Remdesivir for patients hospitalised due to COVID-19

Remdesivir is an intravenous antiviral, which is an adenosine nucleotide prodrug that is metabolised intracellularly to form the pharmacologically active substrate remdesivir triphosphate which inhibits SARS-CoV-2 RNA polymerase, which perturbs viral replication.

Remdesivir has a marketing authorisations for the following indications:

- treatment of COVID-19 in adults and paediatric patients (at least 4 weeks of age and weighing at least 3kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen or other non-invasive ventilation at start of treatment), for a treatment duration of 5-10 days.
- treatment of COVID-19 in adults and paediatric patients (weighing at least 40kg) who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19 within 7 days of symptom onset, for a treatment duration of 3 days.

The Scottish Medicines Consortium (SMC) collaborated with National Institute for Health and Care Excellence (NICE) on the Multiple Technology Appraisals (MTA) 878, which includes positive treatment recommendations for the following licensed COVID-19 treatments relevant to this guideline; nirmatrelvir plus ritonavir (Paxlovid®) and sotrovimab (Xevudy®). The recommendations are also applicable to NHS Scotland.

Final MTA treatment recommendations for molnupiravir (Lagevrio®) and remdesivir (Veklury®) are unlikely to be available until later in 2023 as they are subject to appeal. In the meantime, NICE's COVID-19 rapid guideline covers the use of these medicines.

This policy covers the use of remdesivir for patients hospitalised **due to** symptoms of COVID-19 and to be treated with a 5 day course of remdesivir.

Separate prescribing policies are available which cover the use of remdesivir in patients with hospital-onset COVID-19 and non-hospitalised patients with COVID-19.

1. Allowed Prescribers

Remdesivir for use in patients hospitalised due to symptoms of COVID-19:

- must only be initiated by a consultant
- must be prescribed under the direction of a consultant on the Hospital Electronic Prescribing & Medicine Administration system
- must be prescribed on an Infusion Therapy Recording Chart

2. Patient section

2.1 Eligibility criteria

Remdesivir is indicated as a treatment option for adult and paediatric patients (at least 4 weeks of age and weighing at least 3kg) hospitalised) due to symptoms of COVID-19 who meet the following eligibility criteria:

- SARS-CoV-2 infection is confirmed by polymerase chain reaction (PCR) test or where a multidisciplinary team (MDT) has a high level of confidence that the clinical and/or radiological features suggest that COVID-19 is the most likely diagnosis

AND

- Hospitalised specifically for the management of COVID-19 symptoms

AND

- Requiring low-flow supplemental oxygen *(defined by NICE as oxygen delivered by a simple face mask or nasal cannula at a flow rate usually up to 15 litres/ minute)* (see exemption in immunocompromised patients section 2.1.1 below).

AND

- Presented to hospital not more than 10 days since symptom onset (see exemption in immunocompromised patients section 2.1.1 below).

AND

- Estimated glomerular filtration rate (eGFR) at least 30 mL/min/1.73m^2

AND

- Alanine aminotransferase (ALT) below 5 times the upper limit of normal at baseline.

Exemptions to the above eligibility criteria apply to the following patient groups:

- Patients with end-stage renal disease on haemodialysis are exempt from the eGFR treatment threshold above
- Significantly immunocompromised patients (see section 2.1.1 on 'Immunocompromised patients' for exemptions in this cohort).

2.1.1 Immunocompromised patients

For significantly immunocompromised patients* hospitalised for COVID-19 symptoms:

- A course of remdesivir can be extended to a maximum of 10 days following MDT assessment.
- Criterion on time between symptom onset and treatment initiation does not apply
- Criterion on the need for supplemental oxygen requirement does not apply.

