	Type of Policy: Hospital Wide
	POLICY TITLE: Version 1.9 REMDESIVIR
	Effective Date: 06/17/2020

Background: Veklury® (remdesivir) is an antiviral drug originally developed to treat Ebola. Remdesivir works by inhibiting RNA-dependent RNA polymerase. Remdesivir has been shown to inhibit COVID-19, MERS, and SARS in-vitro and in animal models. Research on the use of remdesivir in COVID-19 is on-going. As of 10/22/2020, remdesivir is the only FDA approved drug for the treatment of COVID-19 in patients ≥ 12 years of age weighing ≥ 40 kg. An updated Emergency Use Authorization (EUA) was approved on 10/22/2020 for suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg **or** hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.

Remdesivir may be utilized via 2 methods:

1) **FDA approved** use for the treatment of COVID-19 in patients ≥ 12 years of age **AND** > 40 kg
2) **Emergency Use Authorization (EUA)**-for hospitalized patients < 12 years weighing ≥ 3.5 kg or hospitalized pediatrics patients weighing ≥ 3.5 kg to < 40 kg

1. FDA approved Patients

a. 12 years of age and ≥ 40 kg
b. No EUA is required for these patients
c. Follow the dosing, preparation, administration, and monitoring recommendations per this guideline and current US Prescribing Information available at www.gilead.com/scienceand-medicine/medicines

2. Emergency Use Authorization (EUA):

https://www.fda.gov/media/137564/download

- A new EUA was issued by the FDA on 10/22/20 approving use in hospitalized pediatric patients < 12 years of age weighing ≥ 3.5 kg or pediatric patients weighing ≥ 3.5 kg to < 40 kg
- For information on the authorized use of remdesivir and mandatory EUA requirements please refer to the Fact Sheet for Healthcare Providers (HCPs) available at: www.gilead.com/remdesivir.
- For the step by step process at CHKD refer to Table 1.

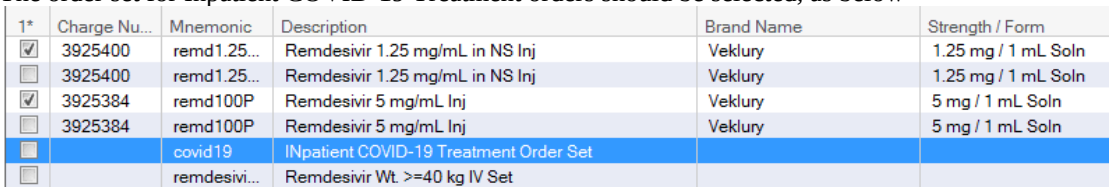
3. CHKD Specific Restriction:

- Only utilize in patients who are ≤ 10 days from the onset of signs and symptoms
- Patients who are > 10 days of symptom onset (i.e., illness), there is little to no benefit with remdesivir or other antivirals, and the risks may outweigh any potential benefit

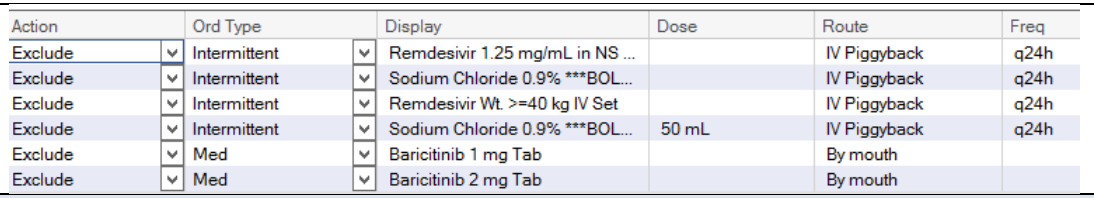
Table 1. CHKD Remdesivir Step-by-Step Treatment Initiation per (10/2020) EUA Requirements

<table>
<tr><th>Step</th><th>Criteria</th><th>Description</th></tr>
<tr><td>1</td><td><u>Confirm Patient Qualification under EUA</u>

