

**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

<b>1. Your name</b>	<b>Dr Susan Walsh</b>
<b>2. Name of organisation</b>	Immunodeficiency UK
<b>3. Job title or position</b>	CEO
<b>4a. Brief description of the organisation (including who funds it). How many members does it have?</b>	Immunodeficiency UK (previously known as PID UK) supports people affected by primary and secondary immuno-deficiency (PID and SID). We help give advice on managing their condition, their treatment; promote awareness and understanding of PID and SID within the general public and medical profession to promote better understanding of these conditions and their impact. We provide a helpline service, events and practical help and advice and advocate for improved healthcare. Our funding comes from public donations, events, legacies, pharmaceutical companies and trusts and foundations ( <a href="#">Immunodeficiency UK - Sponsors</a> ). We currently have over 1000 members.
<b>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?</b>	No
<b>4c. Do you have any direct or indirect links with, or funding from, the tobacco industry?</b>	No
<b>5. How did you gather information about the experiences of patients and carers to include in your submission?</b>	Immunodeficiency UK carried out a survey of its members with questions addressing the issues of this consultation. The survey was a mixture of quantitative and qualitative (free text) questions. Access to the survey was via a link sent by a membership mailing. We received 516 responses: 254 from people directly affected by PID; 194 affected by SID and 68 responses from carers of those affected. Responses were collected from 11 - 27 August 2022. <b>Numbers of people testing positive:</b> Of 254 PID respondees 101 (39.76%) had tested positive for COVID. For 194 SID patients 62 (32%) had tested positive for COVID.
<b>6. How has shielding from COVID-19 affected vulnerable people?</b>	Shielding has had a severe adverse effect on the mental health and quality of life of people affected by primary and secondary immunodeficiency. Anxiety, worry, fear, depression, isolation, lack of social interaction, panic attacks, and PTSD (from having had a COVID infection) were mentioned in our survey responses group. There is

a constant fear from infections brought home by others in the family unit and this fear is likely to increase further as case rates of COVID increase over the coming winter period. Shielding has also affected people's income and ability to earn a living and in some cases led to loss of their job and businesses. This impact is not only on the person who has been shielding but also on the family unit. Through our helpline and survey responses we have heard of broken relationships caused by the strain of shielding, people with immunodeficiency living away from their loved ones so that the unaffected members of the family can get on with their lives. Many carers are still shielding and leading very restrictive lives, in order to protect their relatives. For some of our members shielding has resulted in not being able to invite children to birthday parties for their children, missed celebrations of family events, lack of contact with grandchildren.

There remains considerable anxiety and distress within the community about getting COVID and profound fear about the health consequences of having a COVID-19 infection. **Our survey found that a significantly high proportion of our community are effectively continuing to shield.** Of 439 respondents, in our survey, affected with either SID or PID, 30% were not going out at all, 43% had little confidence in going out; 16% (71) were moderately confident; with only 6% mostly confident and 5% very confident. **Our survey data shows that the quality of life (QoL) for those affected by PID and SID is continuing to be severely affected by COVID.** When asked to rate their quality of life (QoL) on a scale of 1 -100 (poor to excellent) pre-pandemic and now, PID and SID patients reported an average rating pre-pandemic QoL rating of 79 (430 responses) compared to a QoL rating of 30 (426 responses) at the time of the survey.

**Carer data on shielding:** Of 43 carers who responded to this question, 17 were not going out at all, 18 had little confidence in going out; 5 were moderately confident; with 2 mostly confident and 1 very confident. When asked to rate their quality of life (QoL) on a scale of 1 -100 (poor to excellent) pre-pandemic and now, carers reported an average rating pre-pandemic QoL rating of 81 (43 responses) compared to a QoL rating of 25 (43 responses) at the time of the survey.

**Survey data below showed that despite the 'safety net' of access to \*COVID medicines if people test positive, there remains little confidence in entering society. [Confidence of living with COVID in those people with PID/SID who had tested positive and had accessed \\*COVID 19 therapies:](#)** Of 105 respondents (affected by PID or SID) 20% were not going out at all, 38% had little confidence in going out; 21% were moderately confident; 13% were mostly confident and 8% very confident indicating there remains considerable concern about getting COVID again.

