National Institute for Health and Care Excellence

Health Technology Evaluation

AZD 3152 for preventing COVID-19 [ID6282]
Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Anthony Nolan	AZD3152 is a long-acting monoclonal antibody neutralising past and currently circulating variants of SARS-CoV-2. It is expected to confer protection against COVID-19 for six months. It is appropriate for this technology to be evaluated by NICE, using the fastest possible evaluation route. This technology can offer support to patients who have conditions that cause immune impairment and may not mount an adequate protective response after COVID-19 vaccination and, therefore, are at high risk of developing severe COVID-19 if they were to become infected. Without alternative forms of protection, such as prophylactic monoclonal-antibody combination therapies, patients are left unprotected within the community. The status quo poses serious risk factors for most living arrangements; within a family unit, housing of multiple occupancy and single occupancy where the person is self-reliant.	Comments noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public.

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		Patients are potentially otherwise left at risk through any social contact points. This is highly disruptive and distressing to their employment and/or education, family life and even limited socialising, with associated mental health impacts. The ongoing SUPERNOVA Phase I/III trial is evaluating the safety and neutralising activity of AZD3152 for the prevention of symptomatic COVID-19. It has demonstrated efficacy against all known virus variants without evident safety concerns.[1] *1) Webber C et al. Trial in progress: a Phase I/III, randomised, modified double-blind, placebo- and active-controlled pre-exposure prophylaxis study of the SARS-CoV-2–neutralising antibody AZD3152 (SUPERNOVA)*	
	Blood Cancer UK	Blood Cancer UK welcomes the evaluation of AZD 3152 along the single technology appraisal route. With no other preventative treatments currently available to people with immune impairment, such as those with blood cancer, in the UK and with previous technology appraisals having taken too long to benefit this population, we would like to see the appraisal be conducted and recommendations generated as soon as possible. The usual timelines for a single technology appraisal and the funding implementation period do not reflect the urgency of the need for a pre-exposure prophylaxis for COVID-19 in the UK and the evolving nature of the virus and so the timeline should be expedited accordingly.	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation.
	LUPUS UK	None	No action required.

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	Leukaemia Care	This appraisal is highly appropriate for evaluation now, given that some immunocompromised patients, such as leukaemia patients, have not resumed their pre-pandemic daily activities that many of us immunocompetent people are able to do, e.g., using public transport. We recommend that this appraisal be eligible for the new NICE rapid review process and be conducted in a timely manner to ensure that the data on the efficacy of this treatment against certain covid variants remains as relevant as it possibly can at the time of decision making. We also recommend that this initial appraisal be conducted as swiftly as possible, to ensure that the analysis does not become out of date, as happened with other appraisals of this kind.	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	Long Covid SOS	No comment	No action required.
	Faculty of Pharmaceutical Medicine	The Faculty of Pharmaceutical Medicine (FPM) welcomes the proactive approach to early review of AZD3152 within its likely marketing authorisation. The immunocompromised population recommended is unlikely to respond to covid vaccines and remains vulnerable to severe disease and death. FPM considers prevention to be preferable to waiting until these individuals	Comment noted.

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		become ill and then implementing antiviral treatment, as currently recommended, as the use of antiviral treatment in this population risks the potential emergence of viral variants resistant to these treatments, which threatens the health of other vulnerable populations in the UK. This risk may be reduced by considering the use of combination antiviral treatment with both a MAb and a small molecule antiviral, as the Mab will enhance viral clearance within the immunocompromised population. FPM notes the extended eligibility for antiviral treatment recommended in the IAG's March 2023 report, However, FPM suggests that influenza and covid, which can co circulate, may adversely impact the same groups of individuals and it is preferable for treatment recommendations for covid to match those for influenza antiviral therapy. A uniform approach could further reduce risk of hospitalisation/death and it would greatly simplify delivery of care to make these recommendations consistent across both disorders.	
	Cardiothoracic Transplant Patient Group (CTPG), NHS Blood and Transplant	The CTPG considers AZD 3152 for preventing COVID-19 to be an appropriate topic to evaluate and the proposed route also be appropriate.	Comment noted. No action required.
	Forgotten Lives UK	The urgency of the implementation of this drug cannot be understated. The use of this drug represents an opportunity to allow the wide ranging cohorts identified to have a form of protection against Covid 19. WIth so many in this position still shielding or living very restricted lives due to their heightened risk of bad outcomes, its swift implementation is essential to allow them to return to some form of normality as they are presently in their 4th year of facing this way of living. Those in this position are facing physical effects on their health, heightened by exposure to the virus in healthcare settings, causing many to avoid	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients,

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		healthcare settings and cancel critical appointments and procedures, leading to a worsening position for their conditions. On top of this many face ongoing mental health issues as this way of living takes its inevitable toll, much of which is further exacerbated by the cost of living crisis with no financial support, placing further anxiety issues on them The draft guidance for Tixagevimab plus Cilgavimab for preventing COVID-19 [ID6136] stated in its conclusions "The committee agreed that there is an urgent unmet need for an effective prophylactic treatment for people who do not have an adequate response to vaccination." It also stated the following:- The committee recommended that the healthcare system develop a rapid appraisal process for neutralising monoclonal antibodies such as tix–cil so that effective products can be fast-tracked to eligible patients. We are therefore extremely disappointed that this evaluation appears to be going down the Single Technology Evaluation Process, with a possible timeline for evaluation of 40 weeks. We would question why it cannot be placed under the rapid review system since much of the drug has been evaluated under the review for Tixagevimab plus Cilgavimab for preventing COVID-19 [ID6136] If the assessment is to be put down the single technology assessment route then this timeline needs to be significantly foreshortened to allow this drug to be evaluated and provided to those in need of it rapidly at its most effective time against the circulating variants.	carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	AstraZeneca	AstraZeneca agrees that the timely evaluation of AZD 3152 is appropriate, and that guidance should be issued as soon as possible to support with the protection of high-risk patients due to COVID-19. We also agree that the STA process is the most appropriate route for this technology and indication.	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised

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			through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation.
	NHS England	NHS England (NHSE) would support the evaluation of AZD-3152 via NICE's single technology appraisal as the most appropriate route.	Comment noted. No action required.
	Kidney Care UK	There appears to be no choice of an alternative route to evaluate this topic. However, it is vital that the appraisal is carried out as rapidly as possible, so that the evidence is up to date and, if the treatment is shown to be effective, people can access prophylaxis without delay.	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible

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			following the marketing authorisation.
	Myeloma UK	Yes, this topic is highly appropriate for NICE appraisal. There are no preventative COVID-19 treatments available on the NHS in the UK, and COVID-19 still poses a significant risk for the thousands of people with weakened immune systems who don't respond to COVID-19 vaccines. There is an urgent need for a pre-exposure treatment which can help protect this clinically vulnerable group, many of whom are still very cautious about social, day-to-day activities.	Comment noted. No action required.
	Clinically Vulnerable Families	Yes this is appropriate	Comment noted. No action required.
Wording	Anthony Nolan	The remit references the marketing authorisation of AZD3152 for preventing COVID-19. For absolute clarity within the remit itself, it might be helpful to state that its authorisation is for pre-exposure prophylaxis. Also, to state that it is for people with conditions that cause immune impairment.	Comment noted. The scope has been updated to reflect this.
	Blood Cancer UK	The remit references the marketing authorisation of AZD 3152 for preventing COVID-19. For absolute clarity within the remit itself, it might be helpful to state that its authorisation is for pre-exposure prophylaxis.	Comment noted. The scope has been updated to reflect this.
	LUPUS UK	None	No action required.
	Leukaemia Care	Under the technology heading, NICE defines the population as being *"people who are not currently infected with SARS-CoV-2 with conditions causing immune impairment*". This excludes patients for whom the primary cause of their immune impairment could be immunotherapies, for example, rather than the condition itself. As such we would like to see this widened to those with	Comment noted. The scope has been updated to reflect this.

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		immune impairments regardless of whether these are caused by the condition or the treatment.	
	Long Covid SOS	Whilst the remit fits the marketing authorisation for preventing COVID-19, it would be improved by reflecting if the prevention of Covid-19 through this technology would prevent the development of Long Covid, which currently has no treatment and only symptom management.	Comment noted. The committee will consider evidence presented on the impact of long covid.
	Faculty of Pharmaceutical Medicine	Whilst we acknowledge that the recent PreP report is quoted in the introduction to Appendix B, which takes into account a wider public health perspective, the disadvantage of the approach proposed is that it fails to take a population health approach to both the prevention and treatment of covid in the UK. In addition, the change of disease pattern which has accompanied disease caused by omicron variants would warrant a revised assessment of the rates of hospitalisation and death which have significantly decreased since 2020. This can be used as a means of comparing to the data generated in the ongoing clinical trial (which is being conducted internationally with a limited range of UK centres participating) and also to set the baseline assumptions for cost effectiveness modelling based on trial outcomes.	Comment noted. The report referenced describes potential subgroup analysis if the evidence allows. NICE will assess AZD 3152 within its marketing authorisation
	Cardiothoracic Transplant Patient Group (CTPG), NHS Blood and Transplant	Yes	Comment noted. No action required.
	Forgotten Lives UK	None	No action required.

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	AstraZeneca	AstraZeneca suggests updating the wording to include "as a pre-exposure prophylaxis of COVID-19" as it more accurately reflects the remit of this evaluation. Therefore, the wording of the remit should read: '**To appraise the clinical and cost effectiveness of AZD 3152 within its marketing authorisation as a pre-exposure prophylaxis (PrEP) of COVID-19**'. Specifically, AstraZeneca anticipates submitting a NICE STA dossier for a population aligned with the SUPERNOVA trial. This patient group aligns closely with the populations described in the Department of Health and Social Care (DHSC) commissioned independent Pre-Exposure Prophylaxis (PrEP) report(1).	Comment noted. The scope has been updated to reflect this.
	NHS England	NHSE acknowledge there is uncertainty about generalisability of the Study Understanding Pre-Exposure pRophylaxis of NOVel Antibodies (SUPERNOVA) trial data for both the 'at-risk' population and the circulating/future COVID-19 variants. We would be grateful if any recommendations could be underpinned by a mechanism whereby timely assurance can be offered of review of clinical and cost effectiveness for any future variants – such as through the proposed NICE rapid update process. We would welcome financial modelling to include the costs of any new national or local call and recall system that would be required to manage access to the therapy, any new antibody testing programme (if relevant to either eligibility, or treatment intervals or continuation), as well as the costs of the drug and its administration.	Comment noted. The committee will consider all relevant clinical and cost effectiveness when making recommendations. NICE's rapid update process will apply once final recommendations are published. Costs will be considered from an NHS and Personal Social Services perspective and will be based on evidence submitted by the company and stakeholders.

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	Kidney Care UK	We would welcome clarity on what will be included in the 'Personal Social Services perspective' referred to in the cost effectiveness section of Appendix B.	Comment noted. Further information on the Personal Social Services perspective can be found in the Economic evaluation section of the NICE technology appraisals manual.
	Myeloma UK	Yes	Comment noted. No action required.
	Long Covid Support	None	No action required.
	Clinically Vulnerable Families	Yes	Comment noted. No action required.
Timing Issues	Anthony Nolan	It is imperative that NICE and DHSC proactively engage with the pharmaceutical manufacturing company and set a clear and rapid timeline for trials and route to clinic. More than three years into the pandemic, immunocompromised patients still lack adequate protection from COVID-19 and continue to shield to limit their risk exposure. This is intolerable and needs urgent addressing. Eligible patients require timely access to AZD3152 ahead of any potential surge in transmission or development of a new, more dangerous, variant. Therefore, we request that this Single Technology Appraisal be expedited under the new rapid update process so that the recommendations can be	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the

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		published, and the technology potentially be made available to eligible patients as soon as possible. We regret that the previous appraisal of a pre-exposure prophylaxis medicine for COVID-19 was not conducted in time to benefit the UK's immunocompromised population and we hope the lessons learned from that process will be implemented in the appraisal of this new technology.	health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	Blood Cancer UK	We strongly recommend that this evaluation is fast tracked. Those with weakened immune systems, including people with blood cancer, are more likely to be hospitalised and/or to die from COVID-19. Until prophylaxis is available, people with weakened immune systems must rely on post-exposure treatments and many feel they must continue to take significant safety precautions. The time sensitive nature of current post-exposure treatments and the uncertain context surrounding the delivery of post-exposure treatments from 27 June as ICBs take on this responsibility, means that avoiding contracting COVID-19 and developing severe COVID-19 is more important than ever for people with weakened immune systems. People with blood cancer require an effective and accessible option for prophylaxis. Last year, people with weakened immune systems in the UK missed out on the benefits of Evusheld, the first pre-exposure prophylactic treatment for COVID-19, in part because the NICE evaluation took too long and the treatment was no longer effective against currently circulating variants by the time recommendations were made. We do not want this to happen again.	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final

