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COVID-19 UPDATES

Primary-Series Dosing Interval for mRNA Vaccines

The CDC has issued new guidance allowing for an interval of up to 8 weeks between the first and second primary doses of an mRNA COVID-19 vaccine in certain patients 12-64 years old.[1] Product labeling currently recommends a 3-week interval between the first two doses of the Pfizer/BioNTech mRNA vaccine *(Comirnaty)* and a 4-week interval between the first two doses of the Moderna mRNA vaccine *(Spikevax)*. The new guidance is based on data suggesting that a longer interval can decrease the risk of myocarditis and may improve vaccine efficacy.

MYOCARDITIS – The mRNA COVID-19 vaccines have been associated with myocarditis and/or pericarditis. Myocarditis occurs more frequently with the Moderna vaccine than with the Pfizer vaccine. Its incidence is highest in males 12-39 years old following their second primary dose, but even in this cohort, it is rare (<0.05% with either vaccine).[2]

SAFETY DATA – A retrospective population cohort study estimated rates of myocarditis in persons who received at least one dose of an mRNA COVID-19 vaccine in Ontario, Canada over a period of ~8.5-months. The incidence of myocarditis with a second primary dose was significantly greater when the interval from the first dose was ≤30 days than when it was ≥56 days (unadjusted relative risk 5.5 [95% CI 3.1-9.6] with the Pfizer vaccine and 5.2 [95% CI 2.6-10.0] with the Moderna vaccine).[3]

EFFICACY DATA – In an observational study in 589 healthcare workers in the UK who received 2 doses of the Pfizer vaccine, neutralizing antibody and T-cell responses were greater with a longer interval between doses (6-14 weeks) than with a shorter interval (2-5 weeks).[4] In case-control studies in Canada and England, longer dosing intervals were associated with higher vaccine efficacy rates, but these studies were completed before the emergence of the Omicron variant of SARS-CoV-2.[5,6]

RECOMMENDATIONS – According to the CDC, an 8-week interval between the first and second doses of an mRNA COVID-19 vaccine primary series may be optimal for certain persons ≥12 years old, especially males 12-39 years old. A standard 3- or 4-week interval between the first two doses should still be used in adults ≥65 years old, persons who are moderately or severely immunocompromised, and those who require more rapid protection because of high levels of community spread of SARS-CoV-2 infection or a high risk of severe COVID-19.[1] ■

1. CDC. Interim clinical considerations for use of COVID-19 vaccines currently approved or authorized in the United States. February 22, 2022. Available at: https://bit.ly/38i7ClH. Accessed March 3, 2022.
2. D Moulia. Myocarditis and COVID-19 vaccine intervals: international data and policies. ACIP Meeting. February 4, 2022. Available at: https://bit.ly/3IxhPjZ. Accessed March 3, 2022.
3. SA Buchan et al. Epidemiology of myocarditis and pericarditis following mRNA vaccines in Ontario, Canada: by vaccine product, schedule and interval. medRxiv 2021 December 5 (preprint). Available at: https://bit.ly/36PBg9S. Accessed March 3, 2022.
4. RP Payne et al. Immunogenicity of standard and extended dosing intervals of BNT162b2 mRNA vaccine. Cell 2021; 184:5699.
5. DM Skowronski et al. Two-dose SARS-CoV-2 vaccine effectiveness with mixed schedules and extended dosing intervals: test-negative design studies from British Columbia and Quebec, Canada. medRxiv 2021 October 26 (preprint). Available at: https://bit.ly/3K2i9rh. Accessed March 3, 2022.
6. G Amirthalingam et al. Serological responses and vaccine effectiveness for extended COVID-19 vaccine schedules in England. Nat Commun 2021; 12:7217.

Booster Immunization in Persons Who Are Immunocompromised

The CDC has made the following updates to its recommendations for booster vaccination against COVID-19 in persons who are moderately to severely immunocompromised[1]:

1. The recommended length of time between completion of a 3-dose primary series of an mRNA vaccine (Pfizer/BioNTech or Moderna) and administration of a booster mRNA vaccine dose has been reduced from 5 months to 3 months.

2. Persons who have received 1 or 2 doses of the Johnson & Johnson (Janssen) vaccine should continue their vaccination series with an mRNA vaccine until they have received 3 total vaccine doses. An mRNA vaccine should be given ≥4 weeks after an initial Johnson & Johnson vaccine dose and/or ≥2 months after a second vaccine dose of any type. If the completed series will include only one mRNA vaccine dose, it should be a primary dose (Pfizer 30 mcg/0.3 mL or Moderna 100 mcg/0.5 mL). If the completed series will include 2 mRNA vaccine doses, one should be a primary dose and the other a booster dose (Pfizer 30 mcg/0.3 mL or Moderna 50 mcg/0.25 mL).

The Pfizer and Moderna vaccines are preferred over the Johnson & Johnson vaccine for all persons, including those who are immunocompromised. The Johnson & Johnson vaccine can still be offered to persons who would otherwise remain unvaccinated because they have a contraindication or objection to receipt of an mRNA vaccine.[1] ■

1. CDC. Interim clinical considerations for use of COVID-19 vaccines currently approved or authorized in the United States. February 22, 2022. Available at: https://bit.ly/3uXZTLI. Accessed March 3, 2022.

Increased Dosage of Tixagevimab/ Cilgavimab *(Evusheld)*

The FDA has amended its Emergency Use Authorization (EUA) for the investigational long-acting monoclonal antibodies tixagevimab and cilgavimab *(Evusheld)* to increase the recommended dose of each drug from 150 mg to 300 mg.[1] *Evusheld* is authorized for IM pre-exposure prophylaxis of COVID-19 in persons ≥12 years old who weigh ≥40 kg and have either a history of a severe adverse reaction that prevents their vaccination against COVID-19 or moderate or severe immune compromise.[2]

The revision was based on *in vitro* data showing that the neutralizing activity of *Evusheld* is reduced against the SARS-CoV-2 Omicron variants BA.1 (by 12- to 30-fold vs the ancestral virus) and BA.1.1 (by 176-fold). *Evusheld* retains a greater degree of neutralizing activity against the BA.2 Omicron variant (5.4-fold reduction vs the ancestral virus).[3]

The new recommended dosage of *Evusheld* is 300 mg of tixagevimab and 300 mg of cilgavimab administered as consecutive IM injections into separate sites (preferably one in each gluteal muscle). Patients who have already received 150-mg doses of the two drugs should receive an additional 150-mg dose of each as soon as possible. The duration of protection provided by an initial dose of *Evusheld* remains to be established; the FDA will recommend an interval for repeat dosing in the coming months based on changes in the prevalence of different SARS-CoV-2 variants.[1,3] ■

1. FDA Drug Safety Communication. FDA authorizes revisions to Evusheld dosing. February 24, 2022. Available at: https://bit.ly/3K5AcNc. Accessed March 3, 2022.
2. Tixagevimab and cilgavimab (Evusheld) for pre-exposure prophylaxis of COVID-19. Med Lett Drugs Ther 2022; 64:1.
3. FDA. Fact sheet for health care providers: Emergency Use Authorization for Evusheld (tixagevimab co-packaged with cilgavimab). February 2022. Available at: https://bit.ly/3IWpQjg. Accessed March 3, 2022.

Additional Content Available Online: COVID-19 Tables/Charts

Please check our website for the latest information on COVID-19, including our continuously updated tables/charts on treatments, vaccines, and dosing recommendations. Available at: www.medicalletter.org/drugs-for-covid-19.

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