Hospitalized Peds Patients who are either:
a) < 12 years weighing at least ≥ 3.5 kg
b) Weighing ≥ 3.5 kg to < 40 kg

CHKD Restriction: Only utilize in patients who are ≤ 10 days from signs and symptoms</td><td>1. Suspected OR laboratory confirmed COVID-19 <u>AND</u>
2. Severe disease defined as, ≥ 1 of the below:
• SpO2 ≤ 94% on room air
• Requiring supplemental oxygen
• Requiring mechanical ventilation
• Requiring extracorporeal membrane oxygenation (ECMO)</td></tr>
<tr><td>2</td><td>Additional Requirements</td><td>1. Dosing must be in accordance with regimens as detailed in the authorized Facts Sheets
2. MUST be administered in an inpatient hospital setting
3. Patients (>28 days old) MUST have an eGFR determined prior to treatment
4. Full-term neonates (≥7 days to ≤28 days old) MUST have serum creatinine prior to treatment
5. Hepatic labs prior to starting & daily while receiving
6. Obtain prothrombin time before starting & during as clinically appropriate
7. Patients with known hypersensitivity to any ingredient must not receive remdesivir</td></tr>
<tr><td>3</td><td>Obtain ID Approval</td><td>1. At CHKD, Remdesivir is restricted to ID, Contact ASAP if use is anticipated
2. The ID attending will/will not approve
3. If approved, the ID physician will notify:
a) Sarah Parsons Pharm. D., BCPPS (Simon 6491, 8-5447) 07:30-16:00, M-F
b) Pharmacy MEDS on call Pharm. D. (Simon 7337) after hours, holidays, and weekends
▪ To page a Simon when outside of CHKD call 757-668-9494
▪ When prompted enter Simon # 7337
▪ Enter your contact number and follow prompts</td></tr>
<tr><td>4</td><td>Order Entry</td><td>1. The order must be entered via PharmNet and not available via Powerchart
2. The pharmacist will accept a verbal order via prescriber with confirmation of ID approval
3. The order set for Inpatient COVID-19 Treatment orders should be selected, as below
 

4. Once selected, select include for the appropriate order, based on weight per Table 2.
5. Also include the sodium chloride flush to be administered post dose per Table 2.
a. 50 mL flush ≥ 40 kg
b. 30 mL flush < 40 kg, may adjust, ensure sufficient volume to clear line</td></tr>
</table>

		
5	**Discuss & Provide the Info Sheet to Patient/Family**	**1.** **Prior** to receiving, communicate & provide a printed copy of the Fact Sheet for Patients and Parents/Caregivers found at: https://www.gilead.com/-/media/files/pdfs/remdesivir/eua-fact-sheet-for-patients-and-caregivers.pdf?la=en&hash=45C9661BC70F1E1F58B53781B748AC5C **2.** You **MUST** communicate and document that the patient/caregiver has completed and reviewed the below: **a)** Received the Fact Sheet for Patients and Parents/Caregivers **b)** The FDA EUA approves Remdesivir for suspected or confirmed COVID-19 in Hospitalized Peds Patients who are either (*< 12 years weighing at least ≥ 3.5 kg or Weighing ≥ 3.5 kg to < 40 kg)* **c)** The parent/caregiver was given the option to accept or refuse **d)** Reviewed the significant known and potential risks and benefits **e)** Information on available alternative treatments *(none known)*
6	**Obtain Informed Verbal Consent Document in EMR**	Obtain & document informed verbal consent from the patient or designated caregiver. Document in the EMR per template provided below verbal informed consent obtained. **Informed Consent for Remdesivir EUA Treatment** I discussed with the *(patient/caregiver)* ___the benefits and risks of initiating Remdesivir treatment approved under the FDA granted emergency use authorization (EUA) for the treatment of COVID-19. I provided *(patient/caregiver)*____with the Fact Sheet for Patients and Parents/Caregivers, discussed the lack of available alternatives, and informed her that remdesivir is an unapproved drug that is authorized for use under an EUA.I discussed the mechanism of action, use in COVID-19 patients, explained the purpose of an EUA, and discussed any associated risks with remdesivir therapy. I provided the opportunity for her to ask questions and answered those questions. I discussed the risk/benefits with *(patient/caregiver)* _____. The *(patient/caregiver)* _____ agreed to treatment and provided verbal consent. Witness :_____ (*required for telephone consent*)
7	**Maintain Record Transparency**	**1.** Healthcare facilities will ensure any records associated with this EUA are maintained until notified by Gilead and/or FDA **2.** Such records will be made available to Gilead, HHS, and FDA for inspection upon request
8	**Tracking & Reporting Adverse Events**	The prescribing healthcare provider or designee are responsible for: **a)** Submitting a Verge and contacting Elizabeth Rogers Pharm.D.,(8-5285) and Sarah Parsons Pharm. D.(8-5492) **b)** Mandatory responses to requests from FDA for information about adverse events and medication errors following administration