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			recommendations are published to ensure that the recommendations remain up to date.
	LUPUS UK	This evaluation needs to occur as rapidly as possible: • The window during which AZD 3152 is effective may be limited, so it is important that the opportunity to prevent infections in those most vulnerable is not missed. • Access to COVID-19 treatments for people who have tested positive is likely to be disrupted very soon when the pathways change under ICB management. These will be patient-initiated and in some areas will be reliant on already over-pressured GP services. • Some people have been shielding since March 2020 and this is having a very detrimental impact on their physical and mental health, as well as being lost to society. • Precautionary measures in healthcare settings (such as mandates for face coverings) are continuing to be lifted, increasing the risk for the specified population when they need to access routine monitoring or treatment.	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	Leukaemia Care	As mentioned above, this is an urgent appraisal in terms of timelines as the COVID-19 evidence under review is time-sensitive with variants that are quickly changing. The impact COVID-19 continues to have on many	Comment noted. An appraisal of AZD3152 for preventing COVID-

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		immunocompromised patients can impact quality of life significantly causing ongoing inequalities for this population. Protecting the immune compromised from COVID-19 also helps prevent the most serious infections, with these people more likely to go into hospital and need intensive care if they do get COVID. We recommend NICE takes whatever appropriate action to ensure this appraisal is treated with urgency and is conducted as quickly as possible, including making it eligible for a rapid review process. This must not be to the detriment of the patient community being able to comment.	19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	Long Covid SOS	No comment	No action required.
	Faculty of Pharmaceutical Medicine	Although covid is no longer considered a health emergency of international concern, the disease has not disappeared and in the UK currently causing 3-4000 hospital admissions and 3-400 deaths weekly (UKHSA Weekly report May 25 2023). These admissions and deaths may be significantly reduced by appropriate use of targeted chemoprophylaxis/treatment.	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of

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			importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	Cardiothoracic Transplant Patient Group (CTPG), NHS Blood and Transplant	The CTPG consider that the evaluation should be undertaken as rapidly as possible as there is a continuing and ongoing need for an effective treatment to prevent COVID-19. Many patients that the CTPG represent remain susceptible to poor outcomes from COVID-19 despite vaccination and many still have poor quality of life as they continue to "shield".	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing

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			authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	Forgotten Lives UK	At present those represented by the target population and sub-groups exhibit little protection against Covid-19. This large defined cohort is therefore placed at a significant risk, both to themselves in terms of susceptibility of contracting the virus, but also from poor outcomes and complications, necessitating further and often lengthy treatments and interventions. This continues to place a wide ranging burden on the NHS in terms of costs and use of precious staff and resources, and whilst such resources are deployed to deal with this issue the service suffers from the knock on effect to other patients totally unrelated to this issue. It is imperative that the implementation of this drug is made as soon as possible to reduce the burden on the NHS	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.

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	AstraZeneca	There is a significant number of people in the UK who are immunocompromised and amount an insufficient immune response to COVID-19 vaccination and therefore would benefit from PrEP. Although there is another PrEP (Evusheld) approved by MHRA since March 2022(2), there are no PrEPs currently commissioned by the NHS. There is therefore an urgent need for treatment options for this highly vulnerable population who are at high risk of severe adverse clinical outcomes due to COVID-19, and NICE should conduct an appriasal as soon as possible. This urgency and clinical unmet need was further highlighted by a clinical consensus statement published in July 2022 by over 120 clinicians representing 17 different clinical specialities from across all four devolved nations. It stated that PrEP would have clinical benefit to people who are immunocompromised, and that a protective antibody treatment programme should be delivered as soon as possible(3). The NICE appraisal of Evushled also highlgihted the need for urgent and timely decision making as academics, clinicians and patient groups expressed their dissapointment during the appraisal that the process was too lenghty and that patients missed an opportunity to recive treatment(4). NICE have also recognised the importance of arriving at rapid and responsible decisions in the COVID-19 disease area through the development of a new review process to update its recommendations on the clinical and cost effectiveness of COVID-19 treatments(5). Therefore, it is well-established that appraisals of COVID-19 medicines and PrEP should be carried out urgently, rapidly and conducted in a timely manner so not to delay access to this vulnerable and high risk patient group.	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	NHS England	NHSE acknowledge the difficulty in predicting relative urgency given the relatively low prevalence of COVID-19 in the community.	Comment noted. No action required.

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		Given the primary completion date of the Study Understanding Pre-Exposure pRophylaxis of NOVel Antibodies (SUPERNOVA) trial, we would support the current draft timelines.	
	Kidney Care UK	This evaluation is urgent, as there are no other protections against Covid-19 for people who are immunosuppressed and likely to be less well protected by the vaccines. Three years of living restricted lives means access to a protective treatment is extremely significant. Furthermore, the experience of evaluating other Covid-19 treatments and prophylaxis has demonstrated the urgency of rapidly reviewing new antibody treatments – to avoid the risk of efficacy waning if the virus mutates.	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	Myeloma UK	Highly urgent. People with weakened immune systems, including myeloma patients, have been living with the risk of COVID-19 for over three years. Whilst most people get some protection against severe illness due to COVID-19 from vaccination, there is a significant portion of society who do not. Eligible patients need access to preventative treatment as soon as possible to	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised

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		ensure they are protected before there is a change in infection rates or virus severity.	through NICE's topic selection process because it is anticipated that it will be of importance to patients, carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
	Long Covid Support	None	No action required.
	Clinically Vulnerable Families	Extremely urgent to the high-risk individuals who could benefit from this technology. Similar technologies, produced previously, become obsolete (due to viral mutation) before they were made available in the UK	Comment noted. An appraisal of AZD3152 for preventing COVID-19 has been prioritised through NICE's topic selection process because it is anticipated that it will be of importance to patients,

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			carers, professionals, commissioners and the health of the public. NICE intends to publish guidance on AZD3152 as soon as possible following the marketing authorisation. NICE's rapid update process will apply once final recommendations are published to ensure that the recommendations remain up to date.
Additional comments on the draft remit	Anthony Nolan	N/A	No action required.
	Blood Cancer UK	None	No action required.
	LUPUS UK	None	No action required.
	Leukaemia Care	None	No action required.
	Long Covid SOS	None	No action required.
	Faculty of Pharmaceutical Medicine	None	No action required.

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	Cardiothoracic Transplant Patient Group (CTPG), NHS Blood and Transplant	None	No action required.
	Forgotten Lives UK	None	No action required.
	AstraZeneca	None	No action required.
	NHS England	None	No action required.
	Kidney Care UK	None	No action required.
	Myeloma UK	None	No action required.
	Long Covid Support	None	No action required.
	Clinically Vulnerable Families	None	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Anthony Nolan	The background does not provide sufficient information on the risks posed to immunocompromised patients including those with haematological malignancies. Individuals who are immunocompromised are at an increased risk of severe sequelae from coronavirus such as hospitalisation, intensive care unit admission and death.[2] Furthermore, patients with haematological neoplasms who suffer from impaired immunity are at particular risk, with higher morbidity and mortality.[3] With respect to vaccination serving as a primary pharmaceutical intervention for preventing COVID-19, evidence suggests a low seroconversion rate in vaccinated patients with haematological neoplasms compared with healthy controls. It has been demonstrated through OCTAVE trial data and similar vaccine efficacy studies[4] that allogeneic hematopoietic cell transplantation (allo-HCT) recipients display impaired immune response to SARS-CoV-2 vaccination. Patients within 12 months or less of receiving an allo transplant, or undergoing immunosuppression therapies, had the lowest immune responses to vaccination. Therefore, COVID-19 vaccination cannot be considered a means of protection from serious illness as a result of a SARS-CoV-2 infection for HSCT patients. In addition, uptake of continued booster vaccines for people with weakened immune systems is decreasing and there is significant variation in vaccination uptake between populations of different ethnicity and socioeconomic status. Finally, the background should include that the provision of currently available post-exposure treatments is strictly time-limited meaning high-risk patients are only eligible for treatment for COVID-19 within a 5-day timeframe. This greatly	Comment noted. The aim of the background section is to provide context to the disease area and the information provided is not exhaustive – the committee will consider all evidence presented by stakeholders during the appraisal.

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		limits the accessibility of these treatment options. There are also disparities in access between different population sub-groups.[5] *2) Coronavirus monoclonal antibodies as a prophylactic therapy against COVID-19 for immunocompromised groups, National Clinical Expert Consensus Statement, APPG on Vulnerable Groups to Pandemics* https://spiral.imperial.ac.uk/bitstream/10044/1/99831/2/Expertpositionstatement2.pdf *3) Mittleman M et al, 2022, Effectiveness of the BNT162b2mRNA COVID-19 vaccine in patients with hematological neoplasms in a nationwide mass vaccination setting* www.sciencedirect.com/science/article/pii/S0006497121017560 *4) Huang A et al, 2022, Antibody Response to SARS-CoV-2 Vaccination in Patients following Allogeneic Hematopoietic Cell Transplantation, Transplantation and Cellular Therapy* https://doi.org/10.1016/j.jtct.2022.01.019 *5) Antivirals and nMABs for non-hospitalised COVID-19 patients: coverage report, 2022* https://reports.opensafely.org/reports/antivirals-and-nmabs-for-non-hospitalised-covid-19-patients-coverage-report/	
	Blood Cancer UK	While the information is accurate, we recommend that further detail be added in some areas. Such as on the burden and lowering uptake of continued booster vaccines for people with weakened immune systems. As well as their third primary dose, other seasonal booster programmes have followed up to and including Spring 2023. The background also does not include the context that surveillance of COVID-19 and its variants in the UK has been significantly reduced, making it more difficult for vulnerable people to anticipate infection waves and adjust their social behaviour accordingly to try and avoid infection. The background details available post-exposure treatments but fails to mention the context of their delivery, as the responsibility transitions at the end of June 2023. These treatments are time sensitive and any interruption to	Comment noted. The aim of the background section is to provide context to the disease area and the information provided is not exhaustive – the committee will consider all evidence presented by stakeholders during the appraisal.

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		or uncertainty around the delivery pathway could have a significant impact on this population's health outcomes and mental health.	

	LUPUS UK	• More impacts of shielding should be included in the background material of this appraisal. If AZD 3152 is an effective prophylactic treatment, then it is important to fully understand and consider the well-documented and wide-ranging impacts of shielding, to accurately estimate potential improvements to QoL, physical and mental health, and in costs to the NHS. Alongside the already-included impact on mental health, this should include:
		  • The impact on physical health from reduced physical activity.
		  • The impact on management of health conditions due to changes in monitoring and being unable to attend appointments.
		  • The impact on the rest of the household of the person at risk from COVID-19.
		  • The economic impact for the individual and society, for example from worsened mental and/or physical health, lost work days, etc.
		• More elaboration on the number of booster doses and the fall in uptake is needed. Booster doses have been offered to those who are severely immune-suppressed every 6 months, meaning many people have had 6 or more doses of the vaccine. However, uptake for the boosters is dropping. For example, as of the week ending 4th June 2023, only 33.1% of eligible immunosuppressed people in England have received the spring 2023 booster (UKHSA, 2023). Many people are experiencing vaccine fatigue, in part because of the uncertainty around any potential added benefit from each dose. Some in our patient community have also reported that the vaccine triggers a flare of their lupus, and so they are balancing their COVID-19 risk with the vaccine making them unwell, and some do not want to keep having additional doses for this reason. For example, on our patient forum,
			Comment noted. The aim of the background section is to provide context to the disease area and the information provided is not exhaustive – the committee will consider all evidence presented by stakeholders during the appraisal.

