AdventHealth Treatment Algorithm for Non-hospitalized Adults with COVID-19

Last Updated: 01/26/2023

For the management of hospitalized patients with COVID-19, refer to the AH Treatment Algorithm for Hospitalized Adults with COVID-19

For management of pediatrics patients (age <12 years or weight<40 kg), refer to AdventHealth Clinical Pediatric Treatment Algorithm

Table of Contents

Therapeutic Options for COVID-19 Treatment, Non-hospitalized

Due to severely limited supply, most of these agents are being distributed via allocation from the state departments of health and are not widely available at this time.

For patients with mild to moderate COVID-19 who are at high risk of progression to severe or critical COVID-19, the following therapeutics are recommended based on efficacy and side effect profile (in order of preference):

1. Nirmatrelvir with ritonavir (Paxlovid)
2. Remdesivir (3-day course, where operationally feasible)
3. Molnupiravir

Factors to consider in selecting the best treatment option for a specific patient:

- Clinical efficacy
- Regional prevalence of the Omicron variant
- Availability of therapeutic agent and staff
- Feasibility
- Potential for significant drug-drug interactions

Outpatient Therapies in Order of Preference

Treatment	Time from Symptom Onset	Route(s)	Number of Doses	Variant Activity
Preferred:				
Nirmatrelvir with ritonavir (Paxlovid)	≤5 days	Oral	10 (5 days)	Delta: Yes Omicron: Yes Omicron Subvariants (e.g., BQ.1, BQ.1.1): Yes
Remdesivir (where operationally feasible)	≤7 days	IV	3 (3 days)	Delta: Yes Omicron: Yes Omicron Subvariants (e.g., BQ.1, BQ.1.1: Yes
Alternatives: For use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order.				
Molnupiravir	≤5 days	Oral	10 (5 days)	Delta: Yes Omicron and Subvariants (e.g., BQ.1, BQ.1.1: Likely

As of 11/30/2022, bebtelovimab is no longer authorized for use in the U.S.
As of 4/5/2022, sotrovimab is no longer authorized for use in the U.S.

Patient Prioritization in the Setting of Logistical or Supply Constraints

Adopted from the NIH, original available here - Statement on Patient Prioritization for Outpatient Therapies | COVID-19 Treatment Guidelines (nih.gov)

In the event that logistical or supply constraints make it impossible to offer the available therapy to all eligible patients, the following principles apply **only** in this setting:

- Treatment of COVID-19 in unvaccinated or incompletely vaccinated individuals with clinical risk factors for severe illness and vaccinated individuals who are not expected to mount an adequate immune response

Risk groups are based on 3 key elements: age, vaccination status, immune status, and clinical risk factors. Groups are listed by tier in descending order of priority.

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

Tier	Risk Group
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 (age ≥75 years or age ≥65 years with additional risk factors).
2	• Unvaccinated individuals at risk of severe disease not included in Tier 1 (age ≥65 years or age <65 years with clinical risk factors)
3	• Vaccinated individuals at high risk of severe disease (age ≥65 years or age <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.

Monoclonal Antibodies - Outpatient

Bebtelovimab
As of 11/30/2022, bebtelovimab is no longer authorized for use in the U.S. due to the rising prevalence of Omicron subvariants, which bebtelovimab is not active against.

Pre-exposure prophylaxis:
As of 1/26/2023, Tixagevimab/cilgavimab (Evusheld) is no longer authorized for use in the U.S. due to the rising prevalence of SARS-CoV-2 subvariants and unlikely to be active.

COVID-19 Drug Information
Nirmatrelvir with ritonavir (Paxlovid)

<table>
<tr><td>Regulatory Status</td><td>FDA EUA for the for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (≥12 years of age and weight ≥40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death</td></tr>
<tr><td>Dose</td><td>• <u>Nirmatrelvir must be co-administered with ritonavir</u>
• Tablets should be swallowed whole and not chewed, broken, or crushed
<table>
<tr><th>eGFR</th><th>Dose</th></tr>
<tr><td>>60 mL/min</td><td>Nirmatrelvir 300 mg + ritonavir 100 mg PO BID</td></tr>
<tr><td><60 to ≥30 mL/min</td><td>Nirmatrelvir 150 mg + ritonavir 100 mg PO BID</td></tr>
<tr><td><30 mL/min</td><td>Not recommended</td></tr>
</table></td></tr>
<tr><td>Duration</td><td>5 days (10 doses total)
• If hospitalized <u>after starting treatment</u>, patients should complete the full 5-day treatment course per the healthcare provider's discretion.</td></tr>
<tr><td>Contraindications</td><td>• History of hypersensitivity to nirmatrelvir or ritonavir
• Co-administration of strong CYP3A4 substrates for which elevated concentrations are associate with serious and/or life-threatening reactions (Examples: amiodarone, dronedarone, flecainide, propafenone, colchicine, lurasidone, clozapine, lovastatin, simvastatin, sildenafil for PAH, oral midazolam)
• Co-administration with potent CYP3A4 inducers where significantly reduced nirmatrelvir or ritonavir concentrations may be associated with loss of virologic response or possible resistance (Examples: carbamazepine, phenobarbital, phenytoin, rifampin, St. John's Wort)</td></tr>
<tr><td>Drug-drug Interactions and Concomitant Medications</td><td>***Significant interactions*** Paxlovid Drug-Drug Interactions (nih.gov)