		c) Mandatory reporting of all medication errors and serious adverse events considered to be potentially related occurring during treatment within 7 calendar days from the onset of the event ▪ The reports should include unique identifiers and the words "VEKLURY (remdesivir) under Emergency Use Authorization (EUA)" in the description section of the report **d)** Submit adverse event reports to FDA MedWatch using one of the following methods: ▪ Complete and submit the report online www.fda.gov/medwatch/report.htm ▪ By using a postage-paid Form FDA 3500 (available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForm s/Forms/UCM163919.pdf) and returning by mail (MedWatch,5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA-0178) ▪ Call 1-800-FDA-1088 to request a reporting form **e)** Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error" a statement"VEKLURY (remdesivir) under Emergency Use Authorization (EUA)." **f)** In addition please provide a copy of all FDA MedWatch forms to: ▪ Gilead Global Patient Safety, Fax: 1-650-522-5477, E-mail: Safety_fc@gilead.com, or call Gilead at 1-800-GILEAD-5 to report adverse events

Pharmacists Specific Information:

1. **Dosing:**

Refer to the CHKD Treatment Guidance for COVID-19 in Children (Table 4.)

a. Adult dosing:

i. 200 mg IV loading dose (LD) once followed by

ii. 100 mg IV q24h Maintenance Dose (MD), to be given 24 hour post the LD

b. Pediatric dosing*:

Weight	**LD** (once)	**MD** (q24h)
<40 kg	5 mg/kg	2.5 mg/kg
≥40 kg (*powder only)*	200 mg	100 mg

LD-Loading Dose, Max =200 mg
MD-Maintenance Dose, Max= 100 mg
*Pediatric dosing from the WHO

c. Renal Adjustment:

i. Contains SBECD and should not be administered in adults and pediatric patients (> 28 days old) with eGFR < 30 mL/min or in full-term neonates (at least 7 days and ≤ 28 days old) with serum creatinine ≥ 1 mg/dL unless the potential benefit outweighs the risk

d. Hepatic Adjustment:

i. It is not known if dosage adjustment is needed in patients with hepatic impairment

2. **Preparations:**

Supplied in 2 formulations:

a. Veklury® (remdesivir) for Injection (100 mg) Lyophilized **Powder**

For patients < 40 kg: use powder ONLY

b. Veklury® (remdesivir) Injection (5 mg/mL) Concentrated **Solution**

3. **Storage of Vials:**
   - **a.** Lyophilized Powder: Store vials below 30°C (below 86°F) until required for use. The lyophilized powder must be reconstituted and diluted prior to use
   - **b.** Injection Solution: Store 5 mg/mL injection at refrigerated temperature (2°C to 8°C [36°F to 46°F]) until required for use. Dilute within the same day as administration. Prior to dilution, equilibrate remdesivir injection to room temperature (20°C to 25°C [68°F to 77°F]). Sealed vials can be stored up to 12 hours at room temperature prior to dilution. The concentrated solution must be diluted prior to use
4. **Storage of Diluted Solutions:**
   - **a.** After reconstitution, use vials immediately to prepare diluted solution
   - **b.** Diluted remdesivir powder solution in syringe *should be used immediately*
   - **c.** Diluted remdesivir powder or solution in the infusion bags can be stored up to 24 hours at room temperature (20°C to 25°C [68°F to 77°F]) or 48 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) prior to administration