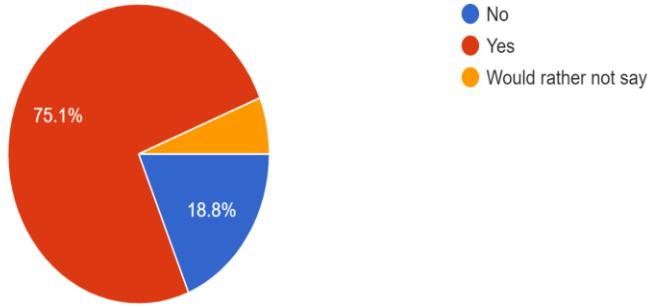
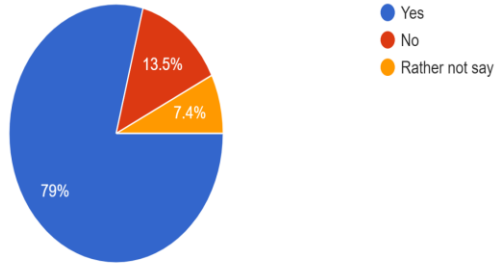
Section	Consultee/ Commentator	Comments [sic]	Action
		there are mixed feelings towards having further vaccines. Users have said (quotes composited for anonymity): • *"Every time I have a vaccine I experience a flare worse than the last. I won't have any more."* • *"I believe vaccination is important, but there is nothing for me against COVID-19 because I experience too many side effects to have any more of those. And we're told they don't work that well for people like us anyway, so what's the point. There's not much empathy for us as people just assume I'm an anti-vaxxer, but I'd love something that works without making me so ill!"* • *"Each vaccine induces a bad flare, but I will keep having them because I am high risk."* The vaccines may be the primary pharmaceutical intervention, but if they are not being accepted by this cohort, or being accepted less and less, then other options, such as a prophylactic treatment, may have additional utility. • The section about the use of treatments for COVID-19 for those at highest risk should include information about access to those treatments. Many of these patients have experienced difficulty accessing the treatments in the required window of time for them to be effective. The forthcoming change from one national system to differing systems for each ICB is likely to exacerbate this issue as patients will not be contacted and it may take time to find out who they need to contact in their local area. The treatments are also under constant review by NICE and changes in current variants could see them withdrawn without alternative options. Without timely access to effective COVID-19 treatments following infection, this cohort requires additional support and/or treatment to reduce the risk of infection.	

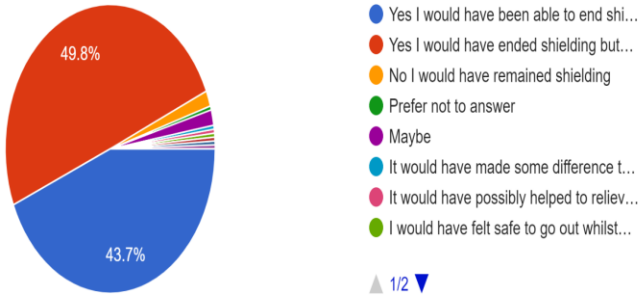
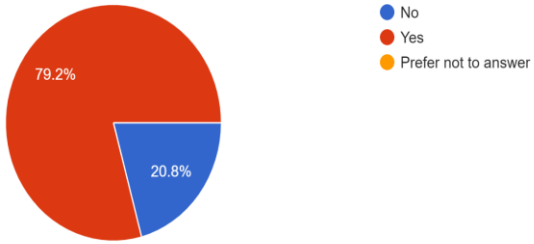
Section	Consultee/ Commentator	Comments [sic]	Action
	Leukaemia Care	The background does not provide sufficient information on the risks posed to immunocompromised patients including those with haematological malignancies. For example, the background description doesn't mention blood cancers as a particularly at-risk group, which we would like to see changed. Blood cancers are also not mentioned in the group least likely to respond to vaccines. The focus instead appears to have been solely on population-wide risk factors (e.g., age, obesity), but it is important that NICE also considers that specific conditions, such as leukaemia, are important risk factors and this should be represented in the scope.	Comment noted. The aim of the background section is to provide context to the disease area and the information provided is not exhaustive – the committee will consider all evidence presented by stakeholders during the appraisal.
	Long Covid SOS	Yes. Two notes to make: Mortality of Covid -19, the data publications are from 2020 and 2021. Are there any updated publications on mortality with more recent strains of Covid-19 to see if it still has the same profile? There are now publications looking at the characteristics of developing post-Covid -19 syndrome and it may be beneficial to include that within the background as well. These populations do not necessarily share the same profile.	Comment noted. Out of date references have now been removed from the final scope.
	Faculty of Pharmaceutical Medicine	The background information is based on data which is 3 years out of date and no longer reflects disease severity as observed in current practice. This will result in discrepant data to that generated in a clinical trial which is currently underway and impact cost effectiveness assessment whatever the outcome of a clinical trial.	Comment noted. Out of date references have now been removed from the final scope.
	Cardiothoracic Transplant Patient Group (CTPG), NHS	The CTPG consider this to be appropriate	Comment noted. No action required.

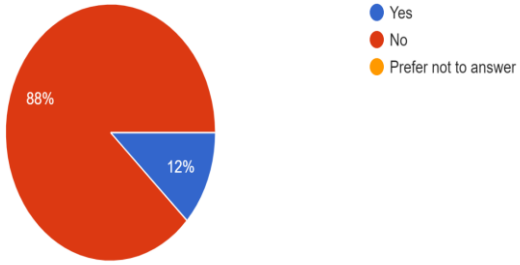
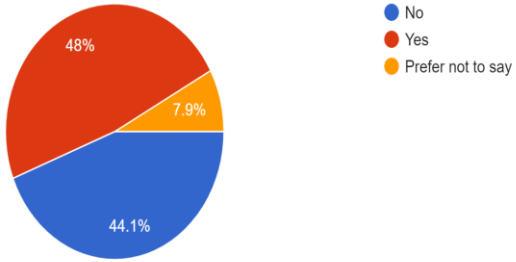
Section	Consultee/ Commentator	Comments [sic]	Action
	Blood and Transplant		
	Forgotten Lives UK	The appraisal of this drug takes place against an ever changing scene with regards to the Covid 19 virus. We have already witnessed how the evaluation of Evusheld and the associated delays resulted in the missed opportunity to provide protection to this large expanded cohort. The present strategy to protect this cohort is the use of prevention principles, which for so many entails shielding or undergoing many restrictions on their lives, and also on their immediate and extended families lives. After such a long time period this cannot continue indefinitely without some consequences. As the time period increases the risk of infection increases, as does shielding fatigue. The mental health toll and anxiety it induces adds to this and in some cases, some are now simply giving up with a fatalistic approach, putting them further in harm's way. Some feel they also no longer have a choice as financial issues from the cost of living crisis place unbearable pressures on them to choose between health or financial survival. It should be recognised that there are many who feel that they would be in position to return to work or the community in some capacity with more protection and are being denied this opportunity, which also has an economic impact for wider society and the national economy. This is already on top of the mental burden they already carry with the diagnosis of their medical conditions. The strategy of relying on regular vaccine boosters, now has to be called into question. With the removal of many of the protective measures in healthcare, and the poor communications surrounding the latest booster rollout, we are seeing an extremely low uptake on the vaccine booster from this cohort. There is a feeling of what is the benefit of taking this is if I have little or no	Comment noted. The committee will consider all patient group submissions and the impact of continued shielding on people's mental health and health-related quality of life when making recommendations.

Section	Consultee/ Commentator	Comments [sic]	Action
		response, and a feeling that the reward is outweighed by the risk of catching covid attending a healthcare setting with little protective measures in place. We are now seeing the change in the administration of post covid infection drugs from CMDUs to ICBs. The change to a local system of assessment and delivery from a national one is likely to exacerbate the many issues with timely delivery that this cohort has already experienced, placing further levels of anxiety on them. Patients in the cohort are now experiencing the very real risk of visiting healthcare settings where in many cases mitigations and testing regimes have reduced dramatically, accompanied by a rise in infection rates in those settings. For those that have spent so much time protecting themselves, they are now making decisions not to attend both routine health appointments, but also for investigative procedures and in some cases more urgent procedures. This is having a large impact on both their physical and mental health. It is also storing up problems for the future as new developments complicate further future treatments. In light of all the above, it is now more critical than ever that the use of drugs such as ADZ3152 are considered and used as an effective protective tool in conjunction with other measures for this large cohort. The notion of leaving patients shielding was raised during the consultation stages with Evusheld due to the fears that patients may take unnecessary risks. This viewpoint cannot be allowed to be repeated within this evaluation. It has not been used for the general population with vaccines and is disingenuous to the cohort. Those in this position value their health more than the general population, due to the need to value and preserve it and are more protective of it than the general population.	

Section	Consultee/ Commentator	Comments [sic]	Action
		The below pie charts show results of a 229 person survey carried out in May 2023 of patients within our group. These results show effects of shielding on immunosuppressed and family members and highlight how this has affected them. We are seeing significant problems being caused with the mental health of both those still shielding and their family members, and the impact cannot be understated. Depression, anxiety and suicidal tendencies have been reported across many of the patient group as a result of the shielding. The graphs illustrate the high percentages still having to live restricted lives and those affected by mental health issues, many of whom are struggling to secure any type of help through normal NHS channels due to backlogs. It is not an option to leave this large cohort to continue living like this. The graphs also show the effect that would have been experienced by the group if they'd had access to Evsheld. showing an overwhelming view from the patients themselves that it would have changed the way they have to live their lives.	

Section	Consultee/ Commentator	Comments [sic]	Action
		17. Has your mental health suffered as a result of shielding? 229 responses  19. Do you think there has been any long term side effects of the Covid-19 pandemic on the ways in which the immunocompromised receive healthcare? 229 responses  	

Section	Consultee/ Commentator	Comments [sic]	Action
		29. If prophylactic (preventative) monoclonal antibody treatments, such as Evusheld, had been made available to you, through a fast track process...uld this have made a difference to your shielding?" 229 responses  30. Did you have any other members of the household who although not immunocompromised or immunosuppressed still undertook shielding to help protect you 226 responses 	

Section	Consultee/ Commentator	Comments [sic]	Action
		31. Did you have any children of school age in the household who had to undertake some form of shielding to help protect you? 225 responses  33. Did any member of your household suffer from any mental health or well being issues as a result of helping you shield? 227 responses  	

Section	Consultee/ Commentator	Comments [sic]	Action
	AstraZeneca	AstraZeneca suggests including the details of the SUPERNOVA trial which studies AZD 3152 as a PrEP. Specifically, we would suggest including the following details: **AZD 3152 is being studied in an ongoing global Phase I/III trial (SUPERNOVA) conducted in patients with conditions causing immune impairment, who are less likely to mount an adequate protective immune response after vaccination and thus are at high risk of adverse outcomes in the event of SARS-CoV-2 infection. SUPERNOVA utilises a novel immuno-bridging approach to build on the generalised safety and efficacy of Evusheld.**	Comment noted. The scope intends to a brief overview of the key trial including the population, intervention and comparator. Further details can be provided in the company submission.
	NHS England	NHSE agree that the background information is accurate, but that it should also include reference to the World Health Organization's decision to no longer constitute COVID-19 as a public health emergency of international concern. In addition, it should reference the Government's 'Living with COVID-19' strategy. We would welcome a rephrasing of the sentence highlighted below to remove any ambiguity and ensure clarity. Currently it may be seen as misleading and infer that eligibility for prophylaxis is agreed, rather than that it is advice on a potential cohort that may be most suitable for prophylaxis that is for consideration as part of the TA process. 'An independent UK government advisory group have identified specific groups of people at highest risk of hospitalisation and death despite receiving COVID-19 vaccination, and groups of people that are eligible to receive pre-exposure prophylaxis for COVID-19.[13,14]'	Comment noted. The aim of the background section is to provide context to the disease area and the information provided is not exhaustive. Comment noted. The sentence has been rephrased to reflect this.

Section	Consultee/ Commentator	Comments [sic]	Action
	Kidney Care UK	We believe this statement should be strengthened. *People at increased risk from COVID-19 have been required to shield long-term during the COVID-19 pandemic, which may also impact their mental health.*[6,7] It should include that: • government guidance continues to recommend additional precautions for this group. • many within this group are continuing to lead restricted lives due to their ongoing risk from Covid and lack of protection from Covid. As well as impact on mental health, shielding and following the recommended additional precautions may also impact on ability to maintain employment and participate in family/community life. • that people who may be eligible for prophylaxis are living in a very different context than the general population who are more likely to have been able to move on from the pandemic and its profound effects.	Comment noted. The aim of the background section is to provide context to the disease area and the information provided is not exhaustive.
	Myeloma UK	The information is accurate. However, the impact does not mention the impact sub-optimal response to vaccination has on immunocompromised people. For example, people with myeloma and other blood cancers are greatly over-represented in COVID-19 death statistics. In 2022, 992 blood cancer patients died of COVID-19; this represents 4.4% of COVID deaths.[1] The current prevalence of blood cancer in England is 0.27 cases per 100 people.[2]	Comment noted. The aim of the background section is to provide context to the disease area and the information provided is not exhaustive. People with myeloma are captured within the subgroups section of the scope under people with anticipated failure of vaccination.

