# NHS Wales National Antiviral Service Clinical Group Treatment Options Evidence Review

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## Document Control

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# 1. Introduction

The National Antiviral Service (NAVS) is hosted within the Welsh Medicines Advice Service of Cardiff and Vale University Health Board (CAVUHB) and is commissioned by Welsh Government, to provide antiviral treatment or referral for antibody treatment for extremely high-risk individuals with COVID-19 symptoms in the community. More information about NAVS and eligibility can be found on at this link National Antiviral Service (NAVS) - Healthcare Professionals site - Welsh Medicines Information Centre (wales.nhs.uk)

The evidence base for COVID-19 treatments is evolving and emerging variants, (such as omicron) and subvariants are changing the role of treatment. It requires regular assessment dependent upon not only the evidence, but also on likely circulating variants.

# 2. Background

In April 2022, the Federal Drug Administration (FDA) in the United States recommended against using Xevudy® (sotrovimab) to treat COVID-19. In September 2022, the World Health Organisation (WHO), via an update to the Living guideline on drugs for COVID-19, strongly advised against the use of sotrovimab for the treatment of COVID-19. Following this statement, in Wales, an evidence review has been completed.

# 3. Evidence review - Results

Following a literature review, a number of studies were identified, demonstrating the efficacy of sotrovimab remains uncertain. Many studies evaluated clinical trials concerning the in vitro neutralisation data of sotrovimab and showed reduced neutralisation activity of sotrovimab against currently circulating variants and subvariants. It is not clear whether, the in vitro neutralisation activity translates to clinical effectiveness and there are few trials to validate this.

Radcliffe *et al* (2022) studied the real-world effectiveness of monoclonal antibodies and oral antiviral agents in solid organ transplant recipients (SOTR) with COVID-19. Rates of hospitalization within 30 days of initiating therapy for Lagevrio® (molnupiravir), Paxlovid® (nirmatrelvir/ritonavir), and sotrovimab were 16% (8/49), 0% (0/1), and 8% (2/24), respectively, compared to 27% (13/48) in patients without outpatient

Neutralising monoclonal antibodies may still be an option for many high-risk patients (Wu *et al* 2022). A recent study only available in pre-print (Zeng *et al*) compared the effectiveness of sotrovimab (a neutralising monoclonal antibody) or molnupiravir (an antiviral) in preventing severe COVID-19 outcomes in non-hospitalised high-risk COVID-19 adult patients. Within 28 days after treatment initiation, 87 (1.4%) COVID-19 related hospitalisations/deaths were lower in those treated with sotrovimab compared with molnupiravir, 32 were treated with sotrovimab and 55 with molnupiravir.

A preliminary analysis of the PANORAMIC study reported 0.8% primary outcome (hospitalisation or death) in both the molnupiravir and usual care groups of vaccinated, high-risk, adults treated in the community. A reduction in recovery time, nine days compared to 15 days, and a reduction in viral load were observed in the molnupiravir arm compared to usual care.

There are still many areas of uncertainty including, the effect of the vaccination programme in high risk cohorts, the effect of variants on virulence and the effects of previous exposures.

## 4. Evidence Review - Recommendations

The clinical review group recommend that the COVID-19 treatment pathway should continue to offer sotrovimab at this current time, especially for SOTR or pregnant patients, until further information becomes available. It is advised that the number of patients receiving Paxlovid® as first choice should be maximised.

The clinical group will develop a visual decision aid and will offer regular training sessions for those involved in COVID-19 triage to increase confidence in the safe use of this medicine.

If Paxlovid® is not suitable despite this, remdesivir should be considered. The group acknowledges the practical difficulties with the administration of remdesivir in the out-patient setting as the schedule requires three doses on three consecutive days

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| **1st line** | Paxlovid® |
| **2nd line** | Remdesevir* |
| **3rd line** | Sotrovimab |
| **4th line** | Molnupiravir |
| * It is appreciated that the practical considerations for the administration of remdesivir renders it unsuitable for community deployment in most cases. | |

## 5. References


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