Remdesivir for Patients Hospitalised due to COVID-19

University Hospitals of Leicester NHS
NHS Trust

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1. Introduction

Remdesivir is an adenosine nucleotide prodrug that is metabolised intracellularly to form the pharmacologically active substrate remdesivir triphosphate. Remdesivir triphosphate produces its antiviral effect by inhibiting SARS-CoV-2 RNA polymerase which perturbs viral replication.

The ACTT-1 trial showed that remdesivir improved time to recovery in patients hospitalised with COVID-19 by 5 days compared to placebo (Beigel et al, 2020). The World Health Organisation Solidarity trial indicated that it did not improve overall mortality, initiation of ventilation or duration of hospitalisation (Pan et al, 2020).

Remdesivir has a conditional marketing authorisation and has been made available to patients in the NHS under an Interim Specialist Commissioning Policy for patients aged 12 years and over, and as such, remdesivir is excluded from tariff and requires Blueteq approval prior to initiation.

2. Scope

This guideline outlines patient eligibility for remdesivir, the prescribing and review requirements, and the procedure to obtain remdesivir for UHL patients that are hospitalised **due to** symptoms of COVID-19 or have hospital onset COVID-19 and has symptoms that require hospital-based treatment.

This guideline applies to all UHL staff involved in the prescribing and administration of remdesivir for adult and paediatric patients (at least 4 weeks of age and weighing at least 3kg) with COVID-19.

3. Recommendations, Standards and Procedural Statements

3.1 Patient selection

Patients are eligible for treatment with remdesivir if they meet ALL of the following criteria unless otherwise stated:

- 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
- Are hospitalised specifically for the management of COVID-19 symptoms (community or hospital acquired)
- Requiring low-flow supplemental oxygen. *Does not apply to significantly immunocompromised patients.*
- Presented to hospital not more than 10 days since symptom onset (or have hospital onset of symptoms within the last 10 days). *Does not apply to significantly immunocompromised patients*
- Have an estimated glomerular filtration rate (eGFR) of at least 30 ml/minute. *Does not apply to patients with end stage renal disease on haemodialysis*
- Alanine aminotransferase (ALT) below five times the upper limit of normal at baseline.

Exclusion criteria:

- Children aged less than 4 weeks of age and/or weighing less than 3kg.
- Have an alanine aminotransferase (ALT) five times above the upper limit of normal at baseline.
- Known hypersensitivity reaction to the active substances or to any of the excipients listed in the Summary of Product Characteristics.

- Patients with hospital onset COVID-19 not requiring hospital-based treatment for their COVID-19 symptoms (refer to Neutralising Monoclonal Antibodies and Intravenous Antivirals Treatment of COVID-19 Hospitalised Patients UHL Guideline for advice on treatment choices in this group).

For patients under 4 weeks of age and/or weighing less than 3kg refer to 'Process for Remdesivir use in children 4 weeks of age' document (trust reference 51/2021)
in the Policy and Guidelines Library.

For patients readmitted for symptoms of COVID-19 (and meeting the eligibility criteria, with the exception of the requirement on the timing from symptom onset) are permitted a second course of up to 5 days upon readmission .

Caution:
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.

3.2 Initiation of treatment

The decision to treat must be made by the admitting consultant (or the consultant caring for the patient if the infection is hospital acquired).

Remdesivir should not be initiated in patients who present to hospital who are unlikely to survive (determined by clinical judgement).

