NICE National Institute for Health and Care Excellence

Single Technology Appraisal
AZD-3152 for preventing COVID-19 [ID6282]
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.

NICE National Institute for Health and Care Excellence

About you

1.Your name	**Robbie Burns**
2. Name of organisation	Cardiothoracic Transplant Patient Group (CTPG), NHS Blood & Transplant (NHSBT)
3. Job title or position	Chair
4a. Brief description of the organisation (including who funds it). How many members does it have?	The CTPG is a patient led group established by NHSBT to represent all people in the UK at any stage of the heart and / or lung transplant pathway (including those with long term ventricular assist devices (VADs) All patient members are voluntary and NHSBT fund the administration. Membership includes over 20 representatives from other cardiothoracic transplant stakeholder organisations (e.g. national disease-based charities and centre specific patient organisations)
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.] **If so, please state the name of the company, amount, and purpose of funding.**	No

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?	In February / March 2024, the CTPG undertook a dedicated online patient survey specifically for the purpose of gathering information to complete this submission. The questions were designed to answer the questions posed by NICE. The survey scope was only for people (or carers of people) who had received a heart and / or lung transplant, as these groups will be among the target populations for preventative COVID-19 treatments. 252 completed surveys were received which represented 6.2% (6.4% lungs & 6.1% hearts) of the 4,080 people living in the UK following a heart and or lung transplant. Other relevant published research articles are also cited in this submission

Living with the condition

6. How does the risk of COVID-19 currently affect people with immune impairment? How does the current situation compare to earlier in the pandemic?	The patient survey investigated this issue, focusing on people's current lifestyle adjustments to reduce the risk of catching COVID-19. Firstly, the survey asked people the following question, "On a scale of 1-10 how would you describe your lifestyle to avoid catching COVID-19. 10 would be behaving as you did during the height of the COVID-19 pandemic restrictions. 1 would be your behaviour is the same as it would be if COVID-19 didn't exist." A complete spectrum of responses was received, with a mean score of 5.7. Each number received at least 6% of the overall total with the top three being 8 (15.5%), 5 (14.7%), 7 (13.1%). The lowest was 1 with 6.0%. The mean for lung transplant recipients (5.9) was higher than heart recipients (5.6). The survey asked specific questions about behaviours to avoid catching COVID-19, as follows, with the positive responses in brackets; Wearing a mask in busy places (46%) Frequent hand washing and / or gelling (73%) Avoiding people who are unwell (89%) Avoiding or reducing my visits to busy indoor places, such as a pub, theatre, cinema, club etc (54%) Reducing my time socialising with friends or family (27%) Sometimes asking people to take a COVID-19 test before I meet them (33%) Trying to only meet people outside (22%) The overwhelming majority of cardiothoracic transplant patients are currently making lifestyle adjustments to avoid catching COVID-19, with over half of patients reporting behaviours closer to full COVID-19 lockdown than acting pre COVID-19 pandemic. Many patients are reporting high levels of anxiety, fear, and depression with poor quality of life. The survey offered an opportunity for respondents to provide a narrative regarding the benefit an effective prophylactic COVID-19 treatment would have on their mental and physical wellbeing. Many took the opportunity to describe their current quality of life due to COVID-19, below are a sample. "Shielding at home is so destroying. I am such an outgoing person and had such a wonderful social life. Now I feel like I've been left behind, I do the same thing more or less every day and just feel a prisoner in my own home." "I am currently treated for depression and anxiety, because of social exclusion from fear of catching COVID, becoming seriously ill or dying and the impact this would have on my loved ones."

