STRAC ID Leads Outpatient Strategies for COVID-19 Infection
Updated: August 4, 2021

- This is a summary of recommendations from STRAC ID Leads for outpatient management of COVID-19.
- There are no oral FDA-approved or authorized therapies for COVID-19.
- NIH and Infectious Diseases Society of America (IDSA) guidelines do not recommend non-FDA authorized or approved therapies for COVID-19 outside of a clinical trial.

Recommended by ID Leads

- **Isolation** – Persons diagnosed with COVID-19 should isolate at home
  - For mild to moderate disease, CDC recommends discontinuing isolation 10 days after the onset of symptoms and resolution of fever for at least 24 hours without the use of fever-reducing medications.
  - For severe disease (requiring hospitalization), CDC recommends discontinuing isolation 20 days after the onset of symptoms and resolution of fever for at least 24 hours without the use of fever-reducing medications; for immunosuppressed persons and those requiring intubation isolation should be continued for 28 days.
  - For asymptomatic persons, isolation for 10 days after the first positive test for SARS-CoV-2 is recommended.


- **General Recommendations**
  - Nutrition/hydration
  - Adequate sleep
  - Stop/limit smoking and vaping
  - Limit alcohol use
  - Acetaminophen or ibuprofen for fever

- **Equipment**
  - Thermometer
  - Pulse oximeter
  - Home blood pressure cuff

- **Warning Signals Warranting Presentation to Health Care Setting for Evaluation**
  - Oxygen saturation <94% at rest
  - Significant desaturation into 85% range upon walking
  - Persistent shortness of breath
  - Persistent fever
  - Decrease in mental status (e.g., confusion, lethargy)
• Significant decrease in blood pressure

• **Monoclonal Antibodies**
  • FDA authorized (under EUA) [https://www.fda.gov/media/145611/download](https://www.fda.gov/media/145611/download)
    ▪ Casirivimab and imdevimab (REGN-COV, Regeneron)
  • **Treatment** (within 10 days of onset)
    ▪ Mild to moderate COVID-19 disease
    ▪ in adult and pediatric patients (12 years of age and older weighing at least 40 kg)
    ▪ with positive results of direct SARS-CoV-2 viral testing,
    ▪ who are at high risk for progression to severe COVID-19, including hospitalization or death

• **Limitations of Authorized Use**
  • *Not* authorized for use in patients who:
    • Are hospitalized due to COVID-19
    • Require oxygen therapy due to COVID-19
    • Require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity
  • Monoclonal antibodies may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

• **Criteria for identifying high risk individuals for monoclonal antibody administration:**
  The following medical conditions or other factors may place adults and pediatric patients (age 12-17 years and weighing at least 40 kg) at higher risk for progression to severe COVID-19:
  • Older age (for example, age ≥65 years of age)
  • Obesity or being overweight (for example, BMI >25 kg/m², or if age 12-17, have BMI ≥85th percentile for their age and gender based on CDC growth charts, [https://www.cdc.gov/growthcharts/clinical_charts.htm](https://www.cdc.gov/growthcharts/clinical_charts.htm))
  • Pregnancy
  • Chronic kidney disease
  • Diabetes
  • Immunosuppressive disease or immunosuppressive treatment
  • Cardiovascular disease (including congenital heart disease) or hypertension
  • Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
  • Sickle cell disease
  • Neurodevelopmental disorders (for example, cerebral palsy)
  • Or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
  • Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19)
• Other factors may place individual patients at high risk for progression to severe COVID-19 and the EUA is not limited to the medical conditions or factors listed above.

Not Recommended

• Oral corticosteroids – not recommended in outpatients not on oxygen for COVID-19
  o RECOVERY trial showed benefit for hospitalized pts requiring supplemental oxygen.
  o Hospitalized pts who did not require oxygen had worse clinical outcomes on steroids


Often Recommended by ID Leads

• Zinc lozenges
  o Antiviral activity
  o Can decrease duration/severity of common cold
  o Well-tolerated
  o High doses over long term – GI side effects, copper deficiency


• Vitamin D
  o Important for immune function and an Immune modulator
  o Vitamin D deficiency associated with worse outcomes
  o Vitamin D supplementation can protect against acute (non-COVID) respiratory infection
  o Supplementation in hospitalized COVID-19 pts – no difference in LOS, intubation, death
  o Consider especially for those at risk for deficiency
    ▪ Elderly
    ▪ Persons with melanin-rich skin
    ▪ Persons with no or limited sun exposure
  o Dose of 2000 IU daily

https://www.thelancet.com/journals/landia/article/PIIS2213-8587%2820%2930183-2/fulltext

https://www.covid19treatmentguidelines.nih.gov/therapies/supplements/vitamin-d/
Melatonin
- Antioxidant and anti-inflammatory
- Production decreased in older adults
- Good safety profile
- Reasonable dose is 3 mg nightly which is easily found in tablet form
- If a smaller dose is needed due to morning grogginess, use the liquid form at 0.3 mg nightly


