Drug Activity Against SARS-CoV-2 Variants and Subvariants – as of 8/1/2023

<table>
<thead>
<tr>
<th>Drug Activity</th>
<th>Omicron XBB</th>
<th>Omicron XBB.1.5</th>
<th>Omicron EG.5</th>
<th>Omicron XBB.1.9.1</th>
<th>Omicron XBB.1.16</th>
<th>Omicron XBB.1.9.2</th>
<th>Omicron XBB.2.3</th>
<th>Omicron XBB.1.16.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evusheld EVUSHELD</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
</tr>
<tr>
<td>(mAb for PrEP, given intramuscularly)</td>
<td>Evusheld Emergency Use Authorization (EUA) amended by FDA on Jan 26, 2023. Evusheld only authorized for use when the combined frequency of non-susceptible variants nationally is less than or equal to 90%. Evusheld is not currently authorized for use in any U.S. Region.</td>
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<tr>
<td>Bebtelovimab</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
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<tr>
<td>(mAb for Covid-19 treatment, given IV)</td>
<td>Due to the high frequency of variants/subvariants that are resistant to it, as of Nov 30, 2022, Bebtelovimab is not authorized for use in any U.S. Region.</td>
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<tr>
<td>Paxlovid</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
</tr>
<tr>
<td>(nirmatrelvir with ritonavir)</td>
<td>(oral Covid-19 antiviral)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Lagevrio</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
</tr>
<tr>
<td>(molnupiravir)</td>
<td>(oral Covid-19 antiviral)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Veklury</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
<td>Active</td>
</tr>
<tr>
<td>(remdesivir)</td>
<td>(IV Covid-19 antiviral)</td>
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<td></td>
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</tbody>
</table>
Key:
- **Active** = drug is currently active or believed to be active against this variant/subvariant
- **Not likely to be active** = based on testing, drug is not likely to be active against this variant/subvariant
- **Not active** = based on testing, drug is inactive against this variant/subvariant
- **No data at this time** = no current testing has been reported about this drug against this variant/subvariant

**Recent Developments / Talking Points:**
- On July 21, 2023, the National Institutes of Health COVID-19 Treatment Guidelines Panel (the Panel) updated the Guidelines with suggestions from some Panel members regarding the management of immunocompromised patients with COVID-19 who have a prolonged and symptomatic course of illness. The Guidelines note there isn’t definitive data to support the following treatment options:
  - Consider a longer and/or additional course of Paxlovid
  - Consider a longer and/or additional course of Veklury
  - Consider the use of high-titer COVID-19 convalescent plasma from a vaccinated donor who recently recovered from COVID-19 likely caused by a similar variant to what the patient has
- Gilead Sciences, Inc. announced that its investigational oral antiviral drug obeldesivir will enter Phase 3 clinical trials to evaluate its safety and efficacy for the treatment of COVID-19. Gilead also manufactures remdesivir (Veklury®), an intravenously administered drug, which is FDA approved for the treatment of COVID-19 in adults and children. Like remdesivir, obeldesivir is an RNA polymerase inhibitor which interferes with SARS-CoV-2 viral replication.
- On May 25, 2023, the U.S. Food and Drug Administration (FDA) approved the oral antiviral drug Paxlovid (nirmatrelvir co-packaged with ritonavir) for the treatment of COVID-19 in adults. The use of Paxlovid in children (aged 12 through 17) remains under Emergency Use Authorization (EUA). Paxlovid continues to be widely available and at no-cost to patients.
- Currently, FDA-approved Paxlovid is not available; therefore, all Paxlovid in use is under the EUA.
- Mutations of the SARS-CoV-2 virus are an expected occurrence and have taken place since the virus was originally discovered (e.g., Alpha, Beta, Delta, Omicron variants).
- The changing epidemiology of Omicron variants and subvariants has substantially diminished the neutralizing ability of monoclonal antibody (mAb) drugs. FDA has paused the EUAs for multiple drugs.
- According to the CDC Nowcast dated 7/22/2023, there are fourteen Omicron variants/subvariants with an estimated prevalence of ≥1% that comprise about 99% of currently circulating SARS-CoV-2 viruses.
- Omicron XBB variants are descendants of the Omicron BA.2 lineage.
- As of July 22, 2023, Omicron variants/subvariants in HHS Region 3 (includes VA, DE, Wash D.C., MD, PA, WV) include:
  - XBB.1.5 estimated prevalence 8.5%
  - XBB.1.16 estimated prevalence 14.4%
  - XBB.1.9.1 estimated prevalence 12.1%
  - XBB.2.3 estimated prevalence 16.2%
  - XBB.1.16.1 est. prevalence 8.1%
  - XBB.1.9.2 estimated prevalence 8.6%
  - XBB.1.5.1 estimated prevalence 0.3%
  - EG.5 estimated prevalence 13.4%
- The three current antiviral drugs (nirmatrelvir with ritonavir [Paxlovid], remdesivir [Veklury], and molnupiravir [Lagevrio]) are expected to have activity against all current circulating variants
- Oral Paxlovid continues to be NIH’s first-choice drug and IV remdesivir the next preferred option for treatment of mild to moderate COVID-19 in high-risk outpatients. See the NIH Treatment Panel’s section on Antiviral Agents, including Antibody Products
- According to its EUA, molnupiravir is a treatment option only if Paxlovid or remdesivir are not appropriate medications for a patient or they are not available.
Prescribers are advised to monitor variant frequency in their area and refer to FDA fact sheets to see if a specific drug is expected to be active against specific variants/subvariants.

