Remdesivir

Coronavirus Treatment

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Emergency Use Authorization (EUA)

- The U.S. Food and Drug Administration has issued an EUA to permit the emergency use of the unapproved product remdesivir for the treatment of suspected or confirmed COVID-19 patients

https://www.fda.gov/media/137565/download

About Remdesivir

- Remdesivir is an investigational antiviral medicine that is still being studied
- There is limited information known about the safety and effectiveness of remdesivir
- Remdesivir was shown in a clinical trial to shorten the time for recovery from COVID-19
- To date, there are no medications approved by the FDA at this time to treat patients with COVID-19

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Who can receive treatment under the EUA

- EUA is permitted for hospitalized children and adults with **severe disease:**
  - Oxygen saturation ≤ 94% on room air
  - Requiring supplemental O2
  - Requiring mechanical ventilation
  - Requiring extracorporeal membrane oxygenation (ECMO)

Adult Treatment and Dosing

- Adults and pediatric patients ≥40kg **requiring mechanical ventilation or ECMO**
  - Single loading dose 200mg IV over 120 min on Day 1
  - Then daily maintenance dose 100mg IV over 120 min for 9 days (days 2 through 10)

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Adult Treatment and Dosing cont.

- Adults and pediatric patients ≥40kg **not requiring mechanical ventilation or ECMO**
  - Single loading dose 200mg IV over 120 min on Day 1
  - Then daily maintenance dose 100mg IV over 120 min for 4 days (days 2 through 5)
  - If patient does not show clinical improvement, treatment may be extended up to 5 additional days (10 days max)

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Pediatric Treatment and Dosing

- Pediatric patients 3.5kg – 40kg **requiring mechanical ventilation or ECMO**
  - Single loading dose 5mg/kg IV over 120 min on Day 1
  - Then daily maintenance dose 2.5mg/kg IV over 120 min for 9 days (days 2 through 10)

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Pediatric Treatment and Dosing cont.

- Pediatric patients 3.5kg – 40kg **not requiring mechanical ventilation or ECMO**
  - Single loading dose 5mg/kg IV over 120 min on Day 1
  - Then daily maintenance dose 2.5mg/kg IV over 120 min for 4 days (days 2 through 5)
  - If patient does not show clinical improvement, treatment may be extended up to 5 additional days (10 days max)

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Guidelines

- May be used at any time after onset of symptoms in hospitalized patients
- Administer via intravenous infusion only (not IM injection)
- All patients must have renal and hepatic function determined before dosing
- Patients with known hypersensitivity to any ingredient of remdesivir must not receive

Renal Impairment

- The pharmacokinetics of remdesivir have not been evaluated in patients with renal impairment
- Use in patients with renal impairment are based on potential risk and potential benefit considerations

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Renal Impairment cont.

- Patients with eGFR ≥ 30 mL/min have received remdesivir for treatment of COVID-19 with no dose adjustment of remdesivir
- Not recommended in adult and pediatric patients (>28 days old) with eGFR < 30 mL/min or in full-term neonates (≥7 days to ≤28 days old) with serum creatinine ≥ 1mg/dL unless potential benefit outweighs the potential risk

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Hepatic Impairment

- Pharmacokinetics have not been evaluated in patients with hepatic impairment
- It is not known if dosage adjustment is needed in patients with hepatic impairment
- Used in patients with hepatic impairment only if potential benefit outweighs the potential risk
- Hepatic lab tests should be performed in all patients prior to starting remdesivir and daily while receiving treatment

Hepatic Impairment cont.

- Not to be initiated in patients with ALT ≥ 5x upper limit of normal at baseline
- Discontinue in patients who develop:
  - ALT ≥ 5x upper limit of normal during treatment with remdesivir (may be restarted with ALT is < 5x upper limit of normal)

  OR

  - ALT elevation accompanied by signs and symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR

Pregnancy

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

Geriatric Use

- Pharmacokinetics have not been evaluated in patients >65 years of age
- In general, appropriate caution should be exercised in administration and monitoring of elderly patients, reflecting:
  - greater frequency of decreased hepatic, renal, or cardiac function
  - concomitant disease or other drug therapy

