Interim Clinical Considerations for COVID-19 Vaccines: Bivalent Boosters

COVID-19 Vaccination Guidance
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COVID-19 Pre-exposure Prophylaxis Guidance
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ACIP Meeting
9/01/2022
cdc.gov/coronavirus
Bivalent Booster Authorized

- On August 31, 2022:
  - Moderna COVID-19 Vaccine, Bivalent authorized for use in people ages 18 years and older.
  - Pfizer-BioNTech COVID-19 Vaccine, Bivalent authorized for use in people ages 12 years and older
- Authorized as single booster dose administered at least 2 months after either:
  - Completion of primary vaccination with any authorized or approved monovalent COVID-19 vaccine, or
  - Receipt of the most recent booster dose with any authorized or approved monovalent COVID-19 vaccine
mRNA COVID-19 Vaccines No Longer Authorized as Booster Doses for People Ages 12 Years and Older

- Monovalent mRNA COVID-19 vaccines are no longer authorized as booster doses for individuals ages 12 years and older, meaning monovalent booster doses can no longer be given to people ages 12 years and older, even if the person had not previously received a monovalent booster dose.
Bivalent Booster Recommendations

- Everyone ages 12 years and older is recommended to receive 1 age-appropriate bivalent mRNA booster dose after completion of any FDA-approved or FDA-authorized monovalent primary series or last monovalent booster dose.
  - People cannot get a bivalent booster without first completing at least a primary series
  - Age-appropriate homologous and heterologous boosters allowed; there is no preference

- At this time, no changes to schedules for children ages 6 months through 11 years.
Previous Monovalent Booster Recommendations

- The bivalent booster recommendation replaces previous booster recommendations for people ages 12 years and older.
- This means that everyone ages 5 years and older who are eligible for a booster dose will now only be eligible for ONE booster dose.
  - People ages 5 through 11 years (who received Pfizer-BioNTech primary series): 1 monovalent booster dose
  - People ages 12 years and older: 1 bivalent booster dose
Fall Booster “Reset”

- Recommendations are simplified
- Change from dose counting to 1 bivalent booster for everyone eligible
- If eligible, a bivalent should not be denied based on total number of doses

<table>
<thead>
<tr>
<th>Vaccination history</th>
<th>Next dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary series</td>
<td>At least 2 months</td>
</tr>
<tr>
<td></td>
<td>1 bivalent booster dose</td>
</tr>
<tr>
<td>Primary series + 1 booster</td>
<td>At least 2 months</td>
</tr>
<tr>
<td></td>
<td>1 bivalent booster dose</td>
</tr>
<tr>
<td>Primary series + 2 booster</td>
<td>At least 2 months</td>
</tr>
<tr>
<td></td>
<td>1 bivalent booster dose</td>
</tr>
</tbody>
</table>
COVID-19 Vaccination Schedule for People who are NOT Moderately or Severely Immunocompromised

**People ages 12 years and older**

- **Primary Dose**
- 3-8 or 4-8 weeks* from primary dose
- **Primary Dose**
- At least 2 months
- **Bivalent Booster†**

*3-8 interval for Novavax and Pfizer-BioNTech; 4-8 interval for Moderna
† The bivalent booster dose is administered at least 2 months after completion of the primary series.

For people who previously received a monovalent booster dose(s), the bivalent booster dose is administered at least 2 months after the last monovalent booster dose. The bivalent booster should be age appropriate; Pfizer-BioNTech is authorized for people ages 12 years and older and Moderna is authorized for people ages 18 years and older.

**Modern, Novavax, or Pfizer-BioNTech Primary Series**

**People ages 18 years and older**

- **Primary Dose**
- At least 2 months
- **Bivalent Booster†**

† The bivalent booster dose is administered at least 2 months after completion of the primary series.