Section	Consultee/ Commentator	Comments [sic]	Action
	Long Covid Support	None	No action required.
	Clinically Vulnerable Families	Ok	Comment noted. No action required.
Population	Anthony Nolan	The population within the draft scope has been defined in the abstract. Without further clarification, this approach may hinder or delay any clinical prioritisation required in the technology's rollout. There remain concerns around global supply, as well as localised logistical issues in clinical delivery since the technology is administered as an intramuscular injection and post-injection patient monitoring is advised. These aspects are relevant to population design and clinical delivery capacity. Should supply constraints form a logistical concern, distinct patient cohorts should be identified and prioritised according to their comparative risk. It is important to note that risk factors for COVID-19 include non-clinical factors such as ethnicity and socioeconomic status.	Comment noted. The population is intentionally kept broad to align with the marketing authorisation. NICE will consider any constraints on implementing its guidance.
	Blood Cancer UK	Yes	Comment noted. No action required.
	LUPUS UK	The population eligible for treatment should be expanded. If there is strong evidence that this treatment can prevent mild infections of COVID-19, it should also be offered to patient groups who are at risk of severe secondary complications from infections which require hospitalisation or changes to their treatment regimens. According to a LUPUS UK survey from 2022, many people with lupus, including those who are not severely immunocompromised, are hospitalised following a COVID-19 infection because of secondary complications such as pneumonia or lupus flares. The JCVI did not expand the criteria for additional	Comment noted. NICE will make recommendations for AZD 3152 within its marketing authorisation.

Section	Consultee/ Commentator	Comments [sic]	Action
		booster vaccines to this group because of the limited effect they have on the prevention of mild infection. If a prophylactic treatment could prevent mild infection, and so prevent these severe secondary complications, it could have wider benefits to physical health and the overall impact of COVID-19, such as reduced disease flares and reduced need for further treatments or hospital appointments.	
	Leukaemia Care	Yes	Comment noted. No action required.
	Long Covid SOS	We would encourage consideration of those that already have Long Covid, especially where the symptom burden may already be debilitating.	Comment noted. NICE will make recommendations for AZD 3152 within its marketing authorisation.
	Faculty of Pharmaceutical Medicine	The population for chemoprophylaxis is appropriately defined in the IAG group report of March 2023.	Comment noted. No action required.
	Cardiothoracic Transplant Patient Group (CTPG), NHS Blood and Transplant	Yes	Comment noted. No action required.
	Forgotten Lives UK	Yes, but it is absolutely essential that the drug is appraised and approval considered for all sub groups as identified by the https://www.gov.uk/government/publications/pre-exposure-prophylaxis-prep-and-covid-19-independent-advisory-group-report/pre-exposure-prophylaxis-prep-report	Comment noted. NICE will make recommendations for AZD 3152 within its marketing authorisation.

Section	Consultee/ Commentator	Comments [sic]	Action
		This represents an exceedingly large group for whom there is no prospect of protection or a return to normality without the approval of this drug. Both target population and sub group should be considered on an equal footing with no differentiation. It is simply not an option to leave this large group still shielding. This would be the equivalent of having given the covid vaccines to only a certain proportion of the general population. It is imperative that all those stuck in this situation be given access to this drug. This will also ensure a fast and effective rollout as has been seen in other countries using Evusheld, where the drug was administered to those in the qualifying cohort, without the need for any testing. This removed any hurdles to accessibility and ensured they received protection as a matter of urgency, and avoided additional burdens on healthcare providers in administration of the drug and avoided additional expenditure. There should be scope for additional discretionary inclusion on the advice of individual clinicians where there is a genuine belief that the patient is “unlikely” to have mounted an adequate vaccine response, regardless of which group they do or don't fall into.	The subgroups which will be considered are outlined in the scope.
	AstraZeneca	The definition accurately describes the indicated population. Further to this, AstraZeneca anticipates submitting a NICE STA dossier for a population aligned with the SUPERNOVA trial population. This patient group aligns closely with the patients who may be eligible for PrEP as described in the DHSC commissioned independent PrEP report(1).	Comment noted. No action required.
	NHS England	NHSE agree that the population is defined appropriately but there is considerable uncertainty in quantifying this population and therefore the number of patients who would be eligible for AZD-3152.	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	Kidney Care UK	It should include individuals whose treatment causes immune impairment (as well as those with conditions causing immune impairment)	Comment noted. The scope has been updated to reflect this.
	Myeloma UK	No, the statement is too general. The statement needs more clarity about eligible conditions and the criteria for identifying eligible patient groups. The scope should outline whether NICE will define eligible patient groups based on the PrEP report or the clinical trial cohort. The wording used to describe the population and subgroups should be consistent with other COVID-19 treatments to prevent confusion around eligibility. Our preference is alignment with the PrEP report.	Comment noted. The population is intentionally kept broad to align with the marketing authorisation. More specific groups are included in the subgroups section and are aligned with the PrEP report.
	Long Covid Support	**1. People with Long Covid should be included in the defined population. Reinfection adversely affects those with a history of Long Covid. Evidence increasingly suggests people with Long Covid are immunocompromised, have a maladaptive immune response and T-cell exhaustion. The following research demonstrates a need for people with Long Covid to be considered as at-risk and therefore eligible for the technology:** i) 'Long-term SARS-CoV-2-specific immune and inflammatory responses in individuals recovering from COVID-19 with and without post-acute symptoms' (Peluso et al 2021). ii)'Neuro-COVID long-haulers exhibit broad dysfunction in T-cell memory generation and	Comment noted. NICE will make recommendations for AZD 3152 within its marketing authorisation.

Section	Consultee/ Commentator	Comments [sic]	Action
		responses to vaccination' (Visvabharathy et al 2021). iii)'Long-term perturbation of the peripheral immune system months after SARS-CoV-2 infection', (Ryan et al 2022). iv)'SARS-CoV-2-specific T cells associate with inflammation and reduced lung function in pulmonary post-acute sequalae of SARS-CoV-2', (Palmer et al 2022). v)'Persistence of SARS CoV-2 S1 Protein in CD16+ Monocytes in Post-Acute Sequelae of COVID-19 (PASC) up to 15 Months Post-Infection' (Patterson et al 2022) vi)'Distinguishing features of Long COVID identified through immune profiling' (Klein et al 2022). vii) 'Immune signatures underlying post-acute COVID-19 lung sequelae' (Cheon et al 2021). viii) Reinfection with Covid causes a worsening of Long Covid symptoms in those who are still suffering, and causes a recurrence of Long Covid in 60% of those who had recovered Reinfections in Long Covid (Long Covid Support 2022).	
	Clinically Vulnerable Families	Yes	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Subgroups	Anthony Nolan	The suggested subgroups are appropriate. These subgroups should be included in the eligible population if demonstrated to be clinically effective. Agree that eligible subgroups should align with those identified in the Pre-exposure prophylaxis (PrEP) report, in order of their priority. However, all patients covered by the draft scope population should be granted *timely* access to AZD3152.	Comment noted. No action required.
	Blood Cancer UK	We agree with the subgroups being aligned with the independent UK advisory group's PrEP report but the evaluation must consider not only which groups are at highest risk from COVID-19 due to disease type (e.g. blood cancer) and treatment type and schedule (e.g. CAR-T therapy, stem cell transplant), but also non-clinical factors that contribute greatly to patient outcomes (e.g. ethnicity and deprivation level, as referenced in the 'Background' section). AZD 3152 will likely be most cost effective for those groups who are at disproportionate risk of dying from COVID-19.	Comment noted.
	LUPUS UK	None	No action required.
	Leukaemia Care	Yes	Comment noted. No action required.
	Long Covid SOS	See above	Comment noted. No action required.
	Faculty of Pharmaceutical Medicine	The IAG group has identified sub populations of interest. If a correlate of immunity were found this may enable a means to identify patients at greatest risk and also patients with pre-existing immunity at a level likely to be protective. This might be particularly relevant for patients in receipt of regular immunoglobulin treatment for their disease condition.	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	Cardiothoracic Transplant Patient Group (CTPG), NHS Blood and Transplant	The CPTG consider that the subgroups of heart and lung transplant recipients should be considered separately. Numerous studies demonstrate these patients remain at high risk of poor outcomes from COVID-19 and hence any effective treatment would derive a greater cost effectiveness.	Comment noted. Solid organ transplant recipients are captured under people with anticipated failure of vaccination in the PrEP report. This subgroup is included in the scope.
	Forgotten Lives UK	As per point above.	Comment noted. No action required.
	AstraZeneca	If data permits, broad and relevant subgroup analyses will be presented. However, as part of the assessment, AstraZeneca may be requested to present subgroup analyses in specific high-risk populations (for example subgroup analyses in groups A1 and A2 that represent the highest risk populations as defined in the DHSC commissioned independent PrEP report(1)). It is extremely unlikely that data will be available at this level of granularity to enable such subgroup analyses to be presented and to be informative.	Comment noted. No action required.
	NHS England	NHSE agree that the sub-group populations as suggested are appropriate. Consideration of sub-group analysis would be welcome (if data are available to do so) to support mobilisation prioritisation, alongside clarity of starting and stopping criteria, particularly in relation to whether six-monthly injections should be continued in perpetuity.	Comment noted. No action required.
	Kidney Care UK	Yes the proposed subgroups are appropriate	Comment noted. No action required.
	Myeloma UK	The suggested subgroups are appropriate. The scope should include the definition and the criteria used to define failure of and suboptimal response to vaccination (primary and booster doses) and how these groups will be	Comment noted. Definitions for groups with failure of

Section	Consultee/ Commentator	Comments [sic]	Action
		identified and subsequently offered prophylactic treatment. If the proposed approach is to use the criteria/patient groups as per the PrEP report, this should be stated/referenced in this section.	vaccination and sub-optimal vaccination response are included in the PrEP report, which is referenced in this section of the scope.
	Long Covid Support	None	No action required.
	Clinically Vulnerable Families	Yes -	Comment noted. No action required.
Comparators	Anthony Nolan	There are no other available prophylaxis pharmaceutical candidates, in which to make a comparative analysis. Vaccination cannot be considered a comparator for this population, since the vast majority will fail in mounting an adequate immune response. Sotrovimab, a neutralising monoclonal antibody (nMAb) is not a prophylactic comparator but can be administered intravenously to non-hospitalised patients with mild-to-moderate disease and at least one risk factor for disease progression. Given allo-transplant patients can be severely immunocompromised and possess multiple risk factors, it should not be considered acceptable that their single line of defence is available only once they are symptomatic. Timely access to post-exposure treatments is also a concern. In real-world practice, the only viable alternative to preventing COVID-19 infections is non-pharmaceutical interventions (NPIs). Limiting social contact	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		and maintaining physical distancing is not always within the control of the patient. Additionally, it requires significant psychological resilience to sustain.	
	Comparators	Yes	Comment noted. No action required.
	LUPUS UK	None	No action required.
	Leukaemia Care	Yes, we agree the only comparator is no prophylaxis, because there are no other available preventative treatments. It is right that vaccination has not been considered a comparator for this population, as many will have sub-optimal immune response to vaccination.	Comment noted. No action required.
	Long Covid SOS	Yes It would be even better if a comparison had been made through a Platform study, though we realise that this may not be the case here.	Comment noted. No action required.
	Faculty of Pharmaceutical Medicine	The clinical trial randomises patients to prophylaxis with AZD3152 or Evusheld. While Evusheld is licensed it has not been widely used for chemoprophylaxis in the UK population. However, as this group are eligible for antiviral treatment of illness, it would also be appropriate to compare outcomes following PrEP with outcomes following treatment of covid. It is unclear whether patients becoming ill with covid in the ongoing clinical trial will be offered antiviral treatment. This should be clarified. A secondary assessment of disease outcomes observed following disease occurring with treatment alone, or chemoprophylaxis plus/minus treatment of breakthrough infection should be conducted – this may utilise up to date outcomes among the UK population currently eligible for antiviral treatment.	Comment noted. The committee will consider the data for AZD3152 and its generalisability to clinical practice in the UK.
	Cardiothoracic Transplant Patient Group (CTPG), NHS	The CTPG consider these to be appropriate	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	Blood and Transplant		
	Forgotten Lives UK	Yes	Comment noted. No action required.
	AstraZeneca	AstraZeneca agree there are no PrEP available and therefore the wording in the scope is appropriate.	Comment noted. No action required.
	NHS England	NHSE agrees that no prophylaxis is the correct comparator for AZD-3152.	Comment noted. No action required.
	Kidney Care UK	Yes, if 'no prophylaxis' incorporates the restrictions some people who are immunosuppressed are placing on their behaviour (see government guidance). Restrictive behaviour comes at a heavy price in terms of quality of life, employment opportunities and mental and physical health An individual's ability to restrict their behaviour as they wish will vary, for example people may wish to avoid public transport at peak times but cannot do so. This may cause significant anxiety. We understand it may be difficult to capture these differences within a model, but it is important the committee are aware and discuss during the evaluation. The balance between no prophylaxis, meaning that some will continue to self-isolate at great mental, financial and emotional cost vs provision of a protective treatment must be openly discussed and evaluated.	Comment noted. The appraisal will aim to cover all important aspects of QoL.
	Myeloma UK	Yes	Comment noted. No action required.
	Long Covid Support	There are no relevant comparators for Long Covid.	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	Clinically Vulnerable Families	There are currently no other available prophylaxes available to people who fail to respond to covid vaccination	Comment noted. No action required.
Outcomes	Anthony Nolan	For transplant patients undergoing active treatment or are considered to be in acute recovery, any adverse effects or disruption to their anticipated treatment pathway, as a result of a SARS-CoV-2 infection, should be recorded as an outcome measure. Health-related quality of life (HRQoL) should play a significant role in this appraisal, as AZD3152 would be a vital tool in protecting the immunocompromised as they manage their day-to-day risk from COVID-19. We urge the committee to strongly consider the socioeconomic and mental health aspects of HRQoL in its analysis.	Comment noted. The committee will consider all relevant adverse event and health-related quality of life outcomes when making recommendations.
	Blood Cancer UK	Health related quality of life (HRQoL) will play a significant role in this appraisal, as AZD3152 will be a vital tool in protecting the immunocompromised as they manage the risks from COVID-19 that arise from going about everyday life. We urge the committee to factor the socioeconomic and mental health aspects of HRQoL into its analysis as a top priority, and to enable patient support organisations to provide evidence of the potential impact of AZD 3152 on HRQoL.	Comment noted. The committee will consider all relevant health-related quality of life outcomes when making recommendations.
	LUPUS UK	• Outcomes should include more secondary impacts of COVID-19 to accurately capture the health and economic impact of preventing COVID-19 infections. During the Partial Rapid Review of TA878 [consultation ID6262], the medical expert raised that mortality and hospitalisations, while important, no longer fully capture the impact of COVID-19. The expert, and practicing medical professionals on the Committee, noted that the main impact on the NHS is now in primary and social care, when COVID-19 causes deterioration in existing health conditions or in health more generally. This includes people that were not hospitalised and people that do not have post-COVID-19	Comment noted. The outcomes listed are not exhaustive and the committee will consider any other relevant factors when making recommendations. The committee will also consider all relevant health-related quality of