Managing Variations in Packaging & Labeling of Gilead's Veklury® (remdesivir)

- Gilead's Veklury® (remdesivir) has been manufactured via EUA & for commercial use, and has different packaging, labeling, & expiration dates depending on the date of manufacture. Packaging and labeling for Gilead's remdesivir EUA **may not** necessarily include the brand name, Veklury
- *To prevent shortages, hospitals **SHOULD** continue to use all unexpired, unopened vials of Gilead's remdesivir – whether or not the vial includes the brand name or is labeled for use under EUA*
- Current packaging variations are described below:
  - **a)** Veklury ® (remdesivir) for injection (100 mg **lyophilized powder** in vial). The lyophilized powder formulation is supplied with a red cap and **may** be marked "for use under Emergency Use Authorization (EUA)"
  - **b)** Veklury ® (remdesivir) injection (100 mg/20 mL [5 mg/mL], **solution** in vial). The solution formulation is supplied with a blue cap and **may** be marked "for use under Emergency Use Authorization (EUA)"

Now FDA Approved:	**Previously authorized for emergency use:**
a) Veklury® (remdesivir) injection solution **b)** Veklury® (remdesivir) for injection (lyophilized powder)	**a)** Veklury (remdesivir) injection solution **b)** Veklury (remdesivir) for injection (lyophilized powder)
	

What hospitals should do with unexpired, unopened vials of Gilead's Remdesivir

Appropriate use of Gilead's remdesivir (brand name VEKLURY), including vials labeled for Emergency Use Authorization (EUA) use		
Product	**Remdesivir for injection, 100 mg, lyophilized powder**	**Remdesivir injection, 100 mg/20 mL (5 mg/mL), solution**
Labeled "For use under Emergency Use Authorization (EUA)" (vials and cartons do not include the brand name, VEKLURY)	Continue use in: • Adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization • Hospitalized pediatric patients weighing 3.5 kg to less than 40 kg ***or*** hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg **under the provisions of the Emergency Use Authorization (EUA) – Please review the EUA Fact Sheet for Healthcare Providers and FDA Letter of Authorization**, available at gilead.com/remdesivir.	Continue use in: • Adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization
FDA-approved VEKLURY (carton and vials will include the brand name, VEKLURY)	Use in: • Adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization • Hospitalized pediatric patients weighing 3.5 kg to less than 40 kg ***or*** hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg **under the provisions of the Emergency Use Authorization (EUA) – Please review the EUA Fact Sheet for Healthcare Providers and FDA Letter of Authorization**, available at gilead.com/remdesivir.	Use in: • Adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization

Table 2. Veklury ® (Remdesivir) Product Specific Preparation and Administration Instructions

<table>
<tr><th colspan="2">Remdesivir 100 mg (Powder) ≥ 40 kg Patients</th></tr>
<tr><th>Step</th><th>Description</th></tr>
<tr><td>Reconstitution</td><td>
1. Remove the required number of single-dose vial(s) from storage
2. For each vial, aseptically reconstitute by addition of 19 mL of Sterile Water (SW) using a suitably sized syringe and needle. Only use SW for Injection to reconstitute remdesivir lyophilized powder
3. Discard the vial if a vacuum does not pull the SW into the vial
4. Immediately shake the vial for 30 seconds
5. Allow the contents of the vial to settle for 2 to 3 minutes. A clear solution should result. If the contents of the vial are not completely dissolved, shake the vial again for 30 seconds and allow the contents to settle for 2 to 3 minutes. Repeat this procedure as necessary until the contents of the vial are completely dissolved
6. Following reconstitution, each vial contains 100 mg/20 mL (5 mg/mL) of remdesivir solution
7. Use reconstituted solution for injection immediately to prepare the diluted solution below
</td></tr>
<tr><td>Dilution</td><td>
1. Determine the volume of 0.9% sodium chloride (NaCl) to withdraw from the infusion bag, see below
2. Withdraw the required volume of NaCl from the bag using an appropriately sized syringe and needle. Discard the NaCl that was withdrawn from the bag
3. Withdraw the required volume of reconstituted remdesivir for injection from the vial using an appropriately sized syringe. Discard any unused portion remaining in the remdesivir vial
4. Transfer the required volume of reconstituted remdesivir for injection to the selected infusion bag
5. Gently invert the bag 20 times to mix the solution in the bag. Do not shake

