COVID-19 Vaccination
Guidelines for Clinical Immunology/Allergy Specialists

Updated 20 September 2021

This resource has been developed for clinical immunology/allergy specialists in Australia as a guide for cases where COVID-19 vaccination should only proceed with precautions, or in cases where COVID-19 vaccination is contraindicated. It includes COVID-19 vaccine skin testing and challenge protocols.

Some information in this guide, including the precautionary notes below, do not apply in New Zealand.

ASCIA has developed the following recommendations, based on the current knowledge regarding allergic reactions to COVID-19 vaccines. These recommendations may change when new information is available.

1. VACCINATE WITHOUT ADDITIONAL PRECAUTIONS

Vaccinate in the community as per national recommendations, with a post-vaccination observation period of **15 minutes**. This includes people with:

- History of allergy, including anaphylaxis to food, drugs, venom, or latex.
- Allergic conditions, including asthma, atopic dermatitis (eczema) or allergic rhinitis (hay fever).

2. VACCINATE WITH PRECAUTIONS*

- Immediate (within four hours) and generalised symptoms of a possible allergic reaction without anaphylaxis to a previous dose of a COVID-19 vaccine.
- Generalised allergic reaction (without anaphylaxis) to one of the ingredients in the COVID-19 vaccine to be administered (Pfizer or Moderna - PEG or AstraZeneca - Polysorbate 80).
- Prior history of anaphylaxis to previous vaccines and/or multiple drugs (injectable and/or oral) where the ingredients PEG or polysorbate 80 may conceivably be the cause and have not been tolerated since on medication review.
- A history of confirmed Mastocytosis with recurrent anaphylaxis that requires treatment.

*** Precautions:**

- Review or discussion prior to vaccination by a clinical immunology/allergy or vaccinology specialist, to develop a risk/benefit assessment for each patient.
- Skin testing to the vaccine and/or graded doses should be considered in some cases.
- Vaccination in a medical facility equipped for the management of anaphylaxis (such as a medical clinic with multiple doctors available, or a hospital clinic).
- Post-vaccination observation period should be at least **30 minutes**.

3. VACCINATION CONTRAINDICATED

- Documented anaphylaxis to one of the ingredients contained in the COVID-19 vaccine to be administered (Pfizer or Moderna - PEG or AstraZeneca - Polysorbate 80).
- Anaphylaxis to a prior dose of a COVID-19 vaccine.

Note: Anaphylaxis with one type of COVID-19 vaccine may not preclude vaccination with another vaccine, but this should only occur if the precautions listed above are met. If there is a high risk of an allergic reaction to one of the vaccines (e.g. known allergy to PEG or Polysorbate 80), it may be possible to have another vaccine which does not contain the ingredient, subject to availability and medical advice.

Information from the Australian Government regarding COVID-19 outbreaks and vaccines is available at www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert

BACKGROUND - COVID-19 VACCINE SKIN TESTING AND CHALLENGES

Allergic reactions have been described for all vaccines, although type 1 mediated reactions comprise only a small proportion of adverse events following immunisation. Allergic reactions need to be distinguished from clinical manifestations co-incidental to vaccination including anxiety and vasovagal reactions. Current data suggest that the reported rates for anaphylaxis are low, with 5 to 20 cases per million doses.

Currently the COVID-19 vaccines available in Australia are Pfizer-BioNTech and Moderna mRNA vaccines, and the AstraZeneca viral vector vaccine. Allergic reactions to vaccines are generally due to excipients or residual proteins used during vaccine production rather than the vaccine antigen:

- **Pfizer-BioNTech and Moderna vaccines** contain a pegylated lipid (polyethylene glycol, molecular weight 2000 Da, abbreviated to PEG2000) although reactions to PEG2000 are rare.
- **AstraZeneca vaccine** contains Polysorbate 80, and unlike PEG2000 this is contained as an excipient in several existing vaccines used routinely in Australia and New Zealand (e.g. DTaP, Hepatitis B, HPV, Influenza vaccines). Whilst polysorbates are derived from PEGs, cross reactivity between the two appears to be extremely rare.[1]

None of these vaccines contain food proteins (egg, dairy, gelatin), latex or antibiotics.

Reactions to previous medications or vaccines

Patients with undiagnosed PEG allergy often have a history of immediate onset anaphylaxis to multiple classes of drugs or idiopathic anaphylaxis. PEG allergic patients should not be vaccinated with the Pfizer-BioNTech vaccine without discussion with a vaccine specialist:

- The AstraZeneca vaccine can be used as an alternative (unless otherwise contraindicated), particularly if they previously tolerated an injected influenza vaccine. The vaccine should be administered in a hospital setting with full resuscitation facilities and a 30-minute observation period is recommended.[2]
- If the Astra-Zeneca vaccine is contraindicated in a possible PEG allergic patient, then the patient should undergo specialist review and consideration for diagnostic testing and/or supervised challenge as per the protocol for reactions to first COVID-19 vaccine (Figure 1).

