The Medical Letter®
on Drugs and Therapeutics

Volume 66 September 16, 2024

ISSUE No. 1711

IN THIS ISSUE

The Medical Letter®
on Drugs and Therapeutics

Volume 66 September 16, 2024

Take CME Exams

COVID-19 Update

New Pfizer and Moderna Vaccine Formulations for 2024-2025

Note: See addendum

New 2024-2025 formulations of the mRNA COVID-19 vaccines manufactured by Pfizer/BioNTech *(Comirnaty)* and Moderna *(Spikevax)* that more closely target currently circulating variants have been licensed by the FDA for persons ≥12 years old and made available under FDA Emergency Use Authorizations (EUAs) for use in persons 6 months to 11 years old.[1-3] A 2024-2025 formulation of the adjuvanted protein subunit COVID-19 vaccine manufactured by Novavax is expected to become available soon for persons ≥12 years old.

THE NEW VACCINES — The new formulations are monovalent vaccines that code for the spike protein of the KP.2 Omicron strain of SARS-CoV-2. KP.2 is a member of the "FLiRT" variant family; as of mid-August 2024, FLiRT variants (e.g., KP.2, KP.2.3, KP.3, KP.3.1.1, LB.1) were causing the majority of COVID-19 cases in the US.[4,5]

CLINICAL STUDIES — No clinical studies evaluating the immunogenicity or effectiveness of the new vaccine formulations are available. Licensure and authorization of both vaccines were based on the immunogenicity, safety, and efficacy of previous vaccine formulations.[1-3]

ADVERSE EFFECTS — Adverse effects of earlier versions of the mRNA COVID-19 vaccines 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.[6]

DOSAGE RECOMMENDATIONS — Generally, **persons ≥5 years old** should receive a single dose of a 2024-2025 vaccine formulation ≥2 months after their previous COVID-19 vaccine dose. **Children 6 months to 4 years old** who have already received

Table 1. Vaccination Recommendations for 2024-2025 mRNA COVID-19 Vaccines[1,2]

Age	Dose/Vial Color	Not Previously Vaccinated	Previously Vaccinated
Pfizer/BioNTech Vaccine *(Comirnaty)*			
6 months-4 years[3]	3 mcg/0.3 mL; yellow cap and label	Three 3-mcg doses: 1st at week 0, 2nd at week 3, and 3rd ≥8 weeks after dose 2[4]	**1 previous Pfizer dose:** One 3-mcg dose ≥3 weeks later and 1 dose ≥8 weeks after dose 2[4] **≥2 previous Pfizer doses:** One 3-mcg dose ≥8 weeks after last dose
5-11 years	10 mcg/0.3 mL; blue cap and label	One 10-mcg dose	One 10-mcg dose ≥2 months after last dose of any mRNA COVID-19 vaccine
≥12 years	30 mcg/0.3 mL; gray cap and label	One 30-mcg dose	One 30-mcg dose ≥2 months after last dose of any COVID-19 vaccine
Moderna Vaccine *(Spikevax)*			
6 months-4 years[3]	25 mcg/0.25 mL; dark blue cap/green label	Two 25-mcg doses 1 month apart	**1 previous Moderna dose:** One 25-mcg dose ≥1 month after last dose **≥2 previous Moderna doses:** One 25-mcg dose ≥2 months after last dose
5-11 years	25 mcg/0.25 mL; dark blue cap/green label	One 25-mcg dose	One 25-mcg dose ≥2 months after last dose of any mRNA COVID-19 vaccine
≥12 years	50 mcg/0.5 mL; dark blue cap/blue label	One 50-mcg dose	One 50-mcg dose ≥2 months after last dose of any COVID-19 vaccine

1. The 2024-2025 vaccines contain a monovalent component that corresponds to the KP.2 Omicron variant of SARS-CoV-2. A 2024-2025 formulation of the adjuvanted protein subunit COVID-19 vaccine manufactured by Novavax is expected to become available soon.
2. For immunocompetent persons. Persons with moderate or severe immunocompromise may receive additional doses of the 2024-2025 COVID-19 vaccines based on the clinical judgement of a healthcare provider and personal preference and circumstances; additional doses should be given ≥2 months after the last 2024-2025 COVID-19 vaccine dose.
3. All doses should be from the same manufacturer.
4. In children who turn 5 years old before completion of the vaccination series, instead administer one 10-mcg Pfizer vaccine dose ≥2 months after the last 3-mcg dose.

