COVID-19 OUTPATIENT THERAPEUTICS

Federal Bureau of Prisons

Clinical Guidance

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WHAT'S NEW IN THIS DOCUMENT

- On January 24, 2022, due to the high frequency of the Omicron variant, the FDA withdrew Emergency Use Authorization for both bamlanivimab-etesevimab and casirivimab-imdevimab (REGEN-COV). Information regarding these two monoclonal antibodies have been removed from this guidance.
- On January 21, 2022, the FDA approval for the antiviral *remdesivir (Veklury)* was extended to include use in non-hospitalized adults with mild-to-moderate COVID-19 and at high risk for progression to severe COVID-19.
- Addition of the antiviral *nirmatrelvir co-packaged with ritonavir (Paxlovid)* for treatment of non-hospitalized adults with mild to moderate COVID-19 and at high risk for progression to severe COVID-19.
- Addition of the antiviral *molnupiravir* for treatment of non-hospitalized adults with mild to moderate COVID-19 and at high risk for progression to severe COVID-19 and for whom alternative COVID-19 treatment options authorized by the FDA and available through the BOP are not accessible or clinically appropriate.

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1. PURPOSE

The purpose of this document is to provide guidance on the use of medications approved through emergency use authorization (EUA) or FDA approval for the treatment of mild to moderate COVID-19 AND for the outpatient prevention of COVID-19 illness before or after exposure in patients with risk factors for progression to severe COVID-19 illness.

2. INTRODUCTION

Infection with SARS-CoV-2, the virus that causes COVID-19, can lead to severe symptoms, hospitalization, and death. Several medications have received FDA approval for prevention of COVID-19 illness before or after exposure or treatment of COVID-19 in patients with mild to moderate symptoms and risk factors for severe COVID-19 illness.

- Studies have shown a 10% or greater absolute risk reduction in the need for emergency department visits and hospitalization with effective treatment.
- Due to rapid mutations of the SARS-CoV-2 virus, available treatments may not always be effective for the prevailing variant in BOP institutions. Providers should be aware of the predominant variant in their local area and review the Antiviral Resistance information in the package insert or Section 15 of the EUA Fact Sheet for Health Care Providers for details regarding specific variants and resistance.
  - ➔ *Providers should also refer to* the *CDC COVID Data Tracker for variant proportions as well as information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.*
- Treatment has the potential to prevent progression to severe disease and decrease the number of inmates who need hospitalization in the local community, thereby reducing the overall strain on the healthcare system during times of peak SARS-CoV-2 transmission.
- Treatment appears to work best when started early after the diagnosis is made in appropriately-selected patients. For that reason, it is recommended that each newly diagnosed inmate with COVID-19 be assessed for possible treatment.
- Each institution should assess their ability to administer an IV infusion and manage severe allergic reactions, including anaphylaxis, in consultation with regional healthcare leadership.

➔ *Patients meeting criteria for treatment will also meet criteria for medical isolation when used to treat COVID-19 illness. Staff who have direct or close contact with the patient will need to wear PPE and follow procedures as described in Modules 2 and 3 of the BOP COVID-19 Pandemic Plan, which may be found on Sallyport.*

3. PATIENT SELECTION - CONFIRMED SARS-COV-2 INFECTION

In addition to the below information, refer to *Section 5. Medications* for medication-specific criteria that must be met in order for a patient to be considered for treatment.

CLINICAL PRESENTATION

Patients with risk factors for severe COVID-19 illness and one or more of the following mild or moderate COVID-19 symptoms **may be considered for treatment**:

- Fever
- Cough

- Sore throat
- Malaise
- Headache
- Muscle pain
- Gastrointestinal symptoms
- Shortness of breath with exertion.

Risk Factors for Severe COVID-19 Illness

Treatment is indicated for patients with *at least one* of the following risk factors for progression to severe disease:

- Body mass index (BMI) ≥25
- Chronic kidney disease (CKD)
- Type 1 or type 2 diabetes
- Immunosuppressive disease
- ≥ 65 years of age
- Currently receiving immunosuppressive treatment
- Cardiovascular disease (CVD) or hypertension
- Chronic obstructive pulmonary disease (COPD) or other chronic respiratory disease
- Sickle cell disease
- Neurodevelopmental disorders or other conditions that confer medical complexity
- Medical-related technological dependence (i.e. tracheostomy, gastrostomy, positive pressure ventilation not related to COVID-19)