• Clinicians who are not experienced in prescribing ritonavir-boosted drugs should refer to resources such as Fact sheet for ritonavir-boosted nirmatrelvir (Paxlovid) and Liverpool COVID-19 Drug Interactions for additional guidance.
<u>Consultation with an expert (e.g., clinical pharmacist and/or specialist providers) should be considered.</u>
• CYP3A inhibition by ritonavir typically resolves 3-5 days after last dose
• Patients with HIV or hepatitis C virus taking ritonavir- or cobicistat-containing regimens should continue those regimens as indicated
• Patients taking concomitant HMG-CoA reductase inhibitors (statins), ACE-inhibitors, or systemic or inhaled corticosteroids, NSAIDs, or acid suppressive therapy should not discontinue these medications unless warranted by their clinical condition</td></tr>
<tr><td>Renal Impairment</td><td>Moderate renal impairment: Dose adjustment
Severe renal impairment: Not recommended</td></tr>
<tr><td>Hepatic Impairment</td><td>Severe hepatic impairment (Child-Pugh Class C): Not recommended</td></tr>
</table>

Monitoring	Hepatotoxicity: Hepatic transaminase elevations, clinical hepatitis, and jaundice have occurred in patients receiving ritonavir
Adverse Effects	• Dysgeusia, diarrhea, hypertension, myalgia • Case reports have described SARS-CoV-2 viral rebound and the recurrence of COVID-19 symptoms in some patients who have completed treatment. The frequency, mechanism, and clinical implications are yet to be determined and there is currently no data on administering longer or second courses of nirmatrelvir with ritonavir.
Patient Education	Paxlovid Patient Fact Sheet (English)
Healthcare Provider References	Paxlovid Health Care Provider Fact Sheet
Notes	• May lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection Nirmatrelvir with ritonavir (Paxlovid) [continued] **Pregnancy:** • Adverse events were observed following exposure to nirmatrelvir in some embryo-fetal developmental toxicity studies. A pregnant rabbit study saw reduced fetal body weights; however, this occurred at exposures that were ~10x higher than the human dose. A full description of the data is available in section 8.1 of FACT SHEET FOR HEALTHCARE PROVIDERS: EUA FOR PAXLOVID • ACOG COVID FAQs - COVID-19 FAQs for Obstetrician-Gynecologists, Obstetrics | ACOG "Obstetric care clinicians may consider the use of the oral SARS-CoV-2 protease inhibitor for the treatment of non-hospitalized COVID-19 positive pregnant individuals with mild to moderate symptoms, particularly if one or more additional risk factors are present (eg BMI >25, CKD, DM, CV disease). Clinicians should weigh the available data against the individual risks of COVID-19 in pregnancy in each situation…The short-term exposure to these medications must be balanced against the maternal and fetal risks associated with untreated COVID-19 in pregnancy." • The Society for Maternal Fetal Medicine statement - Treatment.pdf "SMFM supports the use of Paxlovid (nirmatrelvir [PF-07321332] tablets and ritonavir tablets) for treatment of pregnant patients with COVID-19 who meet clinical qualifications. Any therapy that would otherwise be given should not be withheld specifically due to pregnancy or lactation.

Remdesivir

Regulatory Status	• FDA approved for adults and pediatric patients (≥12 years older and weighing ≥40 kg) for the treatment of COVID-19 requiring:
	  ○ Hospitalized OR
	  ○ Not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death
	• EUA for pediatric patients (3.5 kg to <40 kg or <12 years of age) with positive results of direct SARS-CoV-2 viral testing, and
	  ○ Hospitalized OR
	  ○ Not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death

