Beth Israel Lahey Health

Pharmacy & Therapeutics Antimicrobial Subcommittee:

**REMDESIVIR (VEKLURY®) GUIDELINES**

***** (note: REMDESIVIR will be released ONLY with ID/AST approval)

Remdesivir is FDA approved for treatment of CoVID 19 in hospitalized patients with moderate to severe disease requiring 02 support. The Emergency Use guidelines only pertain to certain pediatric use (hospitalized pediatric patients 12-17 years of age weighing 3.5 kg to <40 kg OR aged <12 Years and weighing ≥3.5 kg).
**PLEASE NOTE: Remdesivir can be used as a replacement for mab therapy given high rates of BA.2 in patients with mild- moderate disease at high risk for progression/hospitalization. For outpatients however given capacity on weekends, bebtelovimab may be preferred.**
For an external review of remdesivir based on scientific evidence and expert opinion, please visit the NIH guideline review.

**CRITERIA FOR USE (must meet all):**

- Confirmed COVID-19 positive with documented initial PCR+ <7 days
- Symptom onset less than or equal to 7 days (an exception would be patients who are significantly immunocompromised given potential inability to mount symptoms: see appendix)

Further criteria by site

Table 1:

| **Moderate to Severe disease with need for supportive oxygen therapy** | **Mild to Moderate Disease in High Risk Patients (Off Label)** |
|---|---|
| Hospitalized | Not Hospitalized |
| Need for oxygen support via nasal cannula or face mask to maintain O2 saturation greater than 94% | Hospitalized for a primary diagnosis that does not include complications of CoVID 19 |
| | Mild to moderate symptoms, e.g. fever, cough, sore throat, malaise, headache, muscle pain, gastrointestinal symptoms, shortness of breath with exertion, loss of taste/smell<br>PLUS high risk for progression due to one or more risk factors listed below. |
| | • Age ≥60 years<br>• High Risk Body-Mass Index (BMI):<br>  • 25-30 kg/m2 AND not fully vaccinated with primary 1-2 dose series (no vaccination or series completed less than 2 weeks prior)<br>  • >30 kg/m2 regardless of vaccination status<br>• Chronic kidney disease<br>• Diabetes<br>• Pregnancy or 3 months after delivery<br>• Immunosuppressive conditions (at least one):<br>  Autoimmune disease requiring ongoing systemic therapy<br>  HIV with any CD4 count<br>  Asplenia or functional asplenia |

| | |
|---|---|
| | Malignancy or primary immunodeficiency as defined in table 2<br>Taking Immunosuppressive medications as defined in table 2<br>• Cardiovascular disease or hypertension<br>• Chronic lung disease (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)<br>• Sickle cell disease or other hemoglobinopathy<br>• Neurodevelopmental disorders (for example, cerebral palsy), genetic/metabolic syndromes<br>• Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID 19))<br>• Race/ethnicity that is associated with a higher risk of hospitalization or death from COVID-19, including Black or African American, Hispanic or Latinx, American Indian or Alaska Native |

Table 2

| **Moderate-Severely Immunocompromising Health Conditions** |
|---|
| Active treatment for solid tumor and hematologic malignancies Defined as any of the following:<br>• Last treatment within 3 months<br>• Remission of malignancy has not been achieved<br>• Receipt of an immunotherapy such as a checkpoint inhibitor within the last year |
| Receipt of solid organ transplant and taking immunosuppressive therapy |
| Receipt of CAR-T cell or hematopoietic stem cell transplant (within 2 years of transplant or taking immunosuppressive therapy) |
| Moderate or severe primary immunodeficiencies (e.g. DiGeorge syndrome, Wiskott-Aldrich, Common Variable Immunodeficiency or hypogammaglobulinemia requiring immunoglobulin therapy) |
| Advanced (CD4<200 or presence of AIDS-defining illness) or untreated HIV infection |
| Active systemic treatment with any of the following immunosuppressive medications:<br>• Chronic daily corticosteroid use (>10mg prednisone or equivalent daily)<br>• Alkylating agents (e.g., cyclophosphamide)<br>• Antimetabolites (e.g., azathioprine, methotrexate)<br>• Transplant-related immunosuppressive drugs (e.g., cyclosporine, tacrolimus, azathioprine, mycophenolate)<br>• Cancer chemotherapeutic agents classified as severely immunosuppressive<br>• Tumor-necrosis (TNF) blockers (e.g. etanercept, adalimumab, infliximab)<br>• B-cell depleting agents (e.g. rituximab)<br>• Other biologic agents or small molecule inhibitors that are immunosuppressive or immunomodulatory (e.g., IL-1 antagonist, PD-L1, VEGF, EGFR, IL-6, JAK kinase inhibitor) |
| End-stage renal disease necessitating hemodialysis |
| Asplenia or functional asplenia |

