

COVID-19 ADULT TREATMENT GUIDANCE

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PURPOSE

The purpose of this document is to provide guidance for the medication management of adult patients with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. For management of pediatric patients, please see [St. Louis Children’s Hospital Guidance for the Management of Acute COVID-19 in Children](#).

Additional information can be found at the following resources:

- [NIH COVID-19 Treatment Guidelines](#)[1]
- [NIH Guidelines for Care of Critically Ill Adult Patients with COVID-19](#)
- [IDSA Guidelines on the Treatment and Management of Patients with COVID-19](#)[2]
- [CDC Interim Clinical Guidance for Management of Patients with COVID-19](#)[3]
- [BJC COVID-19 Resources](#)
- [BJC COVID-19 Monoclonal Antibody Therapy website](#)

MANAGEMENT

Consultation with clinical experts in the treatment of COVID-19 should be considered for management of critically ill patients, pediatric patients, pregnant/breastfeeding patients, and/or patients with risk factors for progression to severe COVID-19 illness*. [4, 5] [6]

Table 1. *Risk Factors for Severe Illness (CDC) [4]

Increasing age, especially over 50 years of age
Younger than one year old
Part of a group with long-standing systemic health and social inequities, including racial and ethnic minorities and people with disabilities
Adults of any age with the following conditions <u>are at increased</u> risk for severe illness (listed in alphabetical order and not in order of risk)
<ul style="list-style-type: none"> • Cancer • Chronic kidney disease • Chronic liver disease • Chronic lung diseases, including COPD, asthma, interstitial lung disease, cystic fibrosis, and pulmonary hypertension • Dementia or other neurological conditions • Diabetes (type 1 or type 2) • Down Syndrome • Heart conditions (such as heart failure, coronary artery disease, cardiomyopathies, or hypertension) • HIV infection • Immunocompromised state • Mental health conditions including depression, and schizophrenia spectrum disorders • Overweight (body mass index [BMI] ≥ 25 mg/m²) and obesity (BMI ≥ 30 kg/m²) • Pregnancy • Sickle cell disease or thalassemia • Smoking, current or former • Solid organ or blood stem cell transplant • Stroke or cerebrovascular disease • Substance use disorders • Tuberculosis

Figure 1. Pharmacologic Prevention and Management of Non-Hospitalized Adults with COVID-19

During times of supply or logistical constraints, patients will be prioritized by highest risk of clinical progression based on age, vaccination status, immune status, and risk factors according to [NIH guidelines](#). Prioritization criteria will be communicated through BJC Incident Command.

