did you gather information about the experiences of patients and carers to include in your submission?** | We receive patient testimonials on a weekly basis – often desperate stories from members of the group asking for advice – and also have our own experiences on which to draw. We have distilled these into a set of essential types (e.g. cases where people are frightened of their workplace covid arrangements) that paint a powerful picture of the ongoing difficulties faced by our patients. |

| | |
|---|---|
| **6. How has shielding from COVID-19 affected vulnerable people?** | While, for most people, the restrictions of the pandemic are a distant memory, for a significant number of patients – estimated at around 500,000 – the ongoing nightmare of shielding has never ended. The immunocompromised, who remain at serious risk from Covid and who cannot respond as well to vaccines, are being forced to take desperate measures to protect themselves. Official NHS guidance at the time of writing recommends that this group "work from home if you can", "keep social distancing", and "avoid meeting with someone who has tested positive". Clearly, although all societal protections have been removed, the health service recognises that this group are *not* safe returning to "normal" and essentially advises shielding, while making this now, supposedly, a matter of "individual choice".<br><br>**Mental Health**<br>We receive approximately one email per fortnight from members that mentions suicide or the intolerable ongoing conditions under which they are living.<br><br>The effects of prolonged isolation that this has entailed are causing serious mental health problems for our members. Length of time shielding/in quarantine is associated with poorer mental health outcomes (Brooks et al. 2020). Furthermore, 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) and with reported increased rates of mental health difficulties over time when comparing two samples (Rettie & Daniels, 2020; Daniels & Rettie, 2022).<br><br>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-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 significantly affected (Daniels & Rettie, 2022). |

| | |
|---|---|
| | 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%).<br><br>These mental health effects also go well beyond just the patient group. Many family members are also shielding and face the same mental pressures. Further, those that are not shielding nonetheless feel additional guilt and strain at the possibility of infecting their loved ones.<br><br>The long-term cost of mental health problems in those with health problems is well documented. 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.<br><br>**Work, Employment, Health and Safety, and Socialisation**<br>Another recurring theme with which we have to deal is members who are being forced back into dangerous working conditions, with inadequate protection. With no formal restrictions on employers and no support for those who are shielding, we hear from members who have left their jobs and are living off savings. In one case, one of our members has had to sell her house as she could no longer safely work and had no other savings.<br><br>We also know of a member who ran a successful carpentry business, employing three other people. He has had to close this down as he cannot work, in person, with other people given his ongoing clinical vulnerability.<br><br>Our members are, essentially, not able fully to be full economic citizens at present. The limitations on their lives as a result of only partial protection from the pandemic through inadequate vaccine response has far-reaching employment and work consequences.<br><br>Finally, we should note that our members are diverse. We span all ages, genders, sexualities, ethnicities, and socio-economic backgrounds. We have younger members whose prime of life has been reduced to Zoom calls and we have older members whose retirement is now effectively an isolation prison. The reduction in quality of life here is significant across an entire spectrum of people. |

## Unmet need

| | |
|---|---|
| **7. Is there an unmet need for patients with this condition?** | Yes.<br><br>We are very used to treating patients with primary and secondary immunodeficiencies using prophylactic IVIG therapies. Pre-exposure prophylaxis (PrEP) is also now widely used in HIV prevention. Indeed, as medical maxims go, “prevention is better than cure” has to be close to the number one spot.<br><br>Evusheld (tixagevimab and cilgavimab) is the first pre-exposure prophylactic monoclonal antibody therapy available to protect those who do not mount an adequate response to vaccination. In several real-world Phase Four observational studies, this drug has been shown to be effective at reducing hospitalisation and death in vulnerable patients (e.g. Kertes et al., 2022; Nyguen et al., 2022). Despite some laboratory in-vitro results showing reduced neutralisation against more recent variant assays, every real-world study has demonstrated extremely strong protection from Evusheld (Al-Obaidi et al., 2022).<br><br>32 other countries are using Evusheld to great effect. The United Kingdom currently stands as an international outlier, acting against international clinical consensus as the only G7 nation not providing this treatment. As the recent clinical consensus letter from 125 clinicians, across 17 specialities, representing all four nations put it: “Patients who would derive meaningful benefit should be offered prophylactic antibody therapy […] there is strong emerging evidence that prophylactic measures using monoclonal antibodies is an effective strategy for immunocompromised individuals.” |

