DELAWARE HEALTH ALERT #455: Expanded COVID-19 Vaccine EUAs for Third Dose in Certain Immunocompromised Persons

The Delaware Division of Public Health (DPH) is issuing this health alert to advise the medical community that the U.S. Food & Drug Administration (FDA) has expanded the Emergency Use Authorizations (EUA) for the Pfizer-BioNTech and Moderna COVID-19 vaccines, to permit administration of a third dose to certain individuals.

Summary

On August 12, 2021, the FDA expanded the EUA for both the Pfizer-BioNTech and Moderna COVID-19 Vaccine to authorize a third dose of the same COVID-19 vaccine administered at least 28 days following the two-dose regimen of either vaccine. This authorization is extremely limited and applies only to eligible individuals (12 years of age or older for Pfizer-BioNTech or 18 years of age or older for Moderna) who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Available data show that these people don't always build adequate levels of protection after an initial 2-dose primary mRNA COVID-19 vaccine series. The data also show that they may benefit from receiving an additional dose of an mRNA vaccine to develop as much protection as possible against COVID-19.

This action does not apply to people who are not immunocompromised. This action also does not apply to those who received the Janssen Johnson & Johnson (J&J) vaccine as their first dose.

In Delaware, providers may administer the third dose of Pfizer-BioNTech or Moderna vaccine for COVID-19 to eligible individuals who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise effective immediately, or as soon as they are in a position to do so.

The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) have defined what other conditions are considered to be 'an equivalent level of immunocompromise'.

Recommendations

ACIP recommends the following individuals be considered for a third dose of an mRNA vaccine, if they received it as the first dose:

- Organ transplant recipients taking immunosuppressive therapy
- Recipient of stem cell transplants (CAR-T-cell or hematopoietic) within two years or taking immunosuppressive therapy
- Active/recent cancer treatments for tumors or hematologic malignancies
- Advanced or untreated HIV infection

- Persons taking medications that weaken the immune system - high-dose corticosteroids (i.e., ≥20mg prednisone or equivalent per day), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, TNF blockers, and other biologic agents that are immunosuppressive or immunomodulatory
- Moderate or severe primary immunodeficiency (e.g., DiGeorge, Wiskott-Aldrich syndromes)

Implementation Considerations:

- The additional dose should be the same mRNA vaccine as the primary series
- Alternate mRNA product can be used if primary series product not available
- The additional dose should be administered at least four weeks (28 days) after completion of the initial primary series
- Currently there are not data to support the use of an additional mRNA COVID-19 vaccine dose after a primary J&J COVID-19 vaccine in immunocompromised people. FDA and CDC are actively working to provide guidance on this issue.
- Immunocompromised people (including those who receive an additional mRNA dose) should be counseled about the potential for reduced immune response to COVID-19 vaccination and need to follow prevention measures*
    - Wear a mask
    - Stay 6 feet apart from others they don't live with
    - Avoid crowds and poorly ventilated indoor spaces until advised otherwise by their healthcare provider
- Close contacts of immunocompromised people should be strongly encouraged to be vaccinated against COVID-19
- Patients may self-attest to their immunocompromised state
- Providers should not use antibody test to determine need for the third dose

Additional considerations

- Patient's clinical team is best able to assess the degree of altered immunocompetence and optimal timing of vaccination, with specific attention paid to current or planned immunosuppressive therapies
- Whenever possible, mRNA COVID-19 vaccination doses (including the primary series and an additional dose) should be given at least two weeks before initiation of immunosuppressive therapies.
- Factors to consider in assessing the general level of immune competence of patients with chronic diseases include disease severity, duration, clinical stability, complications, comorbidities, and any potentially immune-suppressing treatment
- Utility of serologic testing or cellular immune testing to assess immune response to vaccination and guide clinical care (e.g., need for an additional dose) has not been established and is not recommended at this time

If you are a provider with general questions, contact VaccinePlanning@delaware.gov. If you are an enrolled provider and wish to order vaccine e-mail OEMS@delaware.gov, or contact COVIDVaccine@delaware.gov if you wish to enroll as a COVID-19 provider.

Additionally, a reminder that testing is recommended for all persons with symptoms consistent with COVID-19, **regardless of age.** Testing is also recommended for close contacts of persons with COVID-19. Close contact means having been less than 6 feet for a total of at least 15 minutes over a 24-hour period from a person with confirmed or probable case of COVID-19. Unvaccinated persons should get tested 5 – 7 days after an exposure. Fully vaccinated persons should get tested 3-5 days after an exposure. **Exception:** In the **K–12 indoor classroom** setting, the close contact definition excludes students who were within 3 to 6 feet of an infected student (laboratory-confirmed or a clinically compatible illness) if both the infected student and the exposed student(s) correctly and consistently wore well-fitting masks the entire time.

Reporting

Providers are reminded to report all confirmed and suspected cases of COVID-19 to the DPH Office of Infectious Disease Epidemiology (OIDE) at 302-744-4990 (normal business hours) or 1-888-295-5156 (outside of normal business hours), fax to 302-223-1540, or email to reportdisease@delaware.gov.

You may also complete a Notifiable Disease Report PDF Form and mail the form as directed, fax the form to DPH at 302-223-7540, or email to reportdisease@delaware.gov. The form and list of notifiable diseases can be found online at https://dhss.delaware.gov/dhss/dph/dpc/rptdisease.html.

