Peer review comments – Neutralising monoclonal antibodies in the community

Managing COVID-19 rapid guideline (NG191)

Peer review organisations

For a list of stakeholders invited to comment on COVID-19 guidance as part of the targeted peer review, please see the targeted peer review stakeholder list on the NICE website.

For this topic, the following stakeholder organisations were also invited to comment:

- Royal College of Pathologists

Overarching category	Guideline section	Theme of comments	Action taken
General comment	Recommendation	Several reviewers wrote in agreement with content of recommendation.	No action needed.
General comment	Recommendation and Evidence to Decision	3 reviewers suggested updating hyperlinks and other technical/grammatical issues.	Links to current NHS England policy were updated and all technical/grammatical errors were addressed.
General comment	Recommendation	Several reviewers suggested that further clarification of eligibility criteria in relation to symptom onset and disease status was needed.	The studies included in this evidence review included varying criteria on symptom onset (3 days, 5 days and 7 days). The current licensing for

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			sotrovimab recommends treatment within 5 days of symptom onset and for the combination of casirivimab and imdevimab within 7 days of symptom onset. There was no evidence or analyses on data to indicate who may benefit the most from treatment dependent on symptom onset timelines. Lastly, this recommendation addresses neutralising monoclonal antibodies as class agents. Due to this and the potential for differences of treatment timelines of other neutralising monoclonal antibodies we have not specified the onset of treatment. Furthermore, the treatment will be administered in line with current policy and licensing for the specific neutralising monoclonal antibody type.
General comment	Recommendation	1 reviewer suggested that treatment requirements for 12–17-year-olds are specified.	Some of the trials presented to the panel included 12–17-year-old participants, however, no further subgroup analyses were carried out for this age group. This was highlighted by the panel members as a possible equity issue, and they

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			have suggested that this population will remain a subgroup of interest in further research. At present, 12–17-year-olds are licensed to receive this treatment and all those under 18 years old being considered for treatment should be discussed as part of a multidisciplinary team with infectious disease expertise.
General comment	Recommendation, Evidence to Decision	3 reviewers noted that the impact of vaccination on antibody response, viral mechanism and high-risk populations in relation to treatment with neutralising monoclonal antibodies should be considered.	The impact of vaccination on antibody response is important to consider especially in relation to viral mechanism, high risk populations and treatments. At present, the evidence base is scarce, and further studies are needed to evaluate these effects and determine who is expected to benefit the most from treatment. Furthermore, research on viral mechanism and treatment kinetics is needed to elucidate antibody response. As such, we have amended our research question to include vaccinated and unvaccinated people as subgroups of interest.

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General comment	Evidence to decision – Benefits and harms	1 reviewer suggested the need for further clarification on vaccination status of included trial participants.	Some of the included trials were carried out at earlier stages of the pandemic, prior to vaccine availability and when earlier strains of SARS-CoV-2 were dominant. However, the recruitment dates for these trials also coincide with vaccine administration timelines in some countries (Mexico/Romania/USA). As vaccination status was not reported in the trials and no subgroup analyses were carried out, it was not possible to ascertain the possible effects of vaccination on neutralising monoclonal antibodies. We have clarified the statement in the evidence to decision section of the guideline to highlight this further.
General comment	Evidence to decision – Benefits and Harms	2 reviewers wrote in about evidence from new in vitro studies on neutralising monoclonal antibodies against emerging SARS-CoV-2 variants.	In vitro studies were not included in the review protocol eligibility criteria and therefore were not specifically searched for. The in vitro data presented to the expert panel was to provide context around the new Omicron variant but was not used to inform the

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			evidence review on the effectiveness of neutralising monoclonal antibodies against COVID-19. Further research into emerging variants is needed and we continuously monitor databases for any relevant data including real world evidence. Our panel also made a research recommendation looking at the effectiveness of neutralising monoclonal antibodies against different variants.
General comments	Evidence to decision – Certainty of the evidence	2 reviewers highlighted potential difficulties with interpreting adverse event outcomes reported in trials.	Adverse events reported in clinical trials include those that resulted from the disease itself and those in reaction to the treatment. The panel discussed this and agreed that due to the nature of reporting, these outcomes are varied, where the number of adverse events in the treatment arms was lower than the placebo arm. No action needed, as statement on adverse events included in certainty of the evidence section.

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General comments	Evidence to decision - Resources	1 reviewer detailed the need to report on whether cost-effectiveness evidence was identified for inclusion.	Cost-effectiveness was not included in the review question so therefore was not included in our searches for evidence.
General comments	Evidence to decision - Resources	1 reviewer suggested clarifying whether confirmatory PCR testing will be used to guide treatment with neutralising monoclonal antibodies (alongside a positive lateral flow test).	The current recommendation does not specify the need for a PCR test to be carried out prior to treatment and so the new UK government policy on PCR testing will not impact the recommendations.
General comments	Evidence to decision – Resources	1 reviewer noted that collecting evidence on COVID-19 Medicine Delivery Units (CMDUs) would be valuable to understanding the safety profiles of neutralising monoclonal antibodies, however, the administration of treatment through CMDUs may limit access to treatment.	The panel discussed the operational frameworks of CMDUs and acknowledged that there may be resource implications for delivery. These implications are discussed in the equity and accessibility headings of the evidence to the decision section. As such no further action is needed.