Federal Response to COVID-19: Therapeutics Clinical Implementation Guide

Outpatient Administration Guide for Healthcare Providers

Last updated: 3/2/2022

Unclassified
COVID-19 outpatient therapeutics can be used to prevent or treat eligible non-hospitalized patients who have tested positive for COVID-19 and have mild to moderate symptoms. Prevention and early treatment for eligible patients can help improve patient outcomes, reduce stress on healthcare facilities, and even save lives.

HHS/ASPR has purchased supplies of COVID-19 therapeutic products and are working with state and territorial health departments as well as national healthcare and medical organizations and associations to get the treatments into the hands of healthcare providers quickly, with a focus on areas of the country hardest hit by the pandemic.

This Clinical Implementation Guide summarizes key information on COVID-19 outpatient therapeutics and aims to support healthcare providers’ understanding of theses therapies and how to implement their administration.

**IMPORTANT NOTE:** The Clinical Implementation Guide is updated regularly following changes to COVID-19 therapeutics’ Emergency Use Authorizations (EUAs); however, there may be a lag in publishing updated versions. As such it is important for healthcare providers to stay abreast to the latest changes to EUAs and their impact on the allocation, distribution and administration of COVID-19 therapeutics. See the latest information on all FDA products under EUA. [(https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization)](https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization)
HHS’ COVID-19 Therapeutics Homepage & Announcements

**ASPR’s Response to COVID-19 website**
(https://aspr.hhs.gov/COVID-19/Pages/default.aspx)

**New and Notable: COVID-19 Therapeutics Announcements**
(https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx)
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Module 1: COVID-19 Outpatient Therapeutics Overview
Summary of COVID-19 Preventative Agents & Therapeutics

No Illness
- Baseline health status, no infection

Exposed
- Per CDC Close Contact Criteria

Mild to Moderate Symptoms
- Not hospitalized, with limitations\(^1\)

Hospital Admission
- Not hospitalized, with limitations\(^1\)

Hospitalized, no act. medical problems
- Hospitalized, not on oxygen
- Hospitalized, on oxygen

ICU Admission
- Hospitalized, high flow oxygen/ non-invasive ventilation
- Hospitalized, mechanical ventilation/ ECMO

**Not currently authorized for use anywhere in the U.S. due to the prevalence of Omicron.**

COVID-19 VACCINES
- Monoclonal Antibodies for PrEP
  - tixagevimab + cilgavimab (AZ)

Monoclonal Antibodies for PEP
- casirivimab + imdevimab (RGN)**
- bamlanivimab + etesevimab (Lilly)**

Oral Antivirals
- Paxlovid (Pfizer)
- molnupiravir (Merck)

Monoclonal Antibodies for Treatment
- sotrovimab (GSK/Vir)
- bebtelovimab (Lilly)
- bamlanivimab + etesevimab (Lilly)**
- casirivimab + imdevimab (RGN)**

Therapeutic Management of Nonhospitalized Adults With COVID-19
- remdesivir
- tocilizumab
- dexamethasone
- baricitinib

\(^1\) NIH COVID-19 Treatment Guidelines https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/
Tools to Assist in COVID-19 Outpatient Therapeutic Selection

As variant prevalence changes and new therapeutics become available, there are tools and resources available to assist in clinical decision-making for prescribers.


- **Variants of Concern:**
  - The CDC monitors and publishes **variant information** on the CDC Covid-19 Data Tracker ([https://covid.cdc.gov/covid-data-tracker/#variant-proportions](https://covid.cdc.gov/covid-data-tracker/#variant-proportions))
  - Information on variants of concern are updated in Section 15 of FDA fact sheets.
Emergency Use Authorization (EUA) of COVID-19 Therapeutics

- In certain types of emergencies, the FDA can issue an emergency use authorization (EUA), to provide more timely access to critical medical products (including medicines and tests) that may help during the emergency when there are no adequate, approved, and available alternative options.

- The EUA process is different than FDA approval, clearance, or licensing because the EUA standard may permit authorization based on significantly less data than would be required for approval, clearance, or licensing by the FDA. This enables the FDA to authorize the emergency use of medical products that meet the criteria within weeks rather than months to years. Since EUA products are not approved and, thus, do not have labeled indications, “off-label use” of them is not permitted.

- EUAs are in effect until the emergency declaration ends but can be revised or revoked as we evaluate the needs during the emergency and new data on the product’s safety and effectiveness, or as products meet the criteria to become approved, cleared, or licensed by the FDA.

About Emergency Use Authorizations (EUAs)
Current Authorized or Approved COVID-19 Outpatient Therapeutics

• Each product under EUA has an FDA fact sheet for providers and one for patients and caregivers
• For any products with FDA-approved indications, the prescribing information is also included

- nirmatrelvir and ritonavir (Paxlovid)
  - Paxlovid provider fact sheet: https://www.fda.gov/media/155050/download
  - Paxlovid patient fact sheet: https://www.fda.gov/media/155051/download
  - Paxlovid patient fact sheet (Spanish): https://www.fda.gov/media/155075/download

- sotrovimab
  - sotrovimab provider fact sheet: https://www.fda.gov/media/149534/download
  - sotrovimab patient fact sheet: https://www.fda.gov/media/149533/download
  - sotrovimab patient fact sheet (Spanish): https://www.fda.gov/media/154376/download

- bebtelovimab
  - bebtelovimab provider fact sheet: https://www.fda.gov/media/156152/download
  - bebtelovimab patient fact sheet: https://www.fda.gov/media/156153/download
  - bebtelovimab patient fact sheet (Spanish): https://www.fda.gov/media/156155/download
Current Authorized/Approved COVID-19 Outpatient Therapeutics

- Each product under EUA has an FDA fact sheet for providers and one for patients and caregivers
- For any products with FDA-approved indications, the prescribing information is also included

- **remdesivir (Veklury®)**
  - Veklury (remdesivir) Prescribing Information: https://www.vekluryhcp.com/
  - remdesivir provider fact sheet: https://www.fda.gov/media/137566/download
  - remdesivir patient fact sheet: https://www.fda.gov/media/137565/download
  - remdesivir patient fact sheet (Spanish): https://www.fda.gov/media/139460/download

- **molnupiravir**
  - molnupiravir provider fact sheet: https://www.fda.gov/media/155054/download
  - molnupiravir patient fact sheet: https://www.fda.gov/media/155055/download
  - molnupiravir patient fact sheet (Spanish): https://www.fda.gov/media/155115/download

- **tixagevimab and cilgavimab (Evusheld)**
  - Evusheld provider fact sheet: https://www.fda.gov/media/154701/download
  - Evusheld patient fact sheet: https://www.fda.gov/media/154702/download
  - Evusheld patient fact sheet (Spanish): https://www.fda.gov/media/155196/download
Eligibility Criteria for TREATMENT of Mild-to-Moderate COVID-19 Infection in High-Risk Patients

Mild to moderate COVID-19 cases early in infection, who are at high risk for progressing to severe COVID-19 and/or hospitalization\(^1\); with following criteria:

- Adult or pediatric patients 12 years of age and older weighing more than 40kg
- Confirmation via positive PCR or antigen test
- Treatment as soon as possible following positive viral test and within 5-7 days of symptom onset
- Patient symptomatic but not yet progressed to require hospitalization or oxygen therapy (or increase from baseline chronic oxygen therapy)

Monoclonal antibodies (mAbs) and Oral Antivirals (OAVs) given EUA for mild to moderate symptoms of COVID-19 are not authorized for use in patients:

- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who 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

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*Patient eligibility with respect to time since symptom onset varies across agents. See product fact sheets for product-specific durations.
Module 2: Product Information
Products for Pre-Exposure Prophylaxis (PrEP)
Evusheld (tixagevimab and cilgavimab) – AstraZeneca
Monoclonal Antibody for IM Injection

Evusheld Product Information
https://www.evusheld.com
Evusheld Product Information

- FDA Fact Sheets
  - Evusheld provider fact sheet: https://www.fda.gov/media/154701/download
  - Evusheld patient fact sheet: https://www.fda.gov/media/154702/download
  - Evusheld patient fact sheet (Spanish): https://www.fda.gov/media/155196/download

- Manufacturer’s Resources:
  - Website for Healthcare Providers: https://www.evusheld.com/hcp
  - Website for Patients: https://www.evusheld.com/patient

- Additional Resources:
  - NIH COVID-19 Treatment Guidelines Panel’s Statement on Therapies for High-Risk, Nonhospitalized Patients
  - Safety Reporting: https://contactazmedical.astrazeneca.com/
  - Module 4 Monoclonal Antibody Administration
Evusheld (tixagevimab and cilgavimab) Authorization

Evusheld (tixagevimab and cilgavimab) is indicated for PrEP of COVID-19 in adults and pediatric (12 years of age and older, weighing at least 40 kg):

Who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2, **AND**

- Who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination, **OR**
- For whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).

Fact Sheet for Health Care Providers Emergency Use Authorization for EVUSHELD (tixagevimab co-packaged with cilgavimab) (https://www.fda.gov/media/154701/download)
Evusheld (tixagevimab and cilgavimab): Limitations of Authorized Use

• Evusheld is not authorized for use:
  • For treatment of COVID-19.
  • For PEP of COVID-19 in individuals who have been exposed to someone infected with SARS-CoV-2.

• PrEP with Evusheld is not a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended. Individuals for whom COVID-19 vaccination is recommended, including individuals with moderate to severe immune compromise\(^1\) who may derive benefit from COVID-19 vaccination, should receive COVID-19 vaccination.

• In individuals who have received a COVID-19 vaccine, Evusheld should be administered at least 2 weeks after last vaccination.

• Evusheld may only be prescribed by a healthcare provider licensed under state law to prescribe drugs for an individually identified patient and who has the education and training to make the clinical assessment necessary for appropriate use of Evusheld.

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\(^1\) CDC Clinical Considerations for COVID-19 Vaccines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html)
Evusheld (tixagevimab and cilgavimab)

**Dosage and Administration**

- **Initial Dosing:** 300 mg of tixagevimab and 300 mg of cilgavimab administered as two separate consecutive intramuscular injections. preferably one in each of the gluteal muscles, one after the other.

- **Dosing for those previously dosed with 150 mg of tixagevimab and 150 mg of cilgavimab** should receive a second Evusheld dose (150 mg of tixagevimab and 150 mg of cilgavimab) ASAP.

**Contraindications and Precautions**

- History of severe hypersensitivity reactions, including anaphylaxis, to any component of Evusheld.

- Administer with caution to people with any coagulation disorder and at high risk for cardiovascular events.

For more information, see [Fact Sheet for Healthcare Providers: Emergency Use Authorization For EVUSHELD™ (tixagevimab co-packaged with cilgavimab)](https://www.fda.gov/media/154701/download)
Evusheld (tixagevimab and cilgavimab):
Dose Preparation

Each Evusheld carton contains two vials; one of each antibody. Each vial contains an overfill to allow the withdrawal of 150 mg (1.5 mL).

Table 1 Initial Dosage of 300 mg of Tixagevimab and 300 mg of Cilgavimab

<table>
<thead>
<tr>
<th>Evusheld* (tixagevimab co-packaged with cilgavimab)</th>
<th>Antibody dose</th>
<th>Number of vials needed</th>
<th>Volume to withdraw from vial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>tixagevimab 300 mg</td>
<td>2 vials</td>
<td>3 mL</td>
<td></td>
</tr>
<tr>
<td>cilgavimab 300 mg</td>
<td>2 vials</td>
<td>3 mL</td>
<td></td>
</tr>
</tbody>
</table>

* 300 mg of tixagevimab and 300 mg of cilgavimab are to be administered as separate, consecutive intramuscular injections

Table 2 Dosage of 150 mg of Tixagevimab and 150 mg of Cilgavimab^* 150 mg of tixagevimab and 150 mg of cilgavimab are to be administered as separate, consecutive intramuscular injections

<table>
<thead>
<tr>
<th>Evusheld* (tixagevimab co-packaged with cilgavimab)</th>
<th>Antibody dose</th>
<th>Number of vials needed</th>
<th>Volume to withdraw from vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>tixagevimab 150 mg</td>
<td>1 vial</td>
<td>1.5 mL</td>
<td></td>
</tr>
<tr>
<td>cilgavimab 150 mg</td>
<td>1 vial</td>
<td>1.5 mL</td>
<td></td>
</tr>
</tbody>
</table>

^ Dosing for individuals who initially received 150 mg of tixagevimab and 150 mg of cilgavimab

For more information on Dose Preparation and Administration, see Section 2.3 of Fact Sheet for Healthcare Providers: Emergency Use Authorization For EVUSHELD™ (tixagevimab co-packaged with cilgavimab) (https://www.fda.gov/media/154701/download)
Evusheld (tixagevimab and cilgavimab): Repeat Dosing

- The SARS-CoV-2 variants that will be circulating in the United States when Evusheld may need to be redosed are not known at this time and therefore repeat dosing recommendations cannot be made.
- The Fact Sheets will be revised with repeat dosing recommendations in the future when more data are available.

For more information, see [Fact Sheet for Healthcare Providers: Emergency Use Authorization For EVUSHELD™ (tixagevimab co-packaged with cilgavimab)](https://www.fda.gov/media/154701/download)
Products for Treatment of Mild-to-Moderate COVID-19
Paxlovid (nirmatrelvir and ritonavir) – Pfizer

*Oral Antiviral*

Paxlovid Product Information
Paxlovid Product Information

- **FDA Fact Sheets**
  - Paxlovid provider fact sheet: https://www.fda.gov/media/155050/download
  - Paxlovid patient fact sheet: https://www.fda.gov/media/155051/download
  - Paxlovid patient fact sheet (Spanish): https://www.fda.gov/media/155075/download

- **Manufacturer’s Resources:**
  - Website for Healthcare Providers: https://www.covid19oralrx-hcp.com/
  - Website for Patients: https://www.covid19oralrx-patient.com/

- **Additional Resources:**
  - Pfizer Safety Reporting: http://www.pfizersafetyreporting.com/
  - Module 5 Oral Therapeutics Administration
Paxlovid Authorization

- FDA has issued an EUA for the treatment of mild-to-moderate coronavirus disease (COVID-19) in adults (12 years of age and older weighing more than 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization and death, as soon as possible after diagnosis of COVID-19 and within 5 days of symptom onset.

- Paxlovid includes: nirmatrelvir (a SARS-CoV-2 main proteases inhibitor) and ritonavir (a CYP34A inhibitor)

- Limitations of authorized use:
  - Not authorized for initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19
  - Paxlovid is not authorized for pre-exposure or post-exposure prophylaxis for prevention of COVID-19
  - Not authorized for use longer than 5 consecutive days

- Paxlovid may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which Paxlovid belongs (i.e., anti-infectives).