Monitoring Requirements

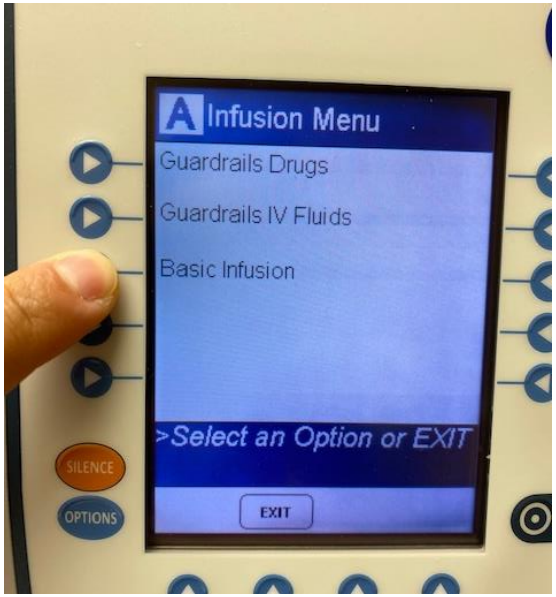
- All receiving patients should be on **tele status**
- VS monitoring guidelines:
  - Monitor HR and BP
    - Baseline at start of infusion
    - Then every 15 min x 2
    - Then every 30 min x 4
- Call physician for SBP < 90 or HR < 60

Monitoring

- Infusion-related reactions (discontinue if noted):
  - Hypotension
  - Nausea/vomiting
  - Diaphoresis
  - Shivering
  - Elevated liver transaminases
- Labs prior to dosing
  - Adult and pediatric patients greater than 28 days old must have an estimated glomerular filtration rate (eGFR) determined and full-term neonates (at least 7 days to less than or equal to 28 days old) must have serum creatinine determined before dosing and daily while receiving remdesivir.
  - Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir.

Administration of Remdesivir

- Requires a dual sign-off (**!!**) in EPIC MAR
- Can be found in Alaris pump Guardrails drug library
- Infuse over 120 min per MAR/label instructions
  - Reprogram Alaris – default is 60 min



Hazardous Drug Precautions

- Remdesivir classified as Non-Antineoplastic (Table 2) Hazardous Drug

- Use PPE chemo gown and double chemo gloves for administration and disposal
  - (glove→gown→glove)

Post-Administration Flush of Tubing

- Perform after completing infusion through secondary IV infusion set
- Ensure patient receives all of IV remdesivir by flushing with primary saline infusion
  - Adults: use 30ml saline (greater than volume of tubing set)
  - Pediatric: use volume necessary to clear line of medication

Disposal

- Following completion of infusion, follow facility disposal waste stream for Table 2 Hazardous Drugs

Adverse Effects

- Health care providers must submit a report on all medication errors and all serious safety events related to remdesivir in RL event reporting and to FDA within 7 calendar days
- Side effects of remdesivir should also be reported by prescriber or designee to FDA MedWatch at www.fda.gov/medwatch/report.htm or by calling 1-800-FDA-1088

Serious Adverse Events Defined as

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant incapacity or substantial disruption of ability to conduct normal life functions
- Congenital anomaly/birth defect
- Medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly

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Storage

- There is no preservative or bacteriostatic agent present in this product
- Diluted remdesivir solution for infusion should be given within
  - 4 hours at room temperature
  - 24 hours at refrigerated temperature
- Inspect visually for particulate matter and discoloration prior to administration and do not administer if observed

Patient Education

- Communicate with patient/family/caregiver info consistent with "Fact Sheet for Patients and Parents/Caregivers" and provide copy prior to patient receiving remdesivir, including:
  - FDA has authorized emergency use of remdesivir (not FDA approved drug)
  - Patient or parent/caregiver has option to accept or refuse treatment
  - The significant known and potential risks and benefits, and extent to which such risks and benefits are unknown
  - Information on available alternative treatments

Summary

- Patients and family/caregivers should be properly educated and consent to treatment before administration
  - Remdesivir Fact Sheet for Patients and Parents/Caregivers (click here)
- Staff should monitor for potential adverse events related to remdesivir

References

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Fact Sheet for Patients and Parent/Caregivers:

- https://www.fda.gov/media/137565/download

- Information on clinical trials of remdesivir for COVID-19 treatment can be found at www.clinicaltrials.gov