➔ *Other medical conditions or risk factors may also place a patient at risk for progression to severe disease. This list is not all-inclusive, and EUA authorization or FDA approval is not limited to the conditions listed above. Providers should consider the risk-benefit of use and discuss with their regional medical director as needed.*

Exclusions to Treatment for COVID-19

Treatment is not authorized for use in patients with any of the following conditions:

- Hospitalized due to COVID-19
- Require oxygen therapy due to COVID-19, OR
- 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

Patients with any of the following criteria should be excluded from further evaluation for outpatient treatment based on clinical indicators of severe infection:

- Oxygen saturation (SpO2) ≤ 93% on room air
- Respiratory rate ≥ 30 per minute
- Heart rate ≥125 per minute

➔ *Inmates with clinical indicators of severe COVID-19 illness should be considered for transfer to an outside hospital, as clinically indicated.*

Other criteria which may exclude a patient from treatment include:

- Pregnancy and lactation: Safety and efficacy of mAb and antiviral medications for prophylaxis and treatment COVID-19 disease may not be known in these populations. Molnupiravir is not recommended in pregnant and lactating women. Other treatments may be considered on a case-by-case basis.
- Treatments for COVID-19 should not be administered to anyone with known allergies to any of the components used in the formulation of the interventions

PATIENT PRIORITY LEVELS

When quantities are limited, patients may need to be prioritized for treatment. In situations where it is necessary to triage patients, treatment of COVID-19 should be prioritized over pre or post-exposure prophylaxis. The following are suggested priority criteria for use in these situations, which may be adapted as appropriate and as needed dependent upon circumstances at each institution.

- *Contact the Regional Medical Director (RMD) to discuss any proposed deviation from the below criteria.*
- *Submission and approval of a non-formulary request is required prior to initiation of any mAb or antiviral for COVID-19.*

PRIORITY 1 PATIENT CRITERIA:

- Three or more risk factors for progression to severe disease ***or***
- ≤ 3 days of symptoms ***or***
- Any one of the following risk factors:
  - Body mass index (BMI) ≥35
  - Type 1 or type 2 diabetes
  - ≥ 65 years of age

PRIORITY 2 PATIENT CRITERIA:

- Two or more risk factors for progression to severe disease

PRIORITY 3 PATIENT CRITERIA:

- One risk factor for progression to severe disease

4. PATIENT SELECTION – PRE-EXPOSURE PROPHYLAXIS (PREP)

- Patients who receive mAbs for PrEP must still follow all required infection control measures.
- MAb for PrEP is not a substitution for vaccination and unvaccinated or not fully vaccinated patients should continue to be offered vaccination regularly.
- Contact the Regional Medical Director (RMD) to discuss any proposed deviation from the below criteria.
- Submission and approval of a non-formulary request is required ***prior to*** initiation of mAb for PrEP.

All of the following criteria must be met in order for a patient to be considered for PrEP with mAb for COVID-19:

- Age ≥ 12 years old; weight ≥ 40 kg (88 lb) *and*
- Not currently infected with SARS-CoV-2 and who have not had a known recent exposure to a person infected with SARS-CoV-2 *and*
- Full vaccination is not possible due to severe allergic reaction to COVID-19 vaccine OR who are not expected to mount an adequate immune response after series completion (i.e. persons who have immunocompromising conditions, or take immunosuppressive medications)

5. MEDICATIONS

Currently, several medications have received either Emergency Use Authorization or FDA approval for treatment of mild to moderate SARS-CoV-2 infection in non-hospitalized patients who are at high risk for progressing to severe disease and/or hospitalization. This guidance will cover those medications available for use in the BOP. Tixagevimab-cilgavimab (EVUSHELD) is indicated for pre-exposure prophylaxis only. It is important for the patient to make an informed decision about treatment, considering both the potential benefit of the treatment and the limited safety and efficacy data upon which the EUA decision was based.

REMDESIVIR (VEKLURY)

Remdesivir is an antiviral approved by the FDA for treatment of both hospitalized and non-hospitalized adult patients at high risk for progression to severe COVID-19.

