

## Single Technology Appraisal

### Tixagevimab–cilgavimab for preventing COVID-19 [ID6136]

#### Patient Organisation Submission

<b>Your name</b>	Victoria Tecca
<b>Name of organisation</b>	Blood Cancer UK
<b>How did you gather information about the experiences of patients and carers to include in your submission?</b>	We gathered the information contained in this report through (1) pre-existing case studies and direct quotes from patients in contact with our support and advocacy service advisors, (2) contact with our network of healthcare professionals, (3) a survey conducted by Blood Cancer UK and disseminated to our patient community, and (4) interviews conducted with people affected by blood cancer. The survey had 779 responses from blood cancer patients. Since it was distributed by Blood Cancer UK, respondents were self-selecting and biased towards our existing networks. Their views, therefore, are less likely to reflect the views of groups who are underrepresented in our networks, some of whom may be marginalised due to e.g., ethnicity. For these groups, the impacts discussed below may be heightened or altered.
<b>Living with the condition</b>	
<b>6. How has shielding from COVID-19 affected vulnerable people?</b>	In our survey conducted with blood cancer patients, 23% of respondents reported being so concerned about Covid-19 that they only left home for essential trips, while over a third avoided meeting people unless necessary and stayed away from indoor places such as restaurants and shops. 82% of respondents reported feeling anxious about Covid-19. Patients tell our service advisors that they want the same opportunities as those who are not immunocompromised. Some of those who are still shielding have high and constant levels of anxiety and fear. One patient describes it as feeling like they're "being told to isolate or play Russian roulette," as they feel abandoned by both the Government and the general public and forced to shield in the absence of other robust, effective, and accessible protection mechanisms. Many feel that leaving their home for any reason is a deadly risk, a perception that has led to some patients refusing to get vaccinated for fear of contracting Covid-19 at the vaccine site. The experiences of one patient attests to this: he had been shielding since 2020 but left his home for the first time for a non-essential reason in October 2022. While in a public space, he contracted Covid-19. Another patient, who has been shielding since 2020 without their family, describes their desperation: "I would sell my home to get Evusheld if it meant I could see my family and live without fear." While Covid-19 prophylaxis, including Evusheld, would not eliminate the risk posed to patients (as is discussed in our response to question 9), it is a

	<p>crucial component of the architecture of protection mechanisms available to patients.</p> <p>As one patient puts his shielding experience, “My diagnosis of Mantle Cell Lymphoma means that I have a potential lifespan of 5 – 10 years, so I would like to spend this time making memories with my family and friends. The fact that I am having to shield means that me and also my family are deprived of this valuable time together, this has a huge psychological impact. The fact I am unable to work [due to high risk in the workplace] means that we are put under a huge financial burden too, especially with the increasing cost of living. Having to shield also takes its toll on relationships, as it adds additional pressure due to the fact my daughter and wife cannot live a normal life either.” For those who live with family members or loved ones, the effects of shielding extend to the entire household. Several patients who speak with our advisors cite significant relationship breakdowns as a result of the enormous mental and financial health impact of shielding.</p> <p>While the impacts of shielding are far-reaching, the committee must also consider the impact of Covid-19 on people who are in particular circumstances that bar them from shielding, or do not have the resources to shield. This includes those who are experiencing financial precarity and must work in public-facing jobs, those who do not have recourse to public funds, and those with school-age children. As the cost-of-living crisis worsens, this group of people will expand. People with blood cancer who cannot shield are at very high risk from Covid-19.</p>
<p><b>Unmet need</b></p>	
<p><b>7. Is there an unmet need for patients with this condition?</b></p>	<p>There is an overwhelming unmet need for people with blood cancer, who remain inadequately protected from Covid-19. As a result of weakened immune systems, people with blood cancer have always been at higher risk from infections than the general population. Yet Covid-19 remains an acute threat to life for this patient group: in the first 6 months of 2022 alone, more people with blood cancer died from Covid-19 than did as a direct result of flu and pneumonia in the past 10 years combined in Wales and England. From January to June 2022, <a href="#">621 people</a> with blood cancer died from Covid-19, while a combined total of <a href="#">577 people</a> died from flu/pneumonia between 2011 and 2021 (an average of 60 people per year), where blood cancer was a contributing factor according to ONS data. While the ONS uses differing death registration data to record these two datasets (the former including all people with blood cancer, and the latter including those for whom blood cancer was listed as a contributory cause), the stark difference in mortality rates underlines</p>

