# COVID-19 Non-Formulary Overview of Remdesivir, Tocilizumab, and Baricitinib

## 1. COVID-19 Treatment Considerations

a. Parkland Antimicrobial Stewardship subcommittee and Pharmacy &Therapeutics (P&T) Committee approved the following criteria for non-formulary requests based on available literature and guidelines

b. For more detailed information, please refer to the drug monograph for each agent that was presented to P&T, as well as IDSA and NIH guidelines

**Treatment Overview**

| Disease Severity | Agents to Consider |
|---|---|
| Room air | Supportive care |
| Supplemental low-flow oxygen including nasal cannula, venturi mask, non-rebreather | Remdesivir<br>+<br>Dexamethasone *or*<br>Baricitinib (if dexamethasone is contraindicated for use) |
| High-flow nasal cannula (HFNC) or non-invasive ventilation (NIV) including CPAP, BiPAP | Dexamethasone<br>+<br>Tocilizumab (if within 48hrs of HFNC/NIV initiation) *or*<br>Baricitinib |
| Mechanical ventilation (MV) or ECMO | Dexamethasone<br>+<br>Tocilizumab (if within 48hrs of MV/ECMO initiation) |

## 2. Non-formulary Medication Process

a. Remdesivir, tocilizumab, and baricitinib are all non-formulary for COVID-19 indications

b. Providers will enter the non-formulary requests

c. Decentral pharmacist will page the appropriate on-call pharmacist when a non-formulary request is entered

| Time | Drug | On-call Pharmacist |
|---|---|---|
| Weekdays (0700 – 1700) | Remdesivir<br>Tocilizumab<br>Baricitinib | Infectious Diseases Pharmacist |
| Weekdays (1700 – 0700) | Tocilizumab<br>Baricitinib | Weekend/Afterhours Pharmacist |
| Weekends or Holidays (0700 – 1700) | Remdesivir<br>Tocilizumab<br>Baricitinib | Weekend/Afterhours Pharmacist |
| Weekends or Holidays (1700 – 0700) | Tocilizumab<br>Baricitinib | Weekend/Afterhours Pharmacist |

d. If approved, the on-call pharmacist will write a chart note detailing the outcome of their review

e. If approved, decentral pharmacist will process the non-formulary order and schedule administration

f. If the patient doesn't meet criteria, the on-call pharmacist will contact the ordering provider to discuss

g. Concerns about approval decisions can be escalated to Dr. Bonnie Prokesch, Director of Antimicrobial Stewardship

### 3. Approval Criteria

| | Remdesivir | Tocilizumab | Baricitinib |
|---|---|---|---|
| **Dose** | 200 mg IV x1 then, 100 mg IV daily x 4 days or until hospital discharge | Single IV dose<br>• > 90 kg: 800 mg<br>• > 65 and ≤ 90 kg: 600 mg<br>• > 40 and ≤ 65 kg: 400 mg<br>• ≤ 40 kg: 8 mg/kg | 4 mg PO daily x 14 days or until hospital discharge |
| **Approval Criteria** | • Confirmed COVID-19<br>• COVID symptoms ≤ 14 days<br>• Low-flow oxygen | • Confirmed COVID-19<br>• CRP > 7.5 mg/dL<br>• Within 48 hours of commencement of respiratory support (HFNC, NIV, MV, or ECMO)<br>• Received or concurrently receiving corticosteroids | • Confirmed COVID-19<br>• HFNC or NIV<br>• Low-flow oxygen or MV/ECMO only if corticosteroids are contraindicated |
| **Denial Criteria** | • On RA, HFNC, NIV, MV, or ECMO<br>• ALT > 10 x ULN<br>• Symptom onset > 14 days ago | • On RA or low-flow oxygen<br>• AST/ALT > 10 x ULN<br>• Significant immunosuppression, including recent use of other biologic immunomodulating drugs<br>• An uncontrolled, serious bacterial, fungal, or non-SARS-CoV-2 viral infection<br>• ANC < 500 cells/µL<br>• Platelet count < 50,000 cells/µL<br>• Gastrointestinal perforation<br>• Prior hypersensitivity reaction to tocilizumab | • On RA<br>• Previously/concurrent receipt of tocilizumab<br>• Significant immunosuppression, including recent use of other biologic immunomodulating drugs<br>• An uncontrolled, serious bacterial, fungal, or non-SARS-CoV-2 viral infection<br>• ALT or AST > 10 x ULN<br>• ANC < 500 cells/µL or ALC < 200 cells/ µL<br>• Severe acute kidney injury or ESRD (eGFR < 15mL/min) and/or are on dialysis<br>• Prior hypersensitivity reaction to baricitinib |
| **Dose Adjustment** | Not needed; CrCl < 30 ml/min, ESRD, or dialysis does not preclude remdesivir use<br>Discontinue if ALT > 10 x ULN | Not needed | eGFR 30 to 59: 2 mg PO daily<br>eGFR 15 to 29: 1 mg PO daily<br>eGFR <15: discontinue therapy |
| **Monitoring** | Baseline and daily LFTs | Baseline LFTs<br>Hypersensitivity reactions | Baseline and daily LFTs, SCr, CBC with differential<br>Discontinue if ANC < 500 cells/µL, ALC < 200 cells/µL, AST/ALT> 10 x ULN<br>Hypersensitivity reactions |
| **Key Clinical Efficacy Findings** | • Reduced time to recovery by 5 days (RRR 1.29; 95% CI, 1.12–1.49; P < 0.001), only patients on low-flow oxygen subgroup demonstrated significant benefit (ACTT-1)<br>• No difference in 5 versus 10 days duration<br>• No mortality benefit | • 8 RCTs performed, however only 2 RCTs identified a mortality benefit (REMAP, RECOVERY)<br>• Both RCTs had > 80% concurrent steroid use, included critically ill patients with increasing inflammatory markers, and recent commencement of respiratory support | • Baricitinib vs. SOC did not improve time to recovery but did reduce mortality by 38% (HR 0.57; 95% CI 0.41–0.78). NNT to prevent 1 death was 9 in HFO/NIV subgroup vs. 20 in all patients (COV-BARRIER)<br>• Baricitinib + RDV vs. RDV improved time to recovery by 1 day in hospitalized patients. In patients on HFNC or NIV, recovery time was shortened by 8 days, RR 1.51; 95% CI 1.10–2.08 (ACTT-2) |

Abbreviations: ALC, absolute lymphocyte count; ANC, absolute neutrophil count; CI, confidence interval; CRP, C-reactive protein: ESRD, end stage renal failure; ECMO, extracorporeal membrane oxygenation; HFNC, high flow nasal cannula, HR, hazard ratio; MV, mechanical ventilation; LFT, liver function tests, NIV, non-invasive ventilation; RDV, remdesivir; RA, room air; RCT, randomized controlled trial, RR, rate or risk ratio; RRR, rate ratio for recovery; SOC, standard of care; ULN, upper limit of normal