- *The package insert for remdesivir can be found here: https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf*

All of the following criteria must be met in order for a patient to be considered for treatment with remdesivir:

- Positive results of direct SARS-CoV-2 viral testing *and*
- A clinical presentation of mild to moderate COVID-19 symptoms *and*
- Symptom onset within 7 days preceding remdesivir
- Risk factors for severe COVID-19 illness (see Risk Factors for Severe COVID-19 Illness) *and*
- Weight ≥ 40 kg (88 lb)

- *Commercial lab PCR test, rapid PCR test or rapid Ag test are all acceptable means of confirming infection.*

HOW SUPPLIED

Remdesivir is available in two different formulations:

- **100mg lyophilized powder** reconstituted with Sterile Water for Injection and further diluted in a 100 mL or 200 mL 0.9% sodium chloride infusion bag
- **100mg/20 mL (5 mg/mL) solution** diluted in a 250 mL 0.9% sodium chloride infusion bag
- Refer to the manufacturer's package insert for instructions on reconstitution, dilution and administration of remdesivir.
- **This product is preservative-free and therefore should NOT be prepared in advance.**
  - The prepared infusion solution should be diluted and administered **immediately** after it is prepared.
  - If the product is prepared in a *biological safety cabinet or laminar flow hood*, under USP <797> standards, store the diluted infusion solution in the refrigerator between 2°C to 8°C (36°F to 46°F) for no more than 48 hours and at room temperature up to 25°C (77°F) for no more than 24 hours, including infusion time.

TESTING REQUIRED PRIOR TO TREATMENT

- eGFR, hepatic transaminase levels and PT/INR must be determined in all patients prior to treatment and while receiving treatment as clinically appropriate.
  - Consider discontinuing remdesivir if ALT levels increase to greater than 10 times the upper limit of normal or if any ALT elevation is accompanied by signs or symptoms of liver inflammation.

DOSING

- For outpatient use, remdesivir is administered as a single loading dose of 200mg on Day 1 followed by once-daily maintenance doses of 100mg on days 2 and 3 via IV infusion over 30 to 120 minutes.
- Administer as soon as possible after a positive SARS-CoV-2 test and within 7 days of symptom onset.
- Renal impairment: remdesivir is not recommended for patients with eGFR < 30 ml/min. Dosing has not been evaluated for patients with hepatic impairment.
- Patients should be monitored for at least 1 hour after infusion is complete for signs and symptoms of hypersensitivity reactions.

STORAGE

- Lyophilized powder may be stored at room temperature (below 86 °F) until required for use.
- Injection solution may be stored under refrigeration in unopened vials at 2°C to 8°C (36°F to 46°F) until required for use.

SOTROVIMAB

Currently circulating SARS-CoV-2 variants may be associated with resistance to sotrovimab. Providers should be aware of the predominant variant in their local area and review the Antiviral Resistance information in Section 15 of the mAb Fact Sheet for Health Care Providers for details regarding specific variants and resistance.

- Providers may also refer to the CDC COVID Data Tracker for variant proportions as well as information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.

The FDA Fact Sheet for Health Care Providers Emergency Use Authorization of sotrovimab can be found here: https://www.fda.gov/media/149534/download

All of the following criteria must be met in order for a patient to be considered for treatment:

- Positive results of direct SARS-CoV-2 viral testing *and*
- A clinical presentation of mild to moderate COVID-19 symptoms *and*
- Symptom onset within the 10 days preceding treatment *and*
- Risk factors for severe COVID-19 illness (see Risk Factors for Severe COVID-19 Illness) *and*
- Weight ≥ 40 kg (88 lb)

Commercial lab PCR test, rapid PCR test or rapid Ag test are all acceptable means of confirming infection.

DOSING - TREATMENT

- Sotrovimab 500mg is administered as a single dose IV infusion
- Administered as soon as possible after a positive SARS-CoV-2 test and within 10 days of symptom onset.

There are no dosing adjustments recommended for renal or hepatic impairment.

DILUTION AND ADMINISTRATION OF INTRAVENOUS INFUSION

- Refer to the EUA for instructions on reconstitution, dilution and administration of sotrovimab.
- **This product is preservative-free and therefore should NOT be prepared in advance.**
  - The diluted infusion solution should be administered **immediately** after it is prepared.
  - If the product is prepared in a *biological safety cabinet or laminar flow hood*, under USP <797> standards, store the diluted infusion solution in the refrigerator between 2°C to 8°C (36°F to 46°F) for no more than 24 hours and at room temperature up to 25°C (77°F) for no more than 6 hours, including infusion time.

STORAGE

- Store under refrigeration in unopened vials at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze, shake, or expose to direct light.

NIRMATRELVIR-RITONAVIR (PAXLOVID)

The antiviral nirmatrelvir co-packaged with ritonavir (Paxlovid) is approved through EUA for the treatment of non-hospitalized adults with mild to moderate COVID-19 and at high risk for progression to severe COVID-19.

