CovenantHealth

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CHS COVID-19 THERAPEUTICS POLICY
Pharmacy & Therapeutics Committee

BACKGROUND:
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (Covid-19), which is most frequently mild but can be severe and life-threatening. Only one agent, remdesivir, has been FDA approved for the treatment of Covid-19. However, the scientific literature is rapidly evolving with a number of investigational agents and drugs approved for other indications under clinical trial evaluation. As this data emerges, the National Institutes of Health (NIH) and the Infectious Diseases Society of America (IDSA) are publishing evidence-based guidance to support clinicians in their decisions about treatment of patients with Covid-19.

PURPOSE:
This document was developed by the Pharmacy & Therapeutics committee to:

- promote adherence to NIH treatment guidelines
- outline CHS P&T approved Covid-19 therapy

This document does not cover ALL treatment modalities. It is neither an attempt to substitute for the practice of medicine nor as a substitute for the provision of any medical professional services.

NIH PHARMACOLOGIC MANAGEMENT BASED ON DISEASE SEVERITY:
The figure below summarizes the updated recommendations by the NIH COVID-19 Treatment Guidelines Panel. CHS P&T suggest clinicians use this as a framework for initiation of pharmacologic agents for the treatment of Covid-19.

CHS SPECIFIC PHARMACOLOGIC TREATMENT GUIDANCE FOR COVID-19:
The following agents have been evaluated by the P&T committee as potential options for the treatment of Covid-19. Listed are the criteria for use or non-use. Agents which have been deemed not to best serve the health interests of our patient population are designated as non-formulary.

ANTIVIRAL THERAPY
Remdesivir

- Dose: 200mg IV loading dose followed 100mg IV daily x 4 days (or until hospital discharge)
- Criteria for use:
    - Hospitalized patient (>12 years of age) with confirmed SARS-CoV-2
    - Requiring supplemental oxygen
    - If known, time since symptom onset ≤ 10 days
- Exclusions:
    - AST/ALT > 10 x ULN
    - CrCl < 30 ml/min
- Use requiring Infectious Diseases/Intensivist approval:
    - Extended treatment up to 10 days
    - Treatment for patients not on supplemental oxygen (i.e. high risk for clinical deterioration)
    - Treatment for patients with >10 days of symptoms
    - Treatment for patients mechanically ventilated or extracorporeal membrane oxygenation (ECMO)
    - Emergency use authorization for hospitalized pediatric patients <12 years old or weighing 3.5-40kg

Hydroxychloroquine ± azithromycin

- Use is NOT recommended
- Randomized controlled trials have not demonstrated a clinical benefit over standard of care alone, and the risk of adverse effects was significantly greater
- Azithromycin is not proven as an adjunctive treatment with HCQ for COVID-19, and may increase the likelihood of prolonged QTc and arrhythmias
- All orders will be considered non-formulary and are subject to non-formulary standard operating procedure

Lopinavir/ritonavir

- Use is NOT recommended
- Randomized controlled trials have not demonstrated a clinical benefit
- All orders will be considered non-formulary and are subject to non-formulary standard operating procedure

Ivermectin

- Standard helminth dose: 200 mcg/kg x 1 (no approved dose for COVID-19)
- NIH guidelines recommend against use, except in context of clinical trial
- Ivermectin plasma concentrations attained with dosages recommended for treatment of parasitic infections are substantially lower than concentrations associated with in vitro inhibition of SARS-CoV-2
    - Pharmacokinetic modeling predicts achieving the plasma concentrations necessary for the antiviral efficacy detected in vitro would require administration of doses up to 100-fold higher than those approved for use in humans
    - The ICON study, a retrospective cohort study of 280 patients in 4 Florida hospitals found a significant reduction in mortality in patients treated with ivermectin 200 mcg/kg vs usual care
        - Caution: in the unmatched cohort, a larger portion of patients in the usual care arm received hydroxychloroquine and/or azithromycin; and less patients received corticosteroids in the usual care arm despite similar severity of illness (propensity score matched analysis revealed similar benefit). Larger RCT needed to validate findings.
- Safety and efficacy has been established for helminth infections; however, there is little evidence to suggest ivermectin is effective for treatment of COVID-19
- Ivermectin is relatively non-cost prohibitive, has a good safety profile, and has suggestive information that it may be beneficial
- Until well designed RCT data is available, we do not endorse the routine use of ivermectin. Prescribers should determine appropriateness on a case-by-case basis. Pharmacy will ensure dosing does not exceed 200 mcg/kg.

ANTIBIOTICS
Routine empiric antibiotics are NOT recommended.