Section	Consultee/ Commentator	Comments [sic]	Action
		syndrome, so without including these secondary impacts there will be uncaptured benefits of preventing infection in any modelling. • Related to our recommendation of expanding the population that this treatment is available to, outcome measures should also consider the incidence and impact of secondary complications and chronic disease flares caused by COVID-19 infection. • The health-related quality of life measure needs to accurately reflect the utility gain for the recipient of the treatment, as well as for carers and/or other people in their household. This means not requiring patients to suggest they will completely stop all protective measures for there to be a utility gain. It is unrealistic to expect patients, who have needed to shield or modify their behaviour for their own safety for over three years, to immediately return to pre-pandemic behaviour, even if a treatment was able to provide 100% protection, not least because patients in recent research have discussed impacts to their mental and physical health, including a loss of confidence and physical decline (e.g. Sloan et al, 2021; Ryan et al, 2022; Maldonado et al, 2021). Additionally, COVID-19 is not the only viral risk for this group, so many would have been practicing enhanced precautionary measures to reduce risk of exposure to viral and bacterial threats before the pandemic. Therefore, it is likely patients will continue to modify their behaviour in some form due to the very real need to reduce risk from infections of all kinds. In the expert patient evidence submitted by Patient Advocacy Group stakeholders and individual patients in the appraisal of Evusheld, they were not necessarily requesting a complete return to their pre-pandemic life, but a desire and need to have more of life open to them (even if that still includes some precautions like masking, for example), and that this could make huge improvements to their mental and physical health. When considering direct utility gains related to changes in shielding behaviours, the committee should consider change over time as	life outcomes when making recommendations.

Section	Consultee/ Commentator	Comments [sic]	Action
		people re-gain confidence and physical strength, rather than just immediate changes in behaviour. Continuing some shielding or protective behaviours should also not be viewed as a lack of impact, as there can still be a significant impact on mental and physical health if people feel able to do more whilst still masking, for example, and some protective behaviours are likely due to increased risk from other viral or bacterial infection for this group.	
	Leukaemia Care	Contracting COVID-19 can cause disruption and halt progress to leukaemia patients who are undergoing treatment or in active recovery. For example, some patients may be required to pause chemotherapy for a cycle if they contract COVID-19 which can have adverse effects on both physical and mental health and wellbeing. It is therefore important that NICE include this within the measured outcomes as AZD 3152 could prevent these disruptions to treatment from taking place. A suggested outcome measure could therefore be to monitor impact AZD 3152 has on the reduction in delayed or paused treatments for pre-existing conditions.	Comment noted. The outcomes listed are not exhaustive and the committee will consider any other relevant factors when making recommendations. The committee will consider any evidence presented on relevant outcomes.
	Long Covid SOS	As far as we are aware	Comment noted. No action required.
	Faculty of Pharmaceutical Medicine	While the outcomes are generally appropriate, there is no consideration of the risk of asymptomatic infection or spread to contacts in the home or hospital setting. An important additional benefit of such treatment may be reduction in nosocomial transmission or, alternatively, harm may occur due to failure to recognise asymptomatic infection with risk of prolonged viral replication causing increased risk of disease in contacts.	Comment noted. The outcomes listed are not exhaustive and the committee will consider any other relevant factors when making recommendations.
	Cardiothoracic Transplant Patient Group	The CTPG consider these to be appropriate	Comment noted. No action required.

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	(CTPG), NHS Blood and Transplant		
	Forgotten Lives UK	The health-related QoL measure needs to accurately reflect the utility gain for the patient and their carers/household. The recommendations from the Evusheld appraisal suggested that, because patients may continue to do some protective behaviour, this reduced the overall utility gain. It needs to be recognised that the use of this drug is not a simple one to measure in terms of simple efficacy and QoL. It has a wide reaching impact on both the patient and immediate family, in terms of physical, mental, social and economic terms. However, it's unrealistic to expect patients to immediately have no protective behaviours due to their increased risk from other viral or bacterial infections, and people may have lost confidence and physical strength while shielding. Patient experts in that appraisal also suggested that they would have improvements to their physical and mental health if they were able to do more even whilst continuing some protective behaviours. The committee should not consider that continuing some shielding or protective behaviours is a lack of impact. Those that previously had Evusheld administered have experienced a transition period from shielding to undertaking a much more active engagement in social interactions. We have seen a gradual rehabilitation back into society that has been facilitated by the use of the drug, whilst risk evaluations for activities and precautions are still taken in conjunction with the use of the drug. We have also seen the effect on the families of those who have benefitted from Evusheld and the lifting of restrictions on them, the removal of anxiety, which has allowed a return to more normal social, educational and economic activities	Comment noted. The committee will consider all relevant health-related quality of life outcomes when making recommendations.

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	AstraZeneca	According to the draft scope, the outcome measures to be considered include: • incidence of symptomatic COVID-19 • mortality • requirement for respiratory support • hospitalisation (requirement and duration) • symptoms of post COVID-19 syndrome • **anxiety and depression** • **time to return to normal activities post COVID-19** • adverse effects of treatment • health-related quality of life AstraZeneca agree with the list of outcomes with the exception of the outcomes listed in **bold.** Firstly, AstraZeneca suggest replacing "anxiety and depression" with "psychosocial impact on quality of life of receiving prophylaxis", as it more accurately captures the full quality of life benefit that patients experience. Secondly, AstraZeneca suggests that "time to return to normal activities post COVID-19" should be removed from the list of outcome measures as no data are available to be presented on this outcome. Instead, "time to return to normal activities post COVID-19" should be considered a benefit for AZD 3152 which is not captured in the QALY calculation.	Comment noted. Outcomes listed are not exhaustive. Psychosocial impact on quality of life of receiving prophylaxis will likely be captured within the health-related quality of life outcome. The committee will consider all relevant outcomes when making recommendations.
	NHS England	NHSE are content with the outcomes listed but it should be noted that some of these will be more challenging to measure given the stepping down of routine COVID-19 testing. In addition, NHSE would also suggest that it might be useful to look at data on hospitalisations with or due to Covid; with respiratory symptoms; and/or ICU admissions. The latter as a good indicator not only of costs but the likely long-term sequelae and length of recovery	Comment noted. The committee will consider all relevant outcomes related to hospitalisation when making recommendations.

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	Kidney Care UK	It is important to capture whether AZD 3152 impacts on a person's ability to work and return to normal activities (leisure/family). We are not sure whether these will be measured by health-related quality of life measures?	Comment noted. The committee will consider all relevant health-related quality of life outcomes when making recommendations.
	Myeloma UK	Yes. We would also ask NICE, if possible, to include outcomes related to the impact of infection on ongoing treatment. Patients actively receiving treatment for their myeloma often have their treatment schedule or hospital appointments delayed or paused when they have COVID-19. The scope should also include the number of individual COVID-19 infections, because immunosuppressed people may have a higher risk of getting COVID-19 multiple times.	Comment noted. The outcomes listed are not exhaustive and the committee will consider any other relevant factors when making recommendations. Delay or pausing of treatment for pre-existing conditions may also be captured by hospitalisation and mortality outcomes.
	Long Covid Support	**1. Acute outcomes are listed and post-COVID-19 syndrome outcomes are listed. But outcomes should also take adequate account of considerable evidence of excess mortality and morbidity following acute Covid infections not classified as post-COVID-19 syndrome. These include cardiovascular events (e.g. heart attacks and strokes), endocrine disorders (diabetes) as well as neurological conditions. Taking account of these will further improve the ICERs associated with the various drugs:** a) Evidence for Excess Mortality:	Comment noted. The committee will consider all relevant mortality health-related quality of life and cost outcomes when making recommendations. Costs will be included from an NHS and Personal and Social Services Perspective in line with the NICE

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		i) 'Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality' (Lancet 2022). ii) 'Coronavirus Pandemic (COVID-19)' (Mathieu et al 2020-22). iii) 'Excess deaths associated with covid-19 pandemic in 2020: age and sex disaggregated time series analysis in 29 high income countries' (Islam et al 2021). iv) WHO Global excess deaths associated with COVID-19, January 2020 - December 2021 (WHO 2021). b) Evidence for Negative Cardiovascular Outcomes: i) 'Long-term cardiovascular outcomes of COVID-19.', (Al-Aly et al 2020). ii) 'Covid can damage the heart' (Topol 2020). iii) 'Risk of Cardiovascular Events after Covid-19: a double-cohort study' (Tereshchenko et al 2021). iv) 'Cardiovascular disease and mortality sequelae of COVID-19 in the UK Biobank' (Raisi-Estabragh et al 2022). c) Evidence for the increase of Diabetes risk:	Health Technology Evaluations Manual

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		i) 'The Incidence of Diabetes Among 2,777,768 Veterans With and Without Recent SARS-CoV-2 Infection.' (Wander et al 2022). ii) 'Risk for newly diagnosed diabetes after COVID-19: a systematic review and meta-analysis', (Zhang et al 2022). iii) 'Association of COVID-19 Vaccination With Risk for Incident Diabetes After COVID-19 Infection', (Botting et al 2023). d) Evidence for the increase of Neurological complications: i) 'Long-term neurologic outcomes of COVID-19' (Al-Aly et al 2022). ii) 'Neuropsychiatric sequelae of COVID-19: long-lasting, but not uniform' (Lewis et al 2022). iii) 'Neuropsychiatric aspects of long COVID: A comprehensive review' (Kubota et al 2023). **2. Evidence indicating further deterioration to health of people with Long Covid on reinfection should beappropriately considered:** i) Long Covid Support Reinfection Survey 80% worsened with reinfection. Of those who had recovered or were in remission from Long Covid, reinfection caused a recurrence in 60%.	

