

- Infrequent larger shifts of the virus: older versions of the virus may be incubating (for example, in people who are immunocompromised, for whom viral clearance may be slower) and mutate to have an advantage over currently circulating variants (for example, the large change that occurred with the Omicron wave).

The committee considered it most likely that new variants would be related to currently circulating variants unless there was a larger shift in the virus. It also considered the possibility that neutralising monoclonal antibodies which currently have low efficacy regain their efficacy against future variants. But it noted that the [World Health Organization therapeutics and COVID-19 living guideline](#) states that 'the likelihood of COVID-19 caused by former variants was extremely low'. So, it considered that the effectiveness of tixagevimab plus cilgavimab (from now, tix-cil) over the appropriate time period for this evaluation would be best indicated by neutralisation potential against currently dominant circulating variants and variants that are currently growing the fastest. The committee noted substantial uncertainty in estimating efficacy for future variants, given the current understanding of COVID-19 and the rapidly evolving virus. It understood from studies such as OpenSAFELY that, broadly, COVID-19 is waning in its severity. It understood that this was because immunity to SARS-CoV-2 has increased in the general population through vaccination and natural exposure, and because later variants of the virus have reduced in pathogenicity. This means that the risks are now very low for the general population and substantially reduced for most people eligible for tix-cil compared with earlier in the COVID-19 pandemic. But the committee noted that the risks have not reduced for some groups such as people who have had transplants.

Patient perspectives

Ongoing impact of COVID-19

- 3.3 The patient experts described the ongoing impact of COVID-19 on their lives and the lives of others with a high risk of severe SARS-CoV-2 infection. One patient expert described how modifying their behaviour was mentally and physically exhausting, needing extensive planning for simple tasks like shopping. They described how nothing had changed for

them since the start of the pandemic. In fact, they added, the situation had worsened for them because the rest of the country has returned to normal, meaning protective measures are no longer in place. They described how removing measures for limiting viral spread, such as mask wearing, working from home and social distancing, has placed all the responsibility for protection on individuals. They added that people who are immunocompromised need to navigate multiple environments that no longer have the COVID-19 mitigation measures that they value. Another patient expert described how they are only able to leave the house for routine medical appointments, and are on high alert to minimise the risk of infection whenever possible. Both patient experts also highlighted that the burden of responsibility extends to household family members, and affects work life and family relationships. People reported that their finances had been affected because of a lack of government support and increased costs of shielding. For people with children, there were concerns about the disruption of education on life chances and the long-lasting impact of this. They said that the availability of a preventative treatment that reduces infection risk could reduce the need for exhausting and isolating behavioural changes. The committee agreed that there is an urgent unmet need for a preventative therapy that would reduce the risk of SARS-CoV-2 infection for people at high risk of severe infection for whom vaccination is not suitable or does not provide sufficient protection.

Benefits of tix-cil

- 3.4 The patient experts discussed their experiences of having tix-cil. One described their relief after having it. They explained that, even after treatment with tix-cil, they continued to be careful and still maintained social distancing. They acknowledged that tix-cil may not stop all SARS-CoV-2 infections, and that returning to normal would be a gradual process as their confidence in the treatment increased. Another patient expert agreed and added that, since having tix-cil, they have met people face to face, but continue to wear a mask and avoid crowded spaces. They added that, even with tix-cil, and with treatments for severe SARS-CoV-2 infection now available, this is not enough for them to abandon all caution.