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Advancing the science and practice of pharmaceutical medicine for the benefit of the public

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FPM NICE Consultation on Remdesivir and tixagevimab plus cilgavimab for treating COVID-19 [ID6261]

Questions:

1. **Has all of the relevant evidence been taken into account?**

The committee has had several meetings at which data supporting the use of antiviral therapies for treating COVID- in hospitalised patients and the community were discussed. The current guideline focuses only on remdesivir and the monoclonal antibody combination of tixagevimab and cilgavimab. The contribution of the antiviral effectiveness of these agents to both clinical effect and, thence, cost-effectiveness is not addressed. The monoclonal antibody combination of tixagevimab and cilgavimab failed to neutralise earlier omicron variants effectively. If this remains the situation, it would not be considered clinically effective. Remdesivir remains effective against circulating variants both in vitro and clinically as shown in the Gilead evidence (Mozaffari et al).
Clinical effectiveness in hospitalised patients in earlier studies was limited to patients treated within ten days of first symptom onset or those in whom immunocompromise was associated with ongoing viral replication. The committee should consider the evidence presented by Gilead in more detail, such as (Beckerman et al) concerning the timing of the use of relative to ongoing viral replication (which can be diagnosed using PCR with cycle times < 25 indicating replication virus or positive lateral flow test) as remdesivir may not be effective in hospitalised patients in whom viral replication has ceased.

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2. **Are the summaries of clinical and cost-effectiveness reasonable interpretations of the evidence?**

The discussion focuses primarily on the cost-effectiveness of remdesivir in hospitalised patients. As noted previously (in response to question 1), the mechanism of remdesivir in treating COVID has not been considered. Additional evidence concerning the timing of use relative to the first onset of symptoms or evidence of ongoing viral replication could be considered. The CE modelling should differentiate vaccinated and non-vaccinated populations (with individuals who had their last vaccination more than six months ago, classified as non-vaccinated. (1. https://link.springer.com/article/10.1007/s10238-023-01036-x, 2. https://www.sciencedirect.com/science/article/pii/S0163445322002006)

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3. **Are the recommendations sound and a suitable basis for guidance to the NHS?**

The committee has continued to ignore the impact of respiratory virus outbreaks in the community and the need for anti-viral treatments to prevent the repercussions and effects on the functioning of the NHS hospitals. Existing guidance is provided for antiviral treatment of influenza, which permits the community use of antiviral therapy. However, COVID-19 treatment guidance in the community needs to be improved. (https://assets.publishing.service.gov.uk/media/62209cd38fa8f549097b87ec/ukhsa-guidance-antivirals-influenza-11v4.pdf).

At this point, COVID has become an endemic disease for which the risk populations overlap with those affected by influenza. While it was reasonable in the early phase of the pandemic, when antiviral therapy was in short supply, to limit the use of such treatments to those at the very highest risk of death from COVID-19, it is no longer reasonable to continue this restriction, instead to consider how best to deploy treatment to reduce hospitalisations and other covid complications, e.g. myocardial infarction and stroke, the incidence of which is increased in patients that have recovered from covid managed within the community (Knight R et al. Association of COVID-19 With Major Arterial and Venous Thrombotic Diseases: A Population-Wide Cohort Study of 48 Million Adults in England and Wales. Circulation. 2022;146: 892-906).

It is also worth considering that parts of the population have been ineligible for COVID-19 vaccination for over two years. Whilst they likely retain some protection from previous vaccination, they may not be adequately protected against current circulating variants, which is likely to contribute to more moderate to severe symptoms, ongoing transmission, and new variant generation. Effective vaccination and treatments for those infected in the community are imperative to prevent this. Clinical experts said hospitalisation and mortality rates are becoming less relevant clinical efficacy measures for COVID-19 treatments. Evidence of the other impacts on QALYs should be considered. The committee should consider the evidence on creating resistant strains and the implications for drug use. It should also look at the volume of distribution data for the drug and ensure that there are no patient types/groups that would be at increased risk of developing a resistant strain. The same is true for the monoclonal antibodies. (1. https://www.cell.com/cell-reports-medicine/pdf/S2666-3791(22)00284-1.pdf, 2. https://pubmed.ncbi.nlm.nih.gov/35482820/, 3. https://academic.oup.com/cid/article/76/2/342/6717535, 4. https://pubmed.ncbi.nlm.nih.gov/35878684/, 5.https://academic.oup.com/jid/article/228/8/1055/7191107, 6. https://www.journalofinfection.com/article/S0163-4453(22)00422-4/fulltext).

Vaccines and anti-virals should be available for private purchase outside the current NHS criteria eligibility, considering NHS criteria for eligible vaccinations and anti-virals have been

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significantly restricted to narrow populations since Autumn 2023. This would further support reducing the impact on the NHS hospitals.

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4. **Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?**

There is a broader population who should be eligible for vaccines and anti-viral use in the community beyond the current criteria of at-risk populations of cancer and immunosuppressed patients. Chronic medical conditions, e.g. ischaemic heart disease, chronic respiratory disease, chronic renal and liver disease, diabetes, and healthy elderly, etc, should be included within the at-risk group. These chronic conditions are associated with an altered immune state and, whilst not the same as an immunocompromised patient, are less effective than an individual of a similar age, gender and ethnicity without the condition(s). The absence of these populations from this guidance to the NHS is discriminatory.