See Table 2 for more information and BJC Criteria for Use

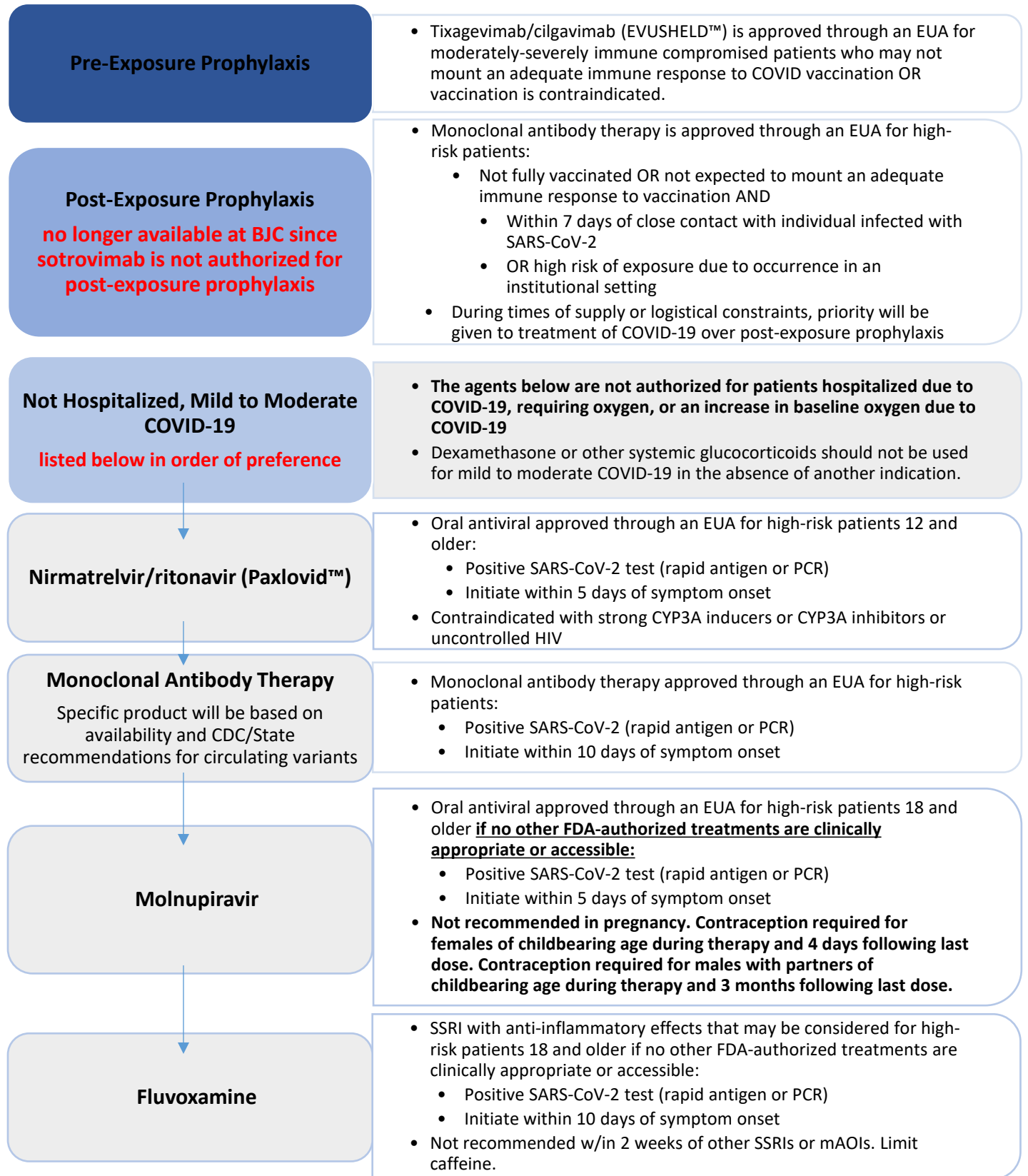


Figure 2. Pharmacologic Management of Hospitalized Adults with COVID-19

See Table 2 for more information and BJC Criteria for Use

Hospitalized But Does Not Require Supplemental Oxygen	<ul style="list-style-type: none">• Remdesivir - Mild to Moderate (3 days) may be considered for patients at high risk of disease progression (see Table 1)• Dexamethasone or other systemic glucocorticoids should not be used in the absence of another indication
Hospitalized and Requires Supplemental Oxygen	<ul style="list-style-type: none">• Use one of the following options:<ul style="list-style-type: none">• Remdesivir - Severe (5 days) (e.g., for patients who require minimal supplemental oxygen)• Dexamethasone + remdesivir (5 days) (e.g., for patients who require increasing amounts of supplemental oxygen)
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	<ul style="list-style-type: none">• Use one of the following options:<ul style="list-style-type: none">• Dexamethasone• Dexamethasone + remdesivir (5 days)• Baricitinib OR tocilizumab* may be added to one of the options above for patients with rapidly increasing oxygen needs and systemic inflammation.
Hospitalized and Requires Invasive Mechanical Ventilation or ECMO	<ul style="list-style-type: none">• Use one of the following options:<ul style="list-style-type: none">• Dexamethasone• Dexamethasone + baricitinib• Dexamethasone + tocilizumab*• A clear benefit of remdesivir has not been demonstrated in this group, but may be considered in patients recently placed on mechanical ventilation (in addition to a regimen above).

*Due to a critical shortage, **tocilizumab** is currently restricted to any of the following: pregnancy, GFR < 15 mL/min, renal replacement therapy, within 24 hours of ICU admission and rapid progression of respiratory failure, or unable to obtain enteral access.

Table 2: Considerations for the management of COVID-19

Recommended as standard of care OR high-quality evidence supporting efficacy and safety [i.e., randomized, controlled trial(s)]

Supportive Care

- Appropriate management of respiratory failure, ARDS, sepsis, septic shock
[NIH Guidelines for Care of Critically Ill Adult Patients with COVID-19](#)
- Unrelenting and high (>39°C) fevers are common in hospitalized COVID-19 patients.
- Antibiotics should only be used for confirmed or strong suspicion of a bacterial infection or sepsis. Antibiotics should be re-evaluated daily and if there is no evidence of bacterial infection, de-escalate or stop antibiotics.

Nirmatrelvir/ritonavir

(Paxlovid™) Outpatient Only

Available through an EUA
[Paxlovid Fact Sheet for Healthcare Providers](#)
[Paxlovid Fact Sheet for Patients](#)

Inclusion Criteria (must meet all)

- Positive SARS-CoV-2 (rapid antigen or PCR)
- One or more symptoms consistent with COVID-19
- Able to receive within 5 days of symptom onset
- One or more high-risk conditions in Table 1

Exclusion criteria (if meets any one)

- < 12 years old
- < 40 kg
- Asymptomatic
- Hospitalized due to COVID-19
- Requiring oxygen therapy due to COVID-19
- Requiring increase in baseline oxygen due to COVID-19 in those on chronic oxygen therapy
- Severe renal impairment (eGFR < 30 mL/min) or severe hepatic impairment (Child-Pugh Class C)
- Drug Interactions*

***Before prescribing Paxlovid, clinicians should review the patient’s medication list to assess the risk of drug-drug interactions. See [Appendix](#) for drug interaction guidance.**

eGFR ≥ 60 mL/min:

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

eGFR 30 to 59 mL/min:

150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet), with both tablets taken together twice daily for 5 days

- May be taken with or without food
- Tablets should be swallowed whole and not chewed, broken, or crushed.
- Nirmatrelvir and ritonavir tablets are co-packaged in a carton containing 30 tablets total, divided in 5 daily-dose blister cards
- Nirmatrelvir must be administered with ritonavir
- Not authorized for use for > 5 consecutive days