	“I don't think I have the words to adequately describe the mental load of thinking about catching covid again.” “Still shielding with no protection after 4 years.Lost everything.” Greig et al (2024) (Exploring the attitudes of solid organ transplant recipients towards COVID-19 shielding communications and the language of ‘clinically extremely vulnerable’: a qualitative study investigating lessons for the future | BMJ Public Health) explored the attitudes of solid organ (including heart) transplant recipients towards COVID -19 shielding and communications. Greig’s findings corroborated those of the patient survey; “for these participants, despite the fact both shielding and mask regulations had ended months prior to them being interviewed, the fear and anxiety they continued to feel towards COVID-19 was clear. Again, this fear relates to leaving one’s home and coming into contact with others, resulting in many participants continuing to self-impose shielding and mask wearing. Hence, while COVID-19 restrictions may have come to an end, their impact—both in terms of how people feel and in terms of how people act persists”

Current treatment of the condition in the NHS

7. Based on your experience, roughly what proportion of people with immune impairment have had COVID-19? What was the impact of this (how severe was the infection and was a hospital stay needed)? Were there any long-lasting effects?	The CTPG have gathered evidence for the post heart and / or lung transplant patient population. Up until 9 March 2022, NHSBT produced a report on all people who had received a solid organ transplant, whether they had tested positive for COVID-19 and the number who had died within 28 days of a positive test (monthly-report-on-covid-19-nhsbt-16-march-2022.pdf (windows.net)). This report revealed that 22.6% of people who had a functioning heart and / or lung transplant had tested positive for COVID-19 by 9 March 2022, with 10.4% (15.5% lungs and 7.5% hearts) of those testing positive dying within 28 days. Callaghan et al (2023) (Vaccine Effectiveness Against the SARS-CoV-2 B.1.1.529 Omicr... : Transplantation (lww.com)) measured vaccine effectiveness against the Covid 19 Omicron B.1.1.529 variant in solid organ or islet transplant recipients. This revealed a Covid 19 mortality rate of 6.2% and 12.0% for heart and lung recipients respectively in the whole study period (Dec 20 – March 22 - which is post UK vaccine deployment). It should be noted the report demonstrated progressive reduction in mortality with increasing vaccine doses. Mortality rates for people who had received 3 or more vaccines were 3.2% and 3.9% for heart and lung transplant recipients. The study also demonstrated that vaccination provided no protection against testing positive for COVID-19 in solid organ transplant patients. The results of the MELODY study have been published, Pearce et al (2023) (Antibody prevalence after 3 or more COVID-19 vaccine doses in 23,000 immunosuppressed individuals: a cross-sectional study from MELODY | medRxiv). This investigated the prevalence of spike-protein antibodies following at least 3 COVID-19 vaccinations in immunocompromised individuals. Three patient groups were included, solid organ transplants, rare autoimmune rheumatic diseases, and lymphoid malignancies. The headline results revealed that solid organ transplant recipients had the highest levels (23.3%) of no detectable IgG spike protein antibodies in the three patient cohorts. The data shows that heart (25.7%) and lung (35.4%) have the highest percentage of undetectable antibodies of the solid organ transplant cohort. When reviewing the data of all three patient groups by sub diagnosis, the highest levels of no detectable IgG spike protein antibodies are lung transplant recipients 35.4%, small vessel vasculitis 27.1%, Indolent B- non-Hodgkins's lymphoma 26.3% and heart transplant recipients 25.7%.

	The CTPG patient survey asked if people had knowingly had COVID-19, a positive response rate was 73.4%, with an identical percentage across lungs and hearts. The CTPG can thus determine that for the post cardiothoracic transplant population 22.6% had first tested positive for COVID-19 by 9 March 2022, 50.8% first between March 2022 and March 2024 and 26.6% have never knowingly had COVID-19. The CTPG patient survey asked people that had been infected with COVID-19, how unwell they had been with their "worst experience of COVID-19". 16.8% (13.4% hearts and 24.1% lungs) had required a hospital stay to treat COVID-19. It should be noted that this survey has only been completed by people who are currently alive, as such the actual admission percentage will likely be higher as the survey excluded patients who had subsequently died of any cause, including COVID-19. The CTPG patient survey asked people that had been infected with COVID-19 whether "suffering from COVID-19 has had any long-term impact on your health". 22.2% (16.5% hearts and 34.5% lungs) answered yes to this question. The survey further asked these people how it has impacted on their long-term health. Fatigue, tiredness, and breathlessness were the most frequently mentioned symptoms. Many people (especially in lung) citing measurable reduction in lung function. Below are examples of the narrative responses provided. "I've never felt the same since. Very short of breath and fatigue is awful" "Reduced lung function and need ambulatory oxygen when walking about" "Very tired all the time, cough that won't go away, pain/ achy body" In summary, all the available evidence, including the patient survey indicates that heart and especially lung transplant recipients remain at high risk of hospitalisation and death from COVID-19. Exact hospitalisation and mortality rates are difficult to accurately quantify. However, current mortality risks in this patient population are highly likely to be 2-4% and hospitalisation more than 10% per COVID-19 infection. Mortality and hospitalisation rates from COVID-19 in lung transplant recipients are probably the highest of any diagnostic group in the entire population. The long term health burden of COVID-19 also appears to be significant with over 20% of patients reporting ongoing physical symptoms from a COVID-19 infection.

