COVID-19 OUTPATIENT THERAPEUTICS

Federal Bureau of Prisons

Clinical Guidance

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WHAT'S NEW IN THIS DOCUMENT

- The BOP provides all medications that are FDA authorized through Emergency Use Authorization (EUA) or approved for the prevention or treatment of COVID-19. Guidance and specific information regarding each of these medications can be found in medical references including UpToDate®, the *National Institutes of Health COVID-19 Treatment Guidelines*, and the *FDA COVID-19 EUA website*. Sites should continue to refer to these resources for the most up to date information and contact *BOP-HSD-CFADpharmacy@bop.gov*, their Regional Chief Pharmacist, or Regional Medical Director to inquire about procurement procedures. Generally, all medications will be shipped to an institution within 24 hours or request.

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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.
- Sites should continue to contact *BOP-HSD-CFADpharmacy@bop.gov*, their Regional Chief Pharmacist, or Regional Medical Director to inquire about procurement procedures. Generally, all medications can be shipped to an institution within 24 hours upon request.

➔ *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 the medical references including UpToDate®, the *National Institutes of Health COVID-19 Treatment Guidelines*, and the *FDA COVID-19 EUA website* for medication-specific criteria that must be met in order for a patient to be considered for pre-exposure prophylaxis or 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

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. 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.

6. PATIENT EDUCATION

- **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.

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 • 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 FDA package Insert or EUA.
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. People who previously received monoclonal antibody products for pre-exposure prophylaxis or treatment of COVID-19 can be vaccinated at any time.

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 medications 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.