# The Medical Letter®
## on Drugs and Therapeutics

Volume 64 April 18, 2022

ISSUE No. 1648

IN THIS ISSUE

The Medical Letter®
on Drugs and Therapeutics

Volume 64 (Issue 1648) April 18, 2022

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COVID-19 UPDATES

## Second Booster Vaccine Dose for Older and Immunocompromised Persons

The FDA has expanded the Emergency Use Authorizations (EUAs) for the mRNA COVID-19 vaccines manufactured by Pfizer-BioNTech *(Comirnaty)* and Moderna *(Spikevax)* to allow for their use as a second booster dose ≥4 months after a first booster dose in adults ≥50 years old and in persons aged ≥12 years (Pfizer) or ≥18 years (Moderna) who have undergone solid organ transplantation or have a condition that compromises the immune system to a similar extent.[1,2]

**EFFICACY —** Expansion of the EUAs was based on the results of a cohort study in healthcare workers in Israel who had received two primary doses and one booster dose of the Pfizer COVID-19 vaccine ≥4 months previously. A total of 274 persons were boosted again with either the Pfizer vaccine (n=154) or the Moderna vaccine (n=120) and then compared with age-matched controls over ~34 days (Pfizer) or ~25 days (Moderna). Geometric mean titers of neutralizing anti-SARS-CoV-2 antibodies 2 weeks after a second booster dose were significantly higher than those in the control group (by 10.4-fold with Pfizer and by 14.3-fold with Moderna) and slightly higher than those observed 2 weeks after the first booster dose (by 1.4-fold with Pfizer and by 2.0-fold with Moderna). The rate of symptomatic COVID-19 from day 8 was lower in persons who received a second booster dose than in those who did not (by 43% [95% CI 7% to 65%] with Pfizer and by 31% [95% CI -18% to 60%] with Moderna).[3]

In a 40-day retrospective cohort study in 563,735 persons 60-100 years old in Israel, the rate of death due to COVID-19 was significantly lower in persons who received a second COVID-19 vaccine booster dose during the study period than in eligible persons who did not (28 vs 99 deaths per 100,000 persons; adjusted HR 0.22 [95% CI 0.17-0.28]).[4]

**SAFETY —** In the cohort study in healthcare workers, adverse effects with a second booster dose were similar to those with previous vaccine doses.[2] According to the FDA, a surveillance study (not published) of ~700,000 persons in Israel who received a fourth dose of the Pfizer vaccine did not generate new safety concerns.[1]

**DOSAGE —** The recommended second booster doses of the mRNA vaccines are the same as the initial booster doses (30 mcg for Pfizer; 50 mcg for Moderna). A second booster dose can be given ≥4 months after an initial booster dose of any FDA-authorized or approved COVID-19 vaccine (Pfizer, Moderna, or Johnson & Johnson/Janssen).[5,6] ■

1. FDA News Release. Coronavirus (COVID-19) update: FDA authorizes second booster dose of two COVID-19 Vaccines for older and immunocompromised individuals. March 29, 2022. Available at: https://bit.ly/38bToLQ. Accessed March 31, 2022.
2. CDC. COVID-19 vaccines for moderately or severely immunocompromised people. March 24, 2022. Available at: https://bit.ly/3iREJYo. Accessed March 31, 2022.
3. G Regev-Yochay et al. Efficacy of a fourth dose of Covid-19 mRNA vaccine against Omicron. N Engl J Med 2022 March 16 (epub).
4. R Arbel et al. Second booster vaccine and Covid-19 mortality in adults 60 to 100 years old. Research Square 2022 March 24 (preprint). Available at: https://bit.ly/3uKhzbY. Accessed March 31, 2022.
5. FDA. Fact sheet for healthcare providers administering vaccine (vaccination providers). Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 vaccine to prevent coronavirus disease 2019 (COVID-19). For 12 years of age and older. March 29, 2022. Available at: https://bit.ly/3bBH5GV. Accessed March 31, 2022.
6. FDA. Fact sheet for healthcare providers administering vaccine (vaccination providers). Emergency Use Authorization (EUA) of the Moderna COVID-19 vaccine to prevent coronavirus disease 2019 (COVID-19). Booster dose only presentation. March 29, 2022. Available at: https://bit.ly/3wQC8WO. Accessed March 31, 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.

## FDA Restricts Use of Sotrovimab

The FDA has begun to restrict use of the anti-SARS-CoV-2 monoclonal antibody sotrovimab in US regions with a high relative prevalence of the BA.2 (Omicron) variant of the virus.[1] Sotrovimab, which is available under an Emergency Use Authorization (EUA) for treatment of mild to moderate COVID-19 in high-risk patients ≥12 years old who weigh ≥40 kg,[2] is unlikely to be effective for treatment of COVID-19 caused by BA.2; it has significantly less neutralizing activity *in vitro* against BA.2 than against other variants.[3]

Sotrovimab is no longer authorized for use in regions where the BA.2 variant of SARS-CoV-2 causes >50% of COVID-19 cases. At the time of publication (March 31, 2022), this was the case in HHS Regions 1 (New England), 2 (NJ, NY, Puerto Rico, Virgin Islands), 5 (Upper Midwest), 9 (AZ, CA, HI, NV, Pacific islands), and 10 (AK, ID, OR, WA).[1] BA.2 is likely to become the predominant strain of SARS-CoV-2 in all regions of the US in the coming weeks[4]; announcements of further restrictions on use of sotrovimab will be published at: https://bit.ly/3wGZNc9.[1] Alternative treatments for mild to moderate COVID-19 that retain efficacy against the BA.2 variant include nirmatrelvir/ritonavir *(Paxlovid)*, remdesivir *(Veklury)*, bebtelovimab, and molnupiravir *(Lagevrio)*.[5] ■


1. FDA Drug Safety and Availability. FDA updates sotrovimab emergency use authorization. March 25, 2022. Available at: https://bit.ly/3wGZNc9. March 31, 2022.
2. An EUA for sotrovimab for treatment of COVID-19. Med Lett Drugs Ther 2021; 63:97.
3. FDA. Fact sheet for health care providers. Emergency Use Authorization (EUA) of sotrovimab. March 2022. Available at: https://bit.ly/2TfoomJ. Accessed March 31, 2022.
4. CDC. COVID data tracker. Variant proportions. Available at: https://bit.ly/3Ka3HhH. Accessed March 31, 2022.
5. Treatment of COVID-19 in high-risk outpatients. Med Lett Drugs Ther 2022 March 3 (epub). Available at: https://secure.medicalletter.org/downloads/1643f_table.pdf.