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# The Medical Letter®

## on Drugs and Therapeutics

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### COVID-19 UPDATE

## 2025-2026 Vaccine Formulations and Recommendations

The FDA has licensed new 2025-2026 formulations of the mRNA COVID-19 vaccines manufactured by Pfizer/BioNTech (*Comirnaty*) and Moderna (*Spikevax*, *mNEXSPIKE*<sup>1</sup>) and the adjuvanted protein subunit COVID-19 vaccine manufactured by Novavax (*Nuvaxovid*). The new formulations are indicated for use in all adults  $\geq 65$  years old and in persons 6 months (*Spikevax*), 5 years (*Comirnaty*), or 12 years (*mNEXSPIKE*, *Nuvaxovid*) through 64 years old who are at high risk for severe COVID-19 because of an underlying condition.<sup>2</sup> An Emergency Use Authorization allowing administration of the Pfizer vaccine to children 6 months through 4 years old has been withdrawn.

**THE NEW FORMULATIONS** — The 2025-2026 formulations of *Comirnaty* and *Spikevax* code for the entire spike protein of the LP.8.1 Omicron strain of SARS-CoV-2; *mNEXSPIKE* codes only for the N-terminal and receptor-binding domains of the LP.8.1 spike protein.<sup>1</sup> *Nuvaxovid* contains the spike protein of the JN.1 Omicron strain of the virus. The XFG Omicron strain of SARS-CoV-2, which was the most prevalent variant in US wastewater as of September 2025,<sup>3</sup> and the LP.8.1 strain are both descended from the JN.1 strain.<sup>4</sup>

**Table 1. FDA-Indicated Populations for the 2025-2026 COVID-19 Vaccines**

| Vaccine                               | Populations                                                                                                   |
|---------------------------------------|---------------------------------------------------------------------------------------------------------------|
| <i>Comirnaty</i><br>(Pfizer/BioNTech) | ▶ Adults $\geq 65$ years old<br>▶ Persons 5-64 years old at high risk for severe COVID-19 <sup>1</sup>        |
| <i>Spikevax</i> (Moderna)             | ▶ Adults $\geq 65$ years old<br>▶ Persons 6 months-64 years old at high risk for severe COVID-19 <sup>1</sup> |
| <i>mNEXSPIKE</i> (Moderna)            | ▶ Adults $\geq 65$ years old<br>▶ Persons 12-64 years old at high risk for severe COVID-19 <sup>1</sup>       |
| <i>Nuvaxovid</i> (Novavax)            | ▶ Adults $\geq 65$ years old<br>▶ Persons 12-64 years old at high risk for severe COVID-19 <sup>1</sup>       |

1. CDC. COVID-19: underlying conditions and the higher risk for severe COVID-19. February 6, 2025. Available at: <https://bit.ly/3UUQffF>. Accessed September 22, 2025.

**EFFICACY** — No clinical studies evaluating the immunogenicity or efficacy of the new vaccine formulations were required. Licensure of the vaccines was based on the immunogenicity, safety, and efficacy of previous vaccine formulations.

**Last Season** — The efficacy of the 2024-2025 COVID-19 vaccine formulations was evaluated in an interim case-control analysis of emergency department and urgent care (ED/UC) visits and hospitalizations occurring between September 2024 and January 2025 that were reported in a large electronic health record (EHR)-based network (VISION). Among 137,543 adults who had an ED/UC visit, receipt of a 2024-2025 COVID-19 vaccine within the previous 7-119 days was associated with a reduced risk of a COVID-19-associated visit; the estimated vaccine efficacy was 33% (30% in adults 18-64 years old and 36% in those  $\geq 65$  years old). Among adults  $\geq 65$  years old who were hospitalized, receipt of a 2024-2025 vaccine 7-119 days previously was associated with a reduced risk of a subsequent COVID-19-associated hospitalization; the estimated vaccine efficacy was 45% in immunocompetent persons (n=26,219) and 40% in immunocompromised persons (n=8192).<sup>5</sup>

Similar results were observed in an analysis of a different EHR-based network (IVY); among 1929 immunocompetent adults  $\geq 65$  years old who were hospitalized during the same time period, those who had received a 2024-2025 vaccine 7-119 days previously had a lower risk of a COVID-19-associated hospitalization (estimated vaccine efficacy 46%).<sup>5</sup>

**ADVERSE EFFECTS** — Adverse effects of previous COVID-19 vaccine formulations have included injection-site reactions, fatigue, irritability, fever, chills, muscle and joint pain, headache, vomiting, decreased appetite, and lymphadenopathy. Severe allergic reactions and Guillain-Barré syndrome have been reported. Myocarditis and pericarditis can occur; the incidence is highest in adolescent and young adult males.<sup>6,7</sup>