Since PEG has not been used in previous vaccines, patients with previous vaccination reactions only, should be able to tolerate the Pfizer-BioNTech or Moderna vaccines containing PEG.

Patients with a history of allergic reactions to vaccines who have not subsequently tolerated vaccination with a Polysorbate 80 containing vaccine should avoid the AstraZeneca vaccine and be considered for referral for specialist assessment and testing to Polysorbate 80 for future vaccination requirements.

Reactions to first doses of COVID-19 vaccines

Patients with possible allergic reactions to the first dose of a COVID-19 vaccine should be referred to a specialist Immunology or Vaccination Clinic for further assessment. Possible vaccine associated anaphylaxis should be assessed using the standardised Brighton collaboration case definition https://brightoncollaboration.us/anaphylaxis-case-definition-companion-guide/.

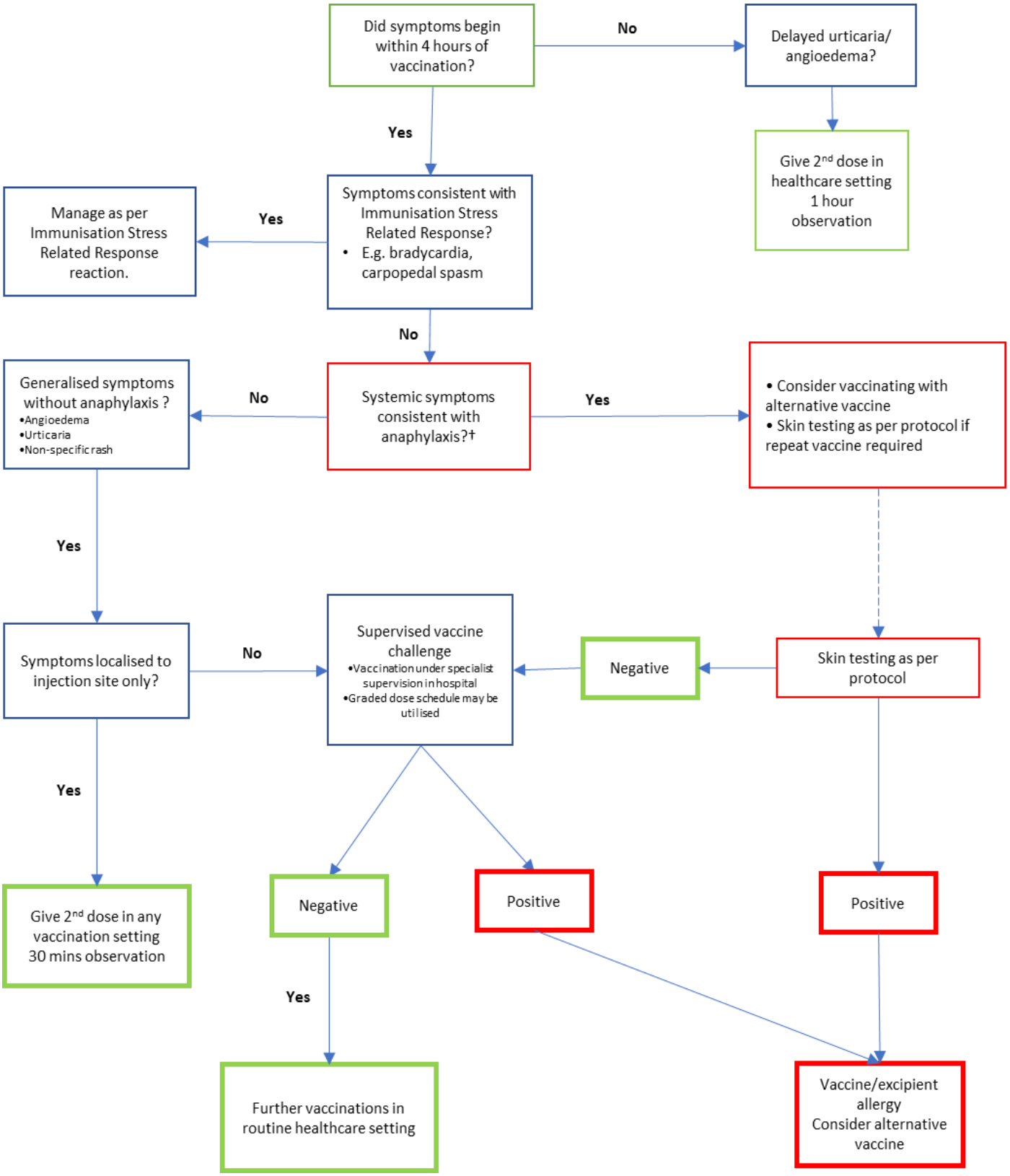
Decisions about the second vaccine dose is dependent on discussions between physician and patient.