8. What do patients or carers think of current treatments and care for COVID-19 available on the NHS?	The CTPG patient survey asked several questions around the responsiveness of COVID-19 treatments and care, and the overall opinion of the NHS COVID-19 treatment services. The survey first asked whether patients were aware of how they obtained free COVID-19 test kits. This is fundamental to proceeding to treatment as this is the only out of hospital route to confirming COVID-19 infection. Since November 2023 eligible patients in all nations apart from Scotland obtain free COVID-19 test kits from pharmacies. The CTPG survey revealed that 44% of patients were unaware that is how they now obtained test kits, 30% had encountered difficulties with obtaining them from pharmacies and the smallest proportion, 26%, had been able to obtain test kits from pharmacies. The CTPG are extremely concerned with this survey result and believe that eligible patients were not informed of the change at an individual level, which had been the case with prior changes to the COVID-19 care pathway. The CTPG survey asked patients who had been infected with COVID-19 since the introduction of community-based treatments (January 2022) and wanted to receive a treatment whether they had received the treatment and if it had been within the effectiveness window of 5 days since symptom onset. 78% of people reported that they had received treatment within 5 days, 11% received treatment after 5 days and 11% were unable to receive a treatment due to system failures. Patients in the latter two categories were asked why they were unable to receive treatment in a timely manner. Multiple reasons were provided, with no overarching common point of failure. However, lack of weekend provision and the inability to provide staff for a Sotrovimab infusion were the most frequently mentioned. The CTPG patient survey asked patients and carers what they thought of the NHS funded treatments and care for COVID-19. The survey offered five responses and the breakdown was as follows, excellent (13%), good (33%), average (34%), poor (10%) and very poor (9%). The results reveal a wide range but with a positive rather than negative tendency. People were also offered the opportunity to provide a narrative on why they gave the rating. Many were positive, for example, “Excellent service, within 4 hours of 1st call to say I had COVID i had managed to book to get antivirals”. Some however, were negative, “It’s difficult to access treatments, most staff at 111 haven’t heard of it, GP’s and hospitals have different interpretations and patients are left caught in the middle”. Based on the patient survey and reports from multiple patients and patient support groups, the quality and responsiveness of COVID-19 treatment appears to be dependant on the patient’s ICB / nation.

9. Where would people prefer to go to receive prophylactic treatment? (hospital / GP surgery /pharmacy / other)	The patient survey specifically asked this question, with the response breakdown as follows, any (54%), GP (25%), transplant centre (11%), pharmacy (7%), local hospital (3%). Whilst the GP was the highest of the named locations, over 50% would be happy to receive the treatment at any location. This shows the enthusiasm the cardiothoracic transplant recipient patient population has for receiving a prophylactic treatment.
10. Is there an unmet need for patients with this condition?	At the time of writing there is no prophylactic treatment for COVID-19 available in the UK and this is a significant unmet need for the cardiothoracic transplant recipient population. The evidence presented in this submission demonstrates that this patient population remain at high risk of death, hospitalisation, and long-term symptoms from COVID-19. This is despite them having good access to COVID-19 vaccines and treatments. Furthermore, the patient survey demonstrates the threat of infection, for which the population has no protection against, is leading to high levels of anxiety, stress and depression which is causing poor quality of life. The CTPG patient survey asked if there was a need for an NHS funded prophylactic treatment for COVID-19, 73% answered yes, 26% maybe, with just 1% responding no. The survey further asked if patients would choose to have the treatment if it was provided by the NHS, 74% answered yes, 23% maybe, with just 3% responding no.

