NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

AZD 3152 for preventing COVID-19

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of AZD 3152 within its marketing authorisation for preventing COVID-19.

Background

COVID-19 is predominantly an acute respiratory illness caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease refers to any symptom resulting from the infection and these can vary widely in clinical severity. People who become critically ill may develop acute respiratory distress syndrome (ARDS), the leading cause of mortality among patients with COVID-19.

The COVID-19 pandemic rapidly evolved globally, with countries facing different stages of the spread of disease. In England and Wales between 13 March 2020 and 17 March 2023, 196,471 deaths occurred involving COVID-19.[1] The gradual mutation of SARS-CoV-2 has led to increased cases of various variants of concern, each with different transmissibility, morbidity, and mortality effects. For cases sequenced in England between 27 March 2023 and 2 April 2023, 53.1% were classified as the Omicron subvariant XBB.1.5.[2] Data from the UK suggest that mortality due to COVID-19 is strongly associated with older age, male gender, deprivation and Black, Asian and minority ethnic family background.[3] Disabled people, people with a learning disability and people with pre-existing conditions, including people with dementia and Alzheimer's disease, diabetes, heart disease or obesity, are more at risk from dying from COVID-19.[4,5] 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]

COVID-19 has a diverse range of clinical manifestations, ranging from mild infection to severe disease accompanied by high mortality.[8] It begins with infection, or the viral replication phase, with symptoms such as cough, fever and breathlessness. This disease stage is when viral shedding occurs and people are at the peak of infectiousness. Some people may also develop post-COVID syndrome, defined by the NICE's rapid guideline on managing the long-term effects of COVID-19 as symptoms continuing for more than 12 weeks after the initial COVID-19 infection.

Vaccination is the primary pharmaceutical intervention for preventing COVID-19. There are 4 vaccines authorised and currently available for use in the UK for preventing COVID-19 in adults. Adults in England are eligible for 2 initial doses of a COVID-19 vaccine followed by at least one booster dose. People with severely weakened immune systems may also be offered an additional (3rd) primary dose.[9] Vaccination may be unsuitable for some people for example, if they have a history of severe allergic reactions or anaphylaxis to any of the ingredients in the vaccine. Some people also have an increased risk of inadequate response to COVID-19 vaccination. The OCTAVE trial showed 40% of people with specific immunocompromised or immunosuppressed conditions generate lower levels of

SARS-CoV-2 antibody reactivity compared to healthy people after 2 COVID-19 vaccines.[10] The MELODY study aims to further improve the understanding of responses to COVID-19 vaccination in individuals who have had 3 doses of vaccine and have had a transplant or have disease treated with immunosuppressants.[11] In the PROVENT study, potential risk factors for poor vaccination response included being older than 60, obesity, being immunocompromised, having congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease or chronic liver disease.[12] 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]

Where COVID-19 infection occurs, NICE recommends the use of nirmatrelvir plus ritonavir, sotrovimab and tocilizumab as options for treating COVID 19 (TA878):

- Nirmatrelvir plus ritonavir is recommended in adults, only if they:
    - do not need supplemental oxygen for COVID 19 and
    - have an increased risk for progression to severe COVID 19, as defined in the independent advisory group report commissioned by the Department of Health and Social Care.

- Sotrovimab is recommended in adults and young people aged 12 years and over and weighing at least 40 kg, only if:
    - they do not need supplemental oxygen for COVID-19 and
    - they have an increased risk for progression to severe COVID-19, as defined in the independent advisory group report commissioned by the Department of Health and Social Care and
    - nirmatrelvir plus ritonavir is contraindicated or unsuitable.

- Tocilizumab is recommended, within its marketing authorisation, in adults who:
    - are having systemic corticosteroids and
    - need supplemental oxygen or mechanical ventilation.

The technology

AZD 3152 (brand name unknown) is administered as an intramuscular injection. AZD 3152 does not currently have a marketing authorisation in the UK for the preventing COVID-19. It has been studied in clinical trials in participants with conditions causing immune impairment compared with AZD 7442 (Evusheld, AstraZeneca).

Intervention(s)	AZD 3152
Population(s)	People who are not currently infected with SARS-CoV-2 with conditions causing immune impairment
Subgroups	If the evidence allows the following subgroups will be considered: • people with known failure of vaccination • people with anticipated failure of vaccination • people with anticipated sub-optimal vaccination response

	These subgroups align with those identified in the Pre-exposure prophylaxis (PrEP) report conducted by an independent UK government advisory group.[14]
Comparators	• no prophylaxis
Outcomes	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.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 (2023) NICE technology appraisal guidance 878. **Related technology appraisals in development:** Molnupiravir, remdesivir and tixagevimab plus cilgavimab for treating COVID-19. NICE technology appraisal guidance [ID6261] Publication date to be confirmed