Regardless of previous monovalent booster doses given
COVID-19 Vaccination Schedule for People who ARE Moderately or Severely Immunocompromised

People ages 12 years and older

- **Moderna or Pfizer-BioNTech**
  - Primary Series
  - 3 or 4 weeks*
  - At least 4 weeks
  - At least 2 months
  - Bivalent Booster†

  Regardless of previous monovalent booster doses given

- **Novavax**
  - Primary Series
  - 3 weeks
  - At least 2 months
  - Bivalent Booster†

  Regardless of previous monovalent booster doses given

People ages 18 years and older who received Janssen

- **Janssen**
  - Primary Series
  - Dose
  - At least 4 weeks
  - At least 2 months
  - Bivalent Booster†

  Regardless of previous monovalent booster doses given

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*3-8 interval for Novavax and Pfizer-BioNTech; 4-8 interval for Moderna
† The bivalent booster dose is administered at least 2 months after completion of the primary series.
For people who previously received a monovalent booster dose(s), the bivalent booster dose is administered at least 2 months after the last monovalent booster dose. The bivalent booster should be age appropriate; Pfizer-BioNTech is authorized for people ages 12 years and older and Moderna is authorized for people ages 18 years and older.
Who may benefit from Evusheld?

- People ages ≥12 years:
  - With moderate to severe immune compromise
  - For whom vaccination with any available COVID-19 vaccine is not recommended due to a history of severe adverse reaction to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s)
Tixagevimab/Cilgavimab (EVUSHELD™)

- Combination of two long-acting human monoclonal antibodies derived from B-cells donated by convalescent patients after SARS-CoV-2 infection

- **FDA’s Emergency Use Authorization (EUA):**
  - Issued 12/8/21 for *pre-exposure prophylaxis* in individuals with moderate/severe immunocompromise or for whom COVID-19 vaccination is not recommended
  - Revised 2/24/22 to **increase dose to 300mg/300mg** (accounting for decreased neutralization activity against Omicron)

- **Fact sheet for healthcare providers** revised 6/29/22 for Evusheld to be administered **every 6 months**

- Evusheld must be prescribed by a healthcare provider

- Doses can be found through the USG therapeutic locator tool: [https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/](https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/)

- There are two ways for providers to order Evusheld:
  - **HHS Health Partner Order Portal** (HPOP), for large orders through the HPOP distribution process
  - A new direct clinical pathway established in July 2022 for **Small Volume Orders** of up to three doses, for providers not participating in the HPOP distribution process
Use of Evusheld is evidence-based

- A randomized clinical trial\textsuperscript{1} and multiple retrospective and other studies\textsuperscript{2-5} show that Evusheld has efficacy against severe COVID-19 outcomes and provides protection against Omicron.

- In vitro studies show that Evusheld is predicted to work against BA.4/5\textsuperscript{6}

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2. Tixagevimab/Cilgavimab for Prevention of COVID-19 during the Omicron Surge: Retrospective Analysis of National VA Electronic Data | medRxiv
3. Serum neutralization of SARS-CoV-2 Omicron sublineages BA.1 and BA.2 in patients receiving monoclonal antibodies | Nature Medicine
4. Al Jurdi et al., American Journal of Transplantation; June 2022
5. Association between AZD7442 (tixagevimab-cilgavimab) administration and SARS-CoV-2 infection, hospitalization and mortality | Clinical Infectious Diseases | Oxford Academic (oup.com)
Most immunocompromised people in the US have not received Evusheld

- Number of individuals age ≥12 in the United States: ~290 million people
- Roughly 3% of U.S. population is immunocompromised: ~8.7 million people
- Therefore, % protected with Evusheld: ~5.3% of individuals who are eligible

Supply far exceeds administration to patients: >390,000 doses available
Evusheld is distributed by the US government at no cost to recipients, although there may be administration fees depending on location

<table>
<thead>
<tr>
<th>Therapeutic (300 mg doses)</th>
<th>Courses Ordered</th>
<th>Courses Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evusheld</td>
<td>850,106</td>
<td>459,572</td>
</tr>
</tbody>
</table>

Data is for states, territories, and federal entities, including HRSA.
Courses administered is based on 92% of sites as of August 21, 2022

1. National population estimates: CDC wonder (wonder.cdc.gov)
Supplementing COVID-19 vaccination with pre-exposure prophylaxis

Monoclonal antibodies (EVUSHELD™) for COVID-19 pre-exposure prophylaxis

People ages 12 years and older (must weigh at least 40 kg)

Any dose (primary or booster) → In at least 2 weeks → EVUSHELD™ dose every 6 months → No minimum interval from EVUSHELD™ to COVID-19 vaccine → Any subsequent COVID-19 vaccine dose → At least 2 weeks from COVID-19 vaccine to EVUSHELD™
CDC Webpage pre-exposure prophylaxis updates for healthcare providers and the public

- Updated website content for healthcare providers:
  - Patient eligibility
  - Evusheld administration guidance

- Updated website content for the public:
  - How to know if you’re eligible for Evusheld
  - How to access Evusheld

- Updated website language for Interim Clinical Considerations
  - How use of Evusheld compliments COVID-19 vaccination in people with moderate or severe immunocompromise
COVID-19 Vaccination Schedule Timing Considerations

- Timing considerations for people with current or prior SARS-CoV-2 infection
- Coadministration
Timing Considerations for People with Current or Prior SARS-CoV-2 Infection

- At a minimum, defer any COVID-19 vaccination, including bivalent booster vaccination, at least until recovery from the acute illness (if symptoms were present) and criteria to discontinue isolation have been met.

- In addition, people who recently had SARS-CoV-2 infection may consider delaying any COVID-19 vaccination, including bivalent booster vaccination, by 3 months from symptom onset or positive test (if infection was asymptomatic).

- Individual factors such as risk of COVID-19 severe disease, COVID-19 community level, or characteristics of the predominant SARS-CoV-2 strain should be taken into account when determining whether to delay getting a COVID-19 vaccination after infection.
Coadministration of COVID-19 Vaccines with Other Vaccines

- Routine administration of all age-appropriate doses of vaccines simultaneously is recommended as best practice for people for whom no specific contraindications exist at the time of the healthcare visit.

- Extensive experience with non-COVID 19 vaccines has demonstrated that immunogenicity and adverse event profiles are generally similar when vaccines are administered simultaneously as when they are administered alone.

- Providers should offer all vaccines for which a person is eligible at the same visit.
Coadministration of Influenza with COVID-19 Vaccines

- Providers should offer influenza and COVID-19 vaccines at the same visit, if eligible.
  - This includes adjuvanted or high-dose influenza vaccines; administer in separate limbs.

- With both influenza and SARS-CoV-2 circulating, getting **both vaccines** is important for prevention of severe disease, hospitalization, and death.

- Getting both vaccines at the same visit increases the chance that a person will be up to date with their vaccinations.
Coadministration of Influenza and COVID-19 Vaccines

- Studies looking at coadministration have shown that **immunogenicity is similar** between those who received coadministered COVID-19 vaccine and seasonal influenza vaccine (SIV) and those who received these vaccines separately\(^2\)-\(^4\)
- 9.4% (~92,000) \(v\)-safe participants reported simultaneous vaccination with an mRNA COVID-19 vaccine and SIV\(^5\)
- 8.7% (~454,000) of persons enrolled in the Vaccine Safety Datalink (VSD) received simultaneous vaccination with a COVID-19 booster and SIV during the 2021-2022 influenza season

**Reactogenicity of Coadministered COVID-19 Vaccine and SIV**

**Percent difference in participants reporting reactogenicity between COVID-19 + SIV vs COVID-19 alone**

<table>
<thead>
<tr>
<th>Vaccine Combination</th>
<th>Systemic Reactions</th>
<th>Local Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna + Any SIV [1]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pfizer + Any SIV [1]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novavax + Either aTIV or QIVc [2]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderna + hdQIV [3]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pfizer + aTIV [4]</td>
<td>-12.9</td>
<td>2.7</td>
</tr>
<tr>
<td>Pfizer + QIVr [4]</td>
<td>-3.7</td>
<td>6.2</td>
</tr>
<tr>
<td>Pfizer + QIVc [4]</td>
<td>-3.3</td>
<td>6.7</td>
</tr>
</tbody>
</table>

**More reactogenicity in COVID-19 alone** | **More reactogenicity in COVID-19 + SIV**


SIV: seasonal influenza vaccine; aTIV: adjuvanted trivalent influenza vaccine; QIVc: quadrivalent influenza cell-based vaccine; hdQIVc: high-dose quadrivalent influenza vaccine; QIVr: recombinant quadrivalent vaccine.
Reactogenicity of Coadministered COVID-19 Vaccine and SIV

- Generally, COVID-19 vaccines administered with seasonal influenza vaccine (SIV) showed similar or slightly higher reactogenicity, however no specific safety concerns were identified.

