COVID neutralising monoclonal antibodies (nMABs) and oral antivirals supply via COVID Medicine Delivery Units (CMDUs)

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Neutralising monoclonal antibody

Casirivimab + imdevimab (Ronapreve)

- Interim clinical commissioning policy for the treatment of COVID-19 in hospitalised patients over 12 years and over 40kg: CAS-ViewAlert (mhra.gov.uk)
- RECOVERY trial findings that casirivimab and imdevimab reduced the relative risk of mortality by 20% (24% in the treatment group vs 30% in those who received standard care alone) in hospitalised patients with COVID-19 who had not mounted an antibody response of their own to the virus (were seronegative) at the time of treatment.

1) Patients hospitalised for acute COVID-19 illness: to be treated at the off-label dose of 2.4g
   - Positive PCR test or MDT diagnosis
   - Hospitalised specifically for the management of COVID-19
   - Negative for baseline serum anti-spike (anti-S) antibodies

2) Patients with hospital-onset COVID-19: to be treated at a dose of 1.2g, in line with the conditional marketing authorisation
   - Positive PCR or MDT diagnosis
   - Hospitalised for indications other than for the management of COVID-19
   - At high risk of progression to severe COVID-19 or COVID-19 infection presents a material risk of destabilising a pre-existing condition or illness or compromising recovery from surgery or other hospital procedure
   - A baseline serum antibody test (anti-S) has been taken prior to treatment

Administration

- IV infusion over 30 minutes or SC injection at multiple injection sites
- Preparation and administration of casirivimab and imdevimab should be initiated and monitored by a qualified healthcare provider using aseptic technique.
- Infusion-related reactions (IRRs) include nausea, chills, dizziness (or syncope), rash, urticaria and flushing. IRRs may present as severe or life-threatening events and may include other signs and symptoms, requiring interrupting, slowing or stopping the infusion and administering appropriate medications and/or supportive care.
- Post-infusion observation period required – approx. 1 hour

Current challenge

- Standing up services for non-hospitalised patients to receive nMABs/antivirals through COVID Medicines Delivery Units (CMDUs) by 13th December.

Oral antivirals

Molnupiravir (Lagevrio)

- Granted a Conditional Marketing Authorisation by the MHRA: Summary of Product Characteristics for Lagevrio - GOV.UK (www.gov.uk)

- Indicated for treatment of mild to moderate COVID-19 in adults with a positive SARS-COV-2 diagnostic test and have at least one risk factor for developing severe illness
- Should be administered asap after diagnosis and within 5 days of symptom onset
- Pro-drug – metabolised to N-hydroxycytidine which eventually leads inhibition of viral replication
- Phase 3 MOVe-OUT placebo controlled RCT:
  - 775 non – hospitalised patients (unvaccinated) with mild to moderate disease who were at risk of progressing to severe disease
  - Hospitalisation reduced from 13.8% to 7.3%
  - Death reduced from 2.1% to 0%

- No dose adjustment necessary in renal or hepatic impairment, or age.
- No drug interactions identified – based on limited data.
- Side effects relatively mild - common: dizziness, headache, diarrhoea, nausea
- Dose 800mg bd for 5 days (200mg capsules: 21.7mm x 7.6mm)
- Not recommended for use during pregnancy or breast feeding. Pregnancy registry under development. Women of child bearing age: effective contraception during the course and 4 days after

Oral antiviral deployment

December 2021

National Study

- From December 2021, some NHS patients will get access through a national study aimed at collecting effectiveness data in vaccinated patients.
- Molnupiravir will be the first antiviral to enter the national study and inclusion of other antivirals will be based on MHRA approval.

Limited Deployment

- From December 2021, patients who are deemed to be at highest risk, that meet the eligibility criteria and are not already receiving antivirals though the study, may have access.

Spring 2022

Wider Deployment

- From early 2022, depending on the outcome of the initial a wider group of patients that meet the eligibility criteria, will have the opportunity to access antivirals – be that in hospitals or in the community.
- Considering options for access for antivirals, including:
  - GP Practice teams
  - NHS 111
  - An online pathway (TBC)
- Expecting second oral antiviral to enter the study depending on MHRA assessment.

From 2023 onwards

Routine use

- Wider availability of antiviral medicines will be dependent a number of factors, including:
  - Clinical trial data
  - Availability of supply
  - Cost of new treatment
- During 2022/23, NHSE&I will be working with DHSC to agree the approach to wider roll out in primary and community settings.

PANORAMIC study - News: NIHR funds community COVID-19 antiviral trial | NIHR

- Recruitment through 1) CRN GP hubs with spoke practices, and 2) central recruitment route.
- Symptoms attributable to COVID-19 started within the past 5 days and ongoing
- A positive PCR SARS-CoV-2 test
- Aged ≥50 years OR aged 18-49 years with one of the following known underlying chronic health condition considered to make them clinically vulnerable:
  - chronic respiratory, heart, vascular, kidney, liver, neurological disease
  - severe and profound learning disability
  - Down's syndrome
  - Diabetes mellitus (Type or Type II)
  - immunosuppression: primary or secondary
  - solid organ, bone marrow and stem cell transplant recipients
  - morbid obesity (BMI >35)
  - severe mental illness
  - care home resident
  - judged by recruiting clinician or research nurse (registered medical practitioner or trained study nurse) to be clinically vulnerable
- Molnupirivir vs. standard care
- Expected to start 6th Dec

Deployment of molnupiravir for high risk cohort - CMDUs

- High risk cohort will have access to oral antivirals outside of the PANORAMIC study
- Same/similar cohort as those eligible for non-hospitalised nMAB treatment (15-43 patients per week in South East ICSs)
- Deployment will be through the CMDUs - nMAB and antiviral treatments within the same pathway
- Clinical commissioning policy for high risk non-hospitalised patients expected imminently, covering both nMABs and oral antivirals
- Referral: Eligible patients will be pre-identified nationally. Local CMDUs will be notified when one of the pre-identified patients has a positive PCR test.
- ICSs should have one or more CMDU services ready from 13th Dec to:
  - Contact eligible patients within 24 hours when notified of a positive PCR test
  - Clinically assess patients (face to face or remote) for suitability for nMAB or antiviral and prescribe appropriate treatment
  - Blueteq forms to be completed for both drugs
  - Prepare and administer IV nMAB infusion to eligible patients at a suitable facility
  - Arrange supply of oral antivirals from an NHS provider pharmacy to eligible patients within 5 days of symptom onset
  - Have appropriate clinical support/follow up arrangements for patients treated
  - Incorporate Health and Justice patients will receive treatment via this model

Numbers of patients expected to qualify for treatment

ICS	Estimated Weekly Activity
HIOW (Hampshire & IOW) ICS	43
Frimley Health and Care	15
Buckinghamshire, Oxfordshire and Berkshire West	36
Surrey Heartlands Health and Care Partnership	22
Sussex Health and Care Partnership	42
Kent and Medway ICS	42

Questions