Dose	200 mg IV x 1 on day 1 followed by 100 mg IV daily
Duration	Non-hospitalized: 3 days Hospitalized: Up to 5 days **Use beyond 5 days requires CMO approval*
Renal Impairment	"Remdesivir is not recommended in patients with eGFR<30 mL/min.", however, expert consensus is that benefits of RDV may outweigh risk for most patients with impaired renal function. (Reference: J Am Soc Nephrol. 2020;31(7):1384-1386. doi:10.1681/ASN.2020050589.)
Hepatic Impairment	RDV should not be initiated in patients with ALT ≥10x ULN
IV Infusion Time	30 minutes
Monitoring	• LFTs, renal function • Heart rate - Post-marketing reports of bradycardia, including severe and even fatal bradycardia, in patients with COVID-19 receiving remdesivir. The frequency of this potential adverse event is not known at this time. • Infusion related reaction (nausea, vomiting, diaphoresis, shaking)
Healthcare Provider References	RDV Prescribing Information
Notes	Risk of reduced antiviral activity when co-administered with chloroquine or hydroxychloroquine

Molnupiravir

Regulatory Status	FDA EUA for treatment of mild-to-moderate COVID-19) in adults with positive results of direct SARS-CoV-2 viral testing who are at high risk for progressing to severe COVID-19, including hospitalization or death, **and** for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate
Dose	800 mg (4 x 200 mg capsules) PO q12hr • Swallow capsules whole, and to not open, break, or crush the capsules
Duration	5 days (10 total doses) • If hospitalized after starting treatment, patients should complete the full 5-day treatment course per the healthcare provider's discretion

Warnings & Precautions	• **Embryo-Fetal Toxicity**: Not recommended for use during pregnancy • Bone and Cartilage Toxicity: Not authorized for use in patients <18 years of age because it may affect bone and cartilage growth
Renal Impairment	No dosage adjustment is recommended
Hepatic Impairment	No dosage adjustment is recommended
Monitoring	N/A
Adverse Effects	Diarrhea, nausea, dizziness
Patient Education	Molnupiravir Fact Sheet for Patients (English)
Healthcare Provider References	Molnupiravir Fact Sheet for Health Care Providers
Notes	• Last line option based on reduced benefits in preventing hospitalization compared to alternatives • Molnupiravir is not authorized under the FDA EUA for pre-exposure or post-exposure prevention of COVID-19 or for initiation of treatment in patients hospitalized due to COVID-19 because benefit of treatment has not been observed in individuals when treatment is started after hospitalization due to COVID-19 ** Prior to initiating treatment with molnupiravir, assess whether an individual of childbearing potential is pregnant or not, if clinically indicated** • Females: Advise females of childbearing potential to use a reliable method of contraception correctly and consistently, as applicable for the duration of treatment and for 4 days after the last dose of molnupiravir • Males: Advise sexually active individuals with partners of childbearing potential to use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose of molnupiravir

Fluvoxamine

Regulatory Status	Off-label; Fluvoxamine is a commonly utilized selective serotonin receptor inhibitor (SSRI) with hypothesized anti-inflammatory properties.
Target Population/ Criteria for Use	There is insufficient evidence to recommend for or against fluvoxamine as early treatment of high-risk outpatients to reduce the need for hospitalization. Current NIH guidelines strongly recommend only using fluvoxamine in the context of a clinical trial among ambulatory patients. The monoclonal antibodies and new antivirals have greater efficacy in preventing hospitalization and death and should be preferred (Therapeutic Options for COVID-19 Treatment, Non-hospitalized).
Dose	100 mg PO BID
Duration	10 days
Formulation(s)	Oral tablet

Adverse Effects	• Restlessness, agitation, insomnia, nausea, diarrhea, headache, dizziness, fatigue, sexual dysfunction, hyponatremia • QT interval prolongation • Increased risk of bleeding
Monitoring	N/A
Notes	• Increased risk of serotonin syndrome when used with other serotonergic drugs. • Contraindicated with MAOIs. • **The monoclonal antibodies have greater efficacy in preventing hospitalization and death (Absolute Risk Reduction 2.2 to 6%, Relative Risk Reduction 70-85% with a significant effect on prevention of death) and should be preferred in high-risk individual to fluvoxamine (Absolute Risk Reduction 5%, Relative Risk Reduction 32%) or colchicine (Absolute Risk Reduction 1.4% Relative Risk Reduction 23% in the PCR confirmed COVID-19 group).

Anticoagulation

Patients receiving chronic anticoagulant or antiplatelet therapy for existing conditions should remain on their current regimen if positive for COVID-19, unless a new clot has developed, or ICU level of care requires a switch to parenteral/SubQ therapy.

