STRAC ID Leads Outpatient Strategies for COVID-19 Infection

Updated: December 30, 2021

- This is a summary of recommendations from STRAC ID Leads for outpatient management of COVID-19. It reflects consensus opinion and overview of treatment options from a group of ID specialists in San Antonio. It is not meant to be an exhaustive or comprehensive review. Prescribers should review information for health care professionals about each product where available. Decisions about individual patient care should be managed by patients' physicians or providers according to individual medical needs. This document is not a substitute for advice from a personal health care provider.
- NIH and Infectious Diseases Society of America (IDSA) guidelines do not recommend non-FDA authorized/approved therapies for COVID-19 outside of a clinical trial.

Recommended by ID Leads

- Isolation – Persons diagnosed with COVID-19 should isolate at home
  - CDC updated isolation and quarantine guidelines on December 27, 2021
  - https://www.cdc.gov/media/releases/2021/s1227-isolation-quarantine-guidance.html
  - If you test positive for COVID-19 – Isolate
    - Stay home for 5 days
    - If you have no symptoms or your symptoms are resolving after 5 days, you can leave your house
    - Continue to wear a mask around others for an additional 5 days
  - For those with severe disease (requiring hospitalization), 20 days of isolation should be considered and for those who are immunosuppressed, longer isolation times may be warranted.
- 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

Locating Therapeutics – to check on availability of limited therapeutic agents, see DSHS link belowL
https://dshs.texas.gov/coronavirus/healthprof.aspx#thera

- Monoclonal Antibodies (mAbs)
- Patient Prioritization for Treatment The Panel prioritized the following risk groups for anti-SARS-CoV-2 mAb therapy based on 4 key elements: age, vaccination status, immune status, and clinical risk factors. The groups are listed by tier in descending order of priority.

Tier Risk Groups for Monoclonal Antibodies (NIH priority groups – see link below)
Tier 1

- Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (see Immunocompromising Conditions below); *or*
- Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors).

Tier 2

- Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors)

Tier 3

- Vaccinated individuals at high risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors)

Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.

Tier 4

- Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged <65 with clinical risk factors)

Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.

Reference:

- *Patient Prioritization for Outpatient Anti-SARS CoV-2 Therapies or Preventive Strategies When There Are Logistical or Supply Constraints*.

- For a list of risk factors, see the CDC webpage Underlying Medical Conditions Associated with High Risk for Severe COVID-19.

    - The previously used mAbs do not have substantial activity against the omicron variant and are not currently recommended. These are:
        - Casirivimab and imdevimab (REGEN-COV, Regeneron) and
        - Bamlanivumab and estevimab (Lilly)
    - FDA authorized (under EUA) and recommended for use with omicron prevalence:
        - Sotrovimab - https://www.fda.gov/media/149534/download
    - Treatment for
        - 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)
- 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 medical conditions or factors (such as race or ethnicity) 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. For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the CDC website: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html
- Circulating SARS-CoV-2 viral variants may be associated with resistance to monoclonal antibodies. Healthcare providers should review the Antiviral Resistance information in Section 15 of this Fact Sheet for details regarding specific variants and resistance, and refer to the CDC website (https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variantproportions.html) as well as information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions. Sotrovimab may only be administered in settings in which healthcare providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

- FDA-authorized (EUA) for ***pre-exposure*** prophylaxis: tixagevimab/cilgavimab (Evusheld) https://www.fda.gov/media/154701/download
    - in adults and pediatric individuals (12 years of age and older weighing at least 40 kg)
    - Note: Efficacy of Evusheld against the omicron variant is not known.
    - ***Pre-exposure prophylaxis*** for those:
        - Who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination or
        - For whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID19 vaccine component(s).
    - Dosage and Administration
        - Injection: • tixagevimab 150 mg/1.5 mL (100 mg/mL) in a single-dose vial. (3) • cilgavimab 150 mg/1.5 mL (100 mg/mL) in a single-dose vial.
    - Limitations of Authorized Use
        - Evusheld is not authorized for use in individuals:

  o For treatment of COVID-19, or
  o For post-exposure prophylaxis of COVID-19 in individuals who have been exposed to someone infected with SARS-CoV-2.