- Nirmatrelvir is a protease inhibitor active against M^{PRO}, a viral protease essential in coronavirus replication. Ritonavir is required to increase nirmatrelvir concentrations to therapeutic ranges.
- **EPIC-HR:** randomized, double-blind, placebo-controlled trial in patients at high risk for progression to severe disease. All patients were unvaccinated and not previously infected and w/in 5 days of symptom onset. Primary outcome was hospitalization or death due to any cause by Day 28. Primary events occurred in 0.8% (8 of 1,039) of paxlovid patients (8 hospitalizations, 0 deaths), and 6.3% (78 of 1,046) of placebo patients (66 hospitalizations, 12 deaths). Relative risk reduction 88%.
- **Pregnancy & Breastfeeding:** there is no data in pregnancy or breastfeeding. Consultation with clinical experts is recommended. Paxlovid should be considered 2nd line in pregnancy after monoclonal antibodies
- **Drug Interactions:**
 - Numerous drug-drug interactions and the potential to cause serious or life-threatening adverse effects.
 - Contraindicated with drugs highly dependent on CYP3A
 - See [Appendix](#) for drug interaction guidance

Adverse Effects: dysgeusia, diarrhea, hypertension, myalgia

Monoclonal Antibody Therapy Outpatient Only

- The selection and availability of monoclonal antibody therapy may change depending upon state allocations and potential efficacy against emerging SARS-CoV-2 variants
- See [BJC COVID-19 Monoclonal Antibody Therapy website](#) for more information
- **All monoclonal antibodies require at least 1 hour of observation after administration and immediate access to medications to treat severe reactions such as anaphylaxis, and the ability to activate the emergency medical system as necessary.**

Monoclonal Antibody Therapy for Pre-Exposure Prophylaxis Outpatient Only

Inclusion Criteria (must meet all criteria)

- Moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medication or treatments AND may not amount an adequate immune response to COVID-19 vaccination
OR
COVID-19 vaccination is not recommended due to history of a severe adverse reaction

Exclusion Criteria (if meets any one criterion)

- Less than 12 years of age
- Less than 40 kg
- Currently infected with SARS-CoV-2
- Recent exposure to someone with SARS-CoV-2

Tixagevimab + cilgavimab (EVUSHELD™)

Available through an EUA
[Tixagevimab + cilgavimab Fact Sheet for Healthcare Providers](#)
[Tixagevimab + cilgavimab Fact Sheet for Patients](#)

Pre-exposure Prophylaxis

Tixagevimab 150 mg + Cilgavimab 150 mg as two separate intramuscular injections, preferably one in each of the gluteal muscles, one after the other.

- **PROVENT:** randomized, double-blind, placebo-controlled trial in adults who had not received a COVID-19 vaccine and not currently or previously infected. Patients were either ≥60 years of age, had a pre-specified co-morbidity (obesity, congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, immunocompromised state, or previous history of severe or serious adverse event after receiving any approved vaccine), or were at increased risk of SARS-CoV-2 infection due to their living situation or occupation. Primary outcome was symptomatic COVID-19 before Day 183. Symptomatic COVID-19 occurred in 0.2% (8 of 3,441) of tixagevimab/cilgavimab patients and 1% (17 of 1,731) of placebo patients. Relative risk reduction 77%. The reduction in risk of developing COVID-19 was maintained through six months.
- 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, tixagevimab/cilgavimab should be administered at least two weeks after vaccination.**
- **Adverse Effects:** Headache, fatigue, cough, allergic reactions, injection site reactions.
 - Serious cardiac adverse events (myocardial infarction and heart failure) were rare, but more frequent than placebo in the trial. Causality not established due to underlying risk factors.

Monoclonal Antibody Therapy for Treatment Outpatient Only

Inclusion Criteria (must meet all criteria)		Exclusion Criteria (if meets any one criterion)
<ul style="list-style-type: none"> • Positive SARS-CoV-2 test (rapid antigen or PCR) • Able to receive monoclonal antibody therapy within 10 days of symptom onset • One or more symptoms consistent with COVID-19 (fever, cough, shortness of breath, fatigue, myalgia, headache, new loss of taste or smell, sore throat, congestion, runny nose, nausea or vomiting, diarrhea) • Has at least one high-risk condition in Table 1 		<ul style="list-style-type: none"> • Asymptomatic • Hospitalized due to COVID-19 • Requiring oxygen therapy due to COVID-19 • Requiring increase in baseline oxygen due to COVID-19 in those on chronic oxygen therapy
<p>Sotrovimab[7] Outpatient Only Available through an EUA Sotrovimab Fact Sheet for Healthcare Providers Sotrovimab Fact Sheet for Patients</p>	<p>Treatment for \geq 12 years old AND $>$ 40 kg</p> <p>500 mg IV x 1 over 30 minutes</p>	<ul style="list-style-type: none"> • Targets an epitope in the receptor-binding domain of the spike protein • Anticipated to have activity against the Omicron variant • COMET-ICE: randomized, multi-center, double-blind, placebo-controlled trial included 583 outpatients with mild to moderate COVID-19 who were at high risk for disease progression. Primary endpoint was hospitalization for $>$ 24 hrs or who died from any cause by Day 29. Endpoint events occurred in 3 of 291 (1%) sotrovimab patients vs. 21 of 292 (7%) placebo patients. Sotrovimab associated with 6% absolute reduction and 85% relative reduction in hospitalizations or death. • Pregnancy: Should be considered 1st line in pregnancy for nonhospitalized patients • Adverse Effects: serious hypersensitivity reactions, anaphylaxis, infusion-related reactions – fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash, urticaria, pruritus, myalgia, dizziness
<p>Molnupiravir[8] Outpatient Only Available through an EUA Molnupiravir Fact Sheet for Healthcare Providers Molnupiravir Fact Sheet for Patients</p> <p><u>Inclusion Criteria (must meet all)</u></p> <ul style="list-style-type: none"> • Positive SARS-CoV-2 test (rapid antigen or PCR) • One or more symptoms consistent with COVID-19 • Able to receive within 5 days of symptom onset • One or more high-risk conditions in Table 1 • Other preferred FDA-Authorized treatments are not clinically appropriate or accessible 	<p>800 mg (four 200 mg capsules) PO every 12 hours for 5 days with or without food</p> <p>Not authorized for use $>$ 5 consecutive days</p>	<ul style="list-style-type: none"> • Oral prodrug of beta-D-N4-hydroxycytidine (NHC), a ribonucleoside that has broad antiviral activity against RNA viruses. NHC uptake by viral RNA-dependent RNA-polymerases results in viral mutations and lethal mutagenesis. • MOVE-OUT: randomized, placebo-controlled, double-blind trial in non-hospitalized high-risk adults. Primary outcome was hospitalization or death due to any cause at Day 29. Primary events occurred in 6.8% (48 of 709) of molnupiravir patients (47 hospitalizations, 1 deaths), and 9.7% (68 of 699) of placebo patients (59 hospitalizations, 9 deaths). Relative risk reduction 30%. • Pediatrics: not recommended in $<$ 18 yrs old due to bone and cartilage toxicity • Pregnancy: May cause fetal harm. Prior to initiating treatment with molnupiravir, health care providers should assess whether an individual of childbearing potential is pregnant or not. Molnupiravir is authorized to be prescribed to a pregnant individual only after the health care provider has determined that the benefits would outweigh the risks for that individual patient and the known and potential benefits and potential risks of using

