COVID-19 OUTPATIENT TREATMENT GUIDELINES ROADMAP

COVID-19 Real-Time Learning Network
Brought to you by CDC and IDSA

Last Updated: April 5, 2022

This resource is intended to serve as a guide on available outpatient COVID-19 treatment options, with links to FDA Emergency Use Authorization information and guideline recommendations from national guideline-developing organizations, where available. **It is not intended to endorse or otherwise promote a specific clinical recommendation or course of action.** Additionally, it does not include other forms of guidance that may be available for specific subsets of populations. Finally, the guidelines referenced here may not consider local allocation and availability of scarce resources. Additional information on where to access these therapeutics can be found at the National Infusion Center Association[16] and HHS.[12]

Risk factors for severe COVID-19[11]

Included here are some medical conditions that may place patients at a higher risk for progression to severe COVID-19:

- Age 65 years and older
- BMI of more than 25 kg/m^2
- Pregnancy
- Chronic kidney disease
- Diabetes mellitus
- Immunosuppressing medications
- Cardiovascular disease or hypertension
- Chronic lung disease
- Sickle cell disease
- Neurodevelopmental disorders or conditions that confer medical complexity
- Medical technological dependence, e.g., tracheostomy

When giving products under Emergency Use Authorization, providers must:

1. Give patient fact sheet for patients.
2. Inform patient of alternatives to treatment.
3. Inform patient that this is an unapproved drug.

Options depicted in gray should be considered AFTER other options, if other options are unavailable, or only in certain clinical situations.

Does your patient have COVID?
Positive results of direct SARS-CoV-2 testing

NO → Tixagevimab plus cilgavimab (Evusheld™) is available for pre-exposure prophylaxis in patients who meet the criteria to the right.

Is Emergency Use Authorization[1] met? Including:

- ONLY FOR USE IN moderate to severe immunocompromise and inadequate vaccine response or inability to be vaccinated or mount adequate vaccine response
- Ages 12 and older
- Weight of 40 kg (88 lbs) and higher
- No known current or recent COVID exposure

(Tixagevimab plus cilgavimab is not a substitute for vaccination)

YES → Has vaccine been given?

YES → Evusheld™ can be given 2 weeks following vaccination. See also IDSA and NIH guidelines.

NO

Dosing: Tixagevimab 300 mg IV plus cilgavimab 300 mg IV

YES → Is your patient hospitalized for COVID-19 or requiring increased O_2 for COVID-19?

YES → See CDC[2] / IDSA[4] / NIH[3] guidance.

NO → Does your patient have any symptoms?

NO → Outpatient treatment options not authorized or recommended. Supportive care only.

YES → How many days since symptom onset?

> 8 DAYS → Outpatient treatment options not authorized or recommended. Supportive care only.

	High-titer convalescent plasma[9, 21] See IDSA and NIH guidelines.	Remdesivir[8, 14] (Veklury®) See IDSA and NIH guidelines.	Nirmatrelvir/ritonavir[18,19] (Paxlovid™) See IDSA and NIH guidelines.	Bebtelovimab[13] See IDSA and NIH guidelines.	Molnupiravir[18,19] (Lagevrio®) See IDSA and NIH guidelines.
≤ 5 DAYS	●	●	●	●	●
≤ 7 DAYS	●	●		●	
≤ 8 DAYS	●				

High-titer convalescent plasma[9, 21] See IDSA and NIH guidelines.

Does patient take immunosuppressive medications or have evidence of immunosuppressive disease?[22]

YES → Is Emergency Use Authorization met?[9]

YES → Dosing: 250 mL high-titer convalescent plasma[9]

Remdesivir[8, 14] (Veklury®) See IDSA and NIH guidelines.

Is patient over 12 years OR over 40 kg?[8, 14]

YES → Dosing: 200 mg IV on day 1, 100 mg IV on days 2 & 3

NO → Is Emergency Use Authorization met for patients < 12 years and down to 3.5 kg?[14]

YES → Dosing: 5 mg/kg IV on day 1 followed by 2.5 mg/kg IV once daily from day 2 to day 3

Nirmatrelvir/ritonavir[18,19] (Paxlovid™) See IDSA and NIH guidelines.

Does patient have severe renal impairment (eGFR <30 mL/min) OR severe hepatic impairment (Child-Pugh class C)?

NO → Is patient taking medicines that cannot be given with Paxlovid™?[5]

YES → Can these medicines be substituted or HELD while Paxlovid™ course is given?*

YES → Is Emergency Use Authorization[10] met? Including:

- Age ≥ 12 years
- Weight ≥ 40 kg
- At high risk for progression to severe COVID-19, including hospitalization or death

YES → Paxlovid™ Dosing:[10]

GFR	Nirmatrelvir	Ritonavir
≥60 mL/min	300 mg 2x daily for 5 days	100 mg 2x daily for 5 days
30 to <60 mL/min	150 mg 2x daily for 5 days	100 mg 2x daily for 5 days

*hold prohibited medicines starting 12 hours before Paxlovid™ and reinitiate 3-5 days after final Paxlovid dose

Bebtelovimab[13] See IDSA and NIH guidelines.