• Pre-exposure prophylaxis with Evusheld is not a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended. Individuals for whom COVID-19 vaccination is recommended, including individuals with moderate to severe immune compromise who may derive benefit from COVID-19 vaccination, should receive COVID-19 vaccination.
• In individuals who have received a COVID-19 vaccine, EVUSHELD should be administered at least two weeks after vaccination.

- Warnings and Precautions
    - Hypersensitivity Including Anaphylaxis: Serious hypersensitivity reactions, including anaphylaxis, have been observed with IgG1 monoclonal antibodies like Evusheld. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy. Clinically monitor individuals after injections and observe for at least 1 hour.
    - Clinically Significant Bleeding Disorders: As with any other intramuscular injection, Evusheld should be given with caution to individuals with thrombocytopenia or any coagulation disorder.
    - Cardiovascular Events: A higher proportion of subjects who received Evusheld versus placebo reported myocardial infarction and cardiac failure serious adverse events. All of the subjects with events had cardiac risk factors and/or a prior history of cardiovascular disease, and there was no clear temporal pattern. A causal relationship between EVUSHELD and these events has not been established. Consider the risks and benefits prior to initiating EVUSHELD in individuals at high risk for cardiovascular events, and advise individuals to seek immediate medical attention if they experience any signs or symptoms suggestive of a cardiovascular event.
- Adverse Reactions
    - Most common adverse events (all grades, incidence ≥3%) are headache, fatigue, and cough.

Not Recommended

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

The Recovery Collaborative Group. Dexamethasone in Hospitalized Patients with Covid-19. New Eng J Med, 2020. doi:10.1056/NEJMoa2021436.

Recommended in certain conditions

- Nirmatrelvir/ritonavir (Paxlovid) –FDA-authorized (EUA) oral antiviral for treatment of COVID-19 https://www.fda.gov/media/155050/download
    - For the treatment of mild-to-moderate coronavirus disease (COVID-19)
    - in adults and pediatric patients (12 years of age and older weighing at least 40 kilograms or about 88 pounds)
        - with positive results of direct SARS-CoV-2 testing,
        - and who are at high risk for progression to severe COVID-19, including hospitalization or death.
    - Paxlovid is available by prescription only
    - and **should be initiated as soon as possible after diagnosis of COVID-19** and ***within five days of symptom onset***.
    - Not recommended in pts with severe kidney or liver impairment.
    - Limitations of authorized use
        - Paxlovid is not authorized for
            - initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19
            - use as pre-exposure or post-exposure prophylaxis for prevention of COVID-19.
            - use for longer than 5 consecutive days.
    - Dosage and Administration
        - Paxlovid is nirmatrelvir tablets co-packaged with ritonavir tablets. Nirmatrelvir must be co-administered with ritonavir.
        - Initiate Paxlovid treatment as soon as possible after diagnosis of COVID-19 and within 5 days of symptom onset.
        - Dosage: 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet), with all three tablets taken together twice daily for 5 days. (2.1)
    - Contraindications
        - history of clinically significant hypersensitivity reactions [e.g., toxic epidermal necrolysis (TEN) or Stevens-Johnson syndrome] to its active ingredients (nirmatrelvir or ritonavir) or any other components of the product.
        - with drugs that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions
          • Alpha1-adrenoreceptor antagonist: alfuzosin
          • Analgesics: pethidine, piroxicam, propoxyphene
          • Antianginal: ranolazine
          • Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine
          • Anti-gout: colchicine
          • Antipsychotics: lurasidone, pimozide, clozapine
          • Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine

• HMG-CoA reductase inhibitors: lovastatin, simvastatin
• PDE5 inhibitor: sildenafil (Revatio®) when used for pulmonary arterial hypertension (PAH)
• Sedative/hypnotics: triazolam, oral midazolam

- Paxlovid is contraindicated with drugs that are potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance. Paxlovid cannot be started immediately after discontinuation of any of the following medications due to the delayed offset of the recently discontinued CYP3A inducer
  • Anticancer drugs: apalutamide
  • Anticonvulsant: carbamazepine, phenobarbital, phenytoin
  • Antimycobacterials: rifampin
  • Herbal products: St. John's Wort (hypericum perforatum)

- Warnings and Precautions
  - The concomitant use of Paxlovid and certain other drugs may result in potentially significant drug interactions. Consult the full prescribing information prior to and during treatment for potential drug interactions.
  - Hepatotoxicity: Hepatic transaminase elevations, clinical hepatitis, and jaundice have occurred in patients receiving ritonavir.
  - HIV-1 Drug Resistance: Paxlovid use may lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.

Molnupiravir (Lagevrio)– FDA-authorized (EUA) oral antiviral for COVID-19
https://www.fda.gov/media/155054/download

- For the treatment of mild-to-moderate disease in adults
  - With positive results of direct SARS-CoV-2 viral testing, and
  - Who are at high-risk for progression to severe COVID, including hospitalization or death, and
  - For whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.
- Limitations on Authorized Use
  - Molnupiravir is not authorized for use in patients who are less than 18 years of age.
  - Molnupiravir is not authorized for initiation of treatment in patients requiring hospitalization due to COVID-19.
  - Benefit of treatment with molnupiravir has not been observed in subjects when treatment was initiated after hospitalization due to COVID-19.
  - Molnupiravir is not authorized for use for longer than 5 consecutive days.
  - Molnupiravir is not authorized for use as pre-exposure or as post-exposure prophylaxis for prevention of COVID-19.

- Dosage and Administration – Available by prescription only
  - 800 mg (four 200 mg capsules) po every 12 hours
  - Take monulpiravir asap after diagnosis of COVID-19, and within 5 days of onset.
- Warnings/Precautions
  - Embryo-Fetal Toxicity: Molnupiravir is not recommended for use during pregnancy.
  - Bone and Cartilage Toxicity: Molnupiravir is not authorized for use in patients less than 18 years of age because it may affect bone and cartilage growth.

- Fluvoxamine – submitted for FDA EUA.
  - Support includes - Two positive RCTs and a positive observational study
  - 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
    - Side effects include nausea, which can be mitigated by taking with food
    - Inexpensive and widely available
  - Lenze EJ, Mattar C, Zorumski CF et al. Fluvoxamine vs. placebo and clinical deterioration with symptomatic COVID-19. JAMA Published online November 12, 2020.
    - 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
  - Seftel D, Boulware D. Prospective cohort of fluvoxamine for early treatment of coronavirus disease 19. Open Forum ID 2021;8(2) ofab050 https://doi.org/10.1093/ofid/ofab050 1 Feb 2021
    - 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
  - NIH multicenter outpatient study underway
    - One option is fluvoxamine dosed 50 mg twice daily x 10 days
    - https://activ6study.org

Often Recommended by ID Leads

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

Prasad AS, Fitzgerald JT, Bao B, Beck FWJ, Chandrasekar PH. Duration of symptoms and plasma cytokine levels in patients with the common cold treated with zinc acetate. Ann Intern Med 2000;133:245-252.