Sometimes Recommended by ID Leads
Fluvoxamine
- SSRI that is an immunomodulator
- Potential mechanisms
  - Sigma-1 activation – reduces cytokine production
  - Inhibits sphingomyelinase, relevant for viral entry
  - Inhibits hyperactivation of platelets and mast cells
  - Inhibits metabolism of melatonin
  - Good safety profile
  - Inexpensive and widely available
  - Positive Phase 2 study in outpatients; Dose 100 mg TID
  - Primary endpoint – clinical deterioration, N=152 outpatients
  - 0% (0/80) in fluvoxamine group vs 8.3% (6/72) in the placebo group. 5/6 to hospital; 4 hospitalized; P=0.009
  - SAEs – 1 in fluvoxamine group (hospitalization for dehydration) vs. 6 in placebo group
  - Dose 50 mg twice daily
  - 0/65 pts on fluvoxamine hospitalized; 0/65 residual sx
  - 6/48 (12/5%) on observation hospitalized; 29/48 (60%) residual sx
- Phase 3 trial underway. Pts can be referred to trial https://stopcovidtrial.wustl.edu/ Dose 100 mg twice daily
• **Inhaled budesonide**
  - Small study, n=146
  - Early administration of inhaled budesonide reduced the likelihood of needing urgent medical care and reduced time to recovery after early COVID-19.

• **Famotidine**
  - Histamine-2 receptor antagonist may modulate cytokine storm
  - Positive preliminary studies warrant further investigation
  - Good safety profile
  - Would not exceed approved dose of 40 mg daily

• **Self-proning**
  - May be used in cooperative patients who have mild desaturation and are comfortable in prone position
  - Benefit usually noticed within 5-10 minutes
  - Usual interval 30-120 minutes
  - Sequence: prone, left lateral decubitus, right lateral decubitis, upright sitting
  - Only maintain if comfortable for patient
  - Avoid with pregnancy, spinal instability, face or neck trauma, hemoptysis

**No Recommendation**

• **Ivermectin**
  - Recent meta-analysis showed improved mortality but two large studies in analysis had flawed data, and without them, no benefit
  - Good safety profile
  - Some concerns about neurotoxicity in inflammatory phase (due to decrease in BBB)
  - Animal preparations should not be used in humans
• **Aspirin (ASA)**
  - Preliminary observational study showed less complications in hospitalized patients who had received ASA within 24 hours of admission or 7 days prior to admission
  - Risk of bleeding
  - Avoid in children due to Reye’s Syndrome
  

• **Nasal irrigation with 1% povidone-iodine**
  - Iodine should not be used in thyroid conditions or pregnancy
  - User must be competent in using irrigation device, including proper cleaning


• **Probiotic *Lactobacillus rhamnosus***
  - Some evidence to suggest immunomodulatory effect in sepsis
  - Clinical trial ongoing in COVID-19

  [https://sites.duke.edu/protectehc/about-our-study/](https://sites.duke.edu/protectehc/about-our-study/)

**Not Recommended Until More Information is Available**

• **Colchicine**
  - Preliminary positive study in hospitalized patients
  - Side effects: GI (diarrhea, nausea/vomiting, abdominal pain), muscle weakness, numbness/tingling, allergic reaction

  - Additional Information:
    - COLCORONA Study
    - [https://www.medrxiv.org/content/10.1101/2021.01.26.21250494v1.full.pdf](https://www.medrxiv.org/content/10.1101/2021.01.26.21250494v1.full.pdf)
    - Dose 0.5 mg BID x 3 days and once daily thereafter for total of 30 days
    - Study in non-hospitalized pts. Primary endpoint death or hospitalization
    - COVID dx by PCR or clinical criteria, N=4488
    - Death or hospitalization decreased 1% (4.7% vs 5.8%; OR 0.79, p 0.08)
    - PCR confirmed Covid, N=4159
    - Death or hospitalization decreased 1.4% (4.6% vs 6.0%, p 0.04)
    - Diarrhea more common in the colchicine group (13.7% vs 7.3%, p 0.0001)
    - Pulmonary embolism more common in the colchicine group 0.5% vs. 0.1%, **11 vs 2 pts**, p 0.01
Generic colchicine no longer available; based on our sources 30 days of colchicine costs ~$250

Not Recommended

- **Hydroxychloroquine**
  - Multiple well-conducted studies show negative results
  - Side effects – GI and prolonged QT interval
  
  Saag MS. Misguided use of hydroxychloroquine for COVID-19. Jour Amer Med Assoc Published online November 9, 2020

- **Azithromycin and Doxycycline**
  - Studies largely done with hydroxychloroquine
  - Well-conducted trials have been negative
  - Unnecessary use contributes to antimicrobial resistance
  - Side effects – prolonged QT interval, GI, *C. difficile* colitis

- **Vitamin C**
  - Antioxidant and anti-inflammatory
  - Studied in sepsis with variable outcomes
  - Few safety concerns
  - COVID-19 studies have been IV doses in hospitalized patients
  - Clinical trials ongoing


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