FDA Emergency Use Authorization (EUA) of Veklury (remdesivir)

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Background

- On May 1st, the FDA issued an Emergency Use Authorization (EUA) to permit the emergency use of remdesivir for the treatment of COVID-19

- Mechanism of action: adenosine nucleotide prodrug; inhibits RNA synthesis

Authorized Use (Patient Criteria)

- Treatment of suspected or laboratory confirmed COVID-19 in adults and children hospitalized with severe disease:
  - Oxygen saturation (SpO2) ≤ 94% on room air,
  - Requiring supplemental oxygen,
  - Requiring mechanical ventilation, or
  - Requiring extracorporeal membrane oxygenation (ECMO)

Mandatory EUA Requirements

- Review and provide copy of FDA Fact Sheet for Patients and Parents/Caregivers
- Document in EMR (use smartphrase ".remdesivir")
  - Given the Fact Sheet for Patients and Parents/Caregivers,
  - Informed of alternatives to receiving remdesivir, and
  - Informed that remdesivir is an unapproved drug that is authorized for use under EUA
- Labs
  - Adult and pediatric patients (>28 days old) must have an eGFR determined and full-term neonates (≥7 days to ≤28 days old) must have SCr determined prior to first dose and daily while receiving remdesivir
  - Hepatic laboratory testing should be performed in all patients prior to first dose and daily while receiving remdesivir

Mandatory EUA Requirements Cont'd

- Do not use in patients with known hypersensitivity to any ingredient of remdesivir
- Must respond to requests from FDA for information about adverse events and medication errors following receipt of remdesivir
- Must report to FDA MedWatch all medication errors and adverse events (death, serious adverse events*) considered to be potentially related to remdesivir occurring during treatment within 7 calendar days from the onset of the event

Ordering

- Use *COVID-19 Orderset – HPH* or remdesivir order panel in Epic
- Dosing
  - Pediatric patients 3.5 to <40kg:
    - 5 mg/kg IV on Day 1, then 2.5 mg/kg IV q24h on Days 2-5
  - Pediatric patients ≥40kg and Adults:
    - 200mg IV on Day 1, then 100mg IV q24h on Days 2-5
- Drug access
  - FDA EUA pathway
    - State has limited EUA supply on hand
    - Contact Dr. Doug Kwock to obtain drug for an eligible patient
  - Pregnant women or pediatric patients <18yo: May use Gilead Compassionate Use pathway
    - Refer to *HPH Instructions - Compassionate Use Request for Remdesivir*
    - Visit https://rdvcu.gilead.com/ for more information

Special Populations

- Pregnancy
  - Well-controlled studies have not been conducted in pregnant women
  - Use only if potential benefit > risk for mother and fetus
- Geriatric use
  - Pharmacokinetics have not been evaluated in patients >65 years old
  - Appropriate caution should be exercised (decreased organ function, concomitant disease/drugs)

Special Populations Cont'd

- Renal impairment
  - All patients must have eGFR determined before dosing
  - Do not use 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 SCr ≥1 mg/dL unless the potential benefit > potential risk
- Hepatic impairment
  - Hepatic laboratory testing should be performed prior to starting therapy and daily while receiving remdesivir
  - Use only if the potential benefit > potential risk

Dosage Forms / Storage

- Lyophilized powder, 100mg vial
  - Store at room temp until expiration date
  - After reconstitution, may be stored up to 4 hours at room temp or 24 hours in refrigerator
- Injection solution, 100mg/20ml (5mg/ml) vial
  - Store in refrigerator until expiration date
  - May be stored up to 12 hours at room temp
- Diluted infusion solution
  - May be stored up to 4 hours at room temp or 24 hours in refrigerator
- No preservatives
  - Single use only
  - Discard any unused portion of drug

Preparation / Dispensing

- Handle as Antineoplastic (Table 2) Hazardous Drug
- Pediatric patients 3.5 - <40kg:
  - **Use lyophilized powder only**
  - Loading dose: 5 mg/kg in NS (base volume: see details in Fact Sheet)
  - Maintenance dose: 2.5 mg/kg in NS (base volume: see details in Fact Sheet)
  - Withdraw (and discard) volume of NS equivalent to drug volume being added to bag
- Pediatric patients ≥ 40kg and adults:
  - May use lyophilized powder or injection solution
  - Loading dose: 200mg in 250ml NS
  - Maintenance dose: 100mg in 250ml NS
  - Withdraw (and discard) volume of NS equivalent to drug volume being added to bag
- Pharmacy to complete drug accountability log prior to dispense

Administration

- Categorized as an investigational, non-antineoplastic (Table 2) hazardous drug
  - RN dual sign off on MAR
  - Chemo gown and double chemo gloves
- Patient on Tele Status
- Give over 120 minutes
- Check BP/HR at baseline, q15min x 2, q30min x 4. Call physician for SBP<90 or HR<60 (adult parameters).
- Do not administer simultaneously with any other medication
  - Compatibility with IV solutions and medications other than NS is not known
- Flush with a volume of NS greater than the priming volume of the tubing to ensure the full dose is delivered (adults = at least 30 ml NS)
- Discard of used IV bag and supplies per facility waste stream for Table 2 hazardous drugs

Monitoring

- Adverse Effects
  - Infusion-related reactions
    - Immediately discontinue if clinically significant reaction occurs
    - Initiate appropriate treatment
  - Transaminase elevations
    - Do not initiate treatment in patients with ALT ≥ 5x ULN at baseline
    - Discontinue treatment in patients who develop ALT ≥ 5x ULN during treatment. May restart when ALT is < 5x ULN, or ALT elevation is accompanied by s/sx of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR

Monitoring Cont'd

- Recommended daily labs
  - Serum chemistries, hematology, ALT, AST, bilirubin, alk phos, SCr and CLcr
- Drug-drug interactions
  - DDI trials have not been conducted in humans
  - In vitro
    - Coadministration with chloroquine or hydroxychloroquine is not recommended based on in vitro data demonstrating an antagonistic effect of chloroquine on the intracellular metabolic activation and antiviral activity of RDV
    - Substrate for CYP2C8, CYP2D6, CYP3A4, Organic Anion Transporting Polypeptides 1B1 (OAPT1B1), and P-glycoprotein (P-gp) transporters
    - Inhibitor of CYP3A4, OATP1B1, OATP1B3, BSEP, MRP4, and NTCP
    - Clinical relevance of these in vitro assessments has not been established

References

- FDA Fact Sheet for Health Care Providers Emergency Use Authorization (EUA) of Remdesivir. Available at: https://www.fda.gov/media/137566/download. Accessed August 5, 2020.

- FDA Fact Sheet for Patients and Parents/Caregivers Emergency Use Authorization (EUA) of Remdesivir for Coronavirus Disease 2019 (COVID-19). Available at: https://www.fda.gov/media/137565/download. Accesed August 5, 2020.