All other patients should be assessed as follows:

1. Confirmed VTE or high clinical suspicion with attending MD (i.e., evidence of DVT/PE/positive Doppler or high clinical suspicion)
    a. Therapeutic anticoagulation needed
        i. Calculate duration of therapy already completed
            1. Continue for minimum of 3 months (long term/indefinite term for idiopathic VTE and low bleeding risk)
        ii. Confirm regimen and dose (all regimens listed below must be adjusted for renal impairment). Subtract any days of treatment initiated as inpatient to determine remaining loading dose and/or maintenance dose.
            1. Apixaban 10 mg PO BID x7 days, followed by 5 mg BID
                a. May be utilized in patients with cancer on a case-by-case basis
            2. Rivaroxaban 15 mg PO BID x 21 days, followed by 20 mg daily with dinner
            3. Enoxaparin 1 mg/kg SubQ BID with CrCL >30 ml/min (alternative for patients with cancer or pregnancy)
                a. NOT preferred due to cost
                b. Round to the nearest syringe (30 mg, 40 mg, 60 mg, 80 mg, 100 mg, 120 mg, 150 mg)
        iii. Obtain prescription
            1. Pharmacist to consult care management to initiate outpatient medication procurement
                a. "Case Management Consult for Medications/Medical Follow Up" à Special Instructions: *Enter drug name*
            2. Care management to send to Rxpress or Hospital outpatient pharmacy (preferred) or patient outpatient pharmacy
                a. Apixaban Eligibility
                    i. for 30-day trial: never filled Eliquis before
                    ii. for Co-pay card: must have commercial insurance (not state or federal insurance, e.g., Medicare)
                b. Rivaroxaban Eligibility
                    i. Commercial or private insurance
                    ii. Not for state or federal insurance, e.g., Medicare
                    iii. Unable to use for 10 mg tabs
            3. Deliver meds to bedside prior to discharge
            4. Pharmacist provides education
            5. Care management sets up outpatient follow up with 7 days

2. High Risk of VTE: Modified International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) VTE risk score ≥4; or Modified IMPROVE VTE risk score ≥2 and D-dimer level >2 times the upper limit of normal.
   Recommendation is based on low level evidence from consensus documents only, use clinical judgement when prescribing

Modified IMPROVE VTE Risk Score	
VTE Risk Factor	**VTE Risk Score**
Previous VTE	3
Known thrombophilia[a]	2
Current lower limb paralysis or paresis[b]	2
History of cancer[c]	2
ICU/CCU stay	1
Complete immobilization[d] ≥1 day	1
Age ≥60 years	1
CCU= cardiac care unit; ICU= intensive care unit; VTE= venous thromboembolism. a: A congenital or acquired condition leading to excess risk of thrombosis (eg, factor V Leiden, lupus anticoagulant, factor C or factor S deficiency). b: Leg falls to bed by 5 seconds but has some effort against gravity (taken from NIH stroke scale). c: Cancer (excluding non-melanoma skin cancer) present at any time in the last 5 years (cancer must be in remission to meet eligibility criteria) d: Immobilization is being confined to bed or chair with or without bathroom privileges.	

   a. Prophylactic anticoagulation needed
      i. Calculate duration of therapy already completed
         1. Continue for a total of 4 weeks
      ii. Confirm regimen and dose
         1. Apixaban 2.5 mg PO BID (regardless of renal function)
         2. Rivaroxaban 10 mg PO daily (regardless of renal function)
         3. Enoxaparin 40 mg SubQ daily (for BMI ≥40: 40 mg SubQ BID)
            a. NOT preferred due to cost
      iii. Obtain prescription
         1. Pharmacist to consult care management to initiate outpatient medication procurement
            a. "Case Management Consult for Medications/Medical Follow Up" - Special Instructions: *Enter drug name*
         2. Care management to send to Rxpress or Hospital outpatient pharmacy (preferred) or patient outpatient pharmacy
         3. Deliver meds to bedside prior to discharge
         4. Pharmacist provides education
         5. Care management sets up outpatient follow up with 7 days

3. Low risk of VTE or contraindication to anticoagulation
   a. No OAC at discharge

Extended VTE prophylaxis is not routinely recommended and should only be prescribed on a case-by-case basis

Convalescent Plasma

- **NIH (Updated August 8, 2022):** There is insufficient evidence for the Panel to recommend either for or against the use of high-titer COVID-19 convalescent plasma (CCP) in patients with COVID-19 who are immunocompromised. Some clinicians would consider the use of CCP in patients who, in their clinical judgment, have severe or progressive COVID-19 and an inadequate response to therapy. In these cases, clinicians should attempt to administer high-titer CCP from a vaccinated donor who recently recovered from COVID-19 likely caused by a similar SARS-CoV-2 variant as the patient.