	<p>the risk from Covid-19 that remains despite the introduction of vaccines and post-exposure Covid-19 treatments.</p> <p>Indeed, the mortality rate from Covid-19 has not lowered at the same pace for people with blood cancer as it has for the general population, which demonstrates the inadequate protection afforded by vaccines for this patient group. In the first half of 2022, among the unvaccinated the immunocompromised made up 2.4% of Covid intensive care admissions according to an <a href="#">ICNARC analysis</a>. Among those with 3 doses, this was 27.7%. Between January and October 2022, people with blood cancer made up <a href="#">1 in 12 people</a> (8.3%) admitted to intensive care where the primary reason was for Covid-19, despite making up less than 1% of the population at just under 580,000 people in the UK.</p> <p>Indeed, <a href="#">a recent publication</a> by Greenberger et al., (2022) in Blood Cancer Cell shows that, in people with blood cancer, the Covid-19 vaccines predominantly induce CD4+ T cells (which merely regulate the immune response) rather than CD8+ T cells, which actively kill viruses. Greenberger and his colleagues also found that only 50% of people with blood cancer mounted a detectable T cell response to the vaccines, and that T cell response was correlated with antibody response. A <a href="#">growing body of literature</a> also demonstrates that people with blood cancer and those on B-cell depleting treatment (including active cancer treatment) do not mount an adequate antibody/B-cell response to the vaccines, with 46% of blood cancer patients left <a href="#">without detectable antibodies</a> following a third vaccine dose. The current Government approach to vaccination relies on T cell responses in the immunosuppressed cohort; it is now well-known that antibody immunity wanes relatively quickly among people with blood cancer, but they are offered vaccine doses only every 6 months based on the assumption that T cell response will protect them. The research above suggests, however, that patients with low or no detectable antibodies also have an impaired T cell response. For those who do mount a T cell response, they are not producing CD8+ T cells, or those needed to eliminate SARS-CoV-2. The failure of the vaccines programme to protect people with blood cancer is evidenced by their disproportionately high mortality and intensive care admission rates, listed above.</p> <p>While post-exposure Covid-19 treatments are available, there are serious barriers to accessing these treatments within the treatment window of 5 to 7 days post-symptom onset. <a href="#">OpenSafely data</a> shows that only 24% of people who register a positive test and are referred for treatment actually receive it. While some of those referred may not be symptomatic, or may not be eligible according to their health condition, there is significant racial and socioeconomic disparity in access which suggests there are also operational failures that contribute to 76% of referred people not being treated. While 25% of those of white ethnicity receive treatment, the same can be said of only 13% of those in the Black or Black British ethnic group.</p>
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	<p>Similarly, 28% of people in the least deprived areas are treated, while only 17% of those in the most deprived areas receive treatment – and those living in urban areas are less likely to be treated than those in rural areas. There is also significant regional variation, with 29% of people in the East of England treated, and only 18% treated in London and the North East, and 17% treated in Yorkshire and the Humber.</p> <p>Case studies gathered by our service advisors show common barriers to access: (1) there is a widespread misunderstanding and lack of knowledge of blood cancer as a condition, as well as the guidance and eligibility criteria for people with blood cancer among healthcare professionals working in Covid-19 Medicines Delivery Units and (2) the assessment system favours patients who ‘perform’ their illness and vulnerability in a way that is often incongruent with how cancer patients present themselves in their day to day lives. Taken together, these barriers mean that patients who have the resources to advocate for themselves and who can ‘perform’ their illness adequately are most likely to receive treatment – which has arguably contributed to the racial and socioeconomic disparity evidenced by the OpenSafely data.</p> <p>People with blood cancer are therefore inadequately protected both by vaccines, and by the post-exposure treatments available. Despite both of these programmes running throughout 2022, people with blood cancer are 12 times more likely to die from Covid-19 than members of the general population. This has led some people to shield, while forcing those who cannot shield (due to, e.g., the reasons outlined in answer to question 6 above) into unsafe environments, putting them at very high risk and leading to further disparity.</p>
<p><b>Advantages of the technology</b></p>	