** Refers to patients with a significant impairment of humoral immune response (antibody production) and/or cellular immune competence*

2.1.2 Clinical decision making

Considerations during clinical decision-making should include the following (see also the clinical pathway in Appendix 1)

Clinical judgement in the initiation, review, escalation and de-escalation of patients receiving remdesivir treatment should be supported where possible by multidisciplinary team assessment

- **Risk assessment**
  - Clinical judgement around treatment with remdesivir can be informed by a risk score. Those with a low 4C Mortality Score (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 judgment). The 4C Mortality Score might be helpful in this assessment.

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. Other clinical risk scores may be deemed appropriate to use instead.

2.2 Exclusions and cautions for use

2.2.1 Exclusion criteria

The following patients are not eligible for treatment:

- Children aged less than 4 weeks of age and/or weighing less than 3kg.
- Estimated glomerular filtration rate (eGFR) <30 mL/min/1.73m^2 (except for patients with end-stage renal disease on haemodialysis)
- Alanine transaminase (ALT) ≥5 times the upper limit of normal
- Known hypersensitivity reaction to the active substances or to any of the excipients of the products as listed in the Summary of Product Characteristics (SmPC).

An individual clinical decision should be made as to whether pre-treatment urea and electrolytes and liver function tests are required based upon whether recent bloods are available or the patient is considered at risk of undiagnosed liver or kidney disease.

2.2.2 Cautions

- Please refer to the SmPC for special warnings and precautions for use.

2.3 Pregnancy, breastfeeding, use in women of childbearing potential and effect on fertility

In **all** cases of pregnancy and breastfeeding, senior Obstetric advice should be sought to ensure that theoretical risks to the fetus (or baby in the case of breastfeeding) do not outweigh proven benefits to the mother. In some cases of breastfeeding, it may be more appropriate to seek advice from a pediatrician.

Clinicians should refer to the SmPCs of the relevant products for further information on their use in pregnancy, breast feeding, women of childbearing potential and effects on fertility. In addition the current guidance from the Royal College of Obstetricians and Gynaecologists on Coronavirus (COVID-19), infection in pregnancy should be followed.

Remdesivir

- There are no or limited amount of data from the use of remdesivir in pregnant women. Remdesivir should be avoided in pregnancy unless clinicians believe the benefits of treatment outweigh the risks to the individual (see SmPC for further information).
- Women of child-bearing potential have to use effective contraception during treatment.
- It is unknown whether remdesivir is excreted in human milk or the effects on the breast-fed infant, or the effects on milk production. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from remdesivir therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

All healthcare professionals are asked to ensure that any patients who receive a COVID antiviral while pregnant are reported to the UK COVID-19 antivirals in pregnancy registry on 0344 892 0909 so that they can be followed up. For more information, go to http://www.uktis.org/.

3 Drug Interactions

- No interactions between remdesivir with corticosteroids (dexamethasone or hydrocortisone) are expected.
- Further information on interactions can be found within the SmPC or via University of Liverpool COVID-19 Drug Interactions website.

4. Dosing schedules, review and stopping criteria

This should be used in conjunction with appendix 1.

4.1. Dosing schedule

- ***Recommended dosage for adults and paediatric patients (weighing at least 40kg) :*** Single loading dose of remdesivir 200mg intravenously on day 1, followed by a once daily maintenance dose of remdesivir 100mg for the remainder of the treatment course. The total duration of treatment should be for a **maximum of 5 days** (except in immunocompromised patients – see below).
- **Recommended dosage for paediatric patients at least 4 weeks old (weighing at least 3kg but less than 40kg**): Single loading dose of remdesivir 5mg/kg intravenously on day 1, followed by a once daily maintenance dose of remdesivir 2.5mg/kg for the remainder of the treatment course. The total duration of treatment should be for a **maximum of 5 days** (except in immunocompromised patients – see below).
- ***Significantly immunocompromised patients*** (see immunocompromised patient section 2.1.1 above), the course of remdesivir can be **extended to a maximum of 10 days**, if agreed following multidisciplinary team assessment.
- ***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.

4.2 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.