Therapies NOT Recommended

Disclaimer: The Scientific Research Committee ensures timely review of emerging experimental therapies, therefore, off-label use of therapies with only published *in vitro* data should NOT be implemented until reviewed and sanctioned by this committee. The recommendations below are subject to change based on emerging data or drug shortage information.

The medications listed below have been reviewed, but due to lack of evidence, these medications are not currently recommended for the treatment of COVID-19.

- **Azithromycin**
  - Based on current evidence demonstrating lack of benefit in preventing invasive mechanical ventilation or death in hospitalized patients, use of azithromycin for treatment of COVID-19 is not recommended.
- **Bamlanivimab/etesevimab and casirivimab/imdevimab**
  - Due to the predominance of the Omicron variant in the US (>99% of COVID-19 cases as of 1/18/22), casirivimab/imdevimab and bamlanivimab/etesevimab are no longer authorized or recommended for the treatment or prophylaxis of COVID-19.
- **Colchicine**
  - Use of colchicine in non-hospitalized patients with COVID-19 is not recommended based on current evidence demonstrating no difference of a composite endpoint of death or hospitalization by Day 30 (COLCORONA Trial) nor the median time to self-reported recovery (PRINCIPLE trial) in the colchicine group versus the control group, nor in other clinically relevant outcomes.
  - Use of colchicine in hospitalized patients with COVID-19 is not recommended.
- **Hydroxychloroquine or chloroquine**
  - Based on studies demonstrating harm and little clinical benefit, the use of hydroxychloroquine for the treatment of COVID-19 is NOT recommended outside of a clinical trial.
- **Ivermectin**
  - Current evidence for the benefit of ivermectin is weak and the results of two high-quality randomized controlled trials showed no evidence of benefit, thus ivermectin should not be used for the treatment of COVID-19. This recommendation will be periodically re-evaluated if new randomized controlled trials become available.
  - International COVID-19 Guidelines & Statements on the Use of Ivermectin for the Treatment of COVID-19:

Merck Statement on Ivermectin use in COVID-19 IDSA Guidelines for Treatment of COVID-19 - Ivermectin
Statement on Ivermectin | COVID-19 Treatment Guidelines

- **Lopinavir/ritonavir**
  - Use of lopinavir/ritonavir is not recommended because of unfavorable pharmacodynamics and negative clinical trial data.
- **Micronutrients (Vitamin C and Zinc)**
  - Adjunctive use of micronutrients in COVID-19 patients beyond the recommended daily allowances for supplementation is not supported by scientific evidence.
  - If utilization is necessary for the treatment of nutritional deficiencies, a once daily dosing strategy should be employed.
- **Famotidine**
  - Data fails to demonstrate beneficial effects of high-dose famotidine in ambulatory patients at day 28
  - Standard dose famotidine also failed to demonstrate benefits in mortality, ICU length of stay, or mechanical ventilation in hospitalized patients with severe COVID-19 infections
- **Inhaled corticosteroids**
  - Among ambulatory patients with mild-to-moderate COVID-19, inhaled corticosteroids did not demonstrate benefit on mortality or hospitalization