**\*Please note that only a proportion of people who are eligible for anti-COVID medicines actually get them. Data from the COVAD study** shows that since the deployment of CMDUs, 61.4% (n=70/114) of treatment eligible patients actually got treatment from a CMDU. The study found significantly lower rates of hospitalisation (4.3% vs 15.9%, p=0.03) amongst individuals treated by CMDU but overall mortality was not affected (2.8% vs 4.5%, p=0.63). **Our survey data** showed that of 154 people who had tested positive for COVID-19 and were on the COVID medicines eligibility list, 46 (30%) were not offered any form of treatment. This uncertainty in accessing COVID-19 treatments, despite being listed on the eligibility list, adds further to the anxiety and uncertainty that people are facing in the context of living with the threat of COVID.

**Patient quote:** 'I do not currently feel safe with the treatments available in the UK. At the moment, if we contract Covid we are given post-exposure therapies. This then relies on us taking the risk of becoming infected and then seeking help. This feels incredibly risky and, as a result, we are still shielding with incredibly limited lives'.

**Carer quote:** 'Despite 5 Pfizer vaccine doses my wife has no antibodies (test paid privately as told not available under NHS) she has no protection to covid and thus our lives are now so different. I've had to stop work to protect her and we have no social life merely living an existence at home and going nowhere.'

**Carer quote:** 'My husband has a PID which, according to recent statistics, would result in a high chance of death if he contracted it. As these are risks we are not prepared to take we therefore remain shielded, and this has had a huge impact on our mental and physical wellbeing as well as the company that we run locally which is a major employer for the area'.

**Carer quote:** The immuno suppressed are expected to live a normal life like everyone else who has been vaccinated, and hope that if they catch Covid (which is highly probable, as the vaccines are not effective for them) they can access the antivirals in time for them to be at their most effective. As a result they are not living a " normal " life, and most are actually still shielding, or living a very restricted and isolated existence. This is having a massive knock-on effect to their physical and, in particular, mental health. **It has left my wife suicidal and needing 12 months of counselling and cognitive behavioural therapy.** Whilst the initial impact is on the 500,000 immunosuppressed, there is also the impact this has on their families and friends. There is the fact that some people have felt the need to give up their jobs or lost them as a result of not feeling safe in the place of work. I go to work in a hospital every day worried that I will bring the virus home, as does our son, to my wife

who is immunosuppressed. We are unable to eat in restaurants, go to the theatre or cinema. We do not have family/friends in the house , nor any workmen.'

**Carer quote:** 'My husband has not caught it due to continued careful shielding, however the shielding itself has had a significant impact on the mental health of all our family. For example our teenage daughter has been diagnosed by CAMHS with moderate depression and is now on antidepressants.'

**Shielding from the fear of getting COVID is also affecting people wanting to access healthcare.** 169 of 437 respondents (38%) were < 20% confident; only 86 of 437 respondents (20%) had > 60% confidence in accessing healthcare in a hospital setting. Some free text responses indicated that people were NOT willing to access ANY healthcare in hospital due to the risk of getting Covid, especially as many COVID restrictions have been lifted.

**Patient quotes:** 'Since freedom day in 2021 I have not been able to safely visit NHS sites. Worried about catching covid whilst travelling to the appointment or in the NHS venue'. 'Attending hospital environment is so traumatic and stressful'. 'Many safeguards have been removed that would help protect me'.

## **7. Is there an unmet need for patients with this condition?**

COVID continues to pose a significant risk to subgroups of patients with PID and SID who have been unable to produce a protective response after repeated vaccination and there is an unmet need. Evidence for this is included in the following 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.

Data from CO-VAD study (antibody deficient patients) 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. CO-VAD data is available on 155 individuals with SARS-CoV-2 infection since the deployment of vaccination (January 2021). Hospitalisation rate with Omicron was 9.9% vs 2.2% for the general population and mortality was 2.7% vs 0.2% for the general population. As of August 2022, the cumulative incidence of infection in this longitudinal cohort is 28.6% which is much, much lower than the ONS cumulative incidence of infection in the general population which was 70% back in February 2022 indicating that many people in this group have not

yet been exposed to the virus. This is probably due to a large proportion of the community continuing to shield.