The FDA Fact Sheet for Health Care Providers Emergency Use Authorization for nirmatrelvir-ritonavir can be found here: https://www.fda.gov/media/155050/download

All of the following criteria must be met in order for a patient to be considered for treatment with nirmatrelvir-ritonavir:

- Positive results of direct SARS-CoV-2 viral testing *and*
- A clinical presentation of mild to moderate COVID-19 symptoms *and*
- Risk factors for severe COVID-19 illness (see Risk Factors for Severe COVID-19 Illness below) *and*
- Symptom onset within 5 days preceding nirmatrelvir-ritonavir *and*

Commercial lab PCR test, rapid PCR test or rapid Ag test are all acceptable means of confirming infection.

DOSING - TREATMENT

- 300mg nirmatrelvir (two 150mg tablets) with 100mg ritonavir (one 100mg tablet) with all three tablets taken together orally with or without food twice daily for 5 days.
- Nirmatrelvir must be co-administered with ritonavir.
- Administered as soon as possible after a positive SARS-CoV-2 test and within 5 days of symptom onset.
- Renal Impairment:
  - eGFR ≥30 to <60 mL/min: 150mg nirmatrelvir (one 150mg tablet) with 100mg ritonavir (one 100mg tablet), with both tablets taken together twice daily for 5 days.
  - eGFR <30 mL/min: not recommended
- Hepatic Impairment: not recommended in severe hepatic impairment (Child-Pugh Class C)
- Nirmatrelvir-ritonavir has the potential for significant drug interactions. Refer to the EUA for additional guidance regarding potential drug interactions.
- Refer to the EUA for additional guidance on what to do if patient misses a dose or is hospitalized prior to completely treatment.

MOLNUPIRAVIR

The antiviral molnupiravir is approved through EUA for the treatment of non-hospitalized adults with mild to moderate COVID-19 and at high risk for progression to severe COVID-19 and for whom alternative COVID-19 treatment options authorized by the FDA and available through the BOP are not accessible or clinically appropriate.

➔ *The FDA Fact Sheet for Health Care Providers Emergency Use Authorization for molnupiravir can be found here: https://www.fda.gov/media/155054/download*

All of the following criteria must be met in order for a patient to be considered for treatment with molnupiravir:

- Positive results of direct SARS-CoV-2 viral testing *and*
- A clinical presentation of mild to moderate COVID-19 symptoms *and*
- Risk factors for severe COVID-19 illness (see Risk Factors for Severe COVID-19 Illness below) *and*
- Symptom onset within 5 days preceding molnupiravir *and*
- Alternative COVID-19 treatment options authorized by the FDA are not accessible or clinically appropriate.

➔ *Commercial lab PCR test, rapid PCR test or rapid Ag test are all acceptable means of confirming infection.*

DOSING - TREATMENT

- Molnupiravir 800g (four 200mg capsules) taken orally every 12 hours for 5 days, with or without food
- Administered as soon as possible after a positive SARS-CoV-2 test and within 5 days of symptom onset.
- Refer to the EUA for additional guidance if patient misses a dose or is hospitalized prior to completely treatment.

➔ *There are no dosing adjustments recommended for renal or hepatic impairment.*

TESTING REQUIRED PRIOR TO TREATMENT

- Molnupiravir should not be used in pregnant or lactating women. Pregnancy testing should be performed prior to initiation when clinically appropriate.

TIXAGEVIMAB AND CILGAVIMAB (EVUSHELD)

Tixagevimab and cilgavimab is authorized for pre-exposure prophylaxis in certain patient populations. It is not authorized for treatment of COVID-19 or for post-exposure prophylaxis in persons exposed to SARS-CoV-2.

➔ *The FDA Fact Sheet for Health Care Providers Emergency Use Authorization of tixagevimab and cilgavimab can be found here: https://www.fda.gov/media/154701/download*

DOSING – PRE-EXPOSURE PROPHYLAXIS

- Tixagevimab 150mg and cilgavimab 150mg is administered as two separate consecutive intramuscular (IM) injections.
- Tixagevimab and cilgavimab should be administered at least two weeks after COVID-19 vaccination.
- Persons who qualify for tixagevimab co-formulated with cilgavimab can be redosed every 6 months while SARS-CoV-2 is in circulation.

➔ *There are no dosing adjustments recommended for renal or hepatic impairment.*

PREPARATION AND ADMINISTRATION OF INTRAMUSCULAR INJECTION

Tixagevimab and cilgavimab cartons contain two vials – one of each antibody. Dilution is not required prior to IM injection.

