COVID-19 Therapeutic Alert

CEM/CMO/2020/028(U) 03 September 2020

This alert replaces CEM/CMO/2020/028 which was issued on 03 July.
The alert has been updated to reflect the publication of revised World Health Organisation (WHO) guidance on the use of corticosteroids in the treatment of COVID-19 (see page 2).

Publication of an interim clinical commissioning policy: Remdesivir for patients hospitalised with COVID-19 (adults and children aged 12 years and older).

Summary

Following confirmation of a Conditional Marketing Authorisation (CMA) by the European Medicines Agency (EMA) for the use of remdesivir in the treatment of COVID-19, the scientific opinion given for remdesivir via the Early Access to Medicines Scheme (EAMS) put in place on 26th May 2020 has now lapsed.

From 3 July 2020, an interim clinical commissioning policy has been put in place to define routine access to remdesivir in the treatment of COVID-19 across the UK. The policy reflects the conditions of the CMA, but also includes secondary criteria to be used should there be limitations in the supply of remdesivir in the UK.

Medicine supply

Remdesivir is supplied to the UK by Gilead. The medicine comes in two forms:

- Remdesivir 100 mg concentrate for solution for infusion (each vial contains 100 mg of remdesivir, each mL of concentrate contains 5 mg of remdesivir).
- Remdesivir 100 mg powder for concentrate for solution for infusion (each vial contains 100 mg of remdesivir, after reconstitution, each vial contains 5 mg/mL of remdesivir solution).

The Medicines and Healthcare products Regulatory products Agency (MHRA) has confirmed that existing UK stocks remaining from either the SIMPLE research studies or the EAMS programme can be utilised.

Access criteria

The interim clinical commissioning policy aims to identify those patients most likely to benefit from remdesivir i.e. those patients at the early stage of a COVID-19 infection who have a high probability of developing severe disease putting their lives at risk. Additional ‘secondary’ criteria have been included in the policy to guide clinicians and are only applicable should demand for remdesivir exceed supply.

Eligibility criteria

Patients will be eligible for treatment with remdesivir in accordance with the product licence. Eligibility criteria within the Remdesivir Summary of Product Characteristics (SmPC) include:

- Hospitalised with coronavirus disease 2019 (COVID-19)
- With pneumonia requiring supplemental oxygen
- Adults, and adolescents ≥ 12 years of age and ≥ 40 kg
- eGFR ≥ 30ml/min
- Alanine Aminotransferase (ALT) below 5 times the upper limit of normal at baseline

Additional criteria
In times of limited supply, additional criteria will be necessary in order to allocate remdesivir to those with the greatest capacity to benefit (patients in the earlier stages of respiratory failure). In this context the following criteria must also be met:

- At the time of decision to treat with remdesivir patients should not be receiving ongoing mechanical ventilation or ECMO. Patients who present with an initial rapid deterioration can, however, be considered for treatment with remdesivir.
- Multi-disciplinary team assessment should determine if patients not suitable for escalation would benefit from initiation of treatment with remdesivir.
- If patients on remdesivir require escalation, continuation of the drug should be considered by multi-disciplinary team assessment.

Pregnancy
Remdesivir should be avoided in pregnancy unless clinicians believe the benefits of treatment outweigh the risks to the individual (please see SmPC for further information).

Please see the full interim clinical commissioning policy for further details, including stopping criteria.

Co-administration

Corticosteroids
Administration of systemic dexamethasone or hydrocortisone is recommended in the management of patients with severe or critical COVID-19[1]. Corticosteroids are not suggested in non severe COVID-19 disease. Updated WHO guidance on the use of systemic corticosteroids in the management of COVID-19 is now available.

There is no interaction of remdesivir with either dexamethasone or hydrocortisone expected. For further information please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker) and see the SmPCs for remdesivir:

- concentrate for solution for infusion: https://www.medicines.org.uk/emc/product/11596/smpc
- powder for concentrate for solution for infusion: https://www.medicines.org.uk/emc/product/11597/smpc

Further information is available in this alert issued via the Central Alerting System on 03 September.