Fact Sheet for Health Care Providers Emergency Use Authorization of PAXLOVID (https://www.fda.gov/media/155050/download)
Paxlovid

Dosage and Administration

- **eGFR 60 or greater**: 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) taken together twice daily for 5 days.
- **eGFR > 30 mL/min to < 60 mL/min**: 150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet) taken together twice daily for 5 days.
- **eGFR <30 mL/min**: currently not recommended
- **Severe hepatic impairment (Child-Pugh Class C)**: currently not recommended

Contraindications and Precautions

- History of clinically significant hypersensitivity reactions to the active ingredients or any other components.
- Co-administration with drugs highly dependent on CYP3A for clearance may result in life-threatening reactions¹.
- Co-administration with potent CYP3A inducers may result in reduced nirmatrelvir plasma concentrations and potential loss of virologic response.
- The concomitant use of Paxlovid and certain other drugs may result in potentially significant drug interactions.
- Hepatic transaminase elevations, clinical hepatitis, and jaundice have occurred in patients receiving ritonavir.
- Paxlovid use may lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.


For more information, see [Fact Sheet for Healthcare Providers: Emergency Use Authorization For PAXLOVID](https://www.fda.gov/media/155050/download).
Paxlovid Provider Checklist

- Positive SARS-CoV-2 test
- Age ≥12 years
- Weight ≥40 kg
- High-risk criteria met
- Symptoms consistent with mild-moderate COVID-19
- Symptom onset with 5 days*
- Not hospitalized due to COVID-19
- If clinically indicated, assess patient renal function
  - eGFR ≥60 mL/min, standard dosing
  - eGFR ≥30 to <60 mL/min, dose modification
  - eGFR <30 mL/min, not recommended
- If clinically indicated, assess patient hepatic function
  - Child-Pugh Class C, contraindicated
- **Assess patient’s home medication list for drug-drug interactions**
  - See next slide for more detail

*Prescriber is encouraged to include a note to the pharmacist in the prescription stating:
Please fill prescription by [insert date]. This prescription fill by date is within 5 days from symptom onset and complies with the patient eligibility criteria under the EUA.
Paxlovid Contraindications*

- Hypersensitivity Reactions
  - History of clinically significant hypersensitivity reactions (e.g., TEN, SJS) to its active ingredients (nirmatrelvir or ritonavir) or any other components of the product

- Drugs highly dependent on CYP3A4 for clearance and for which elevated concentrations are associated with severe/life-threatening reactions*
  - Alpha1-adrenoreceptor antagonists: alfuzosin
  - Analgesics: pethidone, piroxicam, propoxyphene
  - Antianginal: ranolazine
  - Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine
  - Anti-gout: colchicine
  - Antipsychotics: lurasidone, pimozide, clozapine
  - Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine
  - HMG-CoA reductase inhibitors: lovastatin, simvastatin
  - PDE5 inhibitor: sildenafil (Revatio) when used for PAH
  - Sedative/hypnotics: triazolam, oral midazolam

- Drugs that are potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir concentrations may be associated with loss of virologic response or resistance*
  - Anticancer drugs: apalutamide
  - Anticonvulsant: carbamazepine, phenobarbital, phenytoin
  - Antimycobacterials: rifampin
  - Herbal product: St John’s Wort (hypericum perforatum)

*NOT COMPLETE LIST OF ALL DDI’s. ALWAYS USE CLINICAL TOOLS/DDI CHECKER AND USE CLINICAL JUDGMENT

For additional information see: NIH COVID-19 Treatment Guidelines Panel’s Statement on Ritonavir-Boosted Nirmatrelvir (Paxlovid) (https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions/)

Paxlovid provider fact sheet: https://www.fda.gov/media/155050/download
Paxlovid Renal Adjustment Instructions for Pharmacists

Figure 1: Remove the nirmatrelvir tablets circled in red from the blister card

Figure 2: Placement of sticker over empty blister cavities and pre-printed dosing instruction after removal of nirmatrelvir tablets

Figure 3: Placement of sticker over pre-printed dosing regimen on carton

Sotrovimab – GSK/Vir
Monoclonal Antibody for IV Infusion

sotrovimab Product Information
https://www.sotrovimab.com
Sotrovimab Product Information

- **FDA Fact Sheets**
  - sotrovimab provider fact sheet: https://www.fda.gov/media/149534/download
  - sotrovimab patient fact sheet: https://www.fda.gov/media/149533/download

- **Manufacturer’s Resources:**
  - Website for Healthcare Providers: https://www.sotrovimab.com/
  - Website for Patients: https://www.sotrovimab.com/patient

- **Additional Resources:**
  - NIH COVID-19 Treatment Guidelines Panel’s Statement on Therapies for High-Risk, Nonhospitalized Patients
  - Therapeutics Distribution https://protect-public.hhs.gov/pages/therapeutics-distribution
  - Safety Reporting Email: WW.GSKAEReportingUS@gsk.com
  - Module 4 Monoclonal Antibody Administration
Sotrovimab Authorization

- FDA has issued an EUA to permit the emergency use of sotrovimab for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg):
  - With positive results of direct SARS-CoV-2 viral testing, **AND**
  - Who are at high risk for progression to severe COVID-19, including hospitalization or death.

- Sotrovimab is not authorized for use in patients:
  - Who are hospitalized due to COVID-19, **OR**
  - Who require oxygen therapy due to COVID-19, **OR**
  - Who 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).

Sotrovimab Dosage and Administration

- For adults and pediatric patients (12 years of age and older weighing at least 40 kg): **500 mg** administered as a **single IV infusion over 15 minutes** for **50-mL infusion bag** or **30 minutes for 100-mL infusion bag**.

- Sotrovimab injection should be prepared by a qualified healthcare professional using aseptic technique.

- Patients should be clinically monitored during and for one hour after sotrovimab administration.

- Sotrovimab should be given as soon as possible after positive results of direct SARS-CoV-2 viral testing and **within 7 days** of symptom onset.
Bebtelovimab – Eli Lilly
Monoclonal Antibody for IV Injection (IV Push)

bebtelovimab Product Information
http://www.lillyantibody.com/bebtelovimab
Bebtelovimab Product Information

- **FDA Fact Sheets**
  - [bebtelovimab provider fact sheet](https://www.fda.gov/media/156152/download)
  - [bebtelovimab patient fact sheet](https://www.fda.gov/media/156153/download)
  - [bebtelovimab patient fact sheet (Spanish)](https://www.fda.gov/media/156155/download)

- **Manufacturer’s Resources:**
  - Website for Healthcare Providers: [http://www.lillyantibody.com/bebtelovimab](http://www.lillyantibody.com/bebtelovimab)
  - Website for Patients: [http://www.lillyantibody.com/bebtelovimab](http://www.lillyantibody.com/bebtelovimab)

- **Additional Resources:**
  - Safety Reporting Email: mailindata_gsmtindy@lilly.com
  - Module 4 Monoclonal Antibody Administration
Bebtelovimab Authorization

- FDA has issued an EUA to permit the emergency use of bebtelovimab for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg):
  - With positive results of direct SARS-CoV-2 viral testing, **AND**
  - Who are at high risk for progression to severe COVID-19, including hospitalization or death, **AND**
  - For whom alternative COVID-19 treatment options are not clinically appropriate or accessible

*Per EUA: FDA does not consider Veklury® (remdesivir) to be an adequate alternative to bebtelovimab for this authorized use because it may not be feasible or practical for certain patients (e.g., it requires a 3-day treatment duration)*

- Bebtelovimab is not authorized for use in patients:
  - Who are hospitalized due to COVID-19, **OR**
  - Who require oxygen therapy due to COVID-19, **OR**
  - Who 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).