1. Withdraw 1.5mL tixagevimab (dark grey vial cap) and 1.5mL cilgavimab (white vial cap) in TWO separate syringes. **Do not shake.**
2. Discard any product remaining in the vials.

- **This product is preservative-free and therefore should NOT be prepared in advance.**
  - Prepared syringes should be administered **immediately**.
  - If the product is prepared in a *biological safety cabinet or laminar flow hood*, under USP <797> standards, the total time from vial puncture to administration must not exceed 4 hours, regardless if stored in the refrigerator or at room temperature.

The infusion solution should be administered by a qualified healthcare professional using the following instructions:

1. Administer the two syringes consecutively at different injection sites, preferably one in each of the gluteal muscles.
2. Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete

STORAGE

- Store under refrigeration in unopened vials at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze, shake, or expose to direct light.

6. PATIENT EDUCATION

- **Prior to administration of remdesivir**, patients should be educated regarding the risk of hypersensitivity reactions and/or transaminase elevations during or after infusion. Patients should be educated to report to a healthcare provider if they experience any symptoms of hypersensitivity reaction or liver inflammation. Patients may be provided a copy of the FDA-approved patient labeling found in the package insert.
  - Patients should continue to follow required infection control measures to include medical isolation, quarantine and the use of PPE.
- **Prior to administration of a medication with Emergency Use authorization**, the healthcare provider must communicate information consistent with the "Fact Sheet for Patients, Parents and Caregivers" (and provide a copy of the Fact Sheet) to include:
  - FDA has authorized the emergency use of the chosen medication for the treatment of mild to moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.
  - The significant known and potential risks and benefits of the selected treatment for COVID-19, and the extent to which such potential risks and benefits are unknown.
  - Information on available alternative treatments and the risks and benefits of those alternatives.
  - The patient has the option to accept or refuse treatment.
  - Patients should continue to follow required infection control measures to include medical isolation, quarantine and the use of PPE.

- Documentation should be entered in the electronic health record that patient was given the EUA "Fact Sheet for Patients, Parents and Caregivers" (if applicable), informed of alternatives to treatment, informed that the medication is an unapproved drug authorized for use under the EUA (if applicable), and consent was received from the patient prior to preparing the administration.

➔ *The FDA-approved package insert (patient education on pages 29-30) for remdesivir can be found here*: *https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf*

➔ *The FDA Fact Sheet for Patients, Parents and Caregivers Emergency Use Authorization for sotrovimab can be found here*: *https://www.fda.gov/media/149533/download*

➔ *The FDA Fact Sheet for Patients, Parents and Caregivers Emergency Use Authorization for nirmatrelvir-ritonavir can be found here*: *https://www.fda.gov/media/155051/download*

➔ *The FDA Fact Sheet for Patients, Parents and Caregivers Emergency Use Authorization for molnupiravir can be found here*: *https://www.fda.gov/media/155055/download*

➔ *The FDA Fact Sheet for Patients, Parents and Caregivers Emergency Use Authorization for tixagevimab and cilgavimab can be found here*: *https://www.fda.gov/media/154702/download*

7. ADVERSE EVENTS

- There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of mAbs and antivirals. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy.
- Infusion-related reactions have been observed with administration of these medications. Signs and symptoms of infusion-related reactions may include:
  - Fever, chills, nausea, headache, weakness, altered mental status, bronchospasm, hypotension or hypertension, arrhythmias, chest pain or discomfort, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.
- If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.
- Mild to moderate transaminase elevations have been observed in clinical trials for remdesivir that resolved upon discontinuation of use.
- Refer to the medication EUA fact sheet for healthcare providers or package insert for additional information regarding side effects of each medication.
- The prescribing health care provider and/or the provider's designee are/is responsible for **mandatory reporting of all medication errors and serious adverse events** potentially related to treatments authorized under EUA within **7 calendar days** from the onset of the event. Any medication error or serious adverse events related to remdesivir should also be reported.
  - Submit adverse event reports to FDA MedWatch: *https://www.accessdata.fda.gov/scripts/medwatch/index.cfm*
    - The reports should include unique identifiers and the words "[*name of mAb*] treatment under Emergency Use Authorization (EUA)" in the description section of the report.
    - A copy of the FDA MedWatch form should also be submitted to the manufacturer. The address for each is listed in the mAb EUA.
  - Adverse events should also be reported on the *BOP Adverse Events Dashboard*

8. NURSING PROTOCOL FOR ADMINISTERING COVID-19 TREATMENTS

The high transmissibility of SARS-CoV-2 may lead to widespread transmission, which often places increased demands on health care staff. The *Appendix 1. Nursing Protocol for Administering COVID-19 Treatment to Patients who are COVID-19 Positive*, and *Appendix 2. Nursing Protocol for Administering Monoclonal Antibody Treatment to Pre-Exposure Patients* have been developed to extend the capacity of health care staff to offer this treatment to more patients. Use of these protocols requires approval by the institution clinical director and documentation of training for each staff member who will utilize them.