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		ii) 'Acute and postacute sequelae associated with SARS-CoV-2 reinfection. (Al-Aly et al 2022) – "evidence shows that reinfection further increases risks of death, hospitalization and sequelae in multiple organ systems in the acute and post-acute phase". **3. It is important that the appraisal will take account of the considerable psychological and social costs associated with present risks of infection and/or reinfection.** A key benefit associated with treatments for acute covid is the reduction of understandable fear and social isolation for immunocompromised people and people already with Long Covid and who cannot risk further disability through reinfection given their known susceptibility. Taking account of this benefit would greatly improve the cost-effectiveness of the various drugs. Many patients continue to practise social distancing and other strategies to limit infections in order to reduce their risk of reinfection given this would likely threaten to worsen an already existing Long Covid and/or pre-existing health conditions. The availability of treatments for acute covid will reduce legitimate concerns of infection/reinfection and increase health related quality of life (HRQoL). This should be built into the model in order not to underestimate the HRQoL benefits of treatment. **4. It is important that the appraisal takes into account the recent evidence on health related quality of life associated with post-COVID-19 syndrome.** i) Long COVID can impact fatigue and quality of life worse than some cancers . Median EQ-5D index score of 0.60 (IQR 0.41 to 0.71) (Walker et al 2023).	

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		5. It is important that it is not assumed that post-COVID-19 syndrome only lasts 3.5 years. It is impossible for it to have lasted longer as Covid-19 has only existed for 3.5 years. Evidence for theanticipated duration of Long Covid can be derived from SARS1 and ME/CFS evidence. a) Evidence re ME/CFS i) Evidence that around 50% of people with Long Covid are estimated to meet ME Criteria; 46% (Mancini et al., 2021); 50% (Kedor et al., 2021); 50% (Haffke et al., 2022) and 58.7% (Twomey et al. 2022). ii)' A systematic review describing the prognosis of chronic fatigue syndrome' (Cairns et al 2005) – a systematic review of 14 studies of ME/CFS found a median full recovery rate during the follow-up periods of 5%, and the median proportion of patients who improved during follow-up to be 39.5%. iii) Report to the CMO ME/CFS Independent Working Group – "Prognosis is extremely variable. Although many patients have a fluctuating course with some setbacks, most will improve to some degree. However, health and functioning rarely return completely to the individual's previous healthy levels; most of those who feel recovered stabilise at a lower level of functioning than before the illness…", "Overall, there is wide variation in the duration of illness with some people recovering in less than two years while others remain ill after several decades. Those who have been affected for several years seem less likely to recover; full recovery after symptoms persist for more than five years is rare.".	

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		iv) 'Factor analysis of symptoms among subjects with unexplained chronic fatigue: What can we learn about chronic fatigue syndrome?' (Nisenbaum et al 2004) estimated a duration of 6yrs. v) 'The Health-Related Quality of Life for Patients with Myalgic Encephalomyelitis / Chronic FatigueSyndrome (ME/CFS)' (Hvidberg et al 2015) - ME/CFS has an unadjusted disutility scale 0.47 - OLS regression estimated disultility scale 0.29 for ME/CFS, compared to 20 other conditions - ME had the lowest quality of life compared to all 20 conditions, inc. multiple sclerosis, several cancers, stroke and diabetes. v) 'The functional status and well-being of people with myalgic encephalomyelitis/chronic fatigue syndrome and their carers' (Nacul et al 2011) - ME/CFS is as disabling and has a greater impact on functional status and well-being than other chronic diseases, and also has a significant emotional burden on carers. People with ME/CFS experience on average greater disability than those with type 2 diabetes, congestive heart failure, back pain/sciatica, lung disease, osteoarthritis, multiple sclerosis and even most cancers (Buchwald et al 1996). Several studies further confirm the scale of impairment across both physical and mental health and that impacts may be as great or greater than in many other chronic medical conditions (Hvidberg et al 2015, Komaroff et al 1996, Schweitzer et al 1995, Winger et al 2015). 'What is known about severe and very severe chronic fatigue syndrome? A scoping review' (Strassheim 2017) - - 25% of ME patients are severe. Long Covid is being underestimated 50% of people with Long Covid meet ME/CFS criteria.	

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		b) Evidence re SARS1 i) Is 'Long Covid' similar to 'Long SARS'?(Patcai 2022) - A report of a 7 year follow up on 50 healthcare workers who had severe SARS1 from the 2022/3 Toronto outbreak indicated that none of the 50 patients with long term sequelae regained their former state of health over the 7 years. **6. It is important that the wider societal costs of post-COVID-19 syndrome are taken into account** a) Costs to the NHS b) Costs to Social Care c) Costs to Economy i) Of 1041 patients of Long Covid Clinic 25% reported being on long term sick/disabled compared with 2% before Covid; 56% of respondents were employed full time before Covid, dropping to 18% after Covid. Data (unpublished) from the Long Covid Support survey of services for Long Covid in England. ii) Workers Experience of Long Covid (March 2023) joint report by Long Covid Support and the Trades Union Congress found that 1 in 7 people with Long Covid reported having lost their job. d) Welfare Payments	

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	Clinically Vulnerable Families	• anxiety and depression We would like to confirm that this outcome applies to all at-risk individuals who might benefit from this technology, whether or not they become infected with covid	Comment noted. The committee will consider all relevant outcomes related to anxiety and depression when making recommendations.
Equality	Anthony Nolan	**Psychological impact** Without an available prophylactic such as AZD3152, many HSCT patients are left with little alternative but to continue adopting NPIs and shield themselves from their families and communities. Many have done this for over three years now and this is having a significant emotional toll. As the wider population has returned to a form of normalcy, a sense of loneliness and abandonment heightens this impact. Anthony Nolan has surveyed transplant patients throughout the pandemic. Our findings have been consistent in demonstrating an increase in anxiety and low wellbeing when having to shield and take additional social precautions. The psychological impact of shielding, including anxiety, depression and severe stress has been recorded across multiple disease areas.[5,6] **Patients from a minority ethnic background** It has been observed that vaccine hesitancy is greater amongst minority ethnic communities. The UK Government commissioned a study on factors influencing COVID-19 vaccine uptake among minority ethnic groups which shows that Black African and Black Caribbean people are less likely to be vaccinated (50%) compared to White people (70%).[7] Anecdotally, this same hesitancy has been shared by stem cell transplant patients and other haematological patients from the same backgrounds. It	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.

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		remains a risk that a minority of patients will continue to be hesitant around new technologies, especially those that have been recently introduced and which are administered intravenously. **Age and frailty** Analysis of England population-level data indicate that mortality rates for patients aged over 70 are significantly higher than the rest of the population.[8] These risk factors continue for transplant patients of the same age. **Clinical Delivery of COVID-19 therapeutics** How AZD3152 will be clinically delivered will carry its own inequities. The starkest may be between urban and rural patients, given that this technology requires intramuscular injection by a HCP. What's more, a report on antiviral and nMABs delivery shows that for haematological diseases and stem cell transplant recipients, only 50% of those eligible for Sotrovimab were treated. This is significantly lower than for solid organ transplant recipients at 69%.[9] A plan is required for its safe delivery as quickly as possible. In primary care settings, information training is required for patients, GPs, doctors and pharmacists and communities. Primary care pressures would also need to be factored in, including whether the rollout can be completed alongside the wider immunisation programme. At a trust level, there will be a need for sufficient resources to allow delivery in secondary care and beyond. Specialists such as BMT clinicians could administer the IM injections to their own patients rather than for patients to access via a general care centre. All delivery models should be led by the prioritisation of those at the highest risk. This will ensure a rapid rollout to those with the greatest clinical benefit.	

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		5) Spurr L et al, 2022, Psychosocial impact of the COVID-19 pandemic and shielding in adults and children with early-onset neuromuscular and neurological disorders and their families: a mixed-methods study, BMJ Open https://bmjopen.bmj.com/content/12/3/e055430.info *6) Westcott K, 2021, The impact of COVID-19 shielding on the wellbeing, mental health and treatment adherence of* adults with cystic fibrosis, Future Healthcare Journal www.ncbi.nlm.nih.gov/pmc/articles/PMC8004337/ 7) *BAME vaccination hesitancy, NHSE/I, 2021 www.england.nhs.uk/south-east/wp-content/uploads/sites/45/2021/05/BAME-vaccination-hesitancy-A4.pdf* *8) Changes in COVID-19-related mortality across key demographic and clinical subgroups: an observational cohort study using the OpenSAFELY platform on 18* million *adults in England https://doi.org/10.1101/2022.07.30.22278161* *9) Antivirals and nMABs for non-hospitalised COVID-19 patients: coverage report, 2022 https://reports.opensafely.org/reports/antivirals-and-nmabs-for-non-hospitalised-covid-19-patients-coverage-report/*	
	Blood Cancer UK	Please refer to the above comment in the 'Subgroups' section for an outline of how measures of cost effectiveness should consider disparity in risk from COVID-19, including due to both clinical and non-clinical factors. Relevant evidence includes (1) data on mortality and hospitalisation from Covid-19 disaggregated by ethnicity and deprivation level, (2) NHSE COVID-19 vaccine uptake data among the immunosuppressed, disaggregated by ethnicity and deprivation, and (3) data on the percentage of eligible patients who are treated for COVID-19, after testing positive and being referred for post-exposure treatments disaggregated by ethnicity and deprivation level. In each dataset, deprivation and ethnicity are strong indicators of whether a patient will die from COVID-19. Those living in the most deprived areas, for instance, are least likely to easily access vaccines, least likely to be given COVID treatment despite their eligibility and testing positive, and most likely to die from COVID.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.

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		Secondly, cost per QALY is an imperfect unit of measurement in this instance and should be adjusted accordingly. A significant number of those who are unlikely to mount an adequate response to vaccines are, for instance, living with cancer or undergoing cancer treatment. AZD3152 would undoubtedly improve and extend QALYs, not least by helping this patient group to mitigate the risks pervasive in their everyday lives. That said, the cost per QALY will be unreasonably higher for this group than if this treatment were available to healthy patients, because cancer patients are more likely to have a lower baseline quality of life when evaluating it using this scale of measurement. Using the cost per QALY measurement would therefore underestimate the benefit this treatment would have. The threshold of what is considered cost effective based upon cost per QALY should therefore be lowered in this instance, to account for this special circumstance and to adjust for what constitutes a 'healthy life' for those who are disabled, such as cancer patients, and particularly for those who are at highest risk due to clinical factors.	
	LUPUS UK	In previous appraisals of prophylactic and post-infection treatments for COVID-19, there were some inaccurate assumptions made about the precautionary measures made by this patient cohort and their households. We raised these in appraisals for those treatments, and we are repeating them here as they are relevant to the accurate appraisal of AZD 3152. The draft recommendation for the Evusheld appraisal implied that, because (some) people at higher risk from COVID-19 continue to modify their behaviour by shielding, their true risk cannot be fully considered in cost-effectiveness modelling. Section 3.16 of the draft recommendation stated that: "…data for the general population [on infection risk] may not be generalisable to those likely to have Evusheld. The committee considered it likely that the risk of infection in those eligible for Evusheld would be lower	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.

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		than the general population. This is because those eligible for Evusheld modify their behaviour, which remains an effective way to reduce risk of infection, despite the substantial burden." The committee then considered that the model should be sensitive to changes or differences in background levels of risk. It is unreasonable to expect people in the eligible group to continue to modify their behaviour to reduce risk of infection. Using this as evidence of a lower level of risk than the general population could mean recommendations require people to continue to shield and does not account for the large number of eligible people unable to do this. The committee may also need to review any stereotypes of a person who is shielding. We cannot assume that those at risk can reduce their risk of exposure to the virus by modifying just their own behaviour. Many in the at-risk group do not live alone. It is more likely that someone is in a household with family or friends whose behaviour would also need to be modified. This becomes increasingly difficult due to the lack of precautionary measures and governmental support, such as widespread testing. We must also consider the reduced opportunities for at-risk people to practice shielding. Most people in this group are living with a disease and/or treatment which requires attendance to medical settings for medication administration and/or monitoring. Even if an at-risk person can stay safe traveling to and from appointments, the precautionary measures in medical settings are being increasingly abandoned. It is not reasonable to use lower risk values to model cost-effectiveness for this group, because it is not reasonable to assume that all at-risk people and their households are able to adequately modify their behaviour, nor is it reasonable to expect those that are able to, to continue shielding given the difficulties and well-documented mental and physical health impacts of this (e.g. Sloan et al, 2021; Ryan et al, 2022; Maldonado et al, 2021). This is also a matter of health inequalities. A disproportionate number of those unable to shield are from minority ethnic groups, due to the higher	