*For more information see [Fact Sheet for Healthcare Providers: Emergency Use Authorization For bebtelovimab](https://www.fda.gov/media/156152/download).*
Bebtelovimab Dosage and Administration

• For adults and pediatric patients (12 years of age and older weighing at least 40 kg): **175 mg** administered as a **single IV injection** (i.e., IV push) **over at least 30 seconds**.

• **Bebtelovimab** injection should be prepared by a qualified healthcare professional using aseptic technique.

• Patients should be clinically monitored during and for one hour after bebtelovimab administration.

• **Bebtelovimab** should be given as soon as possible after positive results of direct SARS-CoV-2 viral testing, and **within 7 days** of symptom onset.

For more information see [Fact Sheet for Healthcare Providers: Emergency Use Authorization For bebtelovimab](https://www.fda.gov/media/156152/download).
Bebtelovimab Preparation

• Remove bebtelovimab vial from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation.

Do not expose to direct heat. Do not shake vial. Inspect the vial.

• Withdraw 2 mL from the vial into the disposable syringe.
• Discard any product remaining in the vial.
• This product is preservative-free and therefore, should be administered immediately.
  o If immediate administration is not possible, store the syringe for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) and up to 7 hours at room temperature (20°C to 25°C [68°F to 77°F]).
  o If refrigerated, allow the prepared syringe to equilibrate to room temperature for approximately 20 minutes prior to administration
• Attach the syringe extension set.
• Prime the extension set.
• Administer the entire contents of the syringe via IV injection over at least 30 seconds.
• After the entire contents of the syringe have been administered, flush the extension set with 0.9% Sodium Chloride to ensure delivery of the required dose.
Veklury (remdesivir) – Gilead
Antiviral for IV Infusion

Veklury Product Information
https://www.vekluryhcp.com/
Veklury (remdesivir) Product Information

- Prescribing Information & FDA Fact Sheets
  - remdesivir provider fact sheet: https://www.fda.gov/media/137566/download
  - remdesivir patient fact sheet: https://www.fda.gov/media/137565/download
  - remdesivir patient fact sheet (Spanish): https://www.fda.gov/media/139460/download

- Manufacturer’s Resources:
  - Website for Healthcare Providers: https://www.vekluryhcp.com/
  - Website for Patients: https://www.veklury.com/

- Additional Resources:
  - NIH COVID-19 Treatment Guidelines Panel’s Statement on Therapies for High-Risk, Nonhospitalized Patients
  - Safety Reporting Email: Safety_fc@gilead.com
Veklury (remdesivir) – Outpatient Use

- FDA approved expanded use of Veklury (remdesivir) to certain non-hospitalized adults and pediatric patients for treatment of mild-to-moderate COVID-19 disease (Jan 21, 2022), including:
  - adults and pediatric patients (12 years of age and older who weigh at least 40 kilograms) with positive results of direct SARS-CoV-2 viral testing, AND
  - who are not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death

- FDA also revised EUA to authorize Veklury (remdesivir) for treatment of certain non-hospitalized pediatric patients:
  - weighing 3.5 kilograms to less than 40 kilograms OR
  - pediatric patients less than 12 years of age weighting at least 3.5 kilograms, with positive results of direct SARS-CoV-2 viral testing, AND
  - who are not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death

- The treatment course of Veklury (remdesivir) should be initiated as soon as possible after diagnosis of symptomatic COVID-19 has been made and within 7 days of symptom onset. The recommended total duration of treatment for non-hospitalized patients is 3 days.

remdesivir provider fact sheet: https://www.fda.gov/media/137566/download
Veklury (remdesivir)

Dosage and Administration

• Dosage:
  • For adults and pediatric patients 12 years of age and older weighing more than 40kg: **200 mg** on Day 1, followed by once-daily maintenance doses of **100 mg** from Day 2 and Day 3 administered only via intravenous infusion over 30 to 120 minutes\(^1\)
  • For pediatric patients weighing 3.5 kg to <40 kg: **5 mg/kg** on Day 1 followed by **2.5 mg/kg** once daily Days 2-3\(^2\)

• Dosage Forms:
  • For injection: **100 mg** of remdesivir as a lyophilized powder, in a single-dose vial
  • Injection: **100 mg/20mL (5mg/mL)** remdesivir, in a single-dose vial

Contraindications and Precautions

• History of clinically significant hypersensitivity reactions to Veklury or any components of the product
• Hypersensitivity including infusion-related and anaphylactic reactions
• Increased risk of transaminase elevations
• Risk of reduced antiviral activity when coadministered with chloroquine phosphate or hydroxychloroquine sulfate

For more information, see \(^1\)Fact Sheet for Healthcare Providers: Emergency Use Authorization For VEKLURY (https://www.fda.gov/media/137566/download) and \(^2\)Veklury Prescribing Information (https://www.gilead.com/-/media/files/pdfs/medicines/COVID-19/veklury/veklury_pi.pdf)
Veklury (remdesivir) (continued)

Pediatric Dosing and Administration:

<table>
<thead>
<tr>
<th>Body weight</th>
<th>Recommended dosage form</th>
<th>Loading dose (on Day 1)</th>
<th>Maintenance dose (from Day 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5 kg to less than 40 kg</td>
<td>Veklury for injection, lyophilized powder Only</td>
<td>5 mg/kg</td>
<td>2.5 mg/kg</td>
</tr>
<tr>
<td>40 kg and higher</td>
<td>Veklury for injection, lyophilized powder Only</td>
<td>200 mg</td>
<td>100 mg</td>
</tr>
</tbody>
</table>

- Lyophilized powder: **100 mg** of Veklury (remdesivir) reconstituted with 19 mL of Sterile Water for Injection
- Further dilute to a concentration of 1.25 mg/mL using 0.9% Sodium Chloride
- Small 0.9% sodium chloride infusion bags (e.g., 25, 50, or 100 mL) or an appropriate sized syringe should be used for pediatric dosing

For more information, see the [Fact Sheet for Healthcare Providers](#).
### Veklury (remdesivir) (continued)

**Recommended Rate of Infusion-Diluted Veklury for Injection Lyophilized Powder for Pediatric Patients Weighing 3.5 kg to Less than 40 kg**

<table>
<thead>
<tr>
<th>Infusion volume</th>
<th>Infusion time</th>
<th>Rate of infusion(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mL</td>
<td>30 min</td>
<td>3.33 mL/min</td>
</tr>
<tr>
<td></td>
<td>60 min</td>
<td>1.67 mL/min</td>
</tr>
<tr>
<td></td>
<td>120 min</td>
<td>0.83 mL/min</td>
</tr>
<tr>
<td>50 mL</td>
<td>30 min</td>
<td>1.67 mL/min</td>
</tr>
<tr>
<td></td>
<td>60 min</td>
<td>0.83 mL/min</td>
</tr>
<tr>
<td></td>
<td>120 min</td>
<td>0.42 mL/min</td>
</tr>
<tr>
<td>25 mL</td>
<td>30 min</td>
<td>0.83 mL/min</td>
</tr>
<tr>
<td></td>
<td>60 min</td>
<td>0.42 mL/min</td>
</tr>
<tr>
<td></td>
<td>120 min</td>
<td>0.21 mL/min</td>
</tr>
<tr>
<td>7 mL</td>
<td>30 min</td>
<td>0.23 mL/min</td>
</tr>
<tr>
<td></td>
<td>60 min</td>
<td>0.12 mL/min</td>
</tr>
<tr>
<td></td>
<td>120 min</td>
<td>0.06 mL/min</td>
</tr>
</tbody>
</table>