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Summary of Revisions

- 03/15/2020
  - General treatment options, dosing, and monitoring
- 03/19/2020
  - Testing guidance for asymptomatic and symptomatic patients
  - Added therapeutic options based on severity using scale and laboratory monitoring for patients with COVID-19
  - Updated dosing for hydroxychloroquine
  - Corticosteroids: use of steroids in patients with severe disease could be considered as part of the supportive care regimen for *patients with ARDS on a case-by-case basis*
  - ACEi/ARB: advised against adding/removing beyond in standard practice
  - NSAIDs: no evidence for against the management of fever with NSAIDs
  - Guidance for use of nebulized respiratory medications
  - Removed chloroquine, ribavirin, atazanavir/ritonavir, atazanavir/cobicistat, darunavir/cobicistat
  - Added Tocilizumab
  - Post-exposure prophylaxis for patients and health care workers
- 03/21/2020
  - Added: Discharge patients should be offered supportive care (anti-pyretics, MDI, etc.)
- 03/25/2020
  - Updated treatment options based on severity score:
    - Severity score 1: removed hydroxychloroquine, lopinavir/ritonavir, darunavir/ritonavir
    - Severity score 2-3: no change
    - Severity score ≥ 4: Remdesivir for eligible patients first, if not: hydroxychloroquine. Removed combination of hydroxychloroquine plus lopinavir/ritonavir or darunavir/ritonavir
  - Lower dose glucocorticoids (equivalent to methylprednisolone 1-2 mg/kg/day for 3-5 days or ≤0.5-1 mg/kg/day methylprednisolone for ≤ 7 days) have been recommended after *careful consideration of risks and benefits.*
  - Azithromycin: insufficient evidence to recommend the use of azithromycin in addition to hydroxychloroquine
  - ECG monitoring at baseline for all hospitalized patients
- 03/31/2020
  - Revised the duration of treatment
    - Severity score: 2-3: changed from 10 days to 5-7 days
    - Severity score ≥ 4: changed from 10-14 days to 7-10 days
  - Corticosteroids: early initiation of lower dose glucocorticoids (equivalent to methylprednisolone 1-2 mg/kg/day for 3-5 days or ≤0.5-1 mg/kg/day methylprednisolone for ≤ 7 days) have been recommended for *patients with refractory shock and/or ARDS*
  - Removed darunavir/ritonavir
  - Added Sarilumab with criteria for use
- 04/15/2020
  - Added: statement regarding use of off-label experimental therapies with only *in vitro* data
  - Added recommendation against use of ivermectin
  - Added anticoagulation pathway
  - Added guidance on cardiac monitoring
  - Added additional steroid guidance and chart with risk factors for CRS
  - Added restriction to ID for lopinavir/ritonavir
  - Revised daily monitoring parameters
- 04/20/2020
  - Added statement regarding use of micronutrients, Zinc and Vitamin C
- 04/27/2020
  - Removed lopinavir/ritonavir from algorithm
  - Added comment regarding use of hydroxychloroquine
  - Updated remdesivir information for compassionate use
- 04/29/2020
  - Updated anticoagulation algorithm, removal of ROTEM
  - Added statement regarding use of tPA
- 05/12/2020
  - Removed hydroxychloroquine from algorithm
- 05/18/2020
  - Added guidance for outpatient anticoagulation
  - Removed cardiac monitoring for patients receiving hydroxychloroquine
  - Removed statement regarding empiric initiation of experimental/investigational therapies for severity score ≥ 4
  - Included information on remdesivir emergency use authorization
  - Included information on convalescent plasma
- 05/26/2020
  - Clarification of outpatient anticoagulation recommendations
- 06/04/2020
  - Updated allocation information on remdesivir
- 06/09/2020

- Updated DOH link to request remdesivir for State of Florida (outside of CFDS)
- 06/18/2020
  - Addition of low-dose dexamethasone recommendation
  - Removal of remdesivir compassionate use information
  - Edited remdesivir allocation information
- 06/30/2020
  - Added warning against use of hydroxychloroquine
  - Modified IL6 antagonist recommendation to include use for severity score ≥ 2
  - Updated remdesivir access process
- 07/03/2020
  - Removal of sarilumab from algorithm
  - Updated tocilizumab recommendation to include use for severity score ≥ 3
- 07/14/2020
  - Modified remdesivir criteria for use
- 08/05/2020
  - Revised remdesivir criteria for use
  - Updated multi-state convalescent plasma inclusion criteria
  - Removal of HERO study details as trial has stopped enrollment
  - Addition of statement regarding insufficient data on use of tocilizumab
- 08/25/2020
  - Updated convalescent plasma criteria based on FDA's EUA announcement
- 09/03/2020
  - Updated verbiage regarding remdesivir criteria for use
- 10/27/2020
  - Updated remdesivir information to reflect changes in regulatory requirements based on FDA approval of remdesivir on 10/22/20
  - Removed tocilizumab and recommended against routine use
- 11/12/2020
  - Added bamlanivimab
- 11/19/2020
  - Added NIH and IDSA recommendations and references for use of bamlanivimab in outpatients
- 11/24/2020
  - Reviewed available data and EUA information on baricitinib
- 12/3/2020
  - Added casirivimab/imdevimab
- 12/22/2020
  - Revised language regarding baricitinib
- 01/07/2021
  - Updated verbiage regarding use of ivermectin
- 01/12/2021
  - Added tocilizumab back into treatment algorithm
- 02/04/2021
  - Included information on colchicine for non-hospitalized patients
- 02/09/2021
  - Modified tocilizumab recommendation to include only patients with severity score ≥3
  - Updated convalescent plasma EUA criteria
- 02/11/2021
  - Updated EUA information on convalescent plasma
  - Added EUA information for bamlanivimab/etesevimab combination
  - Added additional links to ivermectin
- 02/18/2021
  - Updated information on convalescent plasma severity score recommendations based on EUA
- 03/02/2021
  - Updated inpatient and outpatient anticoagulation algorithm
- 03/10/2021
  - Added additional study evaluating ivermectin
  - Updated information and recommendations on MABs
- 03/25/2021
  - Updated criteria for use for remdesivir to include option to use in patients on high flow oxygen
  - Updated information and recommendations on MABs
- 04/20/2021
  - Updated guideline recommendations on MABs
  - Included FDA EUA updates and information on the revoked EUA for bamlanivimab monotherapy
- 05/03/2021
  - Updated tocilizumab criteria to reflect provider restrictions
- 05/25/2021
  - Updated EUA requirements for MABs