| | |
|---|---|
| **8. What do patients or carers think are the advantages of the technology?**<br><br>• How would having a prophylactic treatment available impact the day-to-day lives of vulnerable people? (for example, how would it change the activities people do, or how they feel?)<br><br>• How would having a prophylactic treatment available impact carers? | The availability of prophylactic antibody therapy for Covid would radically improve the lives of our patients. For close to three years now, many of our members have not been able to see family at Christmas; they have lived apart from their families (some sleeping in summer houses and sheds); and they have lost their livelihoods. Having the additional partial protection of a drug like Evusheld would transform these lives.<br><br>Some of the key points that came from our patient body include:<br><br>• **Safety of medical appointments**. At the moment, a significant number of our members feel unsafe in clinical settings, where mask mandates have been removed and where patients are forced into confined, poorly ventilated hospital spaces with potential infection risks. One of our members, for instance, was placed in a storage cupboard, waiting for eight hours, as this was the only way to keep him safe. Another vulnerable member was placed on an open ward next to a covid patient, separated only by plastic sheeting. Having an additional layer of protection with Evusheld would make it safer for people who require hospital treatments.<br>• **Return to the workforce/employment**. Our members want to be full economic citizens, but at present struggle safely to participate in the workplace. Evusheld would allow those who work “in person” to have additional protection and safety, without worrying about whether their employer will protect them.<br>• **Basic sociality**. Some of our patients have never held newborn family members, cannot see any family members who do not isolate or cannot meet outdoors, and all of our members face a third winter in cruel isolation. One of our members is even living apart from her husband and daughter for safety reasons and sees them only by Skype/Zoom. This is an intolerable standard of life. Evusheld would give some of this life back and improve the mental health situation.<br>• **Reduction of pressure on the NHS**. Recent statistics showed that approximately 1/3 of seriously ill Covid patients admitted to hospital ICUs were immunocompromised. Given the pressure on ICU bed space, Evusheld could reduce the need for hospitalisation in this cohort, thereby alleviating pressure on the health service.<br>• **Impact on family and carers.** While the figure for the number of vulnerable patients is given as 500,000, the impacts of *not* providing Evusheld are felt much more widely. Families and carers are also living under the same conditions of isolation as the vulnerable as they cannot risk becoming a transmission vector. Again, Evusheld could help to free this group.<br>• **Making the most of treatments.** Many of our patients have had expensive previous treatments (chemotherapy, radiotherapy, organ transplants). Some have a limited life expectancy. However, at present they are not able to make the most of their remaining time or to benefit from the richness of life, |

| | |
|---|---|
| | because they remain shielding. Evusheld would allow this group to have a much higher quality of life and to reap the rewards of their other treatments. |

## Disadvantages of the technology

| | |
|---|---|
| **9. What do patients or carers think are the disadvantages of the technology?** | • **Level of protection.** Patients are (and should be) well informed about the level of protection that Evusheld confers. Nobody believes that the technology is a silver bullet. However, the message for this group with vaccines has been that "some protection is better than nothing". We think that the same should apply to Evusheld, as part of a multi-layer protection programme. |

## Patient population

| | |
|---|---|
| **10. Are there any groups of patients who might benefit more or less from the technology than others? If so, please describe them and explain why.** | The cohort who should be given the drug are specified in '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.<br><br>All members of this group are "unlikely to mount an adequate immune response to COVID-19 vaccination", the terms of Evusheld's MHRA authorisation.<br><br>We note that we are <u>strongly opposed</u> to serum antibody testing to identify beneficiaries of this treatment, for several reasons:<br><br>• There is no internationally recognised threshold for understanding how a level of serum antibodies correlates with actual protection against Covid (hence the US's FDA recommends against its use)<br>• Adding an antibody test creates significant additional logistical challenges for implementation<br>• Antibody testing may deter patients, particularly those from ethnic backgrounds who have been shown to exhibit healthcare/vaccine hesitancy<br>• The MHRA authorisation is for those "unlikely" to mount an adequate vaccine response, not those definitively shown not to have |

