Department of Health & Social Care

NHS

COVID-19 Therapeutic Alert

CEM/CMO/2020/035 06 November 2020

The introduction of this guidance supersedes the Supply Disruption Alert SDA/2020/013 which was issued on 29 September 2020

Publication of a revised 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), the use of remdesivir in the treatment of COVID-19 has been supported in the UK by an Early Access to Medicines Scheme (EAMS), implemented from 26th May 2020, and subsequently by an interim clinical commissioning policy, which has been in place since 3 July.

The interim clinical commissioning policy has now been updated to reflect the more positive position on remdesivir supply into the UK (via the European Union Joint Procurement Agreement arrangements) and to reflect the latest available evidence, including the results of the World Health Organization's (WHO's) Solidarity trial.

Action

NHS acute trusts / health boards are asked to take the following immediate steps to support treatment of admitted patients with COVID-19 in line with the updated interim clinical commissioning policy:

1. Ensure only patients with COVID infection 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.

2. Ensure that clinicians prescribe a **maximum treatment course of 5 days**.

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

4. Ensure purchase orders are in place to support the delivery of remdesivir to hospital sites under the new European Union Joint Procurement Agreement arrangements.

5. Provide regular updates on the stock position to trust / hospital and regional procurement pharmacy lead / chief pharmacists.

6. Only order stock where the regional procurement pharmacy lead has advised that there is a confirmed allocation. Please note that a percentage of UK stocks will be held centrally to support allocation to areas of greatest need, using the principles of mutual aid. This will cover the UK, Crown Dependencies and Overseas Territories.

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 supplemental oxygen
- 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.

In addition, the following eligibility criteria, developed on the basis of expert clinical consensus, apply:

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.

Risk assessment

- Clinical judgement around treatment with remdesivir can be informed by a risk score. Those with a low 4C Mortality Score[3] (0 to 3) are highly likely to recover without treatment with remdesivir.
- Remdesivir should not be initiated in patients who present to hospital and are unlikely to survive (determined by clinical judgement). The 4C Mortality Score might be helpful in this assessment.

Duration

- All patients should receive a maximum of 5 days of remdesivir in total (comprising a loading dose plus 4 further days of maintenance doses).

Reassessment and review

The use of remdesivir should be reassessed daily. Consider stopping remdesivir if:

- The patient clinically improves and no longer requires supplemental oxygen 72 hours after commencement of treatment; or
- The patient continues to deteriorate despite 48 hours of sustained mechanical ventilation.

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[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] The 4C Mortality Score (available at https://isaric4c.net/risk/) is a validated risk stratification score, which can help inform clinical decision making for patients admitted to hospital with COVID-19 (Knight et al. 2020). Other clinical risk scores are available.

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

Please see the published interim clinical commissioning policy for further details, including consideration in pregnancy and stopping criteria. 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 comes in two forms (please note that supply in the UK is now predominantly 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).
- Remdesivir 100 mg concentrate for solution for infusion (each vial contains 100 mg of remdesivir, each mL of concentrate contains 5 mg of remdesivir).

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

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

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.

Background

Remdesivir supply has improved significantly with provision into the UK under the European Union Joint Procurement Agreement arrangements. This provides a good level of confidence in the forward supply of remdesivir into the UK over forthcoming months.

The revised interim clinical commissioning policy has been updated on the basis of the latest available clinical evidence, including the results of the WHO Solidarity trial (WHO Solidarity Trial Consortium, 2020), and consensus expert clinical opinion.

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.

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.

[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.