Recommended Dilution Instructions Using Reconstituted Veklury for Injection Lyophilized Powder in Patients ≥ 40 kg
<table>
<tr><th>Veklury ® (Remdesivir) Dose</th><th>0.9% NaCl bag volume to use</th><th>Volume to be withdrawn & discarded from 0.9% NaCl bag</th><th>Required volume of reconstituted Veklury ®</th></tr>
<tr><td rowspan="2">Loading Dose 200 mg (2 vials)</td><td>250 mL</td><td>40 mL</td><td>40 mL (2 × 20 mL)</td></tr>
<tr><td>100 mL</td><td>40 mL</td><td>40 mL (2 × 20 mL)</td></tr>
<tr><td rowspan="2">Maintenance Dose 100 mgf (1 vial)</td><td>250 mL</td><td>20 mL</td><td>20 mL</td></tr>
<tr><td>100 mL</td><td>20 mL</td><td>20 mL</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><td>Administration</td><td>
1. Administer the diluted solution with via the infusion rate per the chart below
2. After infusion is complete, flush with at least 30 mL of 0.9% NaCL

Recommended Rate of Infusion — Diluted Veklury for Injection Lyophilized Powder in Patients ≥ 40 kg
<table>
<tr><th>Infusion Volume</th><th>Infusion time</th><th>Rate of infusion</th></tr>
<tr><td rowspan="3">250 mL</td><td>30 min</td><td>8.33 mL/min</td></tr>
<tr><td>60 min</td><td>4.17 mL/min</td></tr>
<tr><td>120 min</td><td>2.08 mL/min</td></tr>
<tr><td rowspan="3">100 mL</td><td>30 min</td><td>3.33 mL/min</td></tr>
<tr><td>60 min</td><td>1.67 mL/min</td></tr>
<tr><td>120 min</td><td>0.83 mL/min</td></tr>
</table>
</td></tr>
</table>

Table 2. Veklury ® (Remdesivir) Product Specific Preparation and Administration Instructions –*continued*

Remdesivir 100 mg (Powder) <40 kg Patients	
Step	**Description**
Reconstitution	**1.** Remove the required number of single-dose vial(s) from storage **2.** For each vial, aseptically reconstitute by addition of 19 mL of SW using a suitably sized syringe and needle. Only use SW for Injection to reconstitute remdesivir lyophilized powder **3.** Discard the vial if a vacuum does not pull the SW into the vial **4.** Immediately shake the vial for 30 seconds **5.** Allow the contents of the vial to settle for 2 to 3 minutes. A clear solution should result. If the contents of the vial are not completely dissolved, shake the vial again for 30 seconds and allow the contents to settle for 2 to 3 minutes. Repeat this procedure as necessary until the contents of the vial are completely dissolved **6.** Following reconstitution, each vial contains 100 mg/20 mL (5 mg/mL) of remdesivir solution **7.** Use reconstituted solution for injection immediately to prepare the diluted solution below
Dilution	**1.** Following reconstitution as instructed above, each vial will contain a 100 mg/20 mL (5 mg/mL) remdesivir concentrated solution **2.** The 100 mg/20 mL (5 mg/mL) concentrate should be further diluted to a fixed concentration of 1.25 mg/mL using 0.9% NaCl **3.** The total required infusion volume of the 1.25 mg/mL remdesivir solution for infusion is calculated from the pediatric weight-based dosing regimen **4.** Small 0.9% NaCl infusion bags (e.g., 25, 50, or 100 mL) or an appropriately sized syringe should be used **5.** Administer via IV infusion in a total volume target remdesivir concentration of 1.25 mg/mL **6.** A syringe may be used for delivering volumes less than 50 mL **A. <u>Infusion with IV Bag</u>** **a)** Determine the total infusion volume needed to achieve a final infusion volume concentration of 1.25 mg/mL of remdesivir diluted solution based on the patient's calculated dose **b)** Select an appropriately sized infusion bag to prepare diluted solution **c)** If using a prefilled 0.9% NaCl infusion bag, withdraw and discard the amount of diluent equal to the volume of reconstituted solution needed per patient's dose plus a quantity sufficient to achieve a 1.25 mg/mL final volume concentration of remdesivir diluted solution. **d)** Withdraw the required volume of reconstituted remdesivir solution into an appropriately sized syringe.

