NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Tixagevimab–cilgavimab for preventing COVID-19

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of tixagevimab and cilgavimab within its marketing authorisation for the pre-exposure prophylaxis of 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 7 March 2020 and 1 July 2022, 180,642 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. 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.[2] 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.[3,4] 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.[5,6]

COVID-19 has a diverse range of clinical manifestations, ranging from mild infection to severe disease accompanied by high mortality.[7] 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 3 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.[8] 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.[9] 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.[10] 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.[11] An independent UK government advisory group has identified specific groups of people at highest risk of hospitalisation and death despite receiving COVID-19 vaccination.[12]

The technology

Tixagevimab and cilgavimab (Evusheld, AstraZeneca) are monoclonal antibodies used in combination. Tixagevimab and cilgavimab are administered as 2 separate, sequential intramuscular injections. Tixagevimab and cilgavimab in combination has a marketing authorisation in the UK for 'the pre-exposure prophylaxis of COVID-19 in adults who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2 and:

- Who are unlikely to mount an adequate immune response to COVID-19 vaccination or
- For whom COVID-19 vaccination is not recommended.'

Intervention	Tixagevimab and cilgavimab
Population	Adults who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to a person infected with SARS-CoV-2 and • who are unlikely to mount an adequate immune response to COVID-19 vaccination or • for whom COVID-19 vaccination is not recommended
Subgroups	If the evidence allows the following subgroups will be considered: • adults at highest-risk of adverse COVID-19 outcomes
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. The impact of vaccination status or SARS-CoV-2 seropositivity on the clinical evidence base of each intervention, generalisability to clinical practice and interaction with other risk factors will be considered in the context of the appraisal. The impact of different variants of concern of COVID-19 on the clinical evidence base of each intervention will be considered in the context of the appraisal.
Related NICE recommendations	**Related appraisals in development:** 'Therapeutics for people with COVID-19' NICE technology appraisal guidance [ID4038]. Publication date to be confirmed. **Related Guidelines:** 'COVID-19 rapid guideline: managing COVID-19' (2021). NICE guideline 191. 'COVID -19 rapid guideline: managing the long-term effects of COVID-19' (2022). NICE guideline 188.
Related National Policy	UK Health Security Agency (2022) COVID-19 vaccination programme NHS England (2022) UK Interim Clinical Commissioning Policy: Therapies for symptomatic non-hospitalised patients with COVID-19 NHS England (2022) UK Interim Clinical Commissioning Policy. Therapies for patients with symptomatic hospital-onset COVID-19

	NHS England (2022) Interim Clinical Commissioning Policy: Remdesivir for patients hospitalised due to COVID-19 (adults and adolescents 12 years and older) NHS England (2022) Interim Clinical Commissioning Policy: neutralising monoclonal antibodies or antivirals for non-hospitalised patients with COVID-19 NHS England (2022) Interim Clinical Commissioning Policy: Antivirals or neutralising monoclonal antibodies in the treatment of hospital-onset COVID-19 NHS England (2022) Interim Clinical Commissioning Policy: Antivirals or neutralising monoclonal antibodies in the treatment of COVID-19 in hospitalised patients NHS England (2021) Interim Clinical Commissioning Policy: IL-6 inhibitors (tocilizumab or sarilumab) for hospitalised patients with COVID-19 (adults) NHS England (2020) COVID-19 therapy: corticosteroids including dexamethasone and hydrocortisone NHS England (2020) Acute use of non-steroidal anti-inflammatory drugs (NSAIDs) in people with or at risk of COVID-19 NHS England (2021) Rapid Clinical Policy development: COVID-19 The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)

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10. Imperial College London, Faculty of Medicine (2022) MELODY Study. Accessed August 2022

11. 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.

12. 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 August 2022