Hydroxychloroquine
Coadministration of remdesivir and chloroquine phosphate or hydroxychloroquine sulphate is not recommended based on in vitro data demonstrating an antagonistic effect of chloroquine on the intracellular metabolic activation and antiviral activity of remdesivir.

Data collection

Safety reporting

- Adverse Events (AEs), Serious Adverse Events (SAEs) and Special Situation reports (SSRs) (including pregnancies) should be submitted to Gilead Pharmacovigilance & Epidemiology (PVE): Email: Safety_FC@gilead.com; Tel.: 01223 897 500
- Any suspected adverse drug reactions (ADRs) for patients receiving remdesivir can also be reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/

Clinical Outcome reporting

Continued reporting via the ISARIC 4C Clinical Characterisation Protocol (CCP) case report forms (CRFs), as coordinated by the COVID-19 Clinical Information Network (CO-CIN), is encouraged to support ongoing implementation and evaluation (link to forms).

Implementation

In England, access to remdesivir under the interim clinical commissioning policy remains subject to Blueteq registration. Access in Scotland, Northern Ireland and Wales is subject to any further country specific guidance. Mutual aid arrangements should be used in the case of limited supply.

Action

Clinical Teams should:

- share with colleagues the licencing and associated clinical commissioning policy arrangements
- identify patients who may meet the access criteria;
- continue to complete the data entry requirements of those who have initiated treatment, where possible, to support ongoing implementation and evaluation.

Chief Pharmacists / Pharmacy Procurement Leads (Regional Chief Pharmacists and Regional Pharmacy Procurement Leads in England) should:

- retain an oversight of stock levels across the region, including repurposed stock;
- support mutual aid arrangements, if needed

Trust / Hospital Pharmacy Leads should:

- manage the transition to ordering commercial stock, noting MHRA approval to repurpose study and EAMS stock

Deadlines for actions

- Actions underway: on receipt of this alert.
- Actions complete: as soon as possible.

Supporting Information

More detailed information on the the use of remdesivir with COVID-19 infection can be found at the following locations:

New England Journal Medicine https://www.nejm.org/doi/full/10.1056/NEJMoa2007764

Requests for further information on remdesivir supply can be submitted to UKICOVID-19@gilead.com

The ISARIC 4C (Coronavirus Clinical Characterisation Consortium) can be found at: https://isaric4c.net/

Distribution

NHS Trusts (NHS boards in Scotland and Wales)
Regional Medical Directors
Regional Chief Pharmacists
Lead/senior pharmacists
Trust/Hospital Medical Directors to circulate to medical and nursing staff managing COVID-19 patients.

Enquiries

England
Enquiries from NHS trusts in England should in the first instance be directed to your trust pharmacy team who will escalate issues to the Regional Chief Pharmacist and national teams if required. Further information can be requested from the dedicated email address: england.spoc-c19therapeutics@nhs.net.

Northern Ireland
Enquiries from hospitals in Northern Ireland should in the first instance be directed to your hospital pharmacy team.

Scotland
Enquiries from hospitals in Scotland should in the first instance be directed to your hospital pharmacy team who will escalate issues to the Scottish Government's Medicines Policy Team if required. Contact should be made using the email address - CPO-COVID19@gov.scot.

Wales
Enquiries from hospitals in Wales should in the first instance be directed to the health board's Chief Pharmacist who will escalate issues to the Pharmacy and Prescribing Team at Welsh Government if required. Enquiries to the Welsh Government should be directed to: COVID-19.Pharmacy.Prescribing@gov.wales.

[1]Within the WHO guidance, severe COVID-19 is defined as:

- oxygen saturation < 90% on room air.
- respiratory rate > 30 breaths per minute in adults and children > 5 years old; ≥ 60 in children less than 2 months; ≥ 50 in children 2–11 months; and ≥ 40 in children 1–5 years old.
- signs of severe respiratory distress (i.e. accessory muscle use, inability to complete full sentences; and in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs).

Critical COVID-19 is defined by the criteria for acute respiratory distress syndrome (ARDS), sepsis, septic shock or other conditions that would normally require the provision of life-sustaining therapies, such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy.