

# The COVID-19 Treatment Guidelines Panel's Interim Statement on Patient Prioritization for Outpatient Anti-SARS-CoV-2 Therapies or Preventive Strategies When There Are Logistical or Supply Constraints

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The COVID-19 Treatment Guidelines Panel (the Panel) has recommended several therapeutic agents for the treatment and prevention of SARS-CoV-2 infection in individuals who are at high risk for progression to severe COVID-19. These anti-SARS-CoV-2 therapeutics are of greatest benefit for nonhospitalized patients who have risk factors for progression to severe COVID-19. The risks for progression are substantially higher for those who are not vaccinated or who are vaccinated but not expected to mount an adequate immune response to the vaccine.

With the increase in cases of COVID-19 and the emergence of the Omicron (B.1.1.529) variant of concern, there may be logistical or supply constraints that make it impossible to offer the available therapy to all eligible patients, making patient triage necessary.

The purpose of this interim statement is to provide guidance on which individuals might receive the greatest benefit from anti-SARS-CoV-2 therapeutics for treatment or prevention. When it becomes necessary to triage patients for receipt of anti-SARS-CoV-2 therapies or preventive strategies, the Panel suggests prioritizing:

- Treatment of COVID-19 over post-exposure prophylaxis (PEP) of SARS-CoV-2 infection.
- Treatment of COVID-19 in unvaccinated or incompletely vaccinated individuals with clinical risk factors for severe illness and vaccinated individuals who are not expected to mount an adequate immune response (see Immunocompromising Conditions below).
- Use of tixagevimab plus cilgavimab (Evusheld) as pre-exposure prophylaxis (PrEP) for severely immunocompromised individuals over moderately immunocompromised individuals (see Immunocompromising Conditions below).

It is anticipated there may be limitations that make it difficult to provide therapeutic agents (e.g., anti-SARS-CoV-2 monoclonal antibodies [mAbs] that are active against Omicron, small molecule antiviral agents) to all who are at high risk of progression to severe COVID-19 and might benefit from these therapies. In this situation, the Panel's opinion on how to prioritize high-risk ambulatory patients for these interventions is provided below. For more specific guidance, see the [Panel's Statement on using mAbs in nonhospitalized patients when Omicron is the predominant circulating variant](#).

## Prioritization of Patients at Highest Risk of Progression to Severe COVID-19

When logistical or supply constraints limit the availability of anti-SARS-CoV-2 mAbs or small molecule antivirals, the Panel recommends that clinicians prioritize their use for patients at highest risk of clinical progression.

Providers should use their clinical judgment when prioritizing the use of anti-SARS-CoV-2 mAbs for treatment or PEP in a specific situation.

Prioritization schemes should consider how to equitably distribute these scarce resources to populations that may include individuals who may have less knowledge of and/or access to these therapies. The availability and distribution of recommended therapies should be monitored to ensure that access to the

products is equitable.

### ***Patient Prioritization for Treatment***

The Panel prioritized the following risk groups for anti-SARS-CoV-2 mAb therapy based on 4 key elements: age, vaccination status, immune status, and clinical risk factors. The groups are listed by tier in descending order of priority.

For a list of risk factors, see the [CDC webpage Underlying Medical Conditions Associated with High Risk for Severe COVID-19](#).

Tier	Risk Groups
1	<ul style="list-style-type: none"> <li>Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (see Immunocompromising Conditions below); <i>or</i></li> <li>Unvaccinated individuals at the highest risk of severe disease (anyone aged <math>\geq 75</math> years or anyone aged <math>\geq 65</math> years with additional risk factors).</li> </ul>
2	<ul style="list-style-type: none"> <li>Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged <math>\geq 65</math> years or anyone aged <math>&lt; 65</math> years with clinical risk factors)</li> </ul>
3	<ul style="list-style-type: none"> <li>Vaccinated individuals at high risk of severe disease (anyone aged <math>\geq 75</math> years or anyone aged <math>\geq 65</math> years with clinical risk factors)</li> </ul> <p><b>Note:</b> Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.</p>
4	<ul style="list-style-type: none"> <li>Vaccinated individuals at risk of severe disease (anyone aged <math>\geq 65</math> years or anyone aged <math>&lt; 65</math> with clinical risk factors)</li> </ul> <p><b>Note:</b> Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.</p>

### ***Patient Prioritization for Pre-Exposure Prophylaxis***

Tixagevimab plus cilgavimab (Evusheld) is authorized for use as SARS-CoV-2 PrEP for individuals who have moderate to severe immunocompromising conditions that may result in an inadequate immune response to COVID-19 vaccination. Unlike anti-SARS-CoV-2 agents used for treatment, tixagevimab plus cilgavimab (Evusheld) is not authorized for use in unvaccinated individuals unless full vaccination is not possible due to a history of severe allergic reaction to the COVID-19 vaccine. Generally speaking, those who qualify for PrEP because of allergy to the vaccine or contraindication to vaccination are less likely to suffer severe consequences, unless they are also moderately to severely immunocompromised.

### **Immunocompromising Conditions**

The Centers for Disease Control and Prevention (CDC) website [COVID-19 Vaccines for Moderately or Severely Immunocompromised People](#) provides a list of moderate and severe immunocompromising conditions.

If these anti-SARS-CoV-2 agents cannot be provided to all moderately to severely immunocompromised individuals because of logistical constraints or supply limitations, the Panel suggests prioritizing their use for those who are least likely to mount an adequate response to COVID-19 vaccination or SARS-CoV-2 infection and who are at risk for severe outcomes, including (but not limited to) the following patients:

- Patients who are within 1 year of receiving B-cell depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)

- Patients receiving Bruton tyrosine kinase inhibitors
- Chimeric antigen receptor T cell recipients
- Post-hematopoietic cell transplant recipients who have chronic graft versus host disease or who are taking immunosuppressive medications for another indication
- Patients with hematologic malignancies who are on active therapy
- Lung transplant recipients
- Patients who are within 1 year of receiving a solid-organ transplant (other than lung transplant)
- Solid-organ transplant recipients with recent treatment for acute rejection with T or B cell depleting agents
- Patients with severe combined immunodeficiencies
- Patients with untreated HIV who have a CD4 T lymphocyte cell count <50 cells/mm<sup>3</sup>

If supplies are extremely limited, the Panel suggests prioritizing those who are more severely immunocompromised (see above list) and who also have additional risk factors for severe disease for the outpatient therapies.

### Clinical Risk Factors

Some of the most important risk factors for severe COVID-19 include (listed alphabetically) age (risk increases with each decade after age 50),<sup>1</sup> cancer, cardiovascular disease, chronic kidney disease, chronic lung disease, diabetes, immunocompromising conditions or receipt of immunosuppressive medications, obesity (body mass index  $\geq 30$ ), pregnancy, and sickle cell disease. For a complete list of risk factors, including information on the relative risk of severe disease, see the [CDC webpage Underlying Medical Conditions Associated with High Risk for Severe COVID-19](#). Of note, the likelihood of developing severe COVID-19 increases when a person has multiple comorbidities.<sup>2</sup>

Although the data on risk factors for severe COVID-19 in children are limited, there is substantial overlap between risk factors in children and those identified in adults, as listed above. Children who are aged <1 year or with obesity, moderate to severe immunosuppression, or those with complex chronic disease and medical complexity with respiratory technology dependence are at substantially increased risk of severe disease.<sup>3</sup>

The FDA Emergency Use Authorizations (EUAs) provide a broad list of medical conditions or other factors as criteria for use of anti-SARS-CoV-2 agents as treatment or PEP. See [the individual EUAs](#) for the full list of these medical conditions and other factors.

### References

1. Centers for Disease Control and Prevention. COVID-19 risks and vaccine information for older adults. 2021. Available at: <https://www.cdc.gov/aging/covid19/covid19-older-adults.html>. Accessed December 22, 2021.
2. Rosenthal N, Cao Z, Gundrum J, Sianis J, Safo S. Risk factors associated with in-hospital mortality in a US national sample of patients with COVID-19. *JAMA Netw Open*. 2020;3(12):e2029058. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33301018>.
3. Kompaniyets L, Agathis NT, Nelson JM, et al. Underlying medical conditions associated with severe COVID-19 illness among children. *JAMA Netw Open*. 2021;4(6):e2111182. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34097050>.