TO: Vermont Health Care Providers and Health Care Facilities
FROM: Jennifer S. Read, MD, FIDSA, Medical Epidemiologist

Reactogenicity, Contraindications, and Precautions: mRNA COVID-19 Vaccines

Subsequent to the implementation of the COVID-19 vaccine registration system in Vermont, health care providers in the state have had questions regarding language in the screening questions. In response to this, the language in the screening questions has been modified as follows:

Question 3A: Have you had a severe allergic reaction (e.g., anaphylaxis) after a previous dose of the Pfizer or Moderna COVID-19 vaccine or any of its components?

Yes: You should not get another dose of the Pfizer or Moderna COVID-19 vaccine. [Appointment scheduling is blocked]

No: [Appointment scheduling proceeds]

Question 3B: Have had an immediate allergic reaction to any other vaccine or injectable therapy?

Yes: [Proceed to question 3C]

No: [Appointment scheduling proceeds]

Question 3C: [Asked only if patient answers "yes" to question 3B] Have you been told by an allergy/immunology specialist that you can safely receive an mRNA COVID-19 vaccine??

Yes: [Appointment scheduling proceeds]

No: You should not get a Pfizer or Moderna COVID-19 vaccine until an allergy/immunology specialist determines that you can safely receive the vaccine.

Please ask your primary care provider to refer you to an allergy/immunology specialist who can determine if you can safely receive the vaccine. [Appointment scheduling is blocked]

Further information about a history of allergic reactions is provided in Tables 1 and 2 below.

The question about history of a bleeding disorder or use of a blood thinner has been removed from the registration system. All vaccination clinics solicit this history and are prepared to vaccinate people who have this history.

BACKGROUND INFORMATION

The Advisory Committee on Immunization Practices (ACIP) has issued interim recommendations for the use of coronavirus 2019 (COVID-19) vaccines produced by Pfizer-BioNTech and Moderna. Both vaccines are for the prevention of COVID-19 and are lipid nanoparticle-formulated, nucleoside-modified mRNA vaccines encoding the prefusion spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19.

Interim clinical considerations from the Centers for Disease Control and Prevention (CDC) for the use of these vaccines incorporate data submitted to the Food and Drug Administration (FDA) for Emergency Use Authorization (EUA) of the vaccines, other data sources, general best practice guidelines for immunization, and expert opinion. The following information is derived from the CDC's interim clinical considerations:

Reactogenicity

Before vaccination, vaccine recipients should be counseled about expected local (e.g., pain, swelling, erythema at the injection site, localized axillary lymphadenopathy on the same side as the vaccinated arm) and systemic (e.g., fever, fatigue, headache, chills, myalgia, arthralgia) post-vaccination symptoms. Depending on vaccine product, age group, and vaccine dose, approximately:

- 80–89% of vaccinated persons develop at least one local symptom
- 55–83% develop at least one systemic symptom following vaccination

Clinical trial data revealed that some patients (less than 1%) experienced delayed injection site reactions (onset on or after day 8) after the first or second dose of vaccine. Such reactions were characterized by erythema, induration, and tenderness. Resolution occurred over the following 4-5 days.

Systemic symptoms post-vaccination:

- Most are mild to moderate in severity
- Occur within the first three days of vaccination
- Resolve within 1–3 days of onset.
- More frequent and severe
    - Following the second dose
    - Among younger persons compared to older persons

Unless persons develop a contraindication to vaccination (see below), they should be encouraged to complete the series even if they develop local or systemic symptoms following the first dose to optimize protection against COVID-19.

Hypersensitivity-related adverse events following vaccination observed in clinical trials:

- Pfizer-BioNTech: 0.63% (0.51% in placebo-recipients)
- Moderna: 1.5% (versus 1.1% in placebo recipients)

Anaphylaxis following vaccination:

- Not observed in clinical trials for either the Pfizer-BioNTech or Moderna COVID-19 vaccines
- Have been reported following receipt of mRNA vaccines outside of clinical trials.

Contraindications and Precautions

Table 1, based on the CDC's interim clinical considerations, summarizes contraindications and precautions related to the mRNA COVID-19 vaccines currently licensed in the U.S.

Management of Anaphylaxis After mRNA COVID-19 Vaccination

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of mRNA COVID-19 vaccine.

Administration of antihistamines to COVID-19 vaccine recipients prior to vaccination to prevent allergic reactions is not recommended. Antihistamines do not prevent anaphylaxis, and their use may mask cutaneous symptoms, which could lead to a delay in the diagnosis and management of anaphylaxis.