	Nirmatrelvir plus ritonavir for treating COVID-19 (partial rapid review of TA878). NICE technology appraisal guidance [ID6262] Publication date to be confirmed Tixagevimab plus cilgavimab for preventing COVID-19. NICE technology appraisal guidance [ID6136] Publication expected June 2023 **Related NICE guidelines:** COVID-19 rapid guideline: managing COVID-19 (2021, updated 2023) NICE guideline NG191. Review date not stated COVID-19 rapid guideline: vaccine-induced immune thrombocytopenia and thrombosis (VITT) (2021, updated 2022) NICE guideline NG200. Review date not stated COVID-19 rapid guideline: managing the long-term effects of COVID-19 (2020, updated 2021) NICE guideline NG188. Review date not stated COVID-19 rapid guideline: vitamin D (2020, updated 2022) NICE guideline NG187. Review date not stated COVID-19 rapid guideline: haematopoietic stem cell transplantation (2020, updated 2022) NICE guideline NG164. Review date not stated COVID-19 rapid guideline: delivery of systemic anticancer treatments (2020, updated 2022) NICE guideline NG161. Review date not stated COVID 19 rapid evidence summary: anakinra for COVID-19 associated secondary haemophagocytic lymphohistiocytosis (2020) NICE evidence summary 26 COVID-19 rapid evidence summary: Long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) for people with or at risk of COVID-19 (2020) NICE evidence summary 25 COVID-19 rapid evidence summary: angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) in people with or at risk of COVID-19 (2020) NICE evidence summary 24 COVID-19 rapid evidence summary: acute use of non-steroidal anti-inflammatory drugs (NSAIDs) for people with or at risk of COVID-19 (2020) NICE evidence summary 23 **Related NICE diagnostics guidance in development:** Exploratory economic modelling of SARS-CoV-2 viral detection point of care tests and serology tests. NICE diagnostics guidance. Publication date to be confirmed
Related National Policy	Department of Health and Social Care (Nov 2022) Interim Clinical Commissioning Policy: Baricitinib for patients

	hospitalised due to COVID-19 (adults and children aged 2 years and over) Department of Health and Social Care (Nov 2022) Interim Clinical Commissioning Policy: IL-6 inhibitors (tocilizumab or sarilumab) for hospitalised patients with COVID-19 (adults) Department of Health and Social Care (Nov 2022) Interim Clinical Commissioning Policy: Remdesivir for patients hospitalised due to COVID-19 Department of Health and Social Care (Nov 2022) Interim Clinical Commissioning Policy: Treatments for hospital-onset COVID-19 Department of Health and Social Care (Nov 2022) Interim Clinical Commissioning Policy: Treatments for non-hospitalised patients with COVID-19 Department of Health and Social Care (Dec 2021) Withdrawal of the Recommendation for Consideration of Inhaled Budesonide as a Treatment Option for COVID-19 Department of Health and Social Care (Mar 2021) Convalescent Plasma in the Management of Hospitalised Patients with COVID-19 Department of Health and Social Care (Jan 2021) Antimicrobials (azithromycin and doxycycline) Not Beneficial in the Management of COVID-19 (SARS-CoV-2) Positive Patients Department of Health and Social Care (Sept 2020) Corticosteroids in the treatment of suspected or confirmed COVID-19 The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019)

Questions for consultation

Where do you consider AZD 3152 will fit into the existing care pathway for prevention of COVID-19?

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?

Are the subgroups listed appropriate? Are there any other relevant subgroups that should be considered?

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?

Would AZD 3152 be a candidate for managed access?

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?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which AZD 3152 will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Office for National Statistics (2023) Deaths involving coronavirus (COVID-19). Accessed May 2023.
2. UK Health Security Agency (2023) SARS-CoV-2 variants of concern and variants under investigation in England: technical briefing 52. Accessed May 2023.
3. Government Actuary's Department (2020) Mortality Insights from GAD - December 2020. Accessed May 2023.
4. The King's Fund (2021) Deaths from Covid-19 (coronavirus). Accessed May 2023.
5. Public Health England (2020) Deaths of people identified as having learning disabilities with COVID-19 in England in the spring of 2020. Accessed May 2023.
6. Department of Health and Social Care (2022) Guidance for people previously considered clinically extremely vulnerable from COVID-19. Accessed May 2023.
7. Rettie, H and Daniels, J, (2022) The Mental Health Impact of the COVID-19 Pandemic Second Wave on Shielders and their Family Members. International Journal of Environmental Research and Publich Health.

8. Cevik M, Kuppalli K, Kindrachuk J et al. (2020) Virology, transmission, and pathogenesis of SARS-CoV-2. The BMJ.

9. NHS (2022) Coronavirus (COVID-19) vaccine. Accessed May 2023.

10. National Institute for Health and Care Research (2021) OCTAVE trial: Initial data on vaccine responses in patients with impaired immune systems. Accessed May 2023

11. Imperial College London, Faculty of Medicine (2022) MELODY Study. Accessed May 2023.

12. Levin M, Ustianowski A, De Wit S et al. (2022) Intramuscular AZD7442 (Tixagevimab-Cilgavimab) for Prevention of Covid-19. The New England Journal of Medicine.

13. Department of Health and Social Care (2022) Defining the highest-risk clinical subgroups upon community infection with SARS-CoV2 when considering the use of neutralising monoclonal antibodies (nMABs) and antiviral drugs: independent advisory group report. Accessed May 2023.

14. Department of Health and Social Care (2022) Pre-exposure prophylaxis (PrEP) report. Accessed May 2023.