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		likelihood that they are in employment without remote working options, higher likelihood to work in occupations with higher risk of exposure to COVID-19, and higher likelihood of needing to use public transport to travel to work (POST, 2020). Lupus also disproportionately affects those from African-Caribbean or Asian heritage, who also tend to have more severe disease (e.g. Hasan et al, 2022), and so would likely be a high proportion of those eligible for AZD 3152.	
	Leukaemia Care	As alluded to above, many patients who are immunocompromised have a reduced quality of life, which is in part due to the continuing impact of COVID-19 and the lack of effective preventative treatments for this cohort. This directly affects patients' ability to protect themselves from COVID-19, presenting in inequality compared with immunocompetent individuals. The treatment under review has the ability to vastly reduce this inequality and should be considered as such.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.
	Long Covid SOS	Not that we are aware	Comment noted. No action required.
	Faculty of Pharmaceutical Medicine	The restriction of use to immunosuppressed individuals may disadvantage individuals at risk of severe disease for whom vaccination is not appropriate (eg previous vaccine reactions/contraindications).	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.
	Cardiothoracic Transplant Patient Group (CTPG), NHS	The CTPG consider that patient populations with shared protected characteristics should be appraised separately. This will prevent people who would derive a cost-effective benefit from the treatment if they were solely appraised in a wider patient population being excluded.	Comment noted. The committee will consider how the recommendation requires consideration

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	Blood and Transplant	The CTPG consider that heart and lung transplant recipient would be good examples of such defined patient populations.	of equalities issues during the appraisal.
	Forgotten Lives UK	Evidently many of those who will be most affected will be those covered under the equality act due to long-term health problems and disabilities. These groups are known to be most physically and psychologically vulnerable over the pandemic, and it is important that charities and patient representatives are involved in the decision making process so the impact can be fully considered. We are now seeing more of this cohort experiencing an inequality of healthcare access as more healthcare settings reduce or remove preventative measures, meaning many now struggle physically and mentally to attend appointments or are made to feel like second class citizens, waiting outside of healthcare settings in an effort to keep themselves safe. 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. Therefore this should be considered if the prophylactic is distributed outside of a trial (e.g. travel to treatment centres presenting additional costs to those immunocompromised should not lead to economic disadvantage to those most vulnerable, for reasons beyond their control). Those eligible are also more likely to experience mobility difficulties, or be homed in health and social care settings (learning disability, older people, mental health) treatment must be accessible for all groups. It is important that any roll out of this medication is well publicised amongst both patient groups and clinicians. Those from a BAME background and immunocompromised are known to be at higher risk, more likely to be from low socioeconomic backgrounds, and less likely to be engaged with health	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.

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		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.	
	AstraZeneca	AstraZeneca believe that there are important equality considerations to take into account for this appraisal: Firstly, the population included in this scope are high-risk patients who are less likely to mount an adequate protective immune response after vaccination and therefore the underlying risk of developing an adverse outcome from COVID-19 is higher compared to the general population. Therefore, there is an urgent unmet need for an effective PrEP for a vulnerable population who are at a very real risk of severe outcomes from COVID-19. Secondly, members of the general population have either amounted an adequate immune response through vaccination and/or through natural immunity through prior COVID-19 infection while people with immunosuppression are still leading restricted lives and are disadvantaged in the workplace, educationally and socially. People who are immunocompromised should be able to have the same level of protection the general population has through vaccines, and it important that these disadvantaged patients are offered additional layers of protection against COIVID-19. Thirdly, in the STA for Evusheld (TA900) a number of equality issues were identified related to the benefit of PrEP for patients with learning disabilities, minority ethnic groups, and people with mobility issues(6). The NICE STA for Evusheld (TA900) also noted that people eligible for Evusheld are "*more likely to be covered under the protected characteristics of the Equality Act because of the long-term health problems and disabilities.*" AstraZeneca would strongly consider that the equality issues as identified in the NICE STA for Evusheld would also apply to AZD 3152.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.

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	NHS England	NHSE would like to flag that a review of access to COVID medicines, when used to treat COVID-19, to highest risk patients in community settings has highlighted areas of potential inequality of access common to some other areas of healthcare access (including COVID vaccination). For example, access is lower than expected for those in younger or older age groups, for those in more deprived groups, and for those with black African, black Caribbean or mixed-race ethnicity. Similar issues may occur with access to prophylaxis with tixagevimab–cilgavimab.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.
	Kidney Care UK	We know that many people within the highest risk groups (who would generally fall within equality legislation) feel unable to fully participate in society because of their ongoing risk from Covid. This poses the risk of restricted access to employment, fewer opportunities to maintain physical health, and a detrimental impact on mental health. It is important that the NICE appraisal is able to capture the benefits of being able to access an effective preventative treatment and therefore being able to more fully participate in society. By doing so, it will better promote equality between those at continuing high risk and the rest of the population. Conversely, we are aware that some people who are vulnerable have heard only the public messages about the pandemic being over and therefore do not realise that Covid-19 treatments and vaccines are still available, and are therefore at excess risk. As a consequence, some have died.	Comment noted. The committee will consider how the recommendation requires consideration of equalities issues during the appraisal.
	Myeloma UK	As mentioned above, the criteria for defining eligibility and identifying eligible patients should be clear and easy to understand. The definitions should work for both the general population and healthcare professionals. Clear, consistent definitions will help ensure people of different income, education and health literacy levels have equal access to this treatment.	Comment noted. No action required.
	Long Covid Support	None	No action required.

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	Clinically Vulnerable Families	Noted	Comment noted. No action required.
Other considerations	Anthony Nolan	Patients who undergo stem cell transplantation require re-vaccination of all their COVID-19 primary doses. There can be a wait of many weeks before re-vaccination commences (longer for those with late-effects such as Graft vs Host Disease), and it takes some time until patients are 'fully' vaccinated. During this period, they are extremely immunosuppressed with little to no immune protection from COVID-19. Therefore, this group especially are in need of prophylactic protection to fill that stop gap before re-vaccination. To ensure all HSCT and cellular therapy patients can access AZD3152, NICE and NHSE should engage the British Society of Blood and Marrow Transplantation and Cellular Therapies (BSBMTCT) in assessing the latest data including the level of risk, the size of the patient cohort, and the identification and prioritisation of specified subgroups.	Comment noted. Stem cell transplant (HSCT) recipients are covered in the subgroups section of the scope under people with anticipated failure of vaccine.
	Blood Cancer UK	None	No action required.
	LUPUS UK	None	No action required.
	Leukaemia Care	None	No action required.
	Long Covid SOS	Are studies for marketing authorisation being carried out long enough for symptoms of Long Covid to be most effectively measured as an outcome?	Comment noted. The key trial informing the regulatory submission has an end date of January 2025. At the time of submission, it is likely that data on the

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			impact of long COVID will still be maturing. The committee will consider any data presented on long COVID and the uncertainty associated with this.
	Faculty of Pharmaceutical Medicine	None	No action required.
	Cardiothoracic Transplant Patient Group (CTPG), NHS Blood and Transplant	No further considerations	Comment noted. No action required.
	Forgotten Lives UK	The drug needs to be made available both through primary and secondary care to allow the widest possible and quickest access possible. A large number in these cohorts deal with their secondary care on a regular basis and have a much more in depth health relationship with them. Problems accessing vaccines for many of these groups via primary care and the lack of knowledge about their cohort qualifications, has shown that the widest possible access needs to be made and the expert decision making applicable to secondary care should be utilised. If not available through secondary care then there must be a referral pathway for AZD 3152 from secondary to primary care.	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		The rollout of Evusheld both abroad and privately in this country has shown that the drug can be administered quickly, simply, efficiently and cheaply in terms of staffing, on a par with the administration of other vaccines	
	AstraZeneca	Please see response below in the “Questions for consultation” section under Q7.	Comment noted. No action required.
	NHS England	NHSE would suggest that further consideration is given in the evaluation on the delivery requirements of the NHS to administer this treatment if it was subject to a positive recommendation. Understanding the new administration pathways needed will be important as Integrated Care Boards (ICBs) will need to set these up should there be a positive determination. For example, there are unlikely to be similar intramuscular (IM) based pathways which could automatically absorb the delivery of such a therapy currently. The impact of the shift to BAU management of COVID-19 will also need to be factored in – for example, digital enablers supporting the national identification of potentially eligible patients are being stood down and an antibody testing programme is not currently in place for highest risk or potential prophylaxis cohorts (if applicable to the pathway). We would recommend ICB involvement in modelling and relevant appraisal committees will be needed to translate proposed pathways into local service commissioning.	Comment noted. NICE will consider any factors that may affect the implementation of its guidance.
	Kidney Care UK	In the appraisal of Evusheld, the committee found there is uncertainty about how people’s behaviour would change after having tix-cil. We suggest that a NICE appraisal of prophylactic Covid-19 treatment is an opportunity to develop guidance that optimises the benefits of a preventative treatment in terms of quality of life and	Comment noted. The committee will consider all relevant health-related quality of life

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		clinical effectiveness, by ensuring people at high risk are offered advice and guidance on appropriate levels of activity/social mixing following preventative treatment (taking a similar approach to that used in the PrEP guidance). This advice would support people to maximise their quality of life as far as possible while avoiding significant increases in their risk of infection. The model should incorporate these assumptions of how people would behave.	outcomes when making recommendations.
	Myeloma UK	No comment	No action required.
	Long Covid Support	None	No action required.
	Clinically Vulnerable Families	Noted	Comment noted. No action required.
Questions for consultation	Anthony Nolan	*Do you consider that the use of AZD3152 can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?* It is not clear how the QALY includes the varied long-term risks of a COVID-19 infection such as heart, renal, and liver conditions, as well as Long COVID. Additionally, the cost per QALY will be significantly higher for this population group as they are more likely to have lower baseline quality of life compared to the general healthy population so this should be adjusted for in the QALY calculation. It is important to measure the psychosocial and wellbeing effects of AZD3152. Patients would be able to undertake increased social interactions and stop shielding, which has a direct health-related benefit.	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		Where do you consider AZD3152 will fit into the existing care pathway for prevention of COVID-19? Would AZD3152 be used in both primary and secondary care settings? We recommend that AZD3152 be used primarily in secondary care settings. Patients' consultants and specialist teams have a comprehensive and long-term view of their patients' condition, history, treatment type and schedule, immunity and individual risk. Primary care providers and professionals can have lower awareness and understanding of the specific eligibility and access criteria for COVID-19 treatments for immunocompromised groups. For this reason, we anticipate fewer barriers to access AZD3152 in secondary care compared to primary care.	
	Blood Cancer UK	AZD 3152 should be made available to those eligible primarily via the secondary care route (e.g. their specialist teams and consultants). AZD 3152 should be deployed through specialist teams as they have a comprehensive and long-term view of the patient's condition, history, treatment type and schedule, and immune system. For this reason, it should not be delivered in the primary care setting, as primary care providers often do not know whether their patients are eligible for interventions such as additional COVID vaccine doses or post-exposure COVID treatments. It is arguable that eligible patients would encounter similar barriers if attempting to access AZD 3152 via primary care. Specialist teams in secondary care should be responsible for discussing AZD 3152 with their patient and working through any concerns or hesitations the patient may have, but safeguards must be created to ensure that patients who are eligible for AZD 3152 but are not undergoing treatment or do not regularly see their secondary care team for other reasons have equitable access. This includes those on 'watch and wait' or those who completed their cancer treatment course several months prior. Clear procedures must be in	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		place for patients who are unduly refused treatment with AZD 3152 to advocate for themselves and access the treatment, if they are eligible. This is particularly important for the blood cancer cohort, who are largely immunosuppressed as a result of their condition, rather than solely due to their cancer treatment. They are more likely than other cohorts, therefore, to be at highest risk from COVID-19 while not undergoing active cancer treatment. Whichever process is established for the delivery of AZD 3152, it must be ensured that it is equitably accessible.	
	LUPUS UK	• If AZD 3152 is not available in secondary care, there must be a referral pathway for secondary care clinicians. Patient records for primary and secondary care are usually separate, and so primary care does not have accurate data about patients in this cohort who are mainly treated in secondary care. If the only pathway is through primary care, it will be difficult to ensure all eligible patients have access to the treatment. • The health-related benefits for the QALY calculation should include the impact on carers and/or family members. As stated in our response to the section on equalities, it is more likely that a person in an at-risk group lives with others than alone. This means that their household, carers, family, and friends would also need to modify their behaviour to protect them if there are no effective prophylactic treatments, with resultant health and economic impacts.	Comment noted. No action required.
	Leukaemia Care	None	No action required.
	Long Covid SOS	We would welcome the technology being available in all settings.	Comment noted. No action required.