Table 1: Contraindications and precautions: mRNA COVID-19 vaccines

MAY PROCEED WITH VACCINATION	PRECAUTION TO VACCINATION	CONTRAINDICATION TO VACCINATION
CONDITIONS • Immunocompromising conditions • Pregnancy • Lactation **ACTIONS** • 15-minute observation period	**CONDITIONS** • Moderate/severe acute illness **ACTIONS** • Risk assessment • Potential deferral of vaccination • 15-minute observation period if vaccinated	**CONDITIONS** • None **ACTIONS** • None
ALLERGIES • History of allergies that are unrelated to components of an mRNA COVID-19 vaccine†, other vaccines, injectable therapies, or polysorbate, such as: • Allergy to oral medications (including the oral equivalent of an injectable medication) • History of food, pet, insect, venom, environmental, latex, etc., allergies • Family history of allergies **ACTIONS** • 30-minute observation period: Persons with a history of anaphylaxis (due to any cause) • 15-minute observation period: All other persons	**ALLERGIES** • History of any immediate allergic reaction‡ to vaccines or injectable therapies (except those related to component of mRNA COVID-19 vaccines† or polysorbate, as these are contraindicated) **ACTIONS** • Risk assessment • Consider deferral of vaccination and/or referral to allergist-immunologist • 30-minute observation period if vaccinated	**ALLERGIES** • History of the following are contraindications to receiving either of the mRNA COVID-19 vaccines†: • Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components • Immediate allergic reaction‡ of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components^ (including polyethylene glycol)# • Immediate allergic reaction of any severity to polysorbate^# **ACTIONS:** • Do not vaccinate# • Consider referral to allergist-immunologist

† Refers only to mRNA COVID-19 vaccines currently authorized in the United States (i.e., Pfizer-BioNTech, Moderna COVID-19 vaccines)

‡ Immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms consistent with urticaria, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis that occur within four hours following administration.

^ See Table 2 for a list of ingredients. Note: Polyethylene glycol (PEG), an ingredient in both mRNA COVID-19 vaccines, is structurally related to polysorbate and cross-reactive hypersensitivity between these compounds may occur. Information on ingredients of a vaccine or medication (including PEG, a PEG derivative, or polysorbates) can be found in the package insert.

These persons should not receive mRNA COVID-19 vaccination at this time unless they have been evaluated by an allergist-immunologist and it is determined that the person can safely receive the vaccine (e.g., under observation, in a setting with advanced medical care available)

Table 2: Ingredients included in Pfizer-BioNTech and Moderna mRNA COVID-19 vaccines

An immediate allergic reaction to any component or previous dose of an mRNA COVID-19 vaccine is a contraindication to vaccination with both the Pfizer-BioNTech and Moderna vaccines. The following is a list of ingredients for the Pfizer-BioNTech and Moderna COVID-19 vaccines, as reported in the prescribing information for each vaccine.

	Pfizer-BioNTech	Moderna COVID-19 vaccine
mRNA	Nucleoside-modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2	Nucleoside-modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2
Lipids	2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide	PEG2000-DMG: 1,2-dimyristoyl-rac-glycerol, methoxypolyethylene glycol
	1,2-distearoyl-sn-glycero-3-phosphocholine	1,2-distearoyl-sn-glycero-3-phosphocholine
	Cholesterol	Cholesterol
	(4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)	SM-102: heptadecan-9-yl 8-((2-hydroxyethyl) (6-oxo-6-(undecyloxy) hexyl) amino) octanoate
Salts, sugars, buffers	Potassium chloride	Tromethamine
	Monobasic potassium phosphate	Tromethamine hydrochloride
	Sodium chloride	Acetic acid
	Dibasic sodium phosphate dihydrate	Sodium acetate
	Sucrose	Sucrose

Note: Both the Pfizer-BioNTech and Moderna COVID-19 vaccines contain polyethylene glycol (PEG). PEG is a primary ingredient in osmotic laxatives and oral bowel preparations for colonoscopy procedures, an inactive ingredient or excipient in many medications, and is used in a process called pegylation to improve the therapeutic activity of some medications (including

certain chemotherapeutics). Additionally, cross-reactive hypersensitivity between PEG and polysorbates (included as an excipient in some vaccines and other therapeutic agents) can occur.

Requested Actions:

Be aware of current clinical considerations regarding use of currently licensed mRNA COVID-19 vaccines:

1. Hypersensitivity-related adverse events following vaccination with currently licensed mRNA COVID-19 vaccines are rare.
2. Anaphylaxis following vaccination was not observed in the clinical trials of the currently licensed mRNA COVID-19 vaccines but has been reported following receipt of these vaccines outside of clinical trials.
3. Individuals with many different conditions and allergies may proceed with vaccination; only certain specific conditions and allergies represent situations in which vaccination should proceed with caution or in which vaccination is contraindicated.
4. Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of mRNA COVID-19 vaccine.
5. Administration of antihistamines to COVID-19 vaccine recipients prior to vaccination to prevent allergic reactions is not recommended. Antihistamines do not prevent anaphylaxis, and their use may mask cutaneous symptoms, which could lead to a delay in the diagnosis and management of anaphylaxis.

If you have any questions, please contact the HAN Coordinator at 802-859-5900 or vthan@vermont.gov.

HAN Message Type Definitions
Health Alert: Conveys the highest level of importance; warrants immediate action or attention.
Health Advisory: Provides important information for a specific incident or situation may not require immediate action.
Health Update: Provides updated information regarding an incident or situation; unlikely to require immediate action.
Info Service Message: Provides general correspondence from VDH, which is not necessarily considered to be of an emergent nature.