- 05/27/2021
  - Updated bamlanivimab-etesevimab information on distribution to the state of Florida
- 06/03/2021
  - Modified recommendation for use of COVID-19 convalescent plasma
- 06/07/2021
  - Updated FDA EUA information for casirivimab/imdevimab: new dosing and route of administration
- 06/15/2021
  - Clarified language regarding scientific basis for avoiding routine use of remdesivir in patients on room air or mechanical ventilation
  - Removed statement about insufficient data for baricitinib and the warning against use of baricitinib with corticosteroids
  - Updated FDA EUA information for new MAB, Sotrovimab
- 06/25/2021
  - Updated information regarding distribution of bamlanivimab-etesevimab in the U.S.
- 07/13/2021
  - Updated tocilizumab to reflect EUA and results of the RECOVERY trial
- 07/29/2021
  - Added bradycardia and hypotension to Adverse Effects for remdesivir
  - Updated baricitinib information to reflect update to EUA
- 08/05/2021
  - Updated EUA criteria for casirivimab-imdevimab for use in post-exposure prophylaxis
  - Added guidance on utility of IL6 levels
- 08/17/2021
  - Updated recommendations on use of colchicine in non-hospitalized patients and addressed inpatient use
  - Updated ivermectin studies-no change to overall recommendation for use
  - Updated baricitinib drug information to warn against initiation for low ALC, ANC, or Hgb
- 08/24/2021
  - Edited information on baricitinib labs for imitation of therapy (ALC <200 cells/µL instead of <500 cells/µL)
- 08/30/2021
  - Edited information to include tofacitinib and sarilumab as alternatives to baricitinib and tocilizumab in cases of supply issue
- 10/04/2021
  - Updated monoclonal antibody information to reflect renewed availability of bamlanivimab/etesevimab and to incorporate post-exposure prophylaxis
- 11/16/2021
  - Edited inpatient anticoagulation algorithm
  - Added chart on preferred outpatient therapies
  - Added information on fluvoxamine
- 12/17/2021
  - Edited EUA information for bamlanivimab/etesevimab for use in individuals of any age
  - Added EUA information for tixagevimab/cilgavimab (Evusheld) for use as pre-exposure prophylaxis in certain adult and pediatric patients
- 1/4/2022
  - Created new outpatient algorithm
  - Added Paxlovid and molnupiravir
  - Updated monoclonal antibody drug information to reflect Omicron variant and EUA updates
- 1/11/2022
  - Removed colchicine from the proposed therapeutics. Add colchicine to the Therapies Not Recommended.
  - Updated recommendation for fluvoxamine to insufficient evidence to recommend for or against use in COVID-19
- 01/26/2022
  - Removed bamlanivimab/etesevimab and casirivimab/imdevimab from recommended therapies and prophylaxis due to predominance of Omicron variant in the US
  - Updated CMO list
  - Updated regulatory information for RDV to include outpatient therapy as FDA approved
- 3/01/2022
  - Edited monoclonal antibody treatment options to add bebtelovimab
  - Edited dosing information for tixagevimab/cilgavimab (Evusheld)
- 4/6/2022
  - Removed sotrovimab information based on BA.2 subvariant and updated EUA
  - Edited tixagevimab/cilgavimab dosing to match updated EUA
  - Edited information on ivermectin
- 5/31/2022
  - Edited drug-drug interaction and adverse effects of nirmatrelvir and ritonavir
  - Added standard dose of tixagevimab/cilgavimab
  - Added information on use of convalescent plasma in non-hospitalized patients
- 9/20/2022
  - Edited verbiage for molnupiravir to match EUA

- Updated not recommended therapies to add famotidine and inhaled corticosteroids
- Updated fluvoxamine information to align with NIH guidelines
- Updated convalescent plasma recommendations for ambulatory patients to align with NIH guidelines

- 12/02/2022
  - Edited information on the use of tixagevimab plus cilgavimab in the setting of increased prevalence of circulating Omicron subvariants
  - Removed bebtelovimab from algorithm as no longer authorized for treatment in the U.S.
- 01/26/2023
  - Updated information on tixagevimab/cilgavimab as it is no longer authorized for pre-exposure prophylaxis in the U.S.