Table 2. Dosage Recommendations for 2025-2026 COVID-19 Vaccines<sup>1,2</sup>

| Age                                                             | Formulation                                                | Dosage                                      | Cost <sup>3</sup> |
|-----------------------------------------------------------------|------------------------------------------------------------|---------------------------------------------|-------------------|
| <b>Comirnaty (Pfizer/BioNTech) – mRNA vaccine</b>               |                                                            |                                             |                   |
| 5-11 years                                                      | 10 mcg/0.3 mL single-dose vials                            | One 10-mcg dose <sup>4</sup>                | \$83.20           |
| ≥12 years                                                       | 30 mcg/0.3 mL prefilled syringes                           | One 30-mcg dose <sup>4</sup>                | 147.70            |
| <b>Spikevax (Moderna) – mRNA vaccine</b>                        |                                                            |                                             |                   |
| 6-23 months                                                     | 25 mcg/0.25 mL prefilled syringes                          | Two 25-mcg doses 1 month apart <sup>5</sup> | 129.00            |
| 2-11 years                                                      | 25 mcg/0.25 mL prefilled syringes                          | One 25-mcg dose <sup>4</sup>                | 129.00            |
| ≥12 years                                                       | 50 mcg/0.5 mL prefilled syringes                           | One 50-mcg dose <sup>4</sup>                | 141.80            |
| <b>mNEXSPIKE (Moderna) – mRNA vaccine<sup>6</sup></b>           |                                                            |                                             |                   |
| ≥12 years                                                       | 10 mcg/0.2 mL prefilled syringes                           | One 10-mcg dose <sup>4</sup>                | 177.10            |
| <b>Nuvaxovid (Novavax) – adjuvanted protein subunit vaccine</b> |                                                            |                                             |                   |
| ≥12 years                                                       | 5 mcg (plus 50 mcg adjuvant)/<br>0.5 mL prefilled syringes | One 5-mcg dose <sup>4</sup>                 | N.A.              |

N.A. = cost not available at press time

1. The 2025-2026 vaccines contain a monovalent component that corresponds to the LP.8.1 (Pfizer and Moderna) or JN.1 (Novavax) Omicron variant of SARS-CoV-2.

2. For immunocompetent persons. Persons with moderate or severe immunocompromise may receive additional doses of the 2025-2026 COVID-19 vaccines based on the clinical judgment of a healthcare provider, personal preference of the patient, and other circumstances; additional doses should be given ≥2 months after the last 2025-2026 COVID-19 vaccine dose (CDC. Vaccines for moderately to severely immunocompromised people. Available at: <https://bit.ly/3JJZR3c>. Accessed September 22, 2025).

3. Approximate WAC for one dose. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2025. Reprinted with permission by First Databank, Inc. All rights reserved. ©2025. [www.fdbhealth.com/drug-pricing-policy](http://www.fdbhealth.com/drug-pricing-policy)

4. Given at least 2 months after the last dose of any COVID-19 vaccine.

5. Patients 6-23 months old who received one 2024-2025 dose of *Spikevax* should receive a single 25-mcg dose ≥1 month after their previous dose. Those who received ≥2 2024-2025 doses of *Spikevax* should receive a single 25-mcg dose ≥2 months after their previous dose.

6. The *mNEXSPIKE* vaccine codes for the N-terminal and receptor-binding domains of the SARS-CoV-2 spike protein.

**PREGNANCY AND LACTATION** – Pregnancy has been associated with an increased risk of COVID-19 complications, including pneumonia, intensive care unit admission, intubation, and death.<sup>8,9</sup> Vaccination protects pregnant women against COVID-19 complications and provides passive immunity to their infants for the first few months after birth.<sup>10,11</sup> Administration of COVID-19 vaccines to nursing mothers is considered safe.<sup>12</sup> The American College of Obstetricians and Gynecologists has recommended that all pregnant and breastfeeding women be vaccinated against COVID-19.<sup>10</sup>

**DOSAGE AND ADMINISTRATION** – For most patients, a single dose of a 2025-2026 COVID-19 vaccine administered ≥2 months after any previous COVID-19 vaccine dose is recommended. Additional doses, each given ≥2 months after the previous dose, can be considered for persons with immunocompromise (solid-organ transplant recipients and equivalent).<sup>13</sup> Children 6-23 months old who have never been vaccinated against COVID-19 should receive two doses of *Spikevax* 1 month apart (see Table 2).

**RECOMMENDATIONS** – The recently restructured CDC Advisory Committee on Immunization Practices (ACIP) has recommended that vaccination of persons ≥6 months old against COVID-19 during the 2025-2026 season be based on shared clinical decision-making. It has emphasized that, for persons

<65 years old, the benefits of vaccination most greatly outweigh the risks in those who are at increased risk for severe COVID-19.<sup>14</sup>

The **American Academy of Family Physicians (AAFP)** recommends that all adults, including pregnant and lactating women, and all children 6-23 months old receive a COVID-19 vaccine this season. They recommend vaccination of persons 2-18 years old who are at increased risk for severe COVID-19.<sup>15</sup>

The **American Academy of Pediatrics (AAP)** has recommended that all children 6-23 months old and all children who have never been vaccinated against COVID-19 receive a 2025-2026 vaccine (not just those with risk factors for severe disease); it also recommends vaccination of children who reside in long-term care facilities or other congregate settings and those with household contacts who are at high risk for severe COVID-19.<sup>16</sup>

The **American College of Obstetricians and Gynecologists (ACOG)** has recommended that all pregnant and breastfeeding women be vaccinated against COVID-19.<sup>10</sup> ■

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