≥2 Pfizer or Moderna vaccine doses should receive a single dose of the corresponding 2024-2025 vaccine ≥8 weeks (Pfizer) or ≥2 months (Moderna) after their most recent dose. Those 6 months to 4 years old who received <2 previous doses should be given additional doses until they have received 3 total doses of the Pfizer vaccine or 2 total doses of the Moderna vaccine. **Children 6 months to 11 years old with immunocompromise** (solid-organ transplant recipients and equivalent) should receive at least 3 total age-appropriate COVID-19 vaccine doses, including at least 1 dose of a 2024-2025 formulation. Dosage recommendations for the updated vaccine formulations are summarized in Table 1.[2,3]

CDC RECOMMENDATIONS — The CDC recommends that all persons ≥6 months old receive either of the two 2024-2025 mRNA COVID-19 vaccines.[7] ■

1. FDA News Release. FDA approves and authorizes updated mRNA COVID-19 vaccines to better protect against currently circulating variants. August 22, 2024. Available at: https://bit.ly/3T3eGzP. Accessed August 28, 2024.
2. FDA. Fact sheet for healthcare providers administering vaccine: Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 vaccine (2024-2025 formula), for 6 months through 11 years of age. August 22, 2024. Available at: https://bit.ly/4g2dQxa. Accessed August 28, 2024.
3. FDA. Fact sheet for healthcare providers administering vaccine: Emergency Use Authorization (EUA) of Moderna COVID-19 vaccine (2024-2025 formula), for individuals 6 months through 11 years of age. August 2024. Available at: https://bit.ly/3YZmmqo. Accessed August 28, 2024.
4. COVID-19 Real-Time Learning Network. COVID-19 variant update. August 21, 2024. Available at: https://bit.ly/4cLGAqW. Accessed August 28, 2024.
5. CDC. COVID data tracker. Variant proportions. August 27, 2024. Available at: https://bit.ly/3Ka3HhH. Accessed August 28, 2024.
6. CDC. Clinical considerations: myocarditis and pericarditis after receipt of COVID-19 vaccines among adolescents and young adults. October 10, 2023. Available at: https://bit.ly/3yXicot. Accessed August 28, 2024.
7. CDC. Use of COVID-19 vaccines in the United States: interim clinical considerations. August 23, 2024. Available at: https://bit.ly/3yKjLWV. Accessed August 28, 2024.

The Medical Letter®
on Drugs and Therapeutics

Volume 66 Published online October 14, 2024

Online Article

IN THIS ISSUE

Addendum: Effectiveness of mRNA COVID-19 Vaccines

Addendum: Effectiveness of mRNA COVID-19 Vaccines

A reader of our article on the 2024-2025 formulations of the mRNA COVID-19 vaccines manufactured by Pfizer/BioNTech *(Comirnaty)* and Moderna *(Spikevax)*[1] asked us to provide more information on the data that supported their licensure.

The vaccines were initially licensed by the FDA in 2021 (Pfizer) and 2022 (Moderna) based on the results of large, double-blind trials in SARS-CoV-2-naive adolescents and adults. Both vaccines significantly decreased the risk of symptomatic and severe SARS-CoV-2 infection compared to placebo.[2-4] Issuance of the FDA Emergency Use Authorizations (EUAs) allowing use of the vaccines in younger children was initially based primarily on the results of immunogenicity studies. Titer levels of anti-SARS-CoV-2 neutralizing antibodies following vaccination were at least as high in persons 6 months through 11 years old as they were in comparator adult cohorts.[5,6]