<p>Exclusion criteria (if meets any one)</p> <ul style="list-style-type: none"> • < 18 years old due to bone and cartilage toxicity • Asymptomatic • Hospitalized due to COVID-19 • Requiring oxygen therapy due to COVID-19 • Requiring increase in baseline oxygen due to COVID-19 in those on chronic oxygen therapy • Pregnancy 		<p>molnupiravir during pregnancy are communicated to the pregnant individual. Must document that a pregnant individual was made aware of Merck Sharp & Dohme Corp's pregnancy surveillance program at 1-877-888-4231 or pregnancyreporting.msd.com.</p> <ul style="list-style-type: none"> • Breastfeeding: Not recommended during treatment and for four days after the final dose. Pumping and discarding breast milk during treatment and for 4 days after the last dose of molnupiravir may be considered. • Females of Reproductive Potential: Advised to use an effective method of contraception during treatment and for four days after the last dose. • Males of Reproductive Potential: Sexually active individuals with partners of childbearing potential should use an effective method of contraception during treatment and for at least three months after the last dose of molnupiravir. The risk beyond three months is unknown. • Adverse Effects: diarrhea, nausea, dizziness
<p>Remdesivir (Veklury®)[1, 2, 9-12]</p> <p>Inclusion Criteria:</p> <p>Mild to Moderate Illness (3 days)</p> <ul style="list-style-type: none"> • Positive SARS-CoV-2 test (rapid antigen or PCR) • Room air or baseline oxygen • Within 7 days of symptom onset • High-risk for progressing to severe illness <p>Severe (5 days) (must meet all)</p> <ul style="list-style-type: none"> • Positive SARS-CoV-2 test (rapid antigen or PCR) • Hospitalized < 14 days • Oxygen saturation (SpO₂) of ≤94% on room air, OR <ul style="list-style-type: none"> ○ Requiring supplemental oxygen, OR ○ Requiring invasive mechanical ventilation or ECMO* <p><i>*A clear benefit of remdesivir has not been demonstrated in patients who require invasive mechanical ventilation or ECMO, but may be considered in patients recently placed on mechanical ventilation in addition to dexamethasone +/- baricitinib or tocilizumab</i></p>	<p>Treatment for ≥ 12 years old AND > 40 kg</p> <p>Mild to Moderate 200mg IV on day 1, then 100mg IV q24h x 2 days, or hospital discharge, whichever comes first</p> <p>Severe 200mg IV on day 1, then 100mg IV q24h x 4 days, or hospital discharge, whichever comes first</p>	<ul style="list-style-type: none"> • Antiviral that inhibits RNA-dependent RNA polymerase in SARS-CoV-2. • ACTT-1: RCT of 1,059 adults hospitalized with COVID-19. Patients who received remdesivir had significantly faster time to recovery compared to placebo (11 vs. 15 days). Greatest benefit in patients receiving supplemental oxygen • SOLIDARITY: Multinational study by the World Health Organization included 11,266 adults in 30 countries randomized to local standard of care vs. one of four different repurposed antivirals, 2750 were randomized to remdesivir. Compared to standard of care, there was no reduction in mortality, initiation of mechanical ventilation, or duration of hospitalization. • No clear benefit demonstrated in patients requiring invasive mechanical ventilation or ECMO. In ACTT-1, remdesivir did not improve recovery or survival in this subgroup. • PINETREE: 562 nonhospitalized patients >18 years with mild-moderate COVID-19 at high risk of severe disease randomized within 7d of symptom onset to 3d of remdesivir vs. placebo. 87% relative reduction in risk of hospitalization or death at day 28 compared to placebo. • Pregnancy & Breastfeeding: remdesivir has been used during pregnancy and no safety concerns have emerged. • Pediatrics: Lyophilized powder should be used instead of the solution due to the higher amount of SBEC in the solution. • Renal Impairment: Although the manufacturer's labeling recommends against use in patients with eGFR < 30 mL/min, significant toxicity with a 5-day duration is unlikely. • Monitoring: eGFR, hepatic laboratory testing, prothrombin time

