NHS
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Remdesivir 100 mg concentrate for solution

Drug Protocol and Guideline regarding the MHRA approved Early Access to Medicines Scheme (EAMS)

Background

Remdesivir 100mg concentrate for solution for infusion is an unlicensed medicine.

The Medicines and Healthcare Regulatory Agency (MHRA) has approved its use for SARS-CoV-2 infection via an Early Access to Medicines Scheme (EAMS) in collaboration with the manufacturer (Gilead).

COVID-19 has been designated a priority health issue. As a result, data collection for all patients receiving remdesivir through the EAMS is mandatory.

Data collection is to be performed through the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC). For enquiries about ISARIC, please contact: CCP@liverpool.ac.uk. Data collection forms are to be completed by the responsible clinician, which is typically the consultant caring for the patient.

As remdesivir is under surveillance and only available via an EAMS, there are additional requirements with regards adverse drug reactions (ADRs) which must be reported directly to Gilead. Please contact a member of the pharmacy team who will assist with completion to ensure the correct process is followed to alert both the MHRA and Gilead of any potential ADRs. There are further details in the monitoring section below.

Indication for use

Remdesivir is indicated for the treatment of adults and adolescent patients hospitalised with SARS-CoV-2 infection confirmed by PCR collected in the preceding 72 hours. The access criteria recommends that patients receiving supplementary oxygen to maintain SpO2 > 94% or those who are within 24 hours of commencing CPAP or High-Flow Nasal Oxygen are eligible for remdesivir treatment. Remdesivir has not demonstrated clinical benefit in patients receiving ventilation, although some patients starting on ventilation and in the early stage of infection may be deemed suitable following MDT assessment.

Additionally, the following criteria must be met before initiating treatment:

- Aged 12 years or over and weighing at least 40 kg
- eGFR or Creatinine Clearance ≥30 mL/min. Use with caution in patients with eGFR or Creatinine Clearance between 31 and 50 mL/min.
  (Remdesivir is contraindicated in patients with eGFR or Creatinine Clearance <30mL/min and patients receiving dialysis)
- ALT ≤5 times the upper limit of normal at baseline

The decision to use Remdesivir MUST be made by the COVID-19 Multidisciplinary team (MDT). The internal process for obtaining a supply from pharmacy MUST be followed before administering this medication.

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Presentation

Remdesivir 100 mg concentrate for solution for infusion - 20ml vial.

- Containing remdesivir 5mg/ml

- Vials do not have an expiry when they arrive into pharmacy. As part of the unlicensed assessment process within pharmacy, an expiry date is added to the product prior to supplying to ward

Dose and Method of Administration

DOSING

Patients NOT requiring invasive ventilation and/or ECMO

- A single loading dose of remdesivir 200mg on day 1, followed by 100mg daily for a further 4 days

If a patient does not demonstrate clinical improvement, treatment may be extended for up to FIVE additional days (i.e. up to a total of 10 days). This decision must be made after discussion with the COVID-19 MDT.

Patients requiring invasive ventilation and/or ECMO

- A single loading dose of remdesivir 200mg on day 1, followed by 100mg daily for a further 9 days

ADMINISTRATION

- Remdesivir is to be administered via intravenous infusion over 30 to 120 minutes
- The 100mg or 200mg must be added to 250ml 0.9% sodium chloride
- **An equivalent volume of sodium chloride should be removed from the 250mL bag of sodium chloride 0.9%**

Note that the 200mg loading dose can also be diluted in 250mL of 0.9% sodium chloride, there is no need to add the 200mg to 500mL

Infusion bag volume	Infusion time	Rate of infusion
250 mL	30 min	8.33 mL/min
	60 min	4.17 mL/min
	120 min	2.08 mL/min

Concentrate for solution for infusion

- Store at 2 °C to 8 °C until required for use. Dilute within the same day as administration.

Diluted solution for infusion can be

- stored for up to FOUR hours at room temperature (20°C to 25°C)
- 24 hours at refrigerated temperature (2°C to 8°C).

Special populations

Paediatrics
This EAMS does not apply - remdesivir needs to be applied for on an individual patient basis via the approved compassionate use scheme. If use of remdesivir is approved, a powder formulation will be supplied by the manufacturer and is not covered by this document.

There is insufficient data on dosing in paediatric patients under 12 years of age.

Elderly
No dose adjustment of remdesivir is proposed in patients over the age of 65 years.

Renal impairment
The pharmacokinetics of remdesivir have not been evaluated in patients with renal impairment. Patients must have an eGFR determined before dosing and daily while receiving remdesivir.

Remdesivir should not be initiated in patients with an eGFR or Creatinine Clearance <30 ml/min or those on renal replacement therapy.

Hepatic impairment
The pharmacokinetics of remdesivir have not been evaluated in patients with hepatic impairment. It is not known if dosage adjustment is needed in patients with hepatic impairment.

Remdesivir should not be initiated in patients with ALT more than 5 times the upper limit of normal at baseline. Remdesivir should be discontinued in patients who develop ALT more than 5 times the upper limit of normal during treatment with remdesivir or ALT elevation accompanied by signs of symptoms of liver inflammation or increasing conjugated bilirubin or alkaline phosphatase.

Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir.

Pregnancy
This EAMS does not apply - remdesivir needs to be applied for on an individual patient basis via the approved compassionate use scheme. No adequate and well-controlled studies of remdesivir use in pregnant women have been conducted.

Remdesivir should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the foetus.

Breast-feeding
There is no information regarding the presence of remdesivir in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies, remdesivir and metabolites have been detected in the nursing pups of mothers given remdesivir, likely due to the presence of remdesivir in milk. Breast feeding is not recommended due to potential viral transmission to SARS-CoV-2-negative infants and adverse reactions from the drug in breastfeeding infants.

Monitoring & Significant Adverse Drug Reactions

Monitoring
Determine eGFR or Creatinine Clearance before starting treatment. Monitor renal function daily throughout duration of remdesivir treatment.

Check liver function before initial dosing and monitor daily while receiving remdesivir.

Adverse Drug Reactions (ADRs)
Any ADR that a healthcare professional considers might be related to treatment with Remdesivir irrespective of time since dosing initiation, should be reported to the Gilead safety department. These reports must be submitted by the hospital directly to Gilead pharmacovigilance – **please discuss any ADRs with a member of the pharmacy team and they can assist with the paperwork to complete and where to send this to.**

Gilead will forward any reported ADRs onto the MHRA. It is recommended to also inform the MHRA of any suspected ADRs for patients receiving remdesivir. Reports can be submitted via the COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, outcome and results of any test results or investigations.

References

1. https://www.gov.uk/government/publications/early-access-to-medicines-scheme-eams-scientific-opinion-remdesivir-in-the-treatment-of-patients-hospitalised-with-suspected-or-laboratory-confirme/treatment-protocol-for-healthcare-professionals#early-access-to-medicines-scheme--treatment-protocol--information-for-healthcare-professionals