As with the influenza vaccine, efficacy trials are no longer required by the FDA for licensure of new COVID-19 vaccine formulations that only significantly differ from previous formulations in the virus strain that they target. Licensure is based on the immunogenicity, efficacy, and safety of previous formulations, and on the likelihood of the new formulations to protect against currently circulating SARS-CoV-2 variants.[7-9]

Observational studies suggest that all of the COVID-19 vaccine formulations available in the US in 2023-2024 were effective in reducing the incidence of COVID-19. In a case-control analysis of 14,860 COVID-19 nucleic acid amplification tests administered at community pharmacies to immunocompetent adults with COVID-like symptoms between September 2023 and May 2024, receipt of any 2023-2024 COVID-19 vaccine at least 7 days before the test was associated with a decreased incidence of SARS-CoV-2 infection. The estimated adjusted vaccine efficacy was 45%; it was 58% for infections likely caused by the XBB.1.5 variant, which the 2023-2024 vaccines targeted, and 37% for infections likely caused by the JN.1 variant.[10,11]

In similar analyses of tests administered to adults with COVID-like illness within 10 days before or 3 days after an emergency department/urgent care visit (n=245,504) or a hospitalization (n=77,103) between September 2023 and May 2024, receipt of any 2023-2024 COVID-19 vaccine at least 7 days before the test was associated with a decreased incidence of COVID-19 requiring an emergency department/urgent care visit (estimated adjusted vaccine efficacy 36%) or hospitalization (estimated adjusted vaccine efficacy 41%). Among hospitalized immunocompetent persons, the estimated adjusted vaccine efficacy against critical illness was 58%.[10,12]

1. COVID-19 update: New Pfizer and Moderna vaccine formulations for 2024-2025. Med Lett Drugs Ther 2024; 66:151.
2. FP Polack et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020; 383:2603.
3. LR Baden et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021; 384:403.
4. K Ali et al. Evaluation of mRNA-1273 SARS-CoV-2 vaccine in adolescents. N Engl J Med 2021; 385:2241.
5. FDA. Fact sheet for healthcare providers administering vaccine: Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 vaccine (2024-2025 formula), for 6 months through 11 years of age. August 22, 2024. Available at: https://bit.ly/4g2dQxa. Accessed September 26, 2024.
6. FDA. Fact sheet for healthcare providers administering vaccine: Emergency Use Authorization (EUA) of Moderna COVID-19 vaccine (2024-2025 formula), for individuals 6 months through 11 years of age. August 2024. Available at: https://bit.ly/3YZmmqo. Accessed September 26, 2024.
7. FDA News Release. FDA approves and authorizes updated mRNA COVID-19 vaccines to better protect against currently circulating variants. August 22, 2024. Available at: https://bit.ly/3T3eGzP. Accessed September 26, 2024.
8. FDA CBER. Summary minutes. 185th Vaccines and Related Biological Products Advisory Committee. June 5, 2024 Available at: https://bit.ly/4enFzqm. Accessed September 26, 2024.
9. COVID-19 Real-Time Learning Network. COVID-19 variant update. September 17, 2024. Available at: https://bit.ly/3XslucR. Accessed September 26, 2024.
10. R Link-Gelles. Effectiveness of COVID-19 (2023-2024 formula) vaccines. ACIP Meeting COVID-19 Vaccines. June 27, 2024. Available at: https://bit.ly/3TGt41a. Accessed September 26, 2024.
11. R Link-Gelles et al. Early estimates of updated 2023-2024 (monovalent XBB.1.5) COVID-19 vaccine effectiveness against symptomatic SARS-CoV-2 infection attributable to co-circulating Omicron variants among immunocompetent adults - increasing community access to testing program, United States, September 2023-January 2024. MMWR Morb Mortal Wkly Rep 2024; 73:77.
12. J DeCuir et al. Interim effectiveness of updated 2023–2024 (monovalent XBB.1.5) COVID-19 vaccines against COVID-19–associated emergency department and urgent care encounters and hospitalization among immunocompetent adults aged ≥18 Years — VISION and IVY Networks, September 2023–January 2024. MMWR Morb Mortal Wkly Rep 2024; 73:180.