<p><b>8. What do patients or carers think are the advantages of the technology?</b></p> <ul style="list-style-type: none"> <li>• 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?)</li> </ul> <p>How would having a prophylactic treatment available impact carers?</p>	<p>Nearly universally, people with blood cancer tell our service advisors that have an effective, safe, and accessible prophylactic treatment would “give [them their] life back”, lessen their anxiety, and allow them to engage in public life in more meaningful ways than simply going to work or shielding. Many members of our community, even those who must put themselves at risk when going to work or welcoming their children home from school, have not engaged in non-essential trips or visits for over 2 years. They “want to hug and sit closely by family and friends without the worry of catching Covid and dying”. As many households affected by blood cancer are practicing these restrictions together, the impacts of an effective preventative treatment would extend to carers and other household members. For one patient, it would “allow me to go back to work too, but also more importantly make me feel a lot safer when attending hospital appointments for my ongoing care.” He continues, “I think it would also make my life a lot happier, as I can start to spend more time with my daughter too [who is at university].”</p> <p>People with blood cancer who are experiencing financial precarity are forced to work, often in public facing jobs, regardless of whether a preventative treatment is available. Such a treatment would drastically reduce the risks posed to them each day. People whose shielding has led them to financial precarity would also have their risk reduced, potentially to the extent it could be managed while also working. Prophylaxis would certainly allow them to have more informed conversations with their specialist teams about their risk levels as they incorporate risk management in their everyday lives.</p> <p>The vaccine and post-exposure treatment programmes have failed to adequately protect this patient group, as evidenced in response to question 7 above. An effective and accessible prophylactic treatment is vital to ensure that the risk from Covid-19 is reduced for people with blood cancer.</p>
<p><b>Disadvantages of the technology</b></p>	

<p><b>9. What do patients or carers think are the disadvantages of the technology?</b></p>	<p>The disadvantage of this technology is that its efficacy is dependent on the makeup of future variants, similarly to the Covid-19 and flu vaccines, and the already-available post-exposure monoclonal antibody treatments such as sotrovimab. Yet, patients often relay to our service advisors that they understand the technology does not eliminate their risk from both becoming infected with Covid-19, and adverse outcomes associated with infection. One patient says, if the technology to be made available, he would “still continue to take measures to protect myself, such as wearing filtered masks in public places and generally risk assess most situations.” While Evusheld is ineffective against some variants (e.g., BA.4.6) it retains efficacy against others (e.g., BA.2.75), and it may or may not be effective against other variants in the future. Evusheld should therefore be monitored closely if it is made available (alongside sotrovimab, for example, by reviewing emerging evidence and considering input from international bodies and regulators).</p>
<p><b>Patient population</b></p>	