\(^a\) Note: Rate of infusion may be adjusted based on total volume to be infused.
Molnupiravir – Merck
Oral Antiviral

molnupiravir Product Information
https://www.molnupiravir-us.com/
Molnupiravir Product Information

- **FDA Fact Sheets**
  - [Molnupiravir provider fact sheet](https://www.fda.gov/media/155054/download)
  - [Molnupiravir patient fact sheet](https://www.fda.gov/media/155055/download)
  - [Molnupiravir patient fact sheet (Spanish)](https://www.fda.gov/media/155115/download)

- **Manufacturer’s Resources:**
  - Website for Healthcare Providers: [https://www.molnupiravir-us.com/hcp/](https://www.molnupiravir-us.com/hcp/)
  - Website for Patients: [https://www.molnupiravir-us.com/patients/](https://www.molnupiravir-us.com/patients/)
  - Report a Pregnancy Exposure: [https://pregnancyreporting.msd.com/](https://pregnancyreporting.msd.com/)

- **Additional Resources:**
  - Safety Reporting Email: dpoc.usa@msd.com
  - Module 5 Oral Therapeutics Administration
Molnupiravir Authorization

- Molnupiravir has been authorized by FDA under an EUA, for the treatment of mild-to-moderate COVID-19 in adults who are at high-risk for progression to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 outpatient treatment options approved or authorized by FDA are not accessible or clinically appropriate.

- Not authorized for:
  - Patients less than 18 years of age
  - Initiation of treatment in patients requiring hospitalization due to COVID-19
  - Use longer than 5 consecutive days

- Molnupiravir may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which molnupiravir belongs (i.e., anti-infectives).

Fact Sheet for Health Care Providers Emergency Use Authorization of Molnupiravir (https://www.fda.gov/media/155054/download)
Molnupiravir

Dosage and Administration

- **800 mg (four 200 mg capsules)** taken orally every 12 hours for 5 days, with or without food.
- Not authorized for use for longer than 5 consecutive days.

Contraindications and Precautions

- No contraindications have been identified based on the limited available data on the emergency use of molnupiravir authorized under this EUA.
- Not recommended for use during pregnancy and not authorized for use in patients under 18 years of age.
- Hypersensitivity reactions, including anaphylaxis have been reported with molnupiravir. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue molnupiravir.

For more information, see [Fact Sheet for Healthcare Providers: Emergency Use Authorization For Molnupiravir](https://www.fda.gov/media/155054/download).
Molnupiravir Provider Checklist

- Positive SARS-CoV-2 test
- Age ≥18 years
- Alternate COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate
- High-risk criteria met
- Symptoms consistent with mild-moderate COVID-19
- Symptom onset with 5 days*
- Not hospitalized due to COVID-19
- Assessment pregnancy and breastfeeding status (if applicable)
- Provide appropriate counseling
  - Females of childbearing potential treated: should use a reliable method of contraception correctly and consistently, as applicable, for the duration of treatment and for 4 days after the last dose of molnupiravir
  - Breastfeeding is not recommended for the duration of treatment and for 4 days after the last dose of molnupiravir
  - Males of reproductive potential treated: if sexually active with females of childbearing potential, should use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose

*Prescriber is encouraged to include a note to the pharmacist in the prescription stating:

Please fill prescription by [insert date]. This prescription fill by date is within 5 days from symptom onset and complies with the patient eligibility criteria under the EUA.
Molnupiravir Prescriber Requirements

All Patients
1. Provide electronic or hard copy of patient fact sheet
2. Document* that patient has received an electronic or hard copy of the patient fact sheet
3. Review the information contained within the patient factsheet with the patient and counsel patient on the known and potential benefits and risks of molnupiravir
4. Advise patients on need for contraception use as appropriate
   • Females of childbearing potential treated: should use a reliable method of contraception correctly and consistently, as applicable, for the duration of treatment and for 4 days after the last dose of molnupiravir
   • Breastfeeding is not recommended for the duration of treatment and for 4 days after the last dose of molnupiravir
   • Males of reproductive potential treated: if sexually active with females of childbearing potential, should use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose
5. The prescribing healthcare provider and/or the provider’s designee must report all medication errors and serious adverse events potentially related to molnupiravir within 7 calendar days from the healthcare provider’s awareness of the event

*How and where documentation occurs is at the discretion of the prescribing health care provider and their clinical site.
Molnupiravir Prescriber Requirements (continued)

Individuals of Childbearing Potential

1. Assess whether pregnant or not
   - Report of last menstrual period in an individual who has regular menstrual cycles, uses a reliable method of contraception correctly and consistently or has had a negative pregnancy test
   - Negative pregnancy test (recommended but not required if other criteria are not met)

2. If pregnant:
   - Counsel the patient regarding the known and potential benefits and potential risks of molnupiravir use during pregnancy
   - Document* that the patient is aware of the known and potential benefits and potential risks of molnupiravir use during pregnancy
   - Make the individual aware of the pregnancy surveillance program
   - If the pregnant individual agrees to participate in the pregnancy surveillance program and allows the prescribing healthcare provider to disclose patient specific information to Merck, the prescribing healthcare provider must provide the patient’s name and contact information to Merck (at 1-877-888-4231 or pregnancyreporting.msd.com)

3. If not pregnant:
   - Make the individual and their partner aware of the pregnancy surveillance program and encourage them to participate should they become pregnant
   - Review contraception requirements per molnupiravir Providers Fact Sheet (https://www.fda.gov/media/155054/download)

*How and where documentation occurs is at the discretion of the prescribing health care provider and their clinical site.
Module 3: Reimbursement
CMS and HRSA Resources

CMS Resources:
- **COVID-19 Monoclonal Antibodies and outpatient administration of Veklury (remdesivir):**

- **Permissible Flexibilities Related to Oral Antiviral Drugs for Treatment of COVID-19 that May Receive U.S. Food and Drug Administration Emergency Use Authorization and are Procured by the U.S. Government**

- **Oral Antiviral NDC Numbers:**
  - Paxlovid: 0069-1085-06
  - molnupiravir: 0006-5055-06, 0006-5055-07

  *Continue to check CMS website for most up to date information: [www.CMS.gov](http://www.CMS.gov)*

HRSA Resources:
- **COVID-19 Claims Reimbursement for the Uninsured**: [https://www.hrsa.gov/CovidUninsuredClaim](https://www.hrsa.gov/CovidUninsuredClaim)
- **FAQ**: [https://coviduninsuredclaim.linkhealth.com/frequently-asked-questions.html](https://coviduninsuredclaim.linkhealth.com/frequently-asked-questions.html)
## CMS: Coverage of Monoclonal Antibody Products to Treat COVID-19

### Medicare

<table>
<thead>
<tr>
<th>Site of Care</th>
<th>Payable by Medicare</th>
<th>Expected Patient Cost-Sharing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Hospital</td>
<td>✓</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Outpatient Hospital or &quot;Hospital without Walls&quot;</td>
<td>✓</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Outpatient Physician Office/Infusion Center</td>
<td>✓</td>
<td>No patient cost-sharing³</td>
</tr>
<tr>
<td>Nursing Home (See third bullet in Key Facts on CMS enforcement discretion)</td>
<td>✓</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Home</td>
<td>✓</td>
<td>No patient cost-sharing</td>
</tr>
</tbody>
</table>

1 Services must be furnished within the scope of the product’s FDA authorization or approval and within the provider’s scope of practice.