<table>
<tr><td></td><td>
e) Transfer the required volume of reconstituted remdesivir solution to the 0.9% NaCl infusion bag.
f) Gently invert the bag 20 times to mix the solution in the bag. Do not shake.
g) If using an empty infusion bag, transfer the required volume of reconstituted remdesivir solution to the bag, followed by a volume of 0.9% NaCl sufficient to achieve a 1.25 mg/mL final volume concentration of remdesivir diluted solution
B. <u>Infusion with Syringe</u>
a) Determine the total infusion volume needed to achieve a final infusion volume concentration of 1.25 mg/mL of remdesivir diluted solution based on patient’s calculated dose
b) Select an appropriately sized syringe equal to or larger than the calculated total infusion volume of 1.25 mg/mL remdesivir solution needed
c) Withdraw the required volume of reconstituted remdesivir solution from the vial into the syringe based on patient’s calculated dose, followed by the required volume of 0.9% NaCl needed to achieve a 1.25 mg/mL final volume concentration of remdesivir diluted solution.
d) Gently invert the syringe 20 times to mix the solution in the syringe. Do not shake
</td></tr>
<tr><td>Administration</td><td>
1. Administer the diluted solution with the infusion rate per the chart below
2. After infusion is complete, flush with at least 30 mL of 0.9% NaCl

Recommended Rate of Infusion—Diluted Veklury for Injection Lyophilized Powder in Patients < 40 kg
<table>
<tr><th>Infusion Volume</th><th>Infusion Time</th><th>Rate of Infusion</th></tr>
<tr><td rowspan="3">100 mL</td><td>30 min</td><td>3.33 mL/min</td></tr>
<tr><td>60 min</td><td>1.67 mL/min</td></tr>
<tr><td>120 min</td><td>0.83 mL/min</td></tr>
<tr><td rowspan="3">50 mL</td><td>30 min</td><td>1.67 mL/min</td></tr>
<tr><td>60 min</td><td>0.83 mL/min</td></tr>
<tr><td>120 min</td><td>0.42 mL/min</td></tr>
<tr><td rowspan="3">25 mL</td><td>30 min</td><td>0.83 mL/min</td></tr>
<tr><td>60 min</td><td>0.42 mL/min</td></tr>
<tr><td>120 min</td><td>0.21 mL/min</td></tr>
<tr><td rowspan="3">7 mL</td><td>30 min</td><td>0.23 mL/min</td></tr>
<tr><td>60 min</td><td>0.12 mL/min</td></tr>
<tr><td>120 min</td><td>0.06 mL/min</td></tr>
</table>
</td></tr>
</table>

Table 2. Veklury ® (Remdesivir) Product Specific Preparation and Administration Instructions –*continued*

<table>
<tr><th colspan="2">Remdesivir (5 mg/mL) Solution ≥ 40 kg Patients</th></tr>
<tr><th>Step</th><th>Description</th></tr>
<tr><td>Reconstitution</td><td>None</td></tr>
<tr><td>Dilution</td><td>
1. Remove the required number of single-dose vial(s) from storage. Each vial contains 100 mg/20 mL of remdesivir.
2. Equilibrate to room temperature (20°C to 25°C [68°F to 77°F]). Sealed vials can be stored up to 12 hours at room temperature prior to dilution
3. Remdesivir injection must be diluted in an infusion bag containing 250 mL of 0.9% NaCl only, see below