<p>Dexamethasone[1, 2, 13-15]</p> <p><u>Inclusion Criteria:</u></p> <ul style="list-style-type: none"> • Mechanically ventilated, or • Requiring supplemental oxygen <p><u>Exclusion Criteria:</u></p> <ul style="list-style-type: none"> • Patients who do not require supplemental oxygen 	<p>Adults: 6 mg IV/PO daily for up to 10 days or until hospital discharge, whichever comes first.</p>	<ul style="list-style-type: none"> • RECOVERY trial: Multicenter, randomized, open-label trial in hospitalized patients randomized to receive dexamethasone had a lower mortality than those who received standard of care. The benefit was seen in patients who required supplemental oxygen. No benefit was seen in patients who did not require supplemental oxygen. • A meta-analysis of seven randomized controlled trials found that administration of corticosteroids was associated with a lower 28-day mortality in critically ill patients with COVID-19. • Alternative steroid regimens have been evaluated with mixed results; however, the most robust clinical evidence remains with dexamethasone 6 mg IV/PO daily for up to 10 days. • Adverse Effects: related to steroid use should be considered including hyperglycemia, electrolyte and fluid-balance abnormalities, secondary infections, psychiatric effects, and critical-illness related myopathy.
<p>Tocilizumab (Actemra®)[1, 2, 16-22] DUE TO A CRITICAL SHORTAGE, use for COVID-19 is restricted to the following as well as previously established inclusion and exclusion criteria below:</p> <ul style="list-style-type: none"> • Pregnant OR • GFR < 15 mL/min or renal replacement therapy OR • Within 24 hours of ICU admission and rapid progression of respiratory failure OR • Unable to obtain enteral access <p>Tocilizumab is available through the FDA’s Emergency Use Authorization (EUA) Tocilizumab Fact Sheet for Healthcare Providers Tocilizumab Fact Sheet for Patients, Parents, and Caregivers</p> <p><u>Inclusion Criteria:</u></p> <ul style="list-style-type: none"> • Receiving systemic corticosteroids AND <ul style="list-style-type: none"> ○ Requiring high-flow oxygen (>0.4 FiO₂/30 L/min of oxygen flow), noninvasive, or invasive mechanical ventilation OR <ul style="list-style-type: none"> ○ Exhibiting rapid progression of respiratory failure <p><u>Exclusion Criteria (if meets any one criterion)</u></p>	<p>Adults: 8 mg/kg (max 800mg) IV x 1 dose <u>in addition to dexamethasone</u></p>	<ul style="list-style-type: none"> • Tocilizumab, a monoclonal anti-IL-6 receptor blocking antibody, has been proposed as a therapeutic agent to mitigate hyperinflammation associated with COVID-19. To date, no IL-6 inhibitor is FDA-approved or authorized for the treatment of COVID-19. • Several trials have failed to demonstrate improvement in clinical status or a reduction of mortality within 1 month of tocilizumab treatment. • REMAP-CAP trial enrolled 803 critically-ill patients requiring respiratory support who were admitted to an ICU. Compared to placebo, the use of tocilizumab reduced in-hospital mortality and increased the number of organ support-free days. • RECOVERY trial enrolled 4116 adults with hypoxia (oxygen saturation < 92% or requiring oxygen therapy) and C-reactive protein ≥ 75 mg/L. Tocilizumab patients demonstrated improved survival at 28 days and were less likely to progress to mechanical ventilation or death. • Adverse Effects: secondary infections, gastrointestinal perforation, anemia, hepatitis, infusion reaction, neutropenia • Pregnancy & Breastfeeding: there is little safety data in pregnancy or breastfeeding. Consultation with clinical experts is recommended.