4.3 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)

5. Supplies, preparation, administration and monitoring arrangements

Supplies	Remdesivir will be supplied from the pharmacy department. A limited supply of remdesivir will also be available from: • University Hospital Ayr - Emergency Drug cupboard • University Hospital Crosshouse – Emergency Drug cupboard • Arran War Memorial Hospital • Lady Margaret Hospital, Millport
Preparation	Remdesivir requires to be prepared in clinical areas, refer to the drug monograph within the Medusa Injectable Medicines Guide for details.
Administration	• Resuscitation and anaphylaxis treatment facilities must be readily available during the infusion. • Remdesivir should only be administered during daytime hours

	Refer to the drug monograph within the Medusa Injectable Medicines Guide for administration and monitoring instructions.
Monitoring	• Hypersensitivity reactions including infusion-related and anaphylactic reactions have been observed during and following administration of remdesivir. Signs and symptoms may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnoea, wheezing, angioedema, rash, nausea, vomiting, diaphoresis, and shivering. Slower infusion rates, with a maximum infusion time of up to 120 minutes, can be considered to potentially prevent these signs and symptoms. • Patients should be monitored for hypersensitivity reactions during and following administration of remdesivir as clinically appropriate. If signs and symptoms of a clinically significant hypersensitivity reaction occur, administration of remdesivir should be discontinued immediately and appropriate treatment initiated. **Baseline observations** should be recorded using the NEWS (National Early Warning Score) chart (or a PEWS chart if being used in paediatric patients) and repeated every 15 minutes during the infusion and then every 30 minutes until a minimum of 30 minutes post infusion (this may be extended based on clinical judgement). • Renal and liver function should be monitored carefully during treatment with remdesivir as clinically appropriate.

6. Adverse effects

- Refer to the information within sections 4.3 and 5.
- Refer to the SmPC for further information on adverse effects.

7. Safety reporting

Any suspected adverse reactions from any of the treatments should be reported directly to the MHRA via the dedicated COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/. It should be noted that remdesivir is a black triangle medicines.

8. Communication

All handovers of clinical care (including between hospitals if patients are transferred, between levels of care and clinical teams within hospitals, and between hospitals and primary care) should explicitly record that remdesivir has been given along with the dose schedule and date of administration.

9. Bibliography

1 CEM/CMO/2022/016: COVID-19 Therapeutic Alert. Remdesivir for patients hospitalised due to COVID-19, issued 28 November 2022. Available from: COVID-19 Therapeutic Alert: Remdesivir for patients hospitalised due to COVID-19 (scot.nhs.uk) (accessed 05/12/2022).