Background

Rationale behind recommendation for an additional dose

- People with immunocompromising conditions/who take immunosuppressive medications are at increased risk
- Some immunocompromised people have a reduced response compared to non-immunocompromised people
- Including an additional dose after a primary series may enhance the immune response; the reactogenicity/safety profile was similar to prior doses

Pfizer-BioNTech COVID-19 Vaccine:

FDA reviewed safety and effectiveness data reported in two manuscripts on solid organ transplant recipients. The study was a single arm study conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) a median of 97±8 months earlier. A third dose of the Pfizer-BioNTech COVID-19 was administered to 99 of these individuals approximately 2 months after they had received a second dose. Levels of total SARS-CoV-2 binding antibodies meeting the pre-specified criteria for success occurred four weeks after the third dose in 26/59 (44%) of those who were initially

considered to be seronegative and received a third dose of the Pfizer-BioNTech COVID-19 vaccine; 67/99 (68%) of the entire group receiving a third vaccination were subsequently considered to have levels of antibodies indicative of a significant response. In those who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported. Despite the moderate enhancement in antibody titers, the totality of data (i.e., supportive paper by Hall et al. demonstrated efficacy of the product in the elderly and persons with co-morbidities) supports the conclusion that a third dose of the Pfizer-Moderna COVID-19 vaccine may be effective in this population, and that the known and potential benefits of a third dose of Pfizer-BioNTech COVID-19 vaccine outweigh the known and potential risks of the vaccine for immunocompromised individuals at least 12 years of age who have received two doses of the Pfizer-BioNTech COVID-19 vaccine and who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Moderna COVID-19 Vaccine:
FDA reviewed safety and effectiveness data reported in two manuscripts on solid organ transplant recipients. The study was a double-blind, randomized-controlled study conducted in 120 individuals who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years earlier (range 1.99-6.75 years). A third dose of the Moderna COVID-19 vaccine was administered to 60 individuals approximately two months after they had received a second dose (i.e., doses at 0, 1 and 3 months); saline placebo was given to 60 individuals for comparison. The primary outcome was anti-RBD antibody at four months greater than 100 U/mL. This titer was selected based on NHP challenge studies as well as a large clinical cohort study to indicate this antibody titer was possibly protective. Secondary outcome was based on a virus neutralization assay polyfunctional T cell response. Baseline characteristics were comparable between the two study arms as were pre-intervention anti-RBD titer and neutralizing antibodies. Levels of SARS-CoV-2 antibodies indicative of a significant response occurred four weeks after the third dose in 33/60 (55%) of the Moderna COVID-19 vaccinated group and 10/57 (17.5%) of the placebo individuals. In the 60 individuals who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 adverse events were reported. Despite the moderate enhancement in antibody titers, the totality of data (including the supportive paper by Kamar et al. and demonstrated efficacy of the product in the elderly and persons with co-morbidities) supports the conclusion that a third dose of the Moderna COVID-19 vaccine may be effective in this population, and that the known and potential benefit of a third dose of Moderna COVID-19 vaccine outweigh the known and potential risks of the vaccine for immunocompromised individuals at least 18 years of age who have received two doses of the Moderna COVID-19 vaccine and who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Additional Resources:
Interim Clinical Considerations (CDC) - https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

FDA Release - Coronavirus (COVID-19) Update: FDA Authorizes Additional Vaccine Dose for Certain Immunocompromised Individuals | FDA

Pfizer EUA - Pfizer-BioNTech COVID-19 Vaccine EUA LOA reissued August 12 2021 (fda.gov)

Moderna EUA - Moderna COVID-19 Vaccine EUA Letter of Authorization (fda.gov)

Yellow Book APPROACH TO THE IMMUNOCOMPROMISED TRAVELER
https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwwwnc.cdc.gov%2Ftravel%2Fyellowbook%2F2020%2Ftravelers-with-additional-considerations%2Fimmunocompromised-travelers&data=04%7C01%7CAndrea.Wojcik%40delaware.gov%7C3f512e9db43449aac5db08d95e98c6b6%7C8c09e56951c54deeabb28b99c32a4396%7C0%7C0%7C637644832524514685%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=H4Cu4R%2F%2FmSMqNngIzG%2FPJchRGVcx8oPy5sYU4K7BCxI%3D&reserved=0

2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host (Archived)
https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.idsociety.org%2Fpractice-guideline%2Fvaccination-of-the-immunocompromised-host%2F&data=04%7C01%7CAndrea.Wojcik%40delaware.gov%7C3f512e9db43449aac5db08d95e98c6b6%7C8c09e56951c54deeabb28b99c32a4396%7C0%7C0%7C637644832524514685%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=ZtVKSwtYbHuTTlCbA1T9sr7F705QE1JWVedjF8ArRhg%3D&reserved=0

General Best Practice Guidelines for Immunization: Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP)
https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fhcp%2Facip-recs%2Fgeneral-recs%2Fimmunocompetence.html&data=04%7C01%7CAndrea.Wojcik%40delaware.gov%7C3f512e9db43449aac5db08d95e98c6b6%7C8c09e56951c54deeabb28b99c32a4396%7C0%7C0%7C637644832524514685%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=3AhUEefXBSd2Q%2Fns10umtKGPYAJYgdMK%2BW1SlyVpmH0%3D&reserved=0