<ul style="list-style-type: none"> • > 48 hours of ICU admission at BJC hospital • > 10 days of invasive mechanical ventilation • Active systemic bacterial or fungal infection • AST/ALT 10 x upper limit of normal • Neutropenia (ANC < 500 cells/mm³) • Thrombocytopenia (<50,000 cells/mm³) <p><i>In the trials reporting a benefit, tocilizumab was initiated early (within 3 days of hospitalization or within 24 hours of ICU admission.) Tocilizumab may be more beneficial in patients with early rapidly progressing disease.</i></p>		
<p>Baricitinib (Olumiant®)[23, 24]</p> <p>Baricitinib is available through the FDA's Emergency Use Authorization (EUA) Baricitinib EUA Fact Sheet for Health Care Providers Baricitinib EUA Fact Sheet for Patients</p> <p><u>Inclusion Criteria:</u></p> <ul style="list-style-type: none"> • Receiving systemic corticosteroids AND <ul style="list-style-type: none"> ○ Requiring high-flow oxygen (>0.4 FiO₂/30 L/min of oxygen flow), noninvasive, or invasive mechanical ventilation OR ○ Exhibiting rapid progression of respiratory failure <p><u>Exclusion Criteria (if meets any one)</u></p> <ul style="list-style-type: none"> ○ Without enteral access ○ > 48 hours of ICU admission at BJC hospital ○ > 10 days of invasive mechanical ventilation ○ GFR < 15 mL/min or receiving renal replacement therapy or acute kidney injury <p><u>Consider withholding or interruption of therapy for the following:</u></p> <ul style="list-style-type: none"> ○ Absolute lymphocyte count < 200 cell/μL 	<p>Adults: <u>GFR > 60 mL/min:</u> 4 mg PO daily <u>GFR 30-59:</u> 2 mg PO daily <u>GFR: 15-29:</u> 1 mg PO daily Duration: 14 days or until hospital discharge, whichever comes first</p>	<ul style="list-style-type: none"> • Janus kinase (JAK) inhibitor that may prevent cellular immune activation and inflammation in COVID-19. Approved by FDA for severe rheumatoid arthritis. • <u>ACTT-2:</u> multinational, randomized, placebo-controlled trial in 1,033 hospitalized patients with COVID-19 pneumonia found median time to recovery was shorter in the baricitinib plus remdesivir group (7 days) than in the placebo group plus remdesivir group (8 days) in overall cohort. • <u>COV-BARRIER:</u> multinational, randomized, placebo-controlled trial in 1,525 hospitalized patients with pneumonia, and elevation in ≥ 1 inflammatory marker found no significant difference in proportion of patients progressing to high-flow oxygen, noninvasive ventilation, or invasive mechanical ventilation. 28-day mortality and 60-day all-cause mortality was lower in baricitinib group vs. placebo. (8.4% vs. 13.1% and 10.3% vs. 15.2%, respectively). The most pronounced reduction in mortality was in patients hospitalized requiring non-invasive ventilation or high-flow oxygen (23.0% vs. 33.7%, respectively). Encouraging preliminary data suggests mortality benefit in patients on mechanical ventilated or ECMO. Frequency of serious adverse events, infections and VTEs were similar between baricitinib and placebo, respectively.

<ul style="list-style-type: none"> ○ Absolute neutrophil count < 500 cell/μL ○ Suspected drug-induced liver injury 		
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Recommended in the context of a clinical trial OR moderate-quality evidence suggests benefit and has lower potential for harm (i.e., well-designed retrospective, non-randomized studies)

<p>Fluvoxamine[25-27] Outpatient only</p> <p>Based on current available evidence, fluvoxamine may be considered as an alternative for early outpatient treatment of mild-moderate COVID-19 in high-risk patients <u>if no other FDA-authorized treatments are clinically appropriate or available.</u></p> <p><u>Inclusion Criteria (must meet all):</u></p> <ul style="list-style-type: none"> • Laboratory-confirmed COVID-19 (rapid antigen or PCR) • One or more symptoms consistent with COVID-19 • Within 10 days of symptom onset <p>Has at least one high-risk condition in Table</p> <ul style="list-style-type: none"> • Other preferred FDA-authorized treatments are not clinically appropriate or accessible <p><u>Exclusion Criteria (if meets any one criterion)</u></p> <ul style="list-style-type: none"> • Within 2 weeks of receipt of other SSRIs or MAOIs • Asymptomatic • Less than 18 years of age • Hospitalized due to COVID-19 • Requiring oxygen therapy due to COVID-19 • Requiring increase in baseline oxygen due to COVID-19 in those on chronic oxygen therapy 	<p>Adults: 100 mg po twice daily for 10 days</p>	<p>SSRI being studied in COVID as anti-inflammatory</p> <ul style="list-style-type: none"> • WashU study: small, randomized, double-blind, contactless trial vs. placebo in 152 outpatients. Fluvoxamine arm had 8.7% lower likelihood of clinical deterioration over 15 days. • Small observational study: fluvoxamine opt-in group 0/65 hospitalizations vs. 6/48 who chose observation. • <u>TOGETHER Trial:</u> Randomized, double blind, placebo-controlled trial in 1480 patients, fluvoxamine within 7 days of symptom onset reduced risk of ED visit or hospitalization by 29% over 28 days. • <u>Adverse Effects:</u> when used for psychiatric conditions: nausea, diarrhea, insomnia, somnolence, rarely suicidal ideation. • <u>DDIs:</u> <ul style="list-style-type: none"> ○ should not be used within 2 weeks of receipt of other SSRIs or MAOIs due to risk of serotonin syndrome ○ should not be used if taking theophylline, clozapine, olanzapine, or tizanidine ○ may enhance the anticoagulant effects of antiplatelets and anticoagulants ○ should be used with caution with other QT-interval prolonging medications ○ avoid caffeine or limit to ½ of small cup of coffee, one can of soda, or one tea. <p><u>Pregnancy & Breastfeeding:</u> there is little safety data in pregnancy or breastfeeding. Consultation with clinical experts is recommended</p> <p><u>Pediatrics:</u> No data on use for COVID-19</p>
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**Not recommended outside of a clinical trial
Low-quality (i.e., observational) or variable evidence to support use and has higher potential for harm**