**Our survey data concerning patient views on unmet need:** 79.67% (341/428 responses) from people affected by SID or PID indicated an unmet need. Only 3.5% (15/428) of respondents said there was no unmet need; 4.4% (19/428) stated they didn't know. Of those people who said there was an unmet need, 40% (139/341) specifically mentioned the need for Evusheld and 12% (41/341) stated the need for prophylaxis/prevent infection therapies, indicating that people recognise that although COVID-19 medicines may be available via CMDUs if they test positive for COVID-19 they desperately want a protective strategy.

**Patient views:**

'I do not generate memory antibodies – so DoH banging on repeatedly about the success of the vaccine program is very frustrating. Vaccines might be good enough for some vulnerable patients, but vaccination alone is not enough for my needs.'

'Yes, there is prophylactic options available such as Evusheld which is being used in other countries. This has not been made available so consequently life is still anything but normal for me and I am having to be incredibly careful still. If I keep contracting covid and needing months off work then I will lose my job. I still cannot go to the shops or a restaurant or meet friends and family in their homes because I do not want to experience the terrifying experience I have already had once with covid. I think much, much more needs to be done to support the immune compromised in getting back to normal life and being able to function in society and prophylactic medicines would facilitate us being able to take steps to do this.'

'Yes, absolutely. There are many thousands of primary and secondary immune deficient people still living their lives under shielding conditions - removed from society and from 'normal' life, unable to go into public contact situations without fear - people with children, jobs, family, dependents, etc - who still cannot participate in everyday activities because of the lack of protection available. There is an enormous unmet need. None of the therapeutic options currently on offer give any protection for these vulnerable people, and Evusheld is the only option available for these people to be able to return to some kind of 'normal' life.'

It is also noteworthy that the APPG on Vulnerable Groups to Pandemics has produced a 'National Clinical Expert Consensus Statement 'Coronavirus monoclonal antibodies as a prophylactic therapy against COVID-19 for

immunocompromised groups'. This was produced and endorsed by over 120 clinicians indicating that the **medical profession is also of the opinion that there is an unmet need.** <https://bit.ly/3bpE6oO> .

[Continued below – problems in formatting the pages - apologies](#)

**8. What do patients or carers think are the advantages of the technology?**

**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
- Psychological benefits - improved mental health and relief of strong feelings of anxiousness and isolation and increased confidence to reduce shielding.
- Prevention of new pathogenic escape variants due to inability of the immunocompromised to clear COVID-19 infection, even after treatment with anti-viral therapies.

COVID infections in the immunocompromised are a possible driver of mutations (<https://www.nature.com/articles/s41467-022-30163-4>) and can cause the subsequent creation of new variants that escape immunity from vaccines and previous infections. This adds to the argument that protections for people who have immunodeficiency should be bolstered, as part of a wider public health strategy of permanently reducing overall Covid cases.

- Improvement in health as people who are immunocompromised will feel more comfortable in accessing healthcare (see our survey data above) – 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
- Demonstrating that the health system is supporting **all** members of society going forward in the living with COVID-19 plan
- Reduced call on CMDU services and use of anti-virals

It is noteworthy from our survey that in patients who had tested positive for COVID and accessed anti-virals, 37% of respondents reported that the COVID-19 medications offered did not clear their infection, resulting in COVID rebound, recurrence of symptoms and in some cases, people required 2<sup>nd</sup> courses of treatment. This inability to clear infection resulted in time off from work and in some cases long periods of illness and hospitalisation.



