Comparison of Therapeutics for Outpatient Management of COVID-19

November 2022: VHA Pharmacy Benefits Management

Since November of 2020, the FDA has authorized 8 medications for the treatment of mild-to-moderate COVID-19 infection in patients at high-risk for progression to severe disease. Four of those, Bamlanivimab (BAM), Bamlanivimab with Etesevimab (BAM+ETE), casirivimab with imdevimab (CAS+IMD) and sotrovimab (SOT) are not longer authorized for use in any state, given they lack activity against more recent variants of concern. All four remaining therapies outlined in this table target the same patient population: **mild to moderate laboratory confirmed symptomatic COVID-19 in those at high-risk for progression to severe disease.** Risk factors for severe disease can be found on the CDC website. This comparison table is intended as a quick reference to navigate available treatment options for this patient population. Choice should be based on patient factors but may also product availability. Additional information is available: PBM SharePoint COVID-19 EUA Documents folder. This document is a summary developed using information available as of 7/20/2022. Please refer to the EUA documents (linked below) and NIH guidelines for the most up to date information due to rapid updates.

Given a potentially limited supply and to ensure appropriate use consistent with the EUA requirements, COVID-19 testing for the purposes of EUA products should ideally be done through VA facilities. However, if logistical issues preclude testing through VHA, the following guidance should be followed. Testing should be performed in accordance with the FDA EUA instructions and guidance to Veterans regarding at-home testing. **A decreasing order of preference for confidence in self-testing is that**: a. The test is performed under **direct observation (proctored)** e.g. during a VVC telehealth visit., b. the test is not performed under direct observation (un-proctored) but an **image of the test** is made available to the provider (e.g. by secure messaging or during a VVC telehealth visit or c. The test is unproctored and an image is not available but the result is **verbally reported** to the provider

Medication (link to EUA)	Dose	Indication	Time to admin.	Efficacy	Warnings / contraindications (CI) / adverse reactions (ADE)	Pertinent additional factors
Remdesivir (RDV)	200mg once, then 100mg daily for 2 days by IV infusion	FDA approved for severe COVID-19, off-label for outpatients mild-moderate, 12 years and older	Within 7 days (per trial inclusion)	**PINETREE trial:** Death/ hosp. by day 28 was 0.7% (RDV) vs. 5.3% (placebo)	**CI:** History of anaphylaxis to RDV or ingredients **Warnings:** hypersensitivity reactions, transaminase elevations **ADEs**: nausea, elevated AST/ALT	Requires multiple days of IV infusion, and should be administered in a setting where hypersensitivity reactions can be managed Logistics may be challenging Off-label use
Nirmatrelvir /ritonavir (PAXLOVID-PAX)	300mg NIM (2 tablets) with 100mg RTV (1 tablet) twice daily for 5 days with or without food.	EUA for 12 years and older, mild-moderate COVID-19 at high risk for progression **Pharmacists are authorized to prescribe PAX under specific conditions outlined in the EUA**	Within 5 days	**EPIC-HR trial:** Death or hospitalization by day 28: 0.8% (PAX) vs. 6.3% (placebo)	**CI:** Severe renal or hepatic impairment (eGFR< 30 ml/min or Child-Pugh C), CI medications hypersensitivity to any component **Warnings:** Drug interactions, hepatotoxicity, HIV-1 drug resistance **ADEs**: dysgeusia, diarrhea, myalgia	Supplied in carton with 5 daily blister packs Dose adjustment for moderate renal insufficiency to 150mg NIM with 100mg RTV twice daily (by removal of tablets from blister pack **which then must be discarded**) Requires medication profile review due to potential drug-drug interactions (see EUA Fact Sheet, NIH Guidelines statement or University of Liverpool Drug interaction checker for more information Note: rebound symptoms after treatment have been noted but currently repeat administration is not recommended as cases of severe disease are uncommon. Patients should re-isolate as per CDC recommendations.
Molnupiravir (MOV)	800mg (4 capsules) twice daily for 5 days with or without food	EUA for 18 years and older mild-moderate COVID-19 at high risk for progression **only if other alternatives are not accessible or clinically appropriate**	Within 5 days	**MOVe-OUT trial:** Death or hospitalization by day 29 was 6.8% (MOV) vs. 9.7% (placebo)	**CI:** None **Warnings:** Possible embryo-fetal toxicity, possible bone/cartilage toxicity in those <18yrs **ADEs:** diarrhea, nausea, dizziness	**Not recommended in pregnancy and lactation:** potential embryo-fetal toxicity based on animal data –If used, extensive discussion/documentation and pregnancy registry Reliable, consistent contraception required during therapy and for 4 days after (females) of childbearing potential or 3 mo. after last dose (males) of reproductive potential No dose adjustment for renal or hepatic dysfunction
Bebtelovimab (BEB)	175mg IV **over 30 seconds**	EUA for 12 years and older mild-moderate COVID-19 at high risk for progression **only if other alternatives are not accessible or clinically appropriate**	Within 7 days	**Subgroup analyses from BLAZE-4:** Death/hospitalization by D 29 in LOW risk patients randomized to BEB (1.6%) vs. BEB+BAM/ETE** (2.4%) vs. placebo (1.6%). Death or hospitalization by day 29 in HIGH-risk patients was 3% with BEB and 4% with BEB+BAM/ETE (no placebo)	**CI:** None **Warnings:** Hypersensitivity reactions, potential for clinical worsening after administration **ADEs:** nausea and vomiting	**Data to support use more limited than other treatments** **Primary endpoint was viral kinetics** Monitor for injection reactions for 1 hour post-dose No dose adjustment renal/hepatic impairment No drug interactions expected **November 2022: Several emerging variants are rapidly increasing in the U.S. that are resistant to BEB, including BQ.1 and BQ.1.1. VHA will continue to monitor and provide additional guidance as this evolves**

Per VA policy, EUA request must be submitted PRIOR to use via this link: https://dvagov.sharepoint.com/sites/VHAPBM/VA_MedSAFE/App/EUA/SitePages/Home.aspx

References:

- **VHA PBM Formulary Management SharePoint \ Clinical Guidance \ FAQ Sheets \ COVID-19 EUA FAQ Documents**
- **NIH COVID-19 Treatment Guidelines, accessed 7/20/2022**
- **IDSA Guidelines on the Treatment and Management of Patients with COVID-19, Accessed 1/5/2022**
- **Gottlieb RL, Vaca CE, Paredes R, et al. Early remdesivir to prevent progression to severe COVID-19 in outpatients. *N Engl J Med* 2021; https://doi.org/10.1056/nejmoa2116846 (ePub ahead of print, 22 Dec 2021)**
- **Liverpool COVID-19 Drug Interaction Checker, Accessed 1/5/2022**
- **FDA Emergency Use Authorization page, Accessed 1/5/2022**

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