## Equality

| | |
|---|---|
| **11. Are there any potential equality issues that should be taken into account when considering this condition and the technology?** | Yes.<br><br>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.<br><br>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).<br><br>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. |

| | |
|---|---|
| **12. Are there any other issues that you would like the committee to consider?** | **Randomized Control Trials**<br>• **Not guinea pigs.** Our patients have been concerned by the calls for additional randomized control trials of Evusheld at this point. When there is such compelling evidence from overseas of real-world efficacy, testing by randomization to placebo is unethical and not acceptable to our group. 86% of respondents said that if they were offered such a trial, they would not feel safe enough to abandon their current shielding practices, meaning that any such study would remain flawed anyway with altered behavioural profiles. We feel that such an approach would be akin to testing parachutes that have been shown to work 80%-90% of the time in the real world by giving them only to 50% of jumpers from a plane.<br><br>**Bibliography**<br><br>• Al-Obaidi, Mohanad M., Ahmet B. Gungor, Sandra E. Kurtin, Ann E. Mathias, Bekir Tanriover, and Tirdad T. Zangeneh, 'The Prevention of COVID-19 in High-Risk Patients Using Tixagevimab–Cilgavimab (Evusheld): Real-World Experience at a Large Academic Center', The American Journal of Medicine, 2022 <https://doi.org/10.1016/j.amjmed.2022.08.019><br>• Brooks, Samantha K., Rebecca K. Webster, Louise E. Smith, Lisa Woodland, Simon Wessely, Neil Greenberg, and others, 'The Psychological Impact of Quarantine and How to Reduce It: Rapid Review of the Evidence', The Lancet, 395.10227 (2020), 912–20 <https://doi.org/10.1016/S0140-6736(20)30460-8><br>• Daniels, Jo, and Hannah Rettie, '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 (2022), 7333 <https://doi.org/10.3390/ijerph19127333><br>• Kertes, Jennifer, Shirley Shapiro Ben David, Noya Engel-Zohar, Keren Rosen, Beatriz Hemo, Avner Kantor, and others, '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, 2022, ciac625 <https://doi.org/10.1093/cid/ciac625><br>• Nguyen, Yann, Adrien Flahault, Nathalie Chavarot, Cléa Melenotte, Morgane Cheminant, Paul Deschamps, and others, '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, 2022, S1198-743X(22)00383-4 <https://doi.org/10.1016/j.cmi.2022.07.015><br>• Rettie, Hannah, and Jo Daniels, 'Coping and Tolerance of Uncertainty: Predictors and Mediators of Mental Health during the COVID-19 Pandemic', The American Psychologist, 76.3 (2021), 427–37 |

| | |
|---|---|
| | <https://doi.org/10.1037/amp0000710><br><br>We note, for reasons of acknowledgment, that these comments have been jointly prepared by Prof Martin Paul Eve with input from Nikola Brigden, Mark Oakley, and Dr Jo Daniels. |

## Key messages

| | |
|---|---|
| **13. In up to 5 bullet points, please summarise the key messages of your submission.** | • Many of our patients are still living under intolerable life conditions in order to protect themselves from Covid. They are not able to participate in work or social events and are sometimes living away from their families. They face incredible economic hardship as a consequence, with some having sold their houses just to survive. Others have abandoned successful businesses and laid off employees. Finally, many have been unable safely to access medical treatments.<br>• Evusheld could alleviate this situation and has been shown to provide good protection in every real-world study.<br>• Adding antibody testing to the process complicates the logistics significantly and is not necessary given the report identifying patients who should receive this therapy.<br>• Evusheld does not need to provide 100% protection to be of value. As part of a multi-layered strategy, combined with vaccines, it would provide stronger levels of reassurance to this patient body.<br>• The benefits to the NHS in alleviating both long-term mental health problems in this group and in freeing Covid ICU bed space are many. |