Appendix 3. Protocol for Allergic Reactions to Monoclonal Antibody and Antiviral Infusions for COVID-19 has been modified from the standard nursing protocol for allergic reactions to be specific for reactions to this medication.

APPENDIX 1. NURSING PROTOCOL FOR ADMINISTERING COVID-19 TREATMENT TO PATIENTS WHO ARE COVID-19 POSITIVE

All of the following criteria must be met in order for a patient to be considered for treatment with COVID-19 monoclonal antibody or antiviral therapy. See below for a more detailed description.

- Positive results of direct SARS-CoV-2 viral testing *and*
- A clinical presentation of mild to moderate COVID-19 symptoms *and*
- Symptom onset within the 10 days preceding mAb treatment or 7 days preceding antiviral treatment *and*
- Certain risk factors for severe COVID-19 illness *and*
- Age ≥ 18 years old; weight ≥ 40 kg (88 lb). (Patients between the ages of 12 and 18 years are not covered in this protocol.)

Patients who are COVID-19 positive and meet criteria for treatment will also meet criteria for medical isolation. Staff who have direct or close contact with the patient will need to wear PPE and follow procedures as described in Modules 2 and 3 of the BOP COVID-19 Pandemic Plan available on Sallyport.

PRESENTING PROBLEM: Patient is COVID-19 Positive

1. Confirm positive results of direct SARS-CoV-2 viral testing.
2. Commercial lab PCR test, rapid PCR test or rapid Ag test are all acceptable means of confirming infection.

Subjective:

1. Onset and duration of COVID-19 symptoms
2. Nature of symptoms
    a. Loss of sense of taste or smell
    b. Reported fever
    c. Cough
    d. Sore Throat
    e. Malaise
    f. Headache
    g. Muscle Pain
    h. GI Symptoms: N/V/D
    i. Shortness of Breath w/ Exertion
3. Known history of allergies
    a. Food
    b. Medication
    c. Insects
4. Current medications, including over the counter medications

Objective:

1. Vital Signs always including pulse oximetry
2. Positive COVID-19 Test Results; Rapid molecular or antigen testing is acceptable.
3. Weight and BMI
4. Respiratory status
    a. Airway status

b. Respiratory effort
c. Lung sounds

Inclusion Criteria	Exclusion Criteria
Signs/Symptoms of mild to moderate COVID-19 illness *(refer to Section 3. Patient Selection for a list of common signs and symptoms)* *AND* At least one risk factor for severe COVID-19 Illness (*refer to Section 3. Patient Selection for a list of risk factors*)	• Currently 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 • Oxygen saturation (SpO2) ≤ 93% on room air • Respiratory rate ≥ 30 per minute • Heart rate ≥ 125 per minute • Known allergies to any of the components used in the formulation of the interventions • Weight less than 40 kg (88 lbs) • Pregnancy and lactation (Safety and efficacy of COVID-19 mAbs are not known in these populations. Treatment may be considered on a case-by-case basis.)

Assessment:

1. Potential for ineffective airway clearance related to COVID-19
2. Potential for impaired oxygenation secondary to COVID-19

Plan:

1. If patient meets inclusion criteria for administering medication obtain informed consent
   ➔ *All treatment for COVID-19 require a non-formulary request to be submitted and approved.*
2. For instructions on dose, preparation and infusion of mAbs and antivirals, refer to the specific medication under *Section 6. Medications* above.
3. If medication administered through infusion, clinically monitor the patient throughout the infusion and for at least one hour post administration
4. Allergic reaction: If patient develops an allergic reaction to the medication, proceed to the attached Allergic Reaction Protocol (Differs slightly from National Nursing Allergic Reaction Protocol)
5. If patient does not meet inclusion criteria for treatment, continue to monitor as clinically indicated or transfer to local hospital for further monitoring and treatment.
6. Contact the ordering provider for any questions or concerns identified while evaluating the patient, administering the treatment, and during the one-hour post-infusion monitoring period.