Advantages of the technology

11. What do patients or carers think are the advantages of the technology? • How would having a prophylactic treatment available impact the lives of people with immune impairment (for example, how would it change the activities people do, or how they feel?) • How would the effectiveness of treatment impact this? • How would having a prophylactic treatment available impact carers?	The CTPG patient survey asked what impact an effective prophylactic treatment would have on both their physical and mental wellbeing. 70% responded that it would significantly improve (31%) or improve (39%) their physical wellbeing. 73% responded that it would significantly improve (41%) or improve (32%) their mental wellbeing. The CTPG survey asked patients to describe why and how it would improve their mental and / or physical wellbeing. There were hundreds of responses and clearly patients have strong positive feelings about the impact of an effective prophylactic treatment. These are a selection of responses to the benefits of a treatment. “Massively. I would have a reason to get out of bed and some kind of purpose in my life again. Right now I'm existing.” “Not having to risk assess everything I do all the time” “My life at the moment is just an existence. If I had the knowledge that I was being protected, I would be able to start rebuilding my life as to be honest, it feels like I have been in prison.” “I don't go to busy places anymore. If there was a preemptive treatment for covid that would open more things up again for me to enjoy” “I would be less fearful of catching it and would be able to visit theatres and use public transport. It would reduce levels of worry.” “Not feeling I have to analyse every situation for risk and weigh up whether or not I should go to places, see people etc. Would take away one of the many stresses of living with long term medical issues” “I would be able to live normally without the threat of covid every time I step outside my home.” “I would be able to continue living a normal life without becoming very anxious every single time I have to go out and mix with the general public” “Being a part of society again.”

	The CTPG patient survey asked at what level of effectiveness they would choose to receive a prophylactic treatment. Effectiveness was framed as the % chance of reducing the risk of catching COVID19. 86% of respondents stated a required effectiveness of 50% or greater, with the breakdown as follows; 100% effective (16%), 75% effective (36%), 50% effective (34%), 25% effective (6%). 10% or less effective (8%). Lung transplant recipients were slightly more willing to accept lower levels of effectiveness. The CTPG patient survey did not specifically ask what benefits families and carers of cardiothoracic transplant recipients would derive from an effective prophylactic treatment for COVID-19. However, many survey responses spontaneously outlined the wider benefit to the families / carers of cardiothoracic transplant recipients. Similar emotions of anxiety, stress and fear are felt across families and carers, with symptom reductions anticipated from an effective prophylactic COVID-19 treatment for their loved ones; “It would reduce the stress and worry for both myself and my family” “Would relieve mine and my husbands anxiety of mixing with ithers” “The survey did not ask about the effect upon my family and close friends of not receiving effective preventative treatment for myself - the penny pinching decision of NICE upon us. I have lost friends through isolation. My wife is still careful where she goes and who she meets. My children still buy and test before they visit - they don't want to be responsible for me getting COVID. COVID-19 does not just effect the recipients of transplants, instead it is a disease that effects all those around a transplant patient, treat the patient and you treat their family and social network. The economic and social cost of COVID is far more than NICE can calculate.”

	The latter response raises the wider aspect of the benefit that an effective treatment would bring to society as a whole, “Opening up socially and economically in so much as it may be possible to return to some form of work.” “less time off work after being ill with covid, less risk of damaging heart/lungs” “I would not worry about coming into contact with tradespeople children family and friends. And I could resume volunteering in my community.” All cardiothoracic transplant recipients are acutely aware that their lifespan is extended due to an organ from a deceased person. This responsibility weights heavily on many recipients and symptoms of survivor guilt are frequently articulated. This burden, coupled with an awareness of the considerable NHS resources required to fund a cardiothoracic transplant were expressed by many in the survey; “It would reduce the stress about the possibility of catching Covid, which would not only be personally harmful but would also put my donor's heart at risk -- and like many transplant patients I feel duty bound to protect it as best I can.” “What was the point of our donors sacrifice and the money and time of all the NHS staff who worked to save us if the Government/NICE just at best imprison us and at worst let us die of Covid?”