2 Under the Hospital Without Walls initiative, hospitals can provide hospital services in other healthcare facilities and sites that would not otherwise be considered to be part of a healthcare facility; or can set up temporary expansion sites to help address the urgent need to increase capacity to care for patients.

3 Cost-sharing may apply to Medicare beneficiaries when they receive care from a provider that doesn’t participate in Medicare.

### Expected Payment to Providers: Key Facts

- Medicare payment for monoclonal antibody products to treat COVID-19 is similar across sites of care, with some small differences.
- Medicare pays for the administration of monoclonal antibody products to treat COVID-19. For example, Medicare will pay a national average of approximately $450 for the administration of certain monoclonal antibody products. Home infusion is reimbursed at a higher rate.
- CMS will exercise enforcement discretion to allow Medicare-enrolled immunizers working within their scope of practice and subject to applicable state law to bill directly and receive direct reimbursement from the Medicare program for administering monoclonal antibody treatments to Medicare Part A Skilled Nursing Facility residents.
- Medicare will pay the provider for these monoclonal antibody products when they are purchased by the provider. Medicare won’t pay if the product is given to the provider for free by, for example, a government entity.
- When purchased by the provider, Medicare payment is typically at reasonable cost or at 95% of the Average Wholesale Price (an amount determined by the manufacturer). These payment amounts vary depending on which type of provider is supplying the product. Original Medicare will pay for these products for beneficiaries enrolled in Medicare Advantage.
- For more specific information about Medicare payments to providers for these monoclonal antibody products, please see these Frequently Asked Questions.

# CMS: Coverage of Oral Antiviral Therapies to Treat COVID-19

## Medicare

<table>
<thead>
<tr>
<th>Site of Care</th>
<th>Payable by Medicare</th>
<th>Expected Patient Cost-Sharing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Hospital</td>
<td>✔️</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Outpatient Hospital or “Hospital without Walls”</td>
<td>✔️</td>
<td>No patient cost-sharing</td>
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<tr>
<td>Outpatient Physician Office</td>
<td>✔️</td>
<td>No patient cost-sharing³</td>
</tr>
<tr>
<td>Nursing Home</td>
<td>✔️</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>✔️</td>
<td>No patient cost-sharing</td>
</tr>
</tbody>
</table>

1 Services must be furnished within the scope of the product’s FDA authorization or approval and within the provider’s scope of practice.

2 Under the Hospital Without Walls initiative, hospitals can provide hospital services in other healthcare facilities and sites that would not otherwise be considered to be part of a healthcare facility; or can set up temporary expansion sites to help address the urgent need to increase capacity to care for patients.

3 Cost-sharing may apply to Medicare beneficiaries when they receive care from a provider that doesn’t participate in Medicare.

## Expected Payment to Providers: Key Facts

- CMS will provide a list of pharmacies that have provider agreements with the USG to dispense the drug in compliance with the terms and conditions of authorization. CMS will provide a list of these pharmacies, including National Provider Identifier (NPI), on the Health Plan Management Site as soon as it is available.

- Pay dispensing fees: While certain USG-procured oral antiviral drug(s) will be made available at no cost to pharmacies, the procurement does not include payment of a dispensing fee to pharmacies. CMS encourages Part D sponsors to pay a dispensing fee to pharmacies that submit claims for these drugs. No ingredient cost can be paid on these claims.

- Part D sponsors should not charge enrollee cost sharing on dispensing fees paid to the pharmacies.

- Sponsors should consult NCPDP Emergency Preparedness Guidance for “Billing for Reimbursement of a Free Product (No associated cost) with No Administration Fee” as they prepare to implement these changes.

- For more specific information about Medicare payments to providers for these monoclonal antibody products, please see these Frequently Asked Questions.

CMS Code for Outpatient Veklury (remdesivir)

- CMS created **HCPCS code J0248** for the Veklury (remdesivir) antiviral medication when administered in outpatient setting

- Code available for use by all payers

- Effective dates of service on or after December 23, 2021:
  - Long descriptor: Injection, remdesivir, 1 mg
  - Short descriptor: Inj, remdesivir, 1 mg

- Medicare Administrative Contractors (MACs) determine Medicare coverage when no national coverage determination, including when providers use FDA-approved drugs for indications other than what is on approved label

- MACs will determine Medicare coverage for HCPCS code J0248 for Veklury (remdesivir) administered in outpatient setting

- See [CMS Website](https://www.cms.gov/monoclonal) for additional information
Module 4: Monoclonal Antibody Administration
Monoclonal Antibody Administration Can Occur Across a Wide Variety of Models

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Ambulatory center</th>
<th>Nursing homes</th>
<th>Mobile sites</th>
<th>Home</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Hospital-based infusion centers</td>
<td>- Infusion centers</td>
<td>- Skilled nursing facilities</td>
<td>- Bus/trailer</td>
<td>- At patient's home</td>
</tr>
<tr>
<td>- Emergency departments</td>
<td>- Urgent care clinics</td>
<td>- Urgent care facilities</td>
<td>- Other mobile sites</td>
<td></td>
</tr>
<tr>
<td>- Urgent care/Obs units/Fast track areas</td>
<td>- Dialysis centers</td>
<td>- Long-term care facilities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Converted space within hospital for COVID infusion</td>
<td>- Alternate care sites</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Alternate care sites</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Pathway to Monoclonals:
Patient with Confirmed COVID-19 Infection

- Treatment likely most beneficial to patients if given early in symptom progression
- EUA requires administration of treatment as soon as possible after confirmed positive test result and within 7 days of symptom onset
- Strong partnership and communication between patients and HCP to get right treatment to right patients at right time
- Fast testing turnaround needed, to efficiently identify positive tests and schedule for treatment

Example of timeline which would fulfill EUA requirements

<table>
<thead>
<tr>
<th>Onset of symptoms</th>
<th>Clinical visit and diagnostic test</th>
<th>Confirmed positive test</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 3 days post symptom onset</td>
<td>≤ 24 hours post diagnostic test</td>
<td>ASAP post positive test result</td>
<td></td>
</tr>
</tbody>
</table>

Treatment required within 7 days of symptom onset

Testing sites should recommend COVID+ patients that are high risk confer with their HCP on potential suitability for Tx

Early administration of treatment needs fast testing turn-around and patient scheduling

Planning required for "Test and treat" or "Test and refer" models

Please reference EUA factsheet for specific treatment guidelines including recommended treatment window
Patient Flow for Outpatient mAbs Product