Patient Education:

1. Discuss with patient that an adverse reaction may occur, and that they will be monitored throughout and at least one hour post infusion. If any reaction is suspected, the patient should report to staff immediately.
2. If a monoclonal antibody for COVID-19 is administered, patient will not be able to receive the COVID-19 vaccine for 90 days post-treatment. There is no recommended interval for vacation after antiviral therapy for COVID-19.

Disposition:

1. Maintain in medical isolation until patient meets current criteria for release.

APPENDIX 2. NURSING PROTOCOL FOR ADMINISTERING MONOCLONAL ANTIBODY TREATMENT TO PRE-EXPOSURE PATIENTS

This protocol is specifically for administering tixagevimab co-packaged with cilgavimab (EVUSHELD) for the pre-exposure prophylaxis (prevention) of COVID-19 in certain adults.

PRESENTING PROBLEM:

The product is only authorized for those individuals who are not currently infected with COVID-19 virus and who have not recently been exposed to an individual infected with COVID-19. These patients should also have one of the following indications:

- Moderate to severely compromised immune systems due to a medical condition or due to taking immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination:
    - Active treatment for solid tumor and hematologic malignancies
    - Receipt of solid-organ transplant and taking immunosuppressive therapy
    - Receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
    - Moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
    - Advanced or untreated HIV infection (people with HIV and CD4 cell counts <200/mm3, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV)
    - Active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents), or;
- History of severe adverse reactions to a COVID-19 vaccine and/or component(s) of those vaccines, therefore vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended.

Subjective:

1. Documented moderate to severely compromised immune system
2. Symptom screen:
    a. Loss of sense of taste or smell
    b. Reported fever
    c. Cough
    d. Sore Throat
    e. Malaise
    f. Headache
    g. Muscle Pain
    h. GI Symptoms: N/V/D
    i. Shortness of Breath w/ Exertion
3. Known history of allergies

   a. Food
   b. Medication
   c. Insects
4. Current medications, including over the counter medications

Objective:

1. Vital Signs always including pulse oximetry
2. COVID-19 Test Results:
   a. Negative results are required for administration of EVUSHELD
   b. If test results are positive, notify provider for consideration of administering intravenous monoclonal antibody treatment
   c. Rapid molecular or antigen testing is acceptable.
3. Weight and BMI
4. Respiratory status
   a. Airway status
   b. Respiratory effort
   c. Lung sounds

Assessment:

1. Potential for infection related to COVID-19.

Plan:

1. If patient is positive for COVID, symptom screen or testing, and/or has a known exposure to another individual with COVID, then notify provider and do not administer EVUSHELD until cleared by provider.
2. For instructions on dose, preparation and infusion of mAbs, refer to the specific medication under *Section 6. Medications* above.
3. EVUSHELD is two separate injections that are recommended to be administered immediately after preparation, and in the patient's gluteal muscle, one after the other
4. Clinically monitor the patient for at least one hour post administration
5. Allergic reaction: If patient develops an allergic reaction to the medication, proceed to the attached Allergic Reaction Protocol (Differs slightly from National Nursing Allergic Reaction Protocol)
6. Contact the ordering provider for any questions or concerns identified while evaluating the patient, administering the mAb, and during the one-hour post-treatment monitoring period.

Patient Education:

1. Discuss with patient that an adverse reaction may occur, and that they will be monitored for at least one-hour post injection. If any reaction is suspected, the patient should report to staff immediately.

APPENDIX 3. NURSING PROTOCOL FOR ALLERGIC REACTIONS TO MONOCLONAL ANTIBODY AND ANTIVIRAL INFUSIONS FOR COVID-19

PRESENTING PROBLEM: Allergic Reaction to the monoclonal antibody or antiviral treatment

Subjective:

1. Onset and duration of symptoms
2. Nature of symptoms
    a. Difficulty breathing, swelling of throat, cough
    b. Rash, itch, hives
    c. Sneezing, watering eyes
3. Known history of allergies
    a. Food
    b. Medication
    c. Insects
4. Signs and symptoms specific for allergic reaction to mAbs:
        a. Fever
        b. Arrhythmias
            i. Atrial Fibrillation
            ii. Tachycardia
            iii. Bradycardia
        c. Chest pain or discomfort
        d. Weakness
        e. Altered Mental Status
        f. Chills
        g. Nausea
        h. Headache
        i. Bronchospasm
        j. Hypotension or hypertension
        k. Dizziness
        l. Angioedema
        m. Throat Irritation
        n. Rash Including urticarial, pruritus, myalgia
5. Current medications including over the counter medications