Disadvantages of the technology9

12. What do patients or carers think are the disadvantages of the technology?	The CTPG survey asked patients about their experience with the MHRA approved prophylactic treatment Evusheld (tixagevimab/cilgavimab). For those patient's aware of its existence, 87% would have chosen to receive the treatment if it had been available for them on the NHS, 8% choose to pay privately for the treatment and 5% would have declined the treatment even if it were available on the NHS. This shows a strong willingness amongst the patient population for a COVID-19 prophylactic treatment and also an inequity of access based on the ability to privately fund the treatment. If an effective prophylactic treatment were available but could only be accessed privately, patients and carers who would like to receive the treatment but unable to afford to do so would be disadvantaged.

Patient population

13. 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 CTPG believe that all cardiothoracic transplant recipients would derive significant benefit from the availability of an effective NHS funded prophylactic COVID-19 treatment. The clinical evidence base would suggest that the following groups would derive a higher benefit due to their greater risk of progressing to severe COVID-19 and / or reduced ability to generate COVID-19 antibodies following vaccination (see publications cited in section 7) Transplant type: Lungs Age: Over 50 Vaccination Status: Unvaccinated and people who have not received a recent booster (Autumn-Winter-2023-24-COVID-vaccinations-for-SIS-and-IS-29-February-2024.xlsx (live.com)) *Sent email to NHS Stats team to try and get a further breakdown.* Sex: Men Immunosuppressant Regime: Triple therapy of antiproliferative, calcineurin inhibitor and steroid Evusheld (tixagevimab/cilgavimab). was only licensed for people aged 18 and over. If this were the case for Sipavibart then this would disadvantage the paediatric population. The CTPG patient survey results show patients aged under 18 were more likely to catch COVID-19 (93% paediatric v 73% entire population), equally likely to be hospitalised with COVID-19 (20% paediatric v 17% entire population), although less likely to have long term symptoms (7% paediatric v 22% entire population). The paediatric cardiothoracic transplant patient population were equally willing to receive prophylactic treatment and consider that they would gain similar levels of benefit to their physical and mental wellbeing. “I would feel more comfortable seeing my friends, indoors as well as outdoors. The winters are the hardest” If an effective prophylactic treatment was licensed, appraised, and recommended only for those aged 18 and over this would disadvantage children who have received heart and / or lung transplants.

Equality

14. Are there any potential equality issues that should be taken into account when considering this condition and the technology?	The CTPG believe that cost effectiveness of the treatment must be assessed at a diagnostic group level. The CTPG consider that the derived benefit from an effective prophylactic treatment for the cardiothoracic (and especially lung) transplant recipient population will most likely be the highest of any diagnostic group.

Other issues

15. Are there any other issues that you would like the committee to consider?	The CTPG would always advocate for services to be delivered as close as possible to where a patient lives, to enable greatest accessibility. However, the CTPG appreciate this needs to operationally be delivered safely and sometimes services require centralisation to ensure quality. Cardiothoracic transplant recipients are familiar with centralisation of clinical expertise. The CTPG would request that ideally prophylactic COVID-19 treatment is delivered as close as possible to the patient (e.g. in their GP surgery). If this is operationally not feasible then the service should be embedded in a service where the patient already receives treatment (e.g. transplant centres). Cardiothoracic transplant recipients are a small proportion of the worldwide population with a rare, shared characteristic. International cardiothoracic recipient friends are commonplace, with some meeting at events such as European and World Transplant Games. Patients report negative emotions and demoralisation when encountering peers from other countries who are accessing treatments not funded in the UK. The CTPG would also like to raise concerns over the length of time it will take for NICE to assess and publish guidance on Sipavibart. This submission has demonstrated the urgent need for an effective preventative treatment for COVID-19, for the cardiothoracic transplant recipient population to read an expected publication date of 26 February 2025 is painful. The CTPG would urge NICE, where possible, to expedite the assessment and publication of this guidance. The CTPG would also like to highlight the need to ensure that if Sipavibart were recommended by NICE then patients in eligible groups must be contacted individually. The CTPG survey which showed 44% of patients were unaware that free COVID-19 test kits should now be obtained from pharmacies demonstrates the importance of this.

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Key messages

16. In up to 5 bullet points, please summarise the key messages of your submission.	• • • • •

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