**Scenario 1: Confirmed positive patient referred for treatment**

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>Treatment</th>
<th>Post-treatment</th>
</tr>
</thead>
</table>
| Confirm documentation of COVID-19 infection via either  
  • Participant-provided lab report  
  • Medical record lab report  
  • Direct communication from a provider or laboratory  
Discuss treatment with patient  
  • Ensure patient meets treatment requirements and understands risks  
Schedule the patient to come in for treatment ASAP  
  • Provide guidance on site visit protocols to patients  
  • Provide patient education on what to expect with administration  
  **Pre-treatment steps should be completed via telemedicine as possible (~30 mins)** | Pre-book time for administration space and follow clear protocol for coming onsite  
  • Ensure operationally ready to receive and treat the patient  
  • Use CDC recommended practices to minimize exposure to others  
Provide treatment to patient  
  • Infusion duration up to ~1 hr\(^1\) with an additional 1 hr of observation post infusion (checks during infusion and observation)  
  • Infusion pumps or gravity-based infusion acceptable  
Ensure preparation for administration reactions as unlikely but possible side effect  
  • Infusion rate may be reduced based on patient circumstances  
  • Ensure emergency action plan in place; ability to activate EMS if necessary, a requirement for administration under EUA | Discharge patient immediately following monitoring completion  
  • Follow clear protocol to minimize risk of exposure to others  
Post-treatment care encouraged to be via telemedicine as possible  
  • Normal follow-up care, no special data tracking requirements |

---

1. Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing
Patient Flow for Outpatient mAbs Product
Scenario 2 and 3: Patient arrives for testing at site with unknown diagnosis

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>Treatment</th>
<th>Post-treatment</th>
</tr>
</thead>
</table>
| **Direct patient to typical testing process for site (onsite or offsite)**  
  • Quick response testing needed for early diagnosis to enable early treatment  
  **Assuming patient discharged to await test results, once patient confirmed positive**  
  **outreach on treatment (~30 mins):***  
  • Discuss treatment with patient  
    - Ensure patient meets treatment requirements and understands risks  
    - Provide guidance on administration and site visit protocols to patients  
  • Schedule the patient to come in for treatment ASAP  
  • Pre-treatment discussion and scheduling should be via telemedicine as possible  
  **In case of point-of-care rapid testing, consider same-day administration. Needs***  
  • Isolated location for patient to wait  
  Availability of treatment space and staff  
  **Pre-book time for administration space and follow clear protocol for coming onsite***  
  • Ensure operationally ready to receive and treat the patient  
  • Use CDC recommended practices to minimize exposure to others  
  **Provide treatment to patient**  
  • Infusion duration up to ~1 hr\(^1\) with an additional 1 hr of observation post infusion (checks during infusion and observation)  
  • Infusion pumps or gravity-based infusion acceptable  
  **Ensure preparation for administration reactions as unlikely but possible side effect**  
  • Infusion rate may be reduced based on patient circumstances  
  • Ensure emergency action plan in place; ability to activate EMS if necessary, a requirement for administration under EUA  
  **Discharge patient immediately following monitoring completion**  
  • Follow clear protocol to minimize risk of exposure to others  
  **Post-treatment care encouraged to be via telemedicine as possible**  
  • Normal follow-up care, no special data tracking requirements  

---

\(^{1}\) Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing
Sample Staffing Models for Antibody Administration

Examples of staff plans (recommended positions may vary depending on the State’s scope of practice for Paramedics as it related to Subcutaneous and or Intravenous administration of medications or mAbs)

- 8-10 bed mAb infusion/observation site
  - 1 physician / advanced practitioner (present or available via telemedicine)
  - 2 Nurses
  - 1 Nurse or Paramedic
  - 2 Paramedics
  - 1 flex position – administrative/ logistics/ runner

- Single station or mobile visit Subcutaneous administration site
  - 1 physician / advanced practitioner (present or available via telemedicine)
  - 1 Nurse / Paramedic per single mobile visit or single station

Average patient (door to door) visit can range from 80-120 minutes

COVID-19 Monoclonal Antibody Therapeutics Calculator for Infusion Sites: https://www.phe.gov/emergency/mAbs-calculator/Pages/default.aspx
Site Preparation for mAb Administration

- Collect administration site location(s), address, and points of contact
  - For mobile or deployed teams, identify the point of contact at the administration site and make contact
  - Site will need dedicated space for isolation of COVID-19 patients
  - Rededication of existing clinical space is permitted under the CMS Hospital Without Walls Initiative

- Ensure a patient scheduling and referral process is in place

- Identify and understand which therapeutics will be administered

- Determine who is responsible for ordering the monoclonal antibody administration
  - Referring provider
  - On-site or telemedicine provider
  - Standing order

- Brief administration team with site objectives

- Team training
  - Site workflow
  - Monoclonal administration
  - Managing adverse reactions with rescue medications on site as applicable

1 Select recommendations for outpatient setting, for more information reference [CDC guidelines](https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html)
**mAbs Preparation**

**Administration preparation process:**
- Prepare sterile infusions in a manner consistent with local laws, regulations, guidelines and policies
- Obtain new vial(s) and/or IV bags if the drug product contains any visible particulate matter

**Needs for space to prepare mAb drug:**
- Dedicated preparation area with sufficient capacity onsite or nearby

**Acceptable equipment for mAb drug storage:**
- Refrigerated storage (2-8° C)
- Temperature control mechanism including temperature monitoring process

Please see EUA manufacturer fact sheet for drug-specific requirements

*Note: product can be prepared for infusion and subcutaneous administration bedside by any qualified medical professional*
Post-mAbs Administration Observation

- Per EUA, “Clinically monitor patients during dose administration and observe patients for at least 1 hour after intravenous infusion or subcutaneous dosing is complete”
- Provide education on follow-up, required isolation per CDC guidelines after COVID-19 exposure or diagnosis, red flags for seeking emergency care
- Respond to severe adverse events/ anaphylaxis
- “Discharge” patient after one-hour post-administration observation if stable and without symptoms of severe adverse reaction, otherwise consider further observation or emergency department evaluation if clinical concern
- Report any severe adverse events as required by the FDA through the process outlined in the EUA
Managing Adverse Reactions to mAbs

- **Monoclonal antibodies may only be administered** in settings in which health care providers have immediate access to medications to treat a severe infusion or hypersensitivity reactions, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

- Early identification of anaphylaxis. Symptoms may include:
  - Respiratory: throat tightness, stridor, hoarseness, wheezing, respiratory distress, coughing, trouble swallowing/drooling, nasal congestion/drainage, sneezing
  - Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain, cramps
  - Cardiovascular: dizziness, fainting, tachycardia, hypotension, cyanosis, pallor, flushing
  - Skin/mucosal: hives, erythema, itching, swelling of eyes, lips, tongue, mouth, face, or extremities
  - Neurologic: agitation, convulsions, altered mental status, sense of impending doom
  - Other: sudden increase in secretions, urinary incontinence
Managing Adverse Reactions to mAbs: Medications and Equipment

- **Should be available** at all sites:
  - Epinephrine (e.g., prefilled syringe or autoinjector)
  - H1 antihistamine (e.g., diphenhydramine, cetirizine)
  - Blood pressure monitor

- **If feasible**, include at sites (not required)
  - Oxygen
  - Bronchodilator (e.g., albuterol)
  - H2 antihistamine (e.g., famotidine, cimetidine)
  - Intravenous fluids
  - Intubation kit
  - Adult-sized pocket mask with one-way valve (CPR mask)

Adapted from [CDC Interim Considerations: Preparing for the potential management of anaphylaxis at COVID-19 vaccination sites](https://www.cdc.gov/vaccines/covid-19/downloads/IntermConsid-Anaphylaxis-covid19-vaccine-sites.pdf)
mAbs Administration Site Record-Keeping and Adverse Event Reporting Requirements

Sites receiving monoclonal antibody will follow established mechanisms for tracking and reporting serious adverse events

- Events that are potentially attributable to monoclonal antibody use must be reported to the FDA
  - Refer to the Fact Sheet for Healthcare Providers as part of EUA for guidance
  - Complete and submit a MedWatch form or complete and fax FDA Form 3500 to report