All prescriptions for remdesivir prescribed under this guidance must be registered with Blueteq (NHSE web-based approval platform) prior to prescribing. The process is described below:

- Go to: https://www.blueteq-secure.co.uk/Trust/default.aspx
- Register for an account if you do not already have one, or log in to an established account.
- Please note registration can be completed using normal UHL email address and should take no longer than a few minutes. You may need to wait for your account to be activated so ideally this step should be completed ahead of the need to treat an individual patient.
- Select "Patient" then "Add" from the left hand side of the menu bar.
- Complete the details in the Add High Cost Drugs Patient panel. If the Patient is not currently registered with a GP select "Unregistered NHSE patients" as the GP surgery.
- Select "Add request" from the Patient menu bar.
- Make a note of the Blueteq authorisation number –this is required by Pharmacy to release remdesivir
- The Blueteq number should be annotated on the prescription.
- NOTE: remdesivir is to be given only to patients for whom it has been approved under the Blueteq scheme.
- A Blueteq user guide for clinicians is available on INsite

3.3 Dose regimen:

Once Blueteq has been completed, prescribe remdesivir with the following regimens:

Adult and, paediatric patients (weighing at least 40kg):

Remdesivir IV 200mg STAT on day 1
followed by remdesivir IV 100mg OD on days 2-5.

Paediatric patients at least 4 weeks old (weighing at least 3kg but less than 40kg):

Remdesivir IV 5mg/kg STAT on day 1
Followed by remdesivir IV 2.5mg/kg on days 2-5.

Contact the ward pharmacist to order a supply of remdesivir from pharmacy. Out of hours, when the ward pharmacist is unavailable, contact the on-call pharmacist via switchboard.

Significantly immunocompromised patients (defined as significant impairment of humoral immune response (antibody production) and/or cellular immune competence) are eligible for an extended course of remdesivir of up to 10 days, if agreed following multidisciplinary team assessment.

3.4 Reassessment and review

Remdesivir prescriptions should be reassessed daily.

Consider stopping remdesivir if:

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

Remdesivir should be stopped 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 <30ml/min (except in patients with end stage renal failure who are on haemodialysis)

3.5 Pregnancy

There is 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 (please see the relevant SmPC for further information).

3.6 Safety reporting

Any suspected adverse drug reactions (ADRs) for patients receiving remdesivir should be reported directly to the MHRA via the new dedicated COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/

3.7 Co-administration/interactions

There is no interaction expected between remdesivir and other commissioned treatments for COVID-19.

For further information on interactions please visit the University of Liverpool COVID-19 Drug Interactions website (https://www.covid19-druginteractions.org/checker)

3.8 Discharging the patient

The patients discharge letter should explicitly record their treatment with remdesivir, together the dose and and date of administration.

4. Education and Training

No new skills required to implement the guideline.

5. Monitoring and Audit Criteria

All guidelines should include key performance indicators or audit criteria for auditing compliance,

if this template is being used for associated documents (such as procedures or processes) that support a Policy then this section is not required as all audit and monitoring arrangements will be documented in section 8 of the Policy.

Key Performance Indicator	Method of Assessment	Frequency	Lead
Blueteq completed for each prescription	Reviewed by pharmacist	Ongoing – real time	Professionally checking pharmacist

6. Legal Liability Guideline Statement

See section 6.4 of the UHL Policy for Policies for details of the Trust Legal Liability statement for Guidance documents

7. Supporting Documents and Key References

Interim Clinical Commissioning Policy: Remdesivir for Patients Hospitalised due to COVID-19 . NHSEI November 2022
Summary of Product Characteristics: Veklury 100 mg powder for concentrate for solution for infusion. Gilead Sciences Ltd. October 20221

8. Key Words

Remdesivir, COVID-19, Antiviral, SARS-CoV-2, Blueteq

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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Author / Lead Officer:	Dr David Jenkins	**Job Title:** Consultant Microbiologist
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REVIEW RECORD			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
October 2021	1	Corrine Ashton	New document
April 2022	2	Corrine Ashton	Document title updated to better reflect content. Updated introduction to reflect evidence base. Restructuring of sections for clarity. Removal of weight limit exclusion criteria for adults. Removal of requirement for patient not to be receiving invasive ventilation or ECMO at the start of treatment. References added to paediatric guideline and hospital onset guidance. Addition of interactions and pregnancy information
November 2022	3	Corrine Ashton	Inclusion criteria updated to include patients from aged four weeks of age and weighing at least 3kg. Addition of information required on discharge letter.

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