**Patient experience:** ‘It [Paxlovid] definitely improved my condition and I believe I would have ended up in hospital very poorly without it. However I was still positive on day 18, ended up in A&E on day 20, was very poorly for weeks to come and still suffering after effects now’; ‘tested positive for ten weeks after taking paxlovid’; ‘I continued to develop different symptoms and remained very unwell signed off work for 3 weeks. I tested positive continually for 17 days’; ‘I was still testing positive at 21 days but had to return to work on day 19 whilst still feeling terrible.’; ‘Admitted to hospital with a very high viral load 10 days after finishing outpatient treatment’. ‘Molnupiravir did not clear the infection needed to have Sotromivab as a follow-up treatment’. ‘The first course of Paxlovid failed to clear the virus and so I got COVID rebound, recurrence of symptoms and I needed a 2nd course of Paxlovid before I was consistently COVID-free.’

- Reduced cases of chronic coronavirus infections and consequent health costs of long COVID:

From our survey data 59% (93/157) of PID + SID respondents who had tested positive for COVID reported long-term effects of having had COVID. 70% (64 of 92 respondents) reported effects lasting several months. **Physical impacts reported included:** reduced breathing capacity for several months, lung pain, constant coughing, exacerbation of previous health problems, increased susceptibility to infection, mobility issues, fatigue and exhaustion, anosmia, gastrointestinal problems; joint pain, cognitive difficulties with memory/attention /concentration/word finding difficulties (brain fog), dizziness, fainting, headaches & migraines, post exertion symptom exacerbation (PESE/PEM), diarrhoea, neurological symptoms such as vertigo, spells of deafness in one or both ears, spells of agonising headaches, vision problems, heart problems. **The mental health impact, in this group,** was mentioned in 21% (20/93) of responses. Anxiety, worry, fear, depression, isolation, panic attacks, PTSD, frustration at losing previous relatively fit lifestyles were reported. **Impact on ability to work** was mentioned in 13% (12/93) responses and included loss of employment, bedbound/unable to work – on disability benefits, need to take several months off work, taking reduced hours/ inability to work full-time, phased returns to work, occupational health support and reasonable adjustments at work, need to take early retirement and expectation to lose jobs due to continuing health problems. These problems have led to people losing income with resulting financial instability. There was also mention of the on-going need to depend on other people for care and support.

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 alternative therapeutic prevent strategy for

	<p>subgroups of people with primary and secondary immunodeficiency who have not been able to benefit from vaccination.</p> <p><b>View from a carer:</b> ‘Despite all of our best efforts, our immunosuppressed daughter contracted Covid because she had to go into work one day, and despite her wearing high quality masks, because there are no longer any mitigations in place, she was infected. It was absolutely terrifying, our worst nightmare. Fortunately her specialist team accessed Sotrovimab for her really quickly, but it didn't seem to neutralise anything. She was very poorly, dropping SATs which we constantly monitored, isolated her at home and double masking in the house. She tested positive for 15 days, had to come off all of her other disease modifying medications to give her immune system a chance to recover, and has now had to go on a high dose of steroids to help get her back on track before resuming her usual treatments. All because of the position this government is taking that despite all of the real world wide data there is regarding effectiveness, it will not procure Evusheld. She leads a virtually non-existent life, she is a young woman whose life has shrunk to nothing. I have seen her change from a strong person who dealt with her underlying condition as best she could and led as full a life as possible to a shadow of her former self, frightened of contact with people and who I now not only fear for physically, but mentally as well. She used to have a life, she used to socialise, travel, do normal things all of which meant putting money into the economy. She doesn't do any of that now so if we dispassionately take out the physical and mental effects of not being able to live with Covid, the economical impact is significant. Because this doesn't only affect her, it affects us as her carers as well. Our lives have shrunk too, we are in our 60s and cannot enjoy a full life because we have to weigh up everything in the context of what risk might we bring home to her. We only socialise now in a limited way, we have only travelled once and I am reluctant to do so again. So we too aren't putting money into the economy.’</p>
<p><b>9. Disadvantages of the technology?</b></p>	<p>It is an intramuscular injection and will hurt.</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>We absolutely recognise that not all people affected by PID and SID will benefit from Evusheld or are in equal need of Evusheld. People with PID and SID represent an extremely diverse range of patients many of whom will have mounted a good protective response against COVID through the vaccination programme (although there is no routine testing of antibody levels, T cell function in this group). Therefore, there needs to be expert clinical judgement as to which patients would benefit most based on individual vaccine response data and knowledge of the underlying condition and co-morbidities, and subsequent risk level from COVID.</p>