<p>Inhaled Prostanoids[28]</p>	<p>Not routinely recommended</p> <p>While there is insufficient data to provide recommendations specific to COVID-19, patients with ARDS may benefit from inhaled prostanoids. Please</p>	<ul style="list-style-type: none"> • To date, no studies have evaluated use in COVID-19 patients. • A nationwide shortage of available agents exists • Data in patients with non-COVID ARDS indicate inhaled prostanoids may reduce mean pulmonary artery pressure and improve oxygenation; however, data demonstrating clinical benefit are lacking. • Inhaled prostanoids are aerosolized for administration and require filter changes that increase potential exposure of
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	consult Critical Care for guidance	particles within the ventilator circuit to the ambient environment.
<p>Ivermectin[1, 2]</p> <p>Information for Patients</p> <p>A patient handout can be found on the BJC intranet</p> <p><i>In response to requests for prescriptions and reports of patients taking livestock formulations:</i></p> <ul style="list-style-type: none"> • Ivermectin is not authorized or approved by the FDA to prevent or treat COVID-19. • Ivermectin has not been shown to be a safe or effective way to prevent or treat COVID-19 in carefully controlled trials. • Ivermectin is not an antiviral (a drug for treating viruses.) • Medications intended for animals should never be used in humans. Preparations for animals are highly concentrated and have ingredients that are not evaluated in humans. • Taking large doses is dangerous and can cause serious harm. • Toxicities associated with misuse and overdose include rash, nausea, vomiting, abdominal pain, severe hepatitis, seizures, coma, and death. • Vaccination remains our safest and most effective tool to prevent COVID-19 <p>Patient Handout can be found</p>	Not recommended outside of a clinical trial	<ul style="list-style-type: none"> • Ivermectin is an antiparasitic drug being evaluated as a potential treatment for COVID-19 due to <i>in vitro</i> studies suggesting it may have antiviral and anti-inflammatory properties. • Although <i>in vitro</i> data suggests ivermectin may inhibit SARS-CoV-2 in cell cultures, pharmacokinetic and pharmacodynamic studies suggest ivermectin doses up to 100-fold higher than those approved for humans would be required to achieve the concentrations necessary to duplicate the drug's antiviral efficacy <i>in vitro</i>. • Many clinical studies have limitations that make them less definitive and informative. Limitations include: incomplete information and significant methodological limitations such as small sample size, various doses and schedules of ivermectin, open-label in which neither participants nor investigators were blinded to treatment arms, various concomitant medications such as corticosteroids, and poorly defined severity and outcome measures. • The NIH has summarized the most impactful available data here • Adequately powered, well-designed clinical trials are needed.
IV Vitamin C[1]	Not recommended outside of a clinical trial	<ul style="list-style-type: none"> • Insufficient data to support use in COVID-19 • The 2021 Surviving Sepsis Guidelines recommend against using IV Vitamin C for adults with sepsis or septic shock. [29]
<p>Other Therapies</p> <ul style="list-style-type: none"> • Nitazoxanide • GM-CSF inhibitors • Interferons • IL-1 inhibitors (e.g., anakinra) • IVIG (non-SARS-CoV-2 specific) • Leronlimab • Other IL-6 inhibitors (e.g., sarilumab, siltuximab) • Other kinase inhibitors (e.g., tofacitinib, ruxolitinib, acalabrutinib, ibrutinib, zanubrutinib) 	Not recommended outside of a clinical trial	

Do not use (therapies with evidence of no benefit and/or potential for harm)[1, 2]

Hydroxychloroquine (Plaquenil)[30-34]	Not recommended	Multiple randomized, double-blind, placebo-controlled trials have shown no evidence of benefit for post-exposure prophylaxis, nor treatment across the spectrum of disease severity. <ul style="list-style-type: none"> • Reports have documented serious dysrhythmias in patients with COVID-19 • ADRs: bone marrow suppression, hypoglycemia, retinal toxicity
Azithromycin	Not recommended	Not recommended with hydroxychloroquine or as monotherapy in hospitalized and in non-hospitalized patients <ul style="list-style-type: none"> • Associated with QTc prolongation and cardiac adverse events, especially in combination with hydroxychloroquine
Colchicine[1, 35]	Not recommended	<ul style="list-style-type: none"> • COLCORONA outpatient trial did not reduce hospitalizations or death and had significantly increased adverse events. • RECOVERY trial in hospitalized patients closed due to lack of evidence for efficacy
Neuraminidase Inhibitors (oseltamivir, zanamavir, peramivir) Baloxavir	Not recommended	<ul style="list-style-type: none"> • Neuraminidase inhibitors are NOT recommended for treatment of COVID-19 as coronaviruses have not been shown to utilize neuraminidase for replication. • No data to support use of baloxavir. • Should only be utilized with influenza co-infection.
Other therapies <ul style="list-style-type: none"> • Lopinavir/ritonavir (Kaletra) • Vitamin D • Zinc • Oral Ribavirin 	Not recommended	<ul style="list-style-type: none"> • Studies showing lack of clinical efficacy, or insufficient data to support use.