Best Practices for Multiple Injections

- Label each syringe with the name and the dosage (amount) of the vaccine, lot number, initials of the preparer, and exact beyond-use time, if applicable.
- Administer each vaccine in a different injection site; separate injection sites by 1 inch or more, if possible.
- Administer the COVID-19 vaccine and vaccines that may be more likely to cause a local reaction in different limbs, if possible.
  - Example: Adjuvanted or high-dose influenza vaccine and COVID-19 vaccine
# Pfizer-BioNTech COVID-19 Vaccines

<table>
<thead>
<tr>
<th></th>
<th>Monovalent Product</th>
<th>Bivalent Product</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authorized for ages</strong></td>
<td>12 years and older</td>
<td>12 years and older</td>
</tr>
<tr>
<td><strong>Authorized for doses</strong></td>
<td>Primary series doses</td>
<td>Booster doses</td>
</tr>
<tr>
<td><strong>Vial cap color</strong></td>
<td>Gray</td>
<td>Gray</td>
</tr>
<tr>
<td><strong>Dose (mRNA concentration)</strong></td>
<td>30 mcg</td>
<td>30 mcg</td>
</tr>
<tr>
<td></td>
<td>(15 mcg original, 15 mcg Omicron BA.4/BA.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Vaccine composition</strong></td>
<td>Monovalent—Original</td>
<td>Bivalent—Original and Omicron BA.4/BA.5</td>
</tr>
<tr>
<td><strong>Injection volume</strong></td>
<td>0.3 mL</td>
<td>0.3 mL</td>
</tr>
<tr>
<td><strong>Dilution required</strong></td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Beyond-use date</strong></td>
<td>12 hours after puncture</td>
<td>12 hours after puncture</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>Ultra-cold freezer until expiration; Refrigerator (2°C-8°C) up to 10 weeks</td>
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</tr>
</tbody>
</table>
Pfizer-BioNTech Labels

Monovalent label
Primary series only
Ages 12 years and older

Bivalent label
Booster dose only
Ages 12 years and older
# Moderna COVID-19 Vaccines Formulations

<table>
<thead>
<tr>
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<td>12 years and older</td>
<td>6–11 years</td>
<td>18 years and older</td>
</tr>
<tr>
<td><strong>Vial cap color</strong></td>
<td>Red</td>
<td>Dark blue</td>
<td>Dark blue</td>
</tr>
<tr>
<td><strong>Label border color</strong></td>
<td>Light blue</td>
<td>Purple</td>
<td>Gray</td>
</tr>
<tr>
<td><strong>Dose (mRNA concentration)</strong></td>
<td>100 mcg (primary dose)</td>
<td>50 mcg (primary dose)</td>
<td>50 mcg (booster dose) (25 mcg original, 25 mcg Omicron BA.4/BA.5)</td>
</tr>
<tr>
<td><strong>Injection volume</strong></td>
<td>0.5 mL</td>
<td>0.5 mL</td>
<td>0.5 mL</td>
</tr>
<tr>
<td><strong>Dilution required</strong></td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Beyond-use date</strong></td>
<td>12 hours</td>
<td>12 hours</td>
<td>12 hours</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>Freezer (-15°C to -50°C) until expiration; Refrigerator (2°C to 8°C) up to 30 days</td>
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</tr>
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</table>
Modern Labels

Monovalent label
Primary series only
Ages 12 years and older

Bivalent label
Booster dose only
Ages 18 years and older
# Moderna COVID-19 Vaccines Formulations

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Moderna Labels

Monovalent label
Primary series only
Ages 6–11 years

Bivalent label
Booster dose only
Ages 18 years and older

Despite label, do NOT use for booster doses
Staying Up To Date

- CDC encourages people to “Stay up to date with your COVID-19 vaccines”.

- Staying up to date keeps people current with COVID-19 vaccine recommendations.

- You are up to date if you have completed a primary series and received the most recent booster dose recommended for you by CDC.
For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.