	<p>Evusheld would certainly provide an extra layer of protection for those patients with primary antibody failure and secondary antibody failure who will not recover B cell function and for those patients who have had B-cell depleting agents and even more important for those who are older/have co-morbidities e.g. major organ involvement such as significant kidney, liver or lung inflammation or significantly impaired renal, liver and/or lung function. These are common complications of having a PID or a SID.</p> <p>X-linked Agammaglobulinemia and other PID conditions with very low/absent B-cells appear to be specifically associated with inability to clear SARS-CoV-2 virus leading to prolonged infection (Brown et al., J Allergy Clin Immunol. 2022 Feb;149(2):557-561.e1; reviewed in Ponsford et al., Curr Opin Allergy Clin Immunol. 2021 Dec 1;21(6):525-534.). Patients with the PID APS1/APECED have been reported to have had life-threatening COVID-19 (Meisel et al., J Clin Invest. 2021 Jul 15;131(14):e150867 and Bastard et al., J Exp Med. 2021 Jul 5; 218(7):e20210554). Common variable immunodeficiency (CVID the most type of PID) is associated with variable outcomes regarding COVID, likely reflecting the clinical heterogeneity of this group of patients. Co-morbidities known to be associated with worse COVID outcome in the general population, such as pre-existing lung and liver disease have higher prevalence in CVID and are also associated with worse outcome in this group (Shields et al, J Allergy Clin Immunol. 2021 Mar;147(3):870-875.e). Other subgroups that would benefit include people with combined immunodeficiencies which affect T and B cell function, patients with 22q11 have had particularly bad outcomes following COVID infection, people with immune mediated inflammatory disease patients e.g. individuals with stable rheumatoid arthritis, but have terrible lungs with poor pulmonary function, people on rituximab, CD19 CAR-T, BTK inhibitors treatment patients and patients after HSCT who are still considered to be immunosuppressed.</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>Evidence indicates there has been considerable inequality in mortality rates, vaccine uptake and indeed access to COVID medicines amongst different ethnic groups and socioeconomic backgrounds (<a href="#">Antivirals and nMABs for non-hospitalised COVID-19 patients: coverage report   OpenSAFELY: Reports</a>; section: Key demographic and clinical characteristics of treated patients). This means that <b>one</b> measure of cost effectiveness isn't representative of everybody's circumstances and both clinical and non-clinical parameters need to be considered in the NICE analysis.</p> <p>Equitable access is needed via secondary care settings (specialist centres) and not via a CMDU due to reported problems with this delivery system – see below. 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, including</p>

co-morbidities, and are best able to do a comprehensive clinical assessment and make a clinical judgement regarding access to Evusheld.
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## 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>• For people with primary and secondary immunodeficiency shielding has had a severe adverse effect on their mental health, quality of life, ability to earn a living and their confidence in accessing healthcare and a significant proportion of people affected by these conditions, and their carers are continuing to shield because of fear of getting COVID and the serious health complications it could bring.</li> <li>• There are specific subgroups of people with primary and secondary immunodeficiency who would benefit from access to Evusheld as a protect strategy because of an inability, due to their underlying condition, to mount an adequate protective response through vaccination.</li> <li>• Access to COVID medicines (antivirals, Mab therapy) for those people who test COVID positive and are on the eligibility list can be challenging and access is not guaranteed. COVID rebound, lack of access due to contraindications to anti-virals, existing health problems compounded by long-COVID are major problems.</li> <li>• Our patient survey data highlights a major unmet need - an additional strategy is needed based on providing protective therapies such as Evusheld to help people re-enter society and live more normal lives.</li> <li>• People in our community continue to feel that their specific needs are being marginalised and forgotten in the 'living with COVID' planning by the UK Government. This feeling of injustice and inequality is further underlined by UK being the only G7 country where Evusheld is not available. Evusheld should be made available to the subgroups of patients that would benefit most as soon as possible.</li> </ul>
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Thank you for your time.

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