APPENDIX

Ritonavir-boosted nirmatrelvir (Paxlovid) Drug-Drug Interaction Guidance

- Ritonavir-boosted nirmatrelvir (Paxlovid) has numerous drug-drug interactions and the potential to cause serious or life-threatening adverse effects. **Before prescribing Paxlovid, clinicians should review the patient’s medication list, including OTC medicines and herbal supplements to assess the risk of drug-drug interactions.**
- **Clinicians who are not experienced in prescribing ritonavir-boosted drugs should refer to the [EUA fact sheet for ritonavir-boosted nirmatrelvir \(Paxlovid\)](#) and the [Liverpool COVID-19 Drug Interactions website](#) for additional guidance.** Consultation with an expert (e.g., clinical pharmacist, HIV specialist, and/or the patient’s specialist provider[s], if applicable) should also be considered.
- Potential management strategies to facilitate the use of Paxlovid may differ depending on the magnitude and significance of the interaction. Potential strategies include:
 - Dose adjustment of the concomitant medication
 - Use of an alternative to the concomitant medication
 - Increased monitoring for potential adverse reactions to the concomitant medication
 - In some instances, temporary withholding of the concomitant medication
 - Careful consideration should be made regarding withdrawal from abrupt discontinuation, formulation, and half-life of the medication, etc.
- These strategies should be considered for the 5-day duration of Paxlovid treatment and for at least 3 to 5 days after treatment completion.
- The dose of Paxlovid should not be adjusted to avoid or mitigate a drug-drug interaction with a concomitant medication.

- The EUA for Paxlovid suggests that individuals who use products containing ethinyl estradiol for contraception should use a backup, nonhormonal contraceptive method because Paxlovid has the potential to decrease ethinyl estradiol levels. However, the enzyme-inducing effects of Paxlovid that would lead to lower hormone exposure are not expected to be clinically significant during 5 days of therapy and, therefore, would not be expected to decrease contraceptive effectiveness. In addition, ethinyl estradiol is always combined with a progestin for contraception. Progestin concentrations are expected to remain similar or increase when Paxlovid is used concomitantly with combined hormonal contraception, which maintains the effectiveness of the oral contraceptive.
- **Deviation from these recommendations may be appropriate in certain clinical scenarios. Providers should exercise clinical judgment** when assessing the risks and benefits of Paxlovid and determine the most appropriate strategy for managing drug-drug interactions between Paxlovid and concomitant medications. This is particularly important in the outpatient setting, where close monitoring may not be feasible. Expert consultation should be considered.
- This table is a guide and **not a comprehensive list of all possible drugs that may interact or should not be coadministered with Paxlovid. For example, many drugs that may require dose adjustment or increased monitoring when coadministered with Paxlovid are not listed in this table.** The [EUA fact sheet for ritonavir-boosted nirmatrelvir \(Paxlovid\)](#) and the [Liverpool COVID-19 Drug Interactions website](#) should be used to identify and manage drug-drug interactions. Before prescribing Paxlovid for patients receiving highly specialized drugs, such as antineoplastics, consultation with the appropriate specialist providers is recommended.

<p>Contraindicated with Paxlovid</p> <p>Prescribe an alternative COVID-19 therapy for patients who are receiving any of the medications listed.</p>	<p>Before prescribing Paxlovid, determine whether the patient is receiving any of the medications listed in this column:</p> <ul style="list-style-type: none"> • If the patient is receiving any of these medications, withhold the medication if clinically appropriate. • If withholding is not clinically appropriate, use an alternative concomitant medication or COVID-19 therapy.^a • Consultation with an expert (e.g., clinical pharmacist, HIV specialist, and/or the patient’s specialist provider[s], if applicable, is strongly recommended.
<p>Amiodarone Apalutamide Bosentan Carbamazepine Cisapride Clopidogrel Clozapine Colchicine in patients with renal and/or hepatic impairment Disopyramide Dofetilide Dronedarone Eplerenone Ergot derivatives Flecainide Flibanserin Glecaprevir/pibrentasvir Ivabradine Lumateperone Lurasidone Mexiletine Phenobarbital Phenytoin Pimozide</p>	<p>Alfuzosin Alprazolam Atorvastatin Avanafil Clonazepam Codeine Cyclosporine^b Diazepam Everolimus^b Fentanyl (withholding transdermal may not be appropriate) Hydrocodone Lomitapide Lovastatin Meperidine (pethidine) Midazolam (oral) Oxycodone Piroxicam Propoxyphene Rosuvastatin Salmeterol Sildenafil for erectile dysfunction Silodosin Simvastatin Sirolimus^b</p>

<p>Contraindicated with Paxlovid</p> <p>Prescribe an alternative COVID-19 therapy for patients who are receiving any of the medications listed.</p>	<p>Before prescribing Paxlovid, determine whether the patient is receiving any of the medications listed in this column:</p> <ul style="list-style-type: none"> • If the patient is receiving any of these medications, withhold the medication if clinically appropriate. • If withholding is not clinically appropriate, use an alternative concomitant medication or COVID-19 therapy.^a • Consultation with an expert (e.g., clinical pharmacist, HIV specialist, and/or the patient’s specialist provider[s]), if applicable, is strongly recommended.
<p>Propafenone Quinidine Ranolazine Rifampin Rifapentine Rivaroxaban Sildenafil for pulmonary hypertension St. John’s wort Tadalafil for pulmonary hypertension Ticagrelor Vorapaxar</p>	<p>Suvorexant Tacrolimus^b Tadalafil for erectile dysfunction Tamsulosin Tramadol Triazolam Vardenafil</p>
<p>^a Expert consultation may be considered. In some cases, dose reduction of the concomitant medication may be an appropriate management strategy.</p> <p>^b Before prescribing ritonavir-boosted nirmatrelvir (Paxlovid) for a patient receiving this immunosuppressant, the patient’s specialist provider(s) should be consulted, given the significant drug-drug interaction potential between ritonavir and the narrow therapeutic index agent and because close monitoring may not be feasible.</p>	

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