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

Mitchell F. Vitamin-D and COVID-19: do deficient risk a poorer outcome? The Lancet Diabetes and Endocrinology. 2020;8(7):570.
https://www.thelancet.com/journals/landia/article/PIIS2213-8587%2820%2930183-2/fulltext
Jain A, Chaurasia, Sengar NS, Singh M, Mahor S, Narain. Analysis of vitamin D level among asymptomatic and critically ill COVID-19 patients and its correlation with inflammatory markers. Nature Research 2020;10:20191.
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

Hardeland R. Melatonin and inflammation: story of a double-edged blade. J Pineal Res. 2018;65(4):e12525.
Silvestri M, Rossi GA. Melatonin: its possible role in the management of viral infections: a brief review. Ital J Pediatr. 2013;39:61.
Cross KM et al. Melatonin in early treatment for COVID-19: A narrative review of current evidence and possible efficacy. Endocrine Practice 2021
https://doi.org/10.1016/j.eprac.2021.06.001

Sometimes Recommended by ID Leads

- Remdesivir in non-hospitalized patients.
  - Consider especially in immunocompromised patients
  - https://www.natap.org/2021/HIV/120321_01.htm (RCT PINETREE Study)
  - Published in NEJM – Early remdesivir to prevent progression to severe COVID-19 in outpatients. https://www.nejm.org/doi/full/10.1056/NEJMoa2116846
  - Regimen: 200 mg day 1, 100 mg days 2 and 3 in first 7 days of illness
  - Treatment resulted in
    - 87% reduction in hospitalization or death
    - 81% reduction in COVID-19 medically attended visits
  - ***Consider in setting of limited mAb or oral antiviral supply***

- NIH multicenter outpatient study
  - https://activ6study.org 210/567-5262 or 210/488-8054
    (site PI Thomas Patterson, MD, UT Health SA)
    - Criteria: >/= 30 yrs old
    - Tested positive for COVID-19 within past 10 days
    - Have at least 2 COVID-19 symptoms for 7 days or less
  - Treatment arms
    - Fluvoxamine, inhaled fluticasone, ivermection
    - Pts can choose to decline an arm
    - Medications shipped to patient

- Inhaled budesonide
  - Ramakrishnan S et al. Inhaled budesonide in the treatment of early COVID-19: a phase 2, open label, RCT. Lancet Respiratory Medicine 2021;9(7):763-772. April 09, 2021 DOI:https://doi.org/10.1016/S2213-2600(21)00160-0
    - Dose used: 2 inhalations twice daily until symptoms resolved.
    - 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

  Mather JF, Seip RL, McKay RG. Impact of famotidine use on clinical outcomes of hospitalized patients with COVID-19. Am J Gastroenterol 2020

- 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

  Telias I, Katira BH, Brochard L. Is the prone position helpful during spontaneous breathing in patients with COVID-10? Jour Amer Med Assoc 2020;323:22:2265-2267.

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

  Rajter JC, Sherman MS, Fatteh N, Vogel F, Sacks J, Rajter J. Use of ivermectin is associated with lower mortality in hospitalized patients with coronavirus disease 2019. Chest: Oct. 12, 2020.
  Hill A et al. Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection. Open Forum ID ofab358 https://doi.org/10.1093/ofid/ofab358 6 July 2021

- 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

  Chow JH, Khanna, AK, Kethireddy, S, et al. Aspirin Use is Associated with Decreased Mechanical Ventilation, ICU Admission, and In-Hospital Mortality in Hospitalized Patients with COVID-19 Anesthesia & Analgesia Pub ahead of print: Oct. 21, 2020

- 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 Farrell NF et al. Benefits and safety of nasal saline irrigations in a pandemic—washing COVID-19 away. JAMA Otolaryngology-Head & Neck Surgery. 2020;146;787

- 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/

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

  Deftereos SG, Giannopoulos G, Vrachatis DA et al. Effect of colchicine vs. standard care on cardiac and inflammatory biomarkers and clinical outcomes in patients hospitalized with coronavirus disease. JAMA Network Open 2020:3(6):e2013136
  - Additional Information:
    - COLCORONA Study
    - 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

NIH Guidelines https://www.covid19treatmentguidelines.nih.gov/
https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/
Updated December 23, 2021

IDSA Guidelines https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/
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