The potential options include:

1. Allergy testing with skin and/or challenge testing to vaccine and excipients. The suggested algorithm (Figure 1) is recommended for assessment of patients with possible allergic reactions to the first dose.
2. Consider second dose with an alternative vaccine. Whilst data is currently limited on the level of protection offered using a combination of different vaccines, patients unwilling to undergo testing or repeat vaccination may still be suitable to receive an alternative COVID-19 vaccine (unless otherwise contraindicated). The best interval between split schedule doses is unknown but studies of split dosing are currently underway using intervals of between 4 and 12 weeks.
3. Delay until alternative vaccine options are available with reassurance that there is some protection after one dose of Pfizer-BioNTech, Moderna and AstraZeneca vaccines, although duration is not yet established.

For other information about COVID-19 vaccines, allergic reactions and other health issues refer to the ASCIA Position Statement and Guides www.allergy.org.au/members/covid-19

Figure 1. Suggested algorithm for management of patients with possible allergic reactions to first dose of COVID-19 vaccine.



† Recommended for patients meeting anaphylaxis Brighton Collaboration case definition level 1 or 2.

SKIN AND INTRADERMAL TESTING PROTOCOL

The sensitivity and specificity for skin prick or intradermal testing to Pfizer-BioNTech, Moderna and AstraZeneca vaccines is not yet known. Skin prick testing and intradermal testing to PEG has been described although its sensitivity and specificity, as well as the cross-reactivity between PEG molecules, is also not well established.[3-5] Systemic reactions including anaphylaxis have been described to PEG skin testing and intradermal testing.[6]

Based on this data, skin testing should be reserved for patients with previous anaphylactic reactions and after a shared decision-making process with the patient, explaining that the predictive value of testing remains uncertain.

It is recommended that patients should at minimum, undergo testing with either excipient or, if available, vaccine at appropriate concentrations, if the vaccine/excipients that caused anaphylaxis are being considered for repeat administration.

Table 1. Recommended skin prick and intradermal testing concentration for assessment of COVID-19 vaccine allergy.

	PEG 3350 (Macrogol 3350)	**Pfizer-BioNTech or Moderna mRNA vaccines**	**Polysorbate 80**	**Astra-Zeneca viral vector vaccine**
Step 1. Skin Prick	1:100 (1.7mg/ml)			
Step 2. Skin Prick	1:10 (17mg/ml)			
Step 3. Skin Prick	1:1 (170mg/ml)	1:1	1:1	1:1
Step 4. Intradermal		1:100	1:10	1:100
Step 5. Intradermal		1:10		1:10

CHALLENGE PROTOCOL

Patients who have had a non-anaphylactic immediate allergic reaction or anaphylaxis with negative skin and intradermal testing should undergo a supervised challenge under specialist supervision.

To reduce the risk of severe reactions a split dose of 10% of the total vaccine followed by the remainder of the dose (90%) may be administered at 30-minute intervals instead of a full dose challenge.

Patients must be observed for at least one hour after last vaccine dose, although the observation period should be adjusted if patient develops symptoms during challenge or according to their reaction history.

Table 2. Recommended split dose for 2 step vaccine challenge administered at 30-minute intervals.

	Pfizer-BioNTech or Moderna mRNA vaccines	**Astra-Zeneca viral vector vaccine**
1/10th dose	0.03 ml	0.05 ml
Remainder of dose	0.27 ml	0.45 ml

Patients with positive skin testing and with no suitable alternative vaccines can still be considered for vaccine administration, especially in patients at high risk of infection, by utilising multiple graded doses as previously described.[7]

Table 3. Recommended split dose for 5 step high risk vaccine challenge administered at 15-minute intervals.

	Pfizer-BioNTech or Moderna mRNA vaccines	Astra-Zeneca viral vector vaccine
Step 1	0.03 ml of 1:10 dilution	0.05 ml of 1:10 dilution
Step 2	0.03 ml neat	0.05 ml
Step 3	0.06 ml neat	0.10 ml neat
Step 4	0.09 ml neat	0.15 ml neat
Step 5	0.12 ml neat	0.20 ml neat

DISCLAIMER

Recommendations regarding the AstraZeneca COVID-19 vaccines are based on a person's age and circumstances, where the benefits are likely to outweigh the risks of a rare side effect, and the person has made an informed decision based on an understanding of the risks and benefits.

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