If sequencing is available, does the patient have a variant of SARS-CoV-2 against which bebtelovimab is active?

YES → Are alternative COVID-19 treatment options approved or authorized by FDA accessible or clinically appropriate?

NO → Is Emergency Use Authorization[13] met? Including:

- Age ≥ 12 years
- Weight ≥ 40 kg
- At high risk for progression to severe COVID-19, including hospitalization or death

YES → Dosing: 175 mg IV once (over at least 30 seconds)

Molnupiravir[18,19] (Lagevrio®) See IDSA and NIH guidelines.

Are alternative COVID-19 treatment options approved or authorized by FDA accessible or clinically appropriate?

NO → Is your patient age 18 or older?

YES → Is pregnancy ruled out?

YES → Is Emergency Use Authorization[7] met? Including:

- At high risk for progression to severe COVID-19, including hospitalization or death
- People of childbearing potential: Should use reliable contraception for the duration of molnupiravir treatment & for 4 days after it is stopped
- Men: If sexually active, should use a reliable method of contraception during molnupiravir treatment & for 3 months after molnupiravir is stopped

YES → Dosing: Molnupiravir 800 mg (four 200 mg capsules) orally twice daily for 5 days

NO → Due to embryofetal toxicity in animals, **molnupiravir is not recommended for use in pregnancy.**

If the decision is made to use molnupiravir in pregnancy, the prescriber must document that potential benefits and risks of molnupiravir use in pregnancy from the EUA factsheet were discussed with the patient, and the patient was made aware of Merck's pregnancy surveillance program at 1-877-888-4231 or pregnancyreporting.msd.com.

References

1. Evusheld EUA fact sheet: Evusheld Healthcare Providers FS 12202021 (fda.gov)
2. CDC guidelines for clinical management: Management of Patients with Confirmed 2019-nCoV | CDC
3. NIH guidelines: COVID-19 Treatment Guidelines (nih.gov)
4. IDSA guidelines: IDSA Guidelines on the Treatment and Management of Patients with COVID-19 (idsociety.org)
5. NIH Guidelines Panel's Statement on Drug Interactions with Paxlovid: Statement on Paxlovid Drug-Drug Interactions | COVID-19 Treatment Guidelines (nih.gov)
6. Sotrovimab EUA fact sheet: SOTROVIMAB-EUA.PDF (gskpro.com)
7. Molnupiravir EUA fact sheet: FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR MOLNUPIRAVIR (fda.gov)
8. Remdesivir (VekluryTM) Package Insert (Prescribing Information) with the extended approval for outpatient use: veklury_pi.pdf (gilead.com)
9. Convalescent Plasma EUA fact sheet and List of Tests and Cutoffs of High Titers (table on page 9): https://www.fda.gov/media/141477/download
10. Paxlovid EUA Fact Sheet for Healthcare Providers: https://www.fda.gov/media/155050/download
11. CDC List of Medical Conditions with risk of progression to severe COVID-19: Patient-directed format: People with Certain Medical Conditions | CDC Healthcare provider format: Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Providers (cdc.gov)
12. HHS Therapeutics Locator: COVID-19 Therapeutics Locator (arcgis.com)
13. Bebtelovimab EUA fact sheet: Fact Sheet for Healthcare Providers: Emergency Use Authorization for Bebtelovimab
14. Remdesivir EUA fact sheet for use in CHILDREN weighing 3.5 kg to <40 kg OR those less than 12 years old weighing at least 3.5 kg, who are NOT HOSPITALIZED: EUA 046 Veklury (remdesivir) FS for HCPs (01212022) (fda.gov)
15. Combat COVID Website on Treatment Options: COVID-19 Resources For Healthcare Providers | combatCOVID.hhs.gov
16. National Infusion Center Association Website: National Infusion Center Association. Relates to the Access and Availability link.
17. FDA CDER Scientific Review Documents for COVID-19 Related EUAs: CDER Scientific Review Documents Supporting Emergency Use Authorizations for Drug and Biological Therapeutic Products | COVID-19 | FDA
18. University of Liverpool COVID-19 Drug Interactions Page: https://www.covid19-druginteractions.org/prescribing_resources
19. NIH guidance on therapies for high-risk non-hospitalized patients: https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/
20. IDSA guidance on nirmatrelvir/ritonavir (Paxlovid) and molnupiravir: https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management
21. Early Use of High-titer Convalescent Plasma in Outpatients Trial: Randomized Controlled Trial of Early Outpatient COVID-19 Treatment with High-Titer Convalescent Plasma (nih.gov)
22. IDSA guidance on outpatient use of convalescent plasma in immunosuppressed patients: https://www.idsociety.org/globalassets/idsa/practice-guidelines/covid-19/treatment/idsa-covid-19-gl-tx-and-mgmt---convalescent-plasma-2022-02-03.pdf
23. FDA updates Sotrovimab emergency use authorization | FDA

This resource was funded in part by a cooperative agreement with the Centers for Disease Control and Prevention (grant number NU50CK000574). The Centers for Disease Control and Prevention is an agency within the Department of Health and Human Services (HHS). The contents of this resource do not necessarily represent the policy of CDC or HHS, and should not be considered an endorsement by the Federal Government.