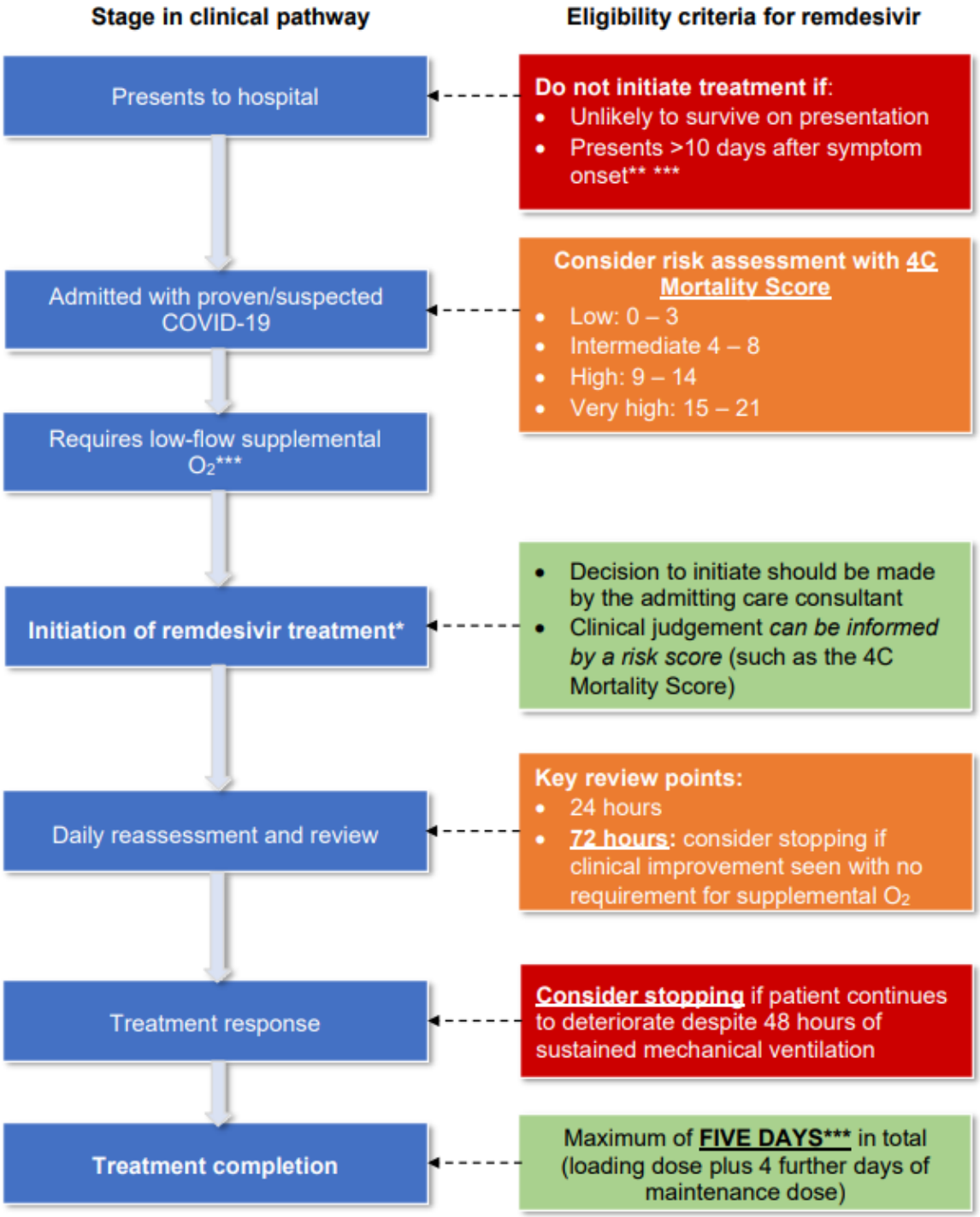
2 Interim Clinical Commissioning Policy: Remdesivir for patients hospitalised due to COVID-19. Published 28 November 2022. Available from: COVID-19 Therapeutic Alert: Remdesivir for patients hospitalised due to COVID-19 (scot.nhs.uk) (accessed 05/12/2022).

3 NICE guideline [NG191]. COVID-19 rapid guideline: managing COVID-19. Published: 23 March 2021, last updated: 29 March 2023. Available from: https://www.nice.org.uk/guidance/ng191 (accessed 21 April 2023).

4 Veklury® (remdesivir) 100 mg powder for concentrate for solution for infusion Summary of Product Characteristics, last updated on eMC 24 January 2023. Available from https://www.medicines.org.uk/emc/product/11597 (accessed 21 April 2023).

Appendix 1

Clinical pathway and criteria for the use of remdesivir in patients hospitalised with COVID-19



*There should be careful consideration before initiating remdesivir treatment
**Unless patient is readmitted with COVID-19 (see main policy document)
***See additional comments on immunocompromised patients

Taken from the Interim Clinical Commissioning Policy: Remdesivir for patients hospitalised due to COVID-19. Published 28 November 2022. Available from: COVID-19 Therapeutic Alert: Remdesivir for patients hospitalised due to COVID-19 (scot.nhs.uk).