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	Faculty of Pharmaceutical Medicine	**Where do you consider AZD 3152 will fit into the existing care pathway for prevention of COVID-19?** See above – chemoprophylaxis for immunosuppressed patients **Which populations would AZD 3152 be used in?** The patient group recommended in the IAG March 2023 report, with the possible exclusion of those receiving chronic immunoglobulin transfusions. **How many people in England would be eligible for treatment with AZD 3152?** Based on QCovid publications potential max 1.5% of UK population or approx. 975,000 **How would these people be identified in practice?** All are under chronic medical care. Many will be listed as eligible for antiviral treatment currently. **Are the subgroups listed appropriate? Are there any other relevant subgroups that should be considered?** If a population health approach were to be utilised there would be a reassessment of potential extension of the groups permitted access to	Comment noted. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		antiviral treatment to include the population recommended for influenza antivirals. **Would AZD 3152 be used in both primary and secondary care settings? If so, about what proportion of use would you expect in each setting?** As it is administered IM it could be prescribed/administered in any setting including community pharmacy **Would AZD 3152 be used at vaccination centres?** If these continue to be used this is an option, but it would likely be preferable to administer this during a hospital visit (all of these patients regularly attend) or via GP/community pharmacy services **Would AZD 3152 be a candidate for managed access?** Yes – as is currently the case for antiviral treatment within the same population **Do you consider that the use of AZD3152 can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** It is possible that use of this treatment within the population concerned would reduce the risk of spread of disease within a hospital/contact setting provided that there is no increase in risk of asymptomatic infection.	

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		Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. It is not clear that this is being evaluated within the ongoing clinical trial. AZ could be asked to consider assessing this additional outcome in the phase III portion of the ongoing SUPERNOVA study.	
	Cardiothoracic Transplant Patient Group (CTPG), NHS Blood and Transplant	No further questions	Comment noted. No action required.
	Forgotten Lives UK	None	No action required.
	AstraZeneca	**1. Where do you consider AZD 3152 will fit into the existing care pathway for prevention of COVID-19?** AstraZeneca anticipates submitting a NICE dossier for patients who are at high risk of an adverse COVID-19 outcome and aligns with the target population in the SUPERNOVA trial (i.e. patients with conditions causing immune impairment, who are less likely to mount an adequate protective immune response after vaccination). In addition to the vulnerability of this patient population there are currently no PrEP options available for these patients and there is a high unmet need for effective therapies. Therefore, AstraZeneca anticipate AZD 3152 to be administered as soon as possible to support extremely high-risk vulnerable patients who would benefit from PrEP. AstraZeneca understands that those patients who are immunocompromised and remain at high risk of adverse clinical outcomes due to COVID-19 will be under the routine care of specialists to manage their underlying conditions.	Comment noted. No action required.

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		We therefore believe that PrEP with AZD 3152 will fit into a patients' existing routine care and can be administered as part of their ongoing care during their outpatient appointments either in secondary care or as part of secondary-care led community service. **2. Which populations would AZD 3152 be used in? How many people in England would be eligible for treatment with AZD 3152? How would these people be identified in practice?** As noted elsewhere AstraZeneca anticipates submitting a NICE STA dossier for a population aligned with the SUPERNOVA trial population. This patient group aligns closely with the patients who may be eligible for PrEP as described in the DHSC commissioned independent PrEP report(1). Approximately 97,000 people in England would be eligible for treatment with AZD 3152 according to the combined population estimates of group A1 and A2 of the DHSC commissioned independent PrEP report sourced from NHS Digital(6). Further to this, available data suggests that a minority of patients in group B would also be eligible for PrEP(7). In terms of identification, as this population reflects people who are high-risk and immunocompromised, they would be expected to attend hospital regularly by way of routine outpatient visits, to manage their underlying health condition. Alternatively, patients may regularly attend secondary care led community services also with the aim of managing their underlying condition. Given the regular contact between this group of patients and NHS services via routine appointments, it is expected that eligible patients for AZD 3152 would be easily identifiable, and the treatment will be administered as part of their routine appointment in this secondary care, or secondary care led community setting. Further to the above, populations who may be eligible for PrEP are clearly defined in the DHSC commissioned independent PrEP report(1). Therefore, digital identification of patients could be utilised in the	

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		same way it has been for access to other COVID-19 therapeutics, vaccinations, and testing. **3. Are the subgroups listed appropriate? Are there any other relevant subgroups that should be considered?** The submission will focus on a population who are at high risk of adverse clinical outcomes due to COVID-19, aligned with the population in the SUPERNOVA trial. If data permits, broad and relevant subgroup analyses will be presented. However, as part of the assessment, AstraZeneca may be requested to present subgroup analyses in specific high-risk populations (for example subgroup analyses in groups A1 and A2 that represent the highest risk populations as defined in the DHSC commissioned independent PrEP report(1)). It is extremely unlikely that data will be available at this level of granularity to enable such subgroup analyses to be presented and to be informative. **4. Would AZD 3152 be used in both primary and secondary care settings? If so, about what proportion of use would you expect in each setting?** Since the target population are high-risk and are immunocompromised, these patients will attend hospital regularly through routine outpatient visits, or attend secondary care led community services to manage their underlying health condition. Therefore AZD 3152 is expected to be administered as part of these regular NHS contacts/visits and prescribed upon specialist advice. AZD 3152 is unlikely to be deployed in primary care. **5. Would AZD 3152 be used at vaccination centres?** According to the World Health Organisation (WHO), COVID-19 is no longer a global health emergency. The NHS is no longer routinely testing the general population for COVID-19 and have decommissioned routine testing for COVID-19 as well as vaccination programmes and centres. Also, there is no	

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		longer a need for COVID-19 Medicine Delivery Units (CMDUs) to provide a resource intensive acute service to administer timely treatment within 5 days of testing as was the case in the pandemic. Therefore, given the current landscape for COVID-19, it is not appropriate to assume that AZD 3152 would be administered in a “pandemic care delivery setting” with an overwhelmed healthcare system, as it is not reflective of current clinical practice. Instead, AZD 3152 should be administered through standard care routes for these patients, specifically as part of routine specialist care in a hospital, or via secondary care led community services. **6. Would AZD 3152 be a candidate for managed access?** AstraZeneca is targeting routine commissioning for this submission and do not consider managed access applicable currently at this stage. **7. Do you consider that the use of AZD 3152 can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** Carer utility is an important consideration given that there is substantial impact of COVID-19 on the carers of immunocompromised patients. For example, families and carers experience anxiety around bringing COVID-19 home causing them to modify behaviour or experience guilt if they cannot afford to do so. As per the NICE reference case, the perspective for outcomes captured in an economic evaluation should include “all direct health effects, whether for patients or, when relevant, carers”. The inclusion of carer disutility into the estimation of cost-effectiveness has been accepted by NICE previously in	

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		appraisals for vutrisiran [TA868(8)] and patisiran [HST10(9)]. In reality, the benefit of a prophylactic therapy also extends to those who live with and care for the patient. The impact on carers was recognised in the Final Guidance for Evusheld (TA900(10)) which states that '*both patient experts also highlighted that the burden of responsibility extends to household family members, and affects work life and family relationships'*. Therefore, given the above, it is important that this STA submission for AZD 3152 accounts for the impact on carers and the improvement in quality of life an effective PrEP would bring. Another important consideration is the "time to return to normal activities post COVID-19". AZD 3152 is an effective PrEP which will avoid COVID-19 and reduce the severity of COVID-19. This implies that patients who receive PrEP will experience less severe COVID-19 and more quickly return to normal activities as compared to patients who do not receive PrEP. There is no data on this duration of time to normal activities, but this outcome should be considered in the assessment outside the QALY calculation given its clear benefit for patients.	
	NHS England	None	No action required.
	Kidney Care UK	*Would AZD 3152 be used in both primary and secondary care settings? If so, about what proportion of use would you expect in each setting?* *Would AZD 3152 be used at vaccination centres?* It is important that we learn from the vaccine rollout about maximising accessibility. Many people will find it easier/would prefer to access the drug at a local site, such as their GP or vaccination centre or pharmacy. We are also hearing more concern about travel costs to hospital appointments leading to	Comment noted. No action required.

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		decisions to cancel. However, some patients may want to have a discussion about risks and benefits with their kidney specialist before making a decision about the treatment. We do not have data on the likely split. Kidney Care UK received a huge number of calls from people who were experiencing significant stress when trying to access the third and subsequent doses of vaccine. Limited understanding of the correct process and eligibility criteria among GPs, hospital specialists, 119 and vaccination sites was a key problem. There have also been problems in the Spring Booster rollout and access to the antivirals, again related to difficulties in accessing correct information as well as lack of understanding about eligibility in some NHS staff. It's important any rollout of AZD 3152 learns from this and ensures communication across all teams is clear and comprehensive, and the responsibility of each part of the system is clear. OpenSafely data on vaccine rollout and use of antivirals in the community shows lower usage among certain groups, including Asian, Black and Mixed ethnic groups and lower socio-economic groups. An AZD 3152 rollout must be designed to avoid unequal access across different groups, and take a procative promotion approach. Kidney Care UK would be pleased to assist with this, as we have done with all Covid treatments, vaccines and information.	
	Myeloma UK	Would AZD3152 be used in both primary care and secondary care settings? AZD3152 should be available in both settings, although primarily in secondary care. We had several calls from patients who struggled to access COVID-19 treatments and vaccines when they were made available on the NHS. Some patients struggled to show their eligibility at primary care centres due to lower awareness of the eligibility criteria and needed intervention from secondary care teams to secure treatment. Allowing clinicians to prescribe	Comment noted. No action required.

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		prophylaxis as part of a patient's ongoing care at secondary care facilities could help prevent this. Patients living in rural settings or with limited transport options would value access to the community via primary care/community settings. Would AZD3152 be used at vaccination centres? AZD3152 should not be given exclusively at vaccination centres. The number of vaccination centres has been declining, and many are not easily accessible for those living in a rural setting or with limited transport options.	
	Long Covid Support	None	No action required.
	Clinically Vulnerable Families	Noted	Comment noted. No action required.
Additional comments on the draft scope	Anthony Nolan	N/A	No action required.
	Blood Cancer UK	There is a wealth of evidence demonstrating that COVID-19 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 AZD 3152.	Comment noted.
	LUPUS UK	References cited in above comments: - Hasan, B., Fike, A., & Hasni, S. (2022). Health disparities in systemic lupus erythematosus – a narrative review. *Clinical Rheumatology, 41(11)*, 3299-3311	No action required.

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		- Maldonado et al (2021). Association of medication access difficulty and COVID-19-related distress with disease flares in rheumatology patients during the COVID-19 pandemic. *Arthritis Care & Research, 73(8)*, 1162-1170 - POST (2020). Impact of COVID-19 on different ethnic minority groups. Rapid response report. https://post.parliament.uk/impact-of-covid-19-on-different-ethnic-minority-groups - Ryan et al (2022). Exploring the physical, psychological and social well-being of people with rheumatoid arthritis during the coronavirus pandemic: a single-centre, longitudinal, qualitative interview study in the UK. *BMJ Open, 12(7)*, e056555 - Sloan et al (2021). COVID-19 and shielding: experiences of UK patients with lupus and related diseases. *Rheumatology advances in practice, 5(1)*, rkab003 - UK Health & Security Agency; UKHSA. (2023). National flu and COVID-19 surveillance report: 8 June (week 23). https://www.gov.uk/government/statistics/national-flu-and-covid-19-surveillance-reports-2022-to-2023-season	
	Leukaemia Care	None	No action required.
	Long Covid SOS	No	No action required.
	Faculty of Pharmaceutical Medicine	None	No action required.
	Cardiothoracic Transplant Patient Group (CTPG), NHS	No further comments	No action required.

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	Blood and Transplant		
	Forgotten Lives UK	None	No action required.
	AstraZeneca	Any additional comments on the draft scope • Please note that the All-Party Parliamentary Group (APPG) on Vulnerable Groups to Pandemics published a clinical expert consensus statement in July 2022 in which it highlighted the urgent need to make prophylaxis treatments available as soon as possible to provide an immunity boost to vulnerable patients(3). This reference should be added to the Related National Policy section. • Please note that NICE published a real-world evidence framework in June 2022 in which it provided the key considerations in informing their guidance(11). This reference should be added to the Related National Policy section. 2. All-Party Parliamentary Group on Vulnerable Groups to Pandemics. July 2022. National Clinical Expert Consensus Statement. Coronavirus monoclonal antibodies as a prophylactic therapy against COVID-19 for immunocompromised groups. 4. National Institute for Health and Care Excellence. June 2022. NICE real-world evidence framework. https://www.nice.org.uk/corporate/ecd9/chapter/overview	Comment noted. No action required.
	NHS England	None	No action required.
	Kidney Care UK	None	No action required.
	Myeloma UK	None	No action required.

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	Long Covid Support	None	No action required.
	Clinically Vulnerable Families	None	No action required.

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

Lymphoma Action