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**Exclusion Criteria for treatment of severe disease (at time of request for remdesivir initiation):**

1. O2 sat > 94% RA
2. Non-ICU with improving clinical trajectory (e.g., decreasing oxygen requirement over time prior to RDV)
3. High-Flow oxygen support, mechanical ventilation or ECMO

***Exclusion Criteria for all indications:***

1. Renal failure, particularly progressive and without plan for renal replacement therapy. FDA-approved package insert states "not recommended in patients with eGFR less than 30 mL per minute"*
2. Liver failure, either COVID-related or pre-existing*
3. Active liver injury*
    a. ALT > 200
    b. ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR
4. Comfort measures or similarly non-aggressive goals of care
5. Pregnancy is **NOT** an exclusion

*These are not absolute inclusion/exclusion criteria and can be considered on a case-by-case basis. Complex cases that deviate from ideal risk/benefit scenario may benefit from ID consultation.

**Monitoring Guidelines:**

| **Moderate to Severe disease with need for supportive oxygen therapy** | **Mild to Moderate Disease in High Risk Patients** |
|---|---|
| Laboratory- Daily monitoring of AST/ALT, alk phos, creatinine and prothrombin time. If CrCl falls below 30 mL/min, or if the ALT rises above 5X upper limit of normal (ULN) or 3XULN accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR, the drug should generally be held with a reassessment of labs the next day. A decision to completely stop therapy will depend on the clinical scenario and level of severity of the drug adverse effect. | If feasible, laboratory- Baseline AST/ALT, alk phos, creatinine and prothrombin time (estimated CrCl), however, given the short course and if used in a patient with limited comorbidities, e.g. young pregnant patient, then labs are not strictly required. |
| Clinical - If the patient rapidly improves within 24 hours of initiation to the extent that she/he would no longer qualify for remdesivir, discontinuation should be considered given the risk of adverse events. If a patient has improved to the extent that she/he otherwise can be discharged from the hospital, remdesivir should be discontinued. | Clinical- Outpatient only: observe for signs or symptoms of rare acute hypersensitivity. |

**Adverse effects**

- Nausea
- ALT and AST elevations
- Hypersensitivity
- Increases in prothrombin time
- Infusion reactions

**Significant Drug- Interactions**

The following hepatic enzyme and p-glycoprotein inducers/inhibitors are **not recommended to be co-administered with** RDV due to the **potential decrease/increase in remdesivir drug concentrations**. See COVID 19 drug interactions.

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- Hydroxychloroquine and chloroquine phosphate should not be co-administered with remdesivir as it may result in reduced antiviral activity of remdesivir and/or increased toxicity due to p-gp inhibition.
- Rifamycins - rifampin, rifapentine - rifabutin may be acceptable alternative.
- Certain anticonvulsant medications- carbamazepine, phenobarbital, phenytoin, primidone. Other carbamazepine congeners such as oxcarbazepine may be acceptable.
- Certain non-nucleoside reverse transcriptase inhibitors - efavirenz, etravirine and nevirapine. Other agents in this category, e.g., rilpivirine, doravirine may be acceptable.

**Dosing:**

| Severity of disease | Recommended dosing (IV only) |
|---|---|
| Inpatient, moderate to severe disease requiring supplemental oxygen, | 200mg on day 1, then 100mg daily for **4 days** |
| Inpatient or outpatient, mild to moderate disease not requiring supplemental oxygen but at high risk for disease progression | 200 mg on day 1, then 100 mg daily for **2 days** |

- Extension of therapy beyond a total prescribed durations is not recommended.

If a patient is well enough to be discharged, stop remdesivir therapy and discharge the patient.

**Pregnancy**

The safety of remdesivir in pregnant women is unknown. Human exposure data is limited to a registry of patients receiving the drug for compassionate use. Animal data did not demonstrate a significant risk of fetal demise.

**Breastfeeding**

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. Providers should consider the clinical need for remdesivir vs. any potential adverse effects on the breastfed child from remdesivir or from the underlying maternal condition.

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