<p><b>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.</b></p>	<p>The blood cancer cohort is heterogenous – due to the varying nature of blood cancer conditions and cancer treatments, some people within this cohort may benefit more from the technology than others. Those who do not mount an adequate cellular or humoral immune response from Covid-19 vaccines would benefit the most. While cellular immunity testing (T cell testing) is expensive and its accuracy is contested, serology testing would provide some insight into whether a humoral response has been elicited. It is important, however, that serology testing is not the sole indicator of who should receive this treatment; antibodies are but one component of the immune response, and those with cancers that affect their T cells may have seroconverted while still being at very high risk from Covid-19. Seronegativity could, however, be used as one key indicator of who might benefit and considered alongside a range of other factors when determining patient eligibility, and results from antibody testing would best be interpreted in light of the research cited in response to question 7 above which investigates the relationship between seroconversion and cellular response.</p> <p>A holistic assessment should be conducted to determine whether an individual would benefit from this treatment, using clinical markers and indicators beyond simply antibody response. Within the blood cancer cohort, Evusheld will likely be most beneficial 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, chemotherapy, monoclonal antibody therapy, and stem cell transplants). Delays to these treatments can lead to disease progression and future treatments that would have not otherwise been necessary. Stem cell transplant patients also rely on donors, and delays can impact donor availability; starting conditioning for transplant and subsequently becoming infected with Covid-19 can be potentially catastrophic for these patients. This is a particularly acute risk for patient groups with historically low donor matches, including those from minoritised ethnic backgrounds. Further, some blood cancer patients may need treatments that require regular hospital visits, e.g., patients with Multiple Myeloma who need dialysis three times per week at a renal unit, or patients with MDS who require weekly transfusions where exposure to staff and other patients is unavoidable.</p> <p>The holistic assessment should also consider people with chronic blood cancers whose lives have been significantly disrupted by their high risk from Covid-19, such as being at risk of poverty and other forms of financial precarity and those with limited prognosis who wish to spend time with loved ones before death. There is also stark disparity in mortality rates from Covid-19, along ethnic and socioeconomic lines. A holistic assessment should take into account social and environmental factors that impact on risk from Covid-19.</p>
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	<p>Over a quarter of intensive care admissions primarily for Covid-19 are from people living in the most deprived areas, and 48.6% of these intensive care admissions live in the two most deprived quintiles, according to <a href="#">ICNARC</a>. People living in these areas are also the <a href="#">least likely</a> to be treated for Covid-19 if they are infected. It is therefore imperative that, were the technology to be made available, it is rolled out in a way that ensures equitable access – with a focus on ensuring access for those living in the most deprived areas and without the resources to pay for this treatment through private channels.</p>
<p><b>Equality</b></p>	
<p><b>11. Are there any potential <a href="#">equality issues</a> that should be taken into account when considering this condition and the technology?</b></p>	<p>There are serious health inequalities in the Covid-19 protection programme for the immunocompromised, constituted by the vaccines and post-exposure treatment initiatives. People of Bangladeshi, Pakistani, Black Caribbean, and Black African backgrounds are <a href="#">less likely to be vaccinated</a> than those of white backgrounds. People of all ethnic groups are less likely to receive post-exposure treatment than those of a white background – with people of Black backgrounds the <a href="#">least likely</a> to receive treatment. Those living in the most deprived areas are both least likely to receive treatment, and most likely to be admitted to intensive care for Covid-19, as has been evidenced in response to questions above. This technology must therefore be rolled out in a way that ensures equitable access to those who are least likely to benefit from the other two components of the Covid-19 protection programme. A failure to do so risks increasing racial and socioeconomic disparity further.</p>
<p><b>Other issues</b></p>	
<p><b>12. Are there any other issues that you would like the committee to consider?</b></p>	<p>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.</p> <p>Further, while people who are immunocompromised make up less than 1% of the population, they are overrepresented in intensive care admissions, making up more than 1 in 9 people admitted primarily for Covid-19. This figure, from <a href="#">an analysis conducted by ICNARC</a>, is conservative. It includes only those who have had chemotherapy, radiotherapy or daily high dose steroid treatment in the previous six months, HIV/AIDS, or congenital immune deficiency. An evaluation of the cost-effectiveness of this technology must also consider the current costs associated with being at high risk from Covid-19. The evaluation should determine whether the costs of administering Evusheld are outweighed by potential savings made elsewhere.</p>



## Key messages

<p><b>13. In up to 5 bullet points, please summarise the key messages of your submission.</b></p>	<ul style="list-style-type: none"><li>• People with blood cancer remain inadequately protected from Covid-19, despite the vaccines and post-exposure treatment programmes.</li><li>• Prophylaxis is a crucial way to address the unmet needs of this patient cohort.</li><li>• This cohort's risk from Covid-19 has significant and far-reaching consequences including adverse outcomes and death from Covid-19, interruptions to life-saving treatments, and blood cancer disease progression.</li><li>• Additional consequences of the risk from Covid-19 include financial precarity, social isolation, and psychological deterioration.</li><li>• The current Covid-19 protection programme reflects and is productive of racial and socioeconomic health inequalities, and this technology must be rolled out in a way that ensures equitable access.</li></ul>
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