From: COVID-19 Scientific Research Committee

To: COVID-19 Pandemic Response Team

Dear Committee:

The Scientific Research Committee (SRC) was asked to review literature surrounding therapeutic treatment of COVID-19 in adult patients. As a committee, we believe the documented algorithm is thought to be the most up to date, comprehensive and scientifically current treatment algorithm. The committee supports the adaptation of the algorithm prepared and approved by the Chief Medical Officer approval board.

Sincerely,

COVID-19 Scientific Committee

Alric Simmonds, MD, Chair
Ariel Watson, OTR/L, CAPM, Project Manager
Nancy Aldrich, MLIS
Atalie Ashley-West, PhD, MPH, CPH
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Alberto Monreal, MD
Okorie, Okorie, MD
Amay Parikh, MD
Richard Pratley, MD
Steve Smith, MD
Jason Sniffen, DO
J. Michael Yurso, MD

Chief Medical Officers

Neil Finkler, MD
Miles Bennett, DO
Dennis deLeon, MD
David Goldman, DO
Victor Herrera, MD
Darin Jordan, MD
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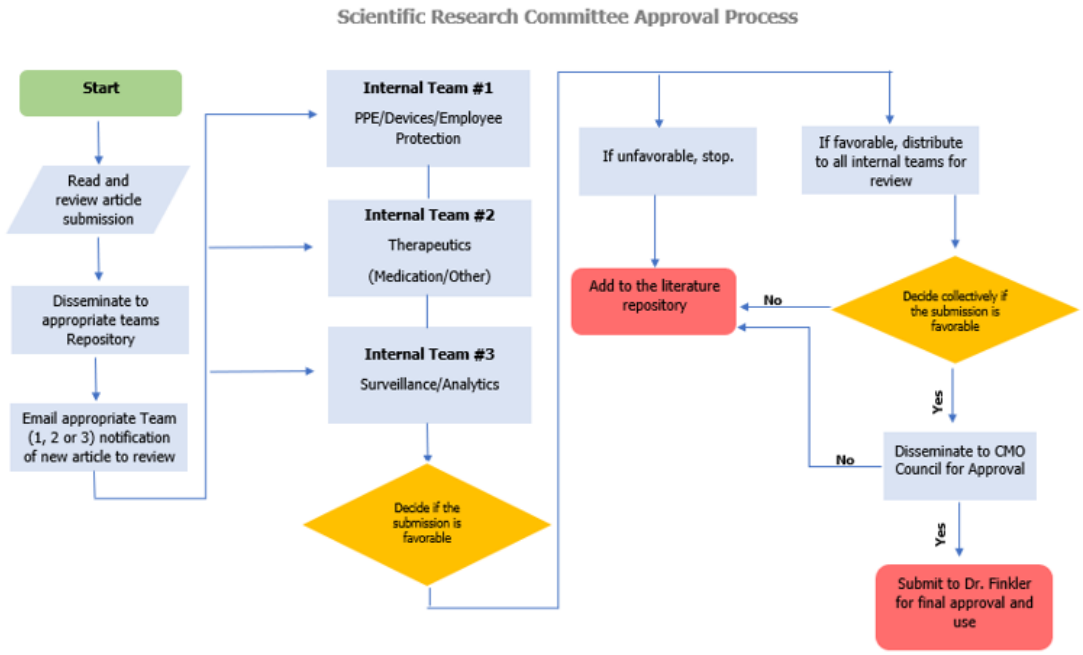
Steve Knych, MD
Omayra Mansfield, MD
Sanjay Pattani, MD
Jason Porter, MD
Floriano Putigna, DO
Thomas Scoggins, MD
David Sinclair, MD
Alric Simmonds Jr., MD
Joe Smith, MD

Disclaimer: The Scientific Committee was formed under the Medical Management Branch of the COVID-19 Pandemic Response Team. The committee's goal is to create a repository, interrogate research literature as it pertains to the treatment of COVID-19 and provides a rapid approval process. The algorithm below is the decision-making process that governs our decisions.



Dr. Neil Finkler	Chief Clinical Officer, CFD	Dr. Jennifer Keehbaugh	Winter Park
Dr. David Sinclair	Altamonte	Dr. Dennis DeLeon	Kissimmee
Dr. Omayra Mansfield	Apopka	Dr. Joe Smith	DeLand
Dr. Alric Simmonds Jr.	Celebration	Dr. David Goldman	New Smyrna
Dr. Sanjay Pattani	Mission Control	Dr. Darin Jordan	FH Health Care Partners
Dr. Jason Porter	East Orlando	Dr. Mark Kilman	AH Palm Coast
Dr. Victor Herrera	Orlando	Dr. Steven Knych	Fish
Dr. Michael Keating	Children's	Dr. Floriano Putigna	Waterman
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Dr. Miles Bennett	Winter Garden		