Recommended Dilution Instructions— Veklury ® Injection (Supplied as Solution in Vial) in Patients ≥ 40 kg
<table>
<tr><th>Veklury ® (Remdesivir) Dose</th><th>0.9% NaCl bag volume to use</th><th>Volume to be withdrawn and discarded from 0.9% NaCl bag</th><th>Required volume of Veklury injection</th></tr>
<tr><td>Loading Dose
200 mg (2 vials)</td><td rowspan="2">250 mL</td><td>40 mL</td><td>40 mL (2 X 20 mL)</td></tr>
<tr><td>Maintenance Dose
100 mgf (1 vial)</td><td>20 mL</td><td>20 mL</td></tr>
</table>
4. Withdraw and discard the required volume of 0.9% NaCl from the bag following instructions using an appropriately sized syringe and needle
5. Withdraw the required volume of remdesivir injection from the vial following instructions outlined above
6. Pull the syringe plunger rod back to fill the syringe with approximately 10 mL of air
7. Inject the air into the remdesivir injection vial above the level of the solution
8. Invert the vial and withdraw the required volume of remdesivir injection solution into the syringe
9. The last 5 mL of solution requires more force to withdraw
10. Transfer the required volume of remdesivir injection to the infusion bag
11. Gently invert the bag 20 times to mix the solution in the bag. Do not shake
</td></tr>
<tr><td>Administration</td><td>
1. Administer the diluted solution with the infusion rate described below
2. After infusion is complete, flush with at least 30 mL of 0.9% NaCl
</td></tr>
</table>

5. **Compatibility:**
    a. Do not administer simultaneously with any other medication. Compatibility with IV solutions and medications other than 0.9% saline is not known. Remdesivir for injection (powder) must be reconstituted with Sterile Water and diluted in 0.9% saline
    b. Remdesivir 5 mg/mL injection must be diluted in 0.9% saline
6. **Pharmacokinetics**:
    a. Peak: active metabolite 3-4 hours
    b. Half-life: prodrug: ~ 1 hour, active metabolite ~ 24 hours
    c. Distribution: Unbound 12.1%; Wide distribution, Poorly crosses blood-brain barrier

d. Metabolism: Prodrug activated by esterases and hydrolase; Active metabolite CYP3A4 substrate, possible CYP2D6, CYP2C8, OAT1b1, and P-gp substrate in vitro

e. Elimination: Renal 63%, biliary 27.8%

7. Monitoring:

a. Vital signs

b. CMP

- Discontinue remdesivir if ALT ≥ 10 time ULN
- Discontinue remdesivir if eGRF < 30 mL/min/1.72m2

c. CBC/diff

d. PT/INR

8. Adverse Events: generally well tolerated

a. ALT/AST increase (onset 5-25 days, resolution 3-4 days)

b. Infusion-related hypotension, Phlebitis

c. Constipation , Dyspepsia, Nausea,

d. Extremity pain, Headache, rare QT prolongation (possible Torsades de pointes risk)

9. Warnings:

a. Pregnancy: only use during pregnancy if the potential benefit justifies the potential risk for the mother and the fetus

b. Hypersensitivity: including infusion-related and anaphylactic reactions

c. Increased risk of transaminase elevations

10. Drug Interactions:

a. CYP450 inhibitors- co-administration is unlikely to result in a clinically significant interaction

b. CYP450 inducers-co-administration should be avoided

c. CYP1A2 and CYP2B6 inducer in vitro- unknown clinical significance

d. Acetaminophen + remdesivir may increase the risk of liver damage, avoid acetaminophen for 15 days post remdesivir completion

References:

1. Tchesnokov EP, Feng JY, Porter DP, Götte M. Mechanism of Inhibition of Ebola Virus RNA-Dependent RNA Polymerase by Remdesivir. Viruses. 2019;11(4):1-16
2. Siegel D, Hui HC, Doerffler E, et al. Discovery and Synthesis of a Phosphoramidate Prodrug of a Pyrrolo[2,1-f][triazin-4-amino] Adenine C-Nucleoside (GS-5734) for the Treatment of Ebola and Emerging Viruses. J Med Chem. 2017;60(5):1648-1661
3. "Covid-19 Drug Interactions." University of Liverpool. http://covid19-druginteractions.org/. Accessed 3/17/2020
4. Brown AJ, Won JJ, Graham RL, et al. Broad spectrum antiviral remdesivir inhibits human endemic and zoonotic deltacoronaviruses with a highly divergent RNA dependent RNA polymerase. Antiviral Res. 2019;169:104541
5. Lo MK, Jordan R, Arvey A, et al. GS-5734 and its parent nucleoside analog inhibit Filo-, Pneumo-, and Paramyxoviruses. Sci Rep. 2017;7(43395):1-7
6. Sheahan TP, Sims AC, Graham RL, et al. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. Sci Transl Med. 2017;9(396)1-10
7. Gordon CJ, Tchesnokov EP, Feng JY, Porter DP, Gotte M. The antiviral compound remdesivir potently inhibits RNA-dependent RNA polymerase from Middle East respiratory syndrome coronavirus. J Biol Chem. 2020;1-14
8. Agostini ML, Andres EL, Sims AC, et al. Coronavirus Susceptibility to the Antiviral Remdesivir (GS-5734) Is Mediated by the Viral Polymerase and the Proofreading Exoribonuclease. mBio. 2018;9(2):1-15
9. Yao X, et al. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Clin Infec Dis. 2020;accepted manuscript. DOI:10.1093/cid/ciaa237
10. Smith EC, Blanc H, Surdel MC, Vignuzzi M, Denison MR. Coronaviruses lacking exoribonuclease activity are susceptible to lethal mutagenesis: evidence for proofreading and potential therapeutics. PLoS Pathog. 2013;9(8):e1003565
11. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res. 2020;30:269-271
12. Jordan PC, Stevens SK, Deval J. Nucleosides for the treatment of respiratory RNA virus infections. Antivir Chem Chemother. 2018;26:1–19
13. De wit E, Feldmann F, Cronin J, et al. Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection. Proc Natl Acad Sci USA. 2020;1-6
14. Sheahan TP, Sims AC, Leist SR, et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nat Commun. 2020;11(1):222
15. Warren TK, Jordan R, Lo MK, et al. Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. Nature. 2016;531(7594):381-5
16. Oh MD, Park WB, Choe PG, et al. Viral Load Kinetics of MERS Coronavirus Infection. N Engl J Med. 2016;375(13):1303-5
17. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med. 2020; DOI: 10.1056/NEJMc2001737
18. Mulangu S, Dodd LE, Davey RT, et al. A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics. N Engl J Med. 2019;381(24):2293-2303
19. Holshue ML, Debolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States. N Engl J Med. 2020;382(10):929-936
20. Al-tawfiq JA, Al-homoud AH, Memish ZA. Remdesivir as a possible therapeutic option for the COVID-19. Travel Med Infect Dis. 2020;101615
21. Remdesivir [EUA Fact Sheet]. Foster City, CA: Gilead Sciences, Inc.; Revised: 10/2020
22. VEKLURY [package insert]. Gilead Sciences, Inc., Foster City, CA; Revised: 10/2020

Helpful Links:

Veklury (Remdesivir) Prescribing Information https://www.remdesivir.com/us/access/ or www.vekluryhcp.com.

Veklury® (remdesivir) Emergency Use for Pediatric Patients

a) Fact Sheet for Healthcare Providers (HCPs) www.gilead.com/remdesivir.
b) Fact Sheet for Parents and Caregivers www.gilead.com/remdesivir.
c) FDA Letter of Authorization available at www.gilead.com/remdesivir.

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