- Unnecessary antibiotic use increases the risk of multi-drug resistant organisms and C.difficile infections
- If empiric antibiotics are given, recommend targeting common CAP pathogens
    - For patients who can tolerate oral therapy, transition from IV to PO as soon a clinically appropriate
    - Recommended duration is 5 days. May discontinue if concern for bacterial pneumonia is low (i.e. confirmation of COVID-19, classic presentation, PCT<0.25)

CORTICOSTEROIDS

Dexamethasone

- Dose: 6mg IV/PO daily x 10 days (or until hospital discharge)
- Criteria for use:
    - Requiring supplemental oxygen, mechanical ventilation, or ECMO
- Exclusion:
    - Patients not receiving supplemental oxygen
        - RCT data did not demonstrate benefit in this population, and some observational data suggest an association with increased risk of mortality
- Alternative corticosteroids if dexamethasone is not available
    - Prednisone 40 mg oral or IV solumedrol 30mg

Inhaled corticosteroids (i.e. budesonide)

- Use is NOT recommended
- No clinical evidence supporting adverse or beneficial effects of premorbid use or continued administration of inhaled corticosteroids in patients with COVID-19. Randomized controlled clinical studies are needed to assess the benefits of inhaled corticosteroids in patients with and without chronic respiratory conditions
- Exception: Patients requiring ICS therapy for their asthma or COPD have real risk for harm (severe exacerbations) if they stop treatment. NIH guidelines recommend ICS used daily for the management of asthma and COPD to control airway inflammation should not be discontinued in patients with COVID-19
- The over prescribing of ICS has placed a large burden on our respiratory therapists and has been a large expenditure for pharmacy
- All orders (with exception for asthma/COPD) will be considered non-formulary and are subject to non-formulary standard operating procedure

IMMUNE-BASED THERAPY

Convalescent plasma

- Available under FDA emergency use authorization
- NIH—insufficient data to recommend either for or against use. Convalescent plasma should not be considered the standard of care.
- Requires ID consultation/approval
    - Hospitalized patients with SARS-CoV-2 infection should be rapidly evaluated and providers should strongly consider offering an opportunity to enroll into randomized clinical trials prior to empiric treatment with convalescent plasma, as some clinical trials exclude concomitant use of convalescent plasma

SARS-CoV-2-specific monoclonal antibodies

- Not commercially available
- See clinical trials section below
- Requires ID consultation for trial eligibility

OTHER IMMUNOMODULATOR THERAPY

Interleukin-6 inhibitors (i.e. tocilizumab, sarilumab)

- Use is NOT recommended
- Randomized, controlled trials failed to demonstrate efficacy
- All orders will be considered non-formulary and are subject to non-formulary standard operating procedure

Interleukin-1 inhibitors (i.e anakinra)

- Use is NOT recommended
- There are case series data but NO clinical trial data on the use of IL-1 inhibitors in patients with COVID-19
- All orders will be considered non-formulary and are subject to non-formulary standard operating procedure

Kinase inhibitors (i.e. BTK inhibitors and JAK inhibitors)

- NIH–Ongoing clinical trials should help clarify their role in the treatment of COVID-19
- See clinical trials section below
- BTK inhibitor (zanubrutinib) use requires ID consultation for trial eligibility
- JAK inhibitors will be considered non-formulary and are subject to non-formulary standard operating procedure

CHS COVID-19 CLINICAL TRIALS:
Contact local principal investigator or study team for guidance regarding enrollment

REGENERON 2066
Anti-spike SARS-COV-2 monoclonal antibodies

- Phase 2/3 trial, plans to enroll 1350 patients
- Principal investigator(s): Dennis Duriex, MD, Prakash Shrestha, MD
- Eligibility criteria:
    - Adult ≥ 18 years of age who provides informed consent
    - SARS-CoV-2-positive test result ≤ 72 hours prior to randomization
        - Outside record acceptable
    - Symptoms consistent w/ COVID-19, onset ≤ 10 days before randomization
    - Hospitalized for ≤ 72 hours AND;
        - Maintains O2 saturation >93% on low-flow oxygen via nasal cannula, simple face mask, or other similar device
- Exclusion: convalescent plasma or IVIG in the past 5 months or plan to receive during the study period

ZANUBRUTINIB (BGB-3111)
Bruton tyrosine kinase (BTK) inhibitor

- Phase 2 trial, plans to enroll 52 patients
- Principal investigator(s): Dennis Duriex, MD
- Eligibility criteria:
    - Adult ≥ 18 years of age who provides informed consent
    - SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR)
    - Radiographic evidence of pulmonary infiltrates
    - Requires supplemental oxygen for pulmonary distress, and has been on supplemental oxygen for no more than 48 hours
      –OR-
    - On mechanical ventilation for ≤ 24 hours from the time of screening
- Exclusion: planned or concurrent use of tocilizumab