Objective:

1. Vital Signs always including pulse oximetry
2. Respiratory status
    a. Airway status
    b. Respiratory effort
    c. Lung sounds
3. Location of any erythema, urticaria, edema, insect stinger
4. EKG

Assessment:

1. Ineffective airway clearance related to pharyngeal swelling
2. Risk for decreased cardiac output related to allergic response
3. Risk for alteration in skin integrity related to allergic response
4. Alteration in comfort related to allergic response/sneezing
5. Potential for Impaired spontaneous ventilation

Plan:

1. Clinically monitor the patient throughout the infusion and for at least one hour post administration
2. Minor allergic reaction, if a reaction is suspected, and is minor,
   a. Slow the infusion down to see if this helps.
   b. Consider administering the medications contained with the moderate allergic reaction section below.
3. Moderate allergic reaction, as defined as generalized rash, scratchy throat, or difficulty breathing with O2 saturations <95% :
   a. Stop infusion
   b. Administer Oxygen to maintain saturations >95%
   c. Administer **diphenhydramine (Benadryl) 50 mg** IV Push
   d. Administer albuterol 0.083% metered dose inhaler (MDI) with spacer if wheezing is present; may repeat every 20 minutes for a total of three treatments. If patient cannot use MDI, albuterol 0.083% solution, 2.5 mg via nebulizer may be used. Follow BOP Pandemic Plan Module 7 for Aerosol Generating Procedures.
   e. Loosen tight clothing and provide calm environment
   f. If based on the nurse's assessment, taking into consideration hours of operations of the department and physician availability, the nurse can determine that the patient is safe to release back to the housing unit, or transfer to the local ER.
4. Severe reaction (*true anaphylaxis*) characterized by hypotension, inability to speak, severe dyspnea, etc.:
   a. Stop infusion
   b. Notify operations LT to initiate transport to local ER without delay.
   c. Administer **Epinephrine Auto-Injector** (Epi-Pen) subcutaneously into mid-outer thigh. May repeat every 5-15 minutes, not to exceed a total of three doses
   d. Place patient in supine position, unless respiratory status requires elevation of the head. Place pregnant patients on their left side.
   e. Monitor vitals every 5 minutes and continuous SpO2
   f. Oxygen 15 liters via NRB, monitor O2 Sat.
   g. Establish IV access with 1 liter of normal saline solution at KVO.
   h. If hypotensive (SBP<100 mmHg), administer fluid bolus in 500 ml increments checking vital signs after each bolus to a total dose of 2000 ml.
   i. If a patient is taking a beta-blocker (most end in –lol; e.g. metoprolol, propranolol, timolol), and is not responding to epi injections, then consider administering glucagon 1-5 mg, IV, over 5 minutes (Glucagon emergency kits only contain 1 mg solution)
   j. Time permitting; consider administering items identified in the Moderate Allergic Reaction section if not already done.

Patient Education:

1. Discuss with patient what caused the allergic reaction and possible methods to avoid exposure in the future.
2. If allergen is unknown, discuss possible suspects with patient. Encourage patient to start journal if appropriate documenting meals, medications, activities, etc.
3. Ensure that patient is fully aware of any changes to his medication regimen ordered by on call provider.
4. Ensure that patient is aware of any newly diagnosed allergens and what groups or classes of foods and medications to avoid.
5. If allergic reaction becomes more severe, report this change to medical.

Disposition:

1. See EMR Disposition field. Mark appropriate response.
2. If the patient was evaluated for a *moderate* reaction, then they will need to follow up the next AM for reevaluation.
3. If the patient was evaluated for a *SEVERE* reaction, then the patient will need to follow-up upon return from the hospital, and if they return after-hours, they will need to ensure they come to medical first thing in the AM for reevaluation.

Adverse Reaction Reporting:

Mandatory reporting of any adverse reaction is required **within 7 calendar days** from the onset of the event. Please report the adverse reaction through the BOP's and FDA's Reporting Systems and to the manufacturer. Links are provided below.

- BOP's Medication Event Reporting Form available on the BOP RX Event Dashboard
- Submit adverse event reports to FDA MedWatch. *https://www.accessdata.fda.gov/scripts/medwatch/index.cfm*
- A copy of the FDA MedWatch form should also be submitted to the manufacturer address listed in the mAb EUA.