Site must maintain records regarding use of the monoclonal antibody by patients

- **Inventory information**: e.g., lot numbers, quantity, receiving site, receipt date, product storage
- **Patient information**: e.g., patient name, age, disease manifestation, number of doses administered per patient, other drugs administered

Ensure that any records associated with this EUA are maintained for inspection upon request

Sites will report utilization daily or weekly through the mechanism indicated by their local, state, or territorial health department
# mAb Administration Site Supplies Needed

## Infrastructure
- Seating area with appropriate spacing for patients to receive mAb
- Steel table for product preparation
- Privacy screens if needed
- Protocol/outline for patient flow (written protocol not required however patient flow and infection control should be addressed at each administration site)
- Emergency response plan (written plan not required, however all staff should be aware of the plan for emergency response)

## General supplies
- Infusion Reaction Kit
- Refrigerator
  - Optional to store prepared solution onsite
- Sharps container
- Biohazard disposal bag
- Trash bins and liners
- Disposable disinfecting wipes
- Hand sanitizer
- Thermometer probe covers (if required)
- 70% alcohol wipes
- Paper towels

## PPE
- NIOSH-certified, disposable N95 filter facepiece respirators or better
- Gloves in appropriate sizes
- Gowns
- Surgical face masks for patients
- Eye and face protection (e.g. goggles, safety glasses, face shields)

## Administration Supplies- Subcutaneous
- Alcohol wipes
- 3 or 5mL luer lock syringes (4 required for each patient for subcutaneous administration)
- Appropriate needles for product preparation and subcutaneous administration
  - 21 gauge 1.5 inch needles for product transfer
  - 25 or 27 gauge needles for subcutaneous administration (4 per each patient course)

## Administration Supplies- Intravenous
- IV poles
- Alcohol wipes
- 2x2 gauze pads
- Adhesive bandages
- Medical tape
- Tegaderm bio-occlusive dressing
- Absorbent underpads (blue pads)
- Normal saline bags for mixing/administration- 50-250 mL
- IV administration sets: PVC infusion set with/without DEHP containing 0.2 or 0.22 micron polyethersulfone (PES) in-line filter
- IV catheters
- IV extension set tubing
- 3mL saline syringes
- Needles – stainless steel 18ga
- Optional: Transilluminator (vein finder)

## Patient Intake
- Vital signs machine
- Pulse oximeter
- Thermometer
- Copies of eligibility checklist for treatment/ PEP

## Administrative
- Site-specific documentation
- Patient fact sheets to provide each patient (copies in English, Spanish and other appropriate languages)
Module 5: Oral Therapeutic Administration
Patient Flow for Antiviral Oral Therapies
Scenario 1: Patient arrives at provider visit and medication available onsite

Visit with Provider

Confirm documentation of COVID-19 infection via either
• Participant-provided lab report
• Medical record lab report
• Direct communication from a provider or laboratory

Discuss treatment with patient
• Ensure patient meets treatment requirements and understands risks

Prescribe therapy for patient & provide the medication fact sheet
• Document required patient assessment in medical record
• Provide patient education on medication therapy being prescribed.

Pre-treatment steps should be completed via telemedicine as possible (~30 mins)

Visit Discharge

Medication and Fact Sheet provided to the patient
• Ensure patient is understands medication therapy being provided
• Ensure medication therapy being dispensed complies with federal/state dispensing laws.

Post-visit

Patient to begin prescribed therapy immediately and continue x 5 days

Patient to report any adverse effect to FDA MedWatch
• Patients that present for hospital visit may continue their prescribed antiviral during hospitalization (at discretion of provider).
Patient Flow for Antiviral Oral Therapies

Scenario 2: Patient arrives at provider visit and medication NOT available onsite

### Visit with Provider

Confirm documentation of COVID-19 infection via either
- Participant-provided lab report
- Medical record lab report
- Direct communication from a provider or laboratory

Discuss treatment with patient
- Ensure patient meets treatment requirements and understands risks

Prescribe therapy for patient & provide the medication fact sheet
- Document required patient assessment in medical record
- Provide patient education on medication therapy being prescribed.

Determine locations medication is available in local area.


### Visit Discharge

Prescription and Fact Sheet provided to the patient
- Ensure patient is understands medication therapy being prescribed
- Ensure patient is advised where to go pick up the medication therapy

### Post-visit

Pharmacy receives patient prescription
- Pharmacy should prioritize the prescription fill and ensure timely turnaround to support same day start for therapy.
- Pharmacist verifies prescription is appropriate for patient. Any concerns are clarified with prescribing provider.

Pharmacy staff dispenses product to the patient
- Patient is counseled on medication therapy and reminded to start immediately.

Patient to begin prescribed therapy immediately and continue x 5 days

Patient to report any adverse effect to FDA MedWatch
- Patients that present for hospital visit may continue their prescribed antiviral during hospitalization (at discretion of provider).
Pharmacy Journey

Pharmacy receives antiviral Rx (either product) for patient

Pharmacist reviews fill-by date to ensure Rx still valid

molnupiravir

Dispense prescribed product & molnupiravir EUA Fact Sheet 
(if not provided by prescriber)

If pharmacist has question regarding dosing, possible drug interaction or known contraindication, will need to contact prescriber same day in order to have minimal dispensing delay to patient (time-sensitive nature of drug)

STOP: No fill if outside 5-day therapeutic window & contact prescriber!

Paxlovid

Review patient chart for major drug interactions (if information available)

Dispense prescribed product & Paxlovid EUA Fact Sheet 
(if not provided by prescriber)

Review prescribed dosing for any required renal adjustment requirements prior to dispensing

Dispense prescribed product per EUA required renal dosing packaging requirements & Paxlovid EUA Fact Sheet 
(if not provided by prescriber)

Responsibility of Prescriber to provide EUA Fact Sheet
Module 6: Additional Resources
COVID-19 Vaccination after mAb Administration

Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the US

• Non-hospitalized Covid-19 patients who previously received passive antibody therapy
  ➢ There is no longer any need to delay vaccination following receipt of monoclonal antibody or convalescent plasma beyond recovery from the acute illness (if symptoms were present) and criteria to discontinue isolation have been met.

• Hospitalized Covid-19 patients
  ➢ Follow guidelines from CDC Advisory Committee on Immunization Practices: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#CoV-19-vaccination

Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html)
Update: C19 to HPOP Migration

• USG-purchased Covid-19 Therapeutics Ordering
  ➢ Migrated from C19 to HPOP

• USG-purchased Covid-19 Therapeutic Reporting
  ➢ Existing reporting process will remain in place across four systems (NHSN, HHS Protect, TeleTracking, and HPOP)
  ➢ New therapeutics to be reported in HPOP
Reporting Requirements

For sotrovimab, bam/ete**, REGEN-COV®**

- Long Term Care / Skilled Nursing Facilities
  - NHSN

- Hospitals / Hospital Pharmacies
  - HHSProtect/TeleTracking/Health Departments

- Non-hospital Facilities
  - HHS TeleTracking

Reporting required by 11:59 pm each Wednesday

For Evusheld, Paxlovid, molnupiravir, bebtelovimab

- Reporting required by 11:59 pm daily

**Not currently authorized for use anywhere in the U.S. due to the prevalence of Omicron.

Sites administering/dispensing USG-purchased COVID-19 therapeutics must provide information on product utilization and stock on hand
Thank you!

Questions?

https://ASPR.HHS.gov
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