**Evusheld:**
- On January 26, 2023, FDA amended the drug’s Emergency Use Authorization stating that Evusheld is only authorized when the combined frequency of non-susceptible variants is less than or equal to 90% according to the CDC Nowcast. In HHS Region 3 (which includes VA) approximately 99% of currently circulating variants are resistant to Evusheld and the drug is not authorized for use in this or any U.S. Region.
  - Evusheld Fact Sheet updated on January 26, 2023. Table 6 (see page 20) notes that Evusheld is not likely to be active against Omicron variants and subvariants.

**Immunocompromised patients:** Currently, Evusheld is not authorized for use in any U.S. Region. Therefore, patients with moderate to severe immunocompromise should have a plan of action in place if they become ill with COVID-19-like symptoms. They are advised to: 1) have a supply of home COVID-19 tests available, 2) test themselves right away, 3) contact their medical provider promptly with the result of the COVID-19 test, 4) have a mechanism in place to obtain Paxlovid promptly if the patient’s healthcare provider prescribes it, and 5) if the patient is unable to take oral Paxlovid, talk with their medical provider about using an alternate drug such as remdesivir, Lagevrio, or COVID-19 convalescent plasma for treatment.
  - To be eligible for treatment with Paxlovid or Lagevrio, patients must start the medication within 5 days of COVID-19 symptom onset. With remdesivir, the drug must be started within 7 days of symptom onset.
  - Patients should be treated as early as possible. Patients with mild symptoms who meet EUA criteria should receive treatment.

“Legacy” monoclonal antibodies (Bamlanivimab/Etesevimab [“Bam/Ete”), REGEN-COV [casirivimab plus imdevimab], and sotrovimab), do NOT have an EUA for any current use including treatment of COVID-19 or postexposure prophylaxis. These drugs are not active against newer Omicron variants.

**Treatment and Testing Resources**

- [COVID-19 Test to Treat Locator](https://www.cdc.gov/coronavirus/2019-ncov/testing/t2t-locator.html) - Test to Treat initiative aims to help people quickly access lifesaving treatments for COVID-19 at little to no cost.

**Sources:**

- [CDC COVID Data Tracker](https://data.cdc.gov/)
- [Evusheld](https://www.fda.gov/drugs/drugs-by-indication/evusheld-tixagevimab-co-packaged-cilgavimab)
- [Evusheld](https://www.cdc.gov/pre-exposure-prophylaxis-evusheld.html)
- [National Institutes of Health (NIH)](https://www.nih.gov/)
- [Paxlovid](https://www.fda.gov/)
  - FDA. Approved package insert (May 2023)