COVID-19 Therapeutic Alert

CEM/CMO/2021/013 14 June 2021

This guidance updates and replaces the COVID-19 Therapeutic Alert CEM/CMO/2020/035 which was issued on 06 November 2020

Remdesivir for patients hospitalised with COVID-19 (adults and children aged 12 years and older)

Summary

Remdesivir has been available to UK clinicians treating hospitalised patients with COVID-19 since May 2020.

The UK interim clinical commissioning policy has been updated to allow an extended treatment duration and other exemptions for immunocompromised patients, clarify when a further treatment course might be given following readmission, and reflect exceptions in the eligibility criteria for patients with end-stage renal disease on haemodialysis.

Action

NHS acute trusts / health boards are asked to take the following immediate steps to support treatment of admitted patients with COVID-19:

1. Cascade the updated UK interim clinical commissioning policy to relevant clinical teams

2. Ensure that only patients with COVID-19 pneumonia are treated with remdesivir. In the absence of a confirmed virological diagnosis, remdesivir should only be used when a multidisciplinary team has a high level of confidence that the clinical and radiological features suggest that COVID-19 is the most likely diagnosis.

3. Ensure that clinicians prescribe a **maximum treatment course of 5 days** (this may be extended to a maximum of 10 days in significantly immunocompromised patients).

4. Ensure the full criteria as described in the remdesivir interim clinical commissioning policy are being applied by treating clinicians (please see section below).

5. Continue to adhere to the existing ordering, supply and reporting arrangements for remdesivir (including pre-authorisation through Blueteq™ in England).

Clinical Criteria

Clinicians are asked to prescribe within the scope of the product licence:

- Hospitalised with coronavirus disease 2019[1] (COVID-19)
- With pneumonia requiring low-flow oxygen (oxygen delivered by a simple face mask or nasal cannula at a flow rate usually up to 15 litres/minute).
- Adults, and adolescents 12 years and older who weigh 40kg and over
- Estimated glomerular filtration rate (eGFR) at least 30ml/minute
- Alanine aminotransferase (ALT) below 5 times the upper limit of normal at baseline.

Exemptions

- Patients with end-stage renal disease on haemodialysis are exempt from the eGFR treatment threshold above
- See later section on 'Immunocompromised patients' for exemptions in this cohort

Initiation of treatment

- The decision to initiate treatment with remdesivir should be made by the admitting care consultant[2].
- Remdesivir should not be initiated in patients who present to hospital more than 10 days after symptom onset (see later section on 'Immunocompromised patients' for how this criterion applies to this group).

Duration

- Patients should receive a maximum of 5 days of remdesivir in total (comprising a loading dose plus 4 further days of maintenance doses).
- Patients re-admitted with COVID-19 (and meeting the eligibility criteria above, with the exception of the requirement on the timing from symptom onset) are permitted a second course of up to 5 days upon readmission.
- Significantly immunocompromised patients (see below) are eligible for an extended course of remdesivir (up to 10 days), if agreed following multidisciplinary team assessment.

Dose

The recommended dosage is a single loading dose of remdesivir 200 mg intravenously on day 1, followed by a once daily maintenance dose of remdesivir 100 mg for the remainder of the treatment course, which should not exceed five days (see exemption in immunocompromised patients below).

Immunocompromised patients

For significantly immunocompromised patients[3]:

- A course of remdesivir can be extended to 10 days
- The criterion on time between symptom onset and treatment initiation does not apply
- The criterion on the need for supplemental oxygen requirement does not apply

[1] In the absence of a confirmed virological diagnosis, remdesivir should only be used when a multidisciplinary team have a high level of confidence that the clinical and radiological features suggest that COVID-19 is the most likely diagnosis.

[2] The decision to treat with remdesivir is not an emergency and should be made judiciously after assessment and in a timely manner.

[3] Patients with a significant impairment of humoral immune response (antibody production) and/or cellular immune competence.

Stopping criteria

Remdesivir should be discontinued in patients who develop **any** of the following:

- ALT ≥ 5 times the upper limit of normal during treatment with remdesivir (remdesivir may be restarted when ALT is < 5 times the upper limit of normal)
- ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR)
- eGFR <30 mL/min (except in patients with end-stage renal disease on haemodialysis)

Please see the published interim clinical commissioning policy for further details, including initiation of treatment, risk assessment, reassessment and consideration in pregnancy. The published clinical access criteria may be further refined on the basis of expert clinical advice, as required.

Product Details

Remdesivir is supplied to the UK by Gilead. The medicine is now only available in the powder form:

- 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 summaries of product characteristics (SmPCs) for remdesivir can be found here:

- 100mg powder for concentrate for solution for infusion (Great Britain): https://www.medicines.org.uk/emc/product/11597/smpc

- 100mg powder for concentrate for solution for infusion (Northern Ireland): https://www.medicines.org.uk/emc/product/12115/smpc

Co-Administration

Corticosteroids

Administration of systemic dexamethasone or hydrocortisone is recommended in the management of patients with severe or critical COVID-19[4]. 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 can be found here.

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).

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[4] 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

Distribution

NHS Trusts (NHS boards in Scotland and Wales)

Regional Medical Directors
Regional Chief Pharmacists
Lead/Senior Pharmacists and Regional Procurement Pharmacy Leads
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 who will escalate issues to the Regional Pharmaceutical Procurement Service or Pharmaceutical Directorate at the Department of Health if required. Further information can be obtained by contacting RPHPS.Admin@northertrust.hscni.net

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 following emails: nss.nhssmedicineshortages@nhs.scot or medicines.policy@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.