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Joint Position Statement on BioNTech Vaccination in Adolescents with Allergic Diseases

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Hong Kong Society for Paediatric Immunology Allergy and Infectious Diseases

Abstract This Statement was prepared to encourage Hong Kong adolescents aged 12-17 years old to receive BioNTech vaccine and recommend when to refer them for vaccine allergy evaluation. Importantly, the personal and societal benefits of BioNTech vaccination outweigh the risk of non-severe adverse vaccine reactions. BioNTech is currently contraindicated only in individuals with history of anaphylaxis to this vaccine or its components (e.g., polyethylene glycol [PEG]) by appropriate allergy testing. Subjects with history of immediate and severe allergic reactions to PEG-containing drugs or vaccines or immediate allergic reaction to the first dose of BioNTech warrant paediatric allergy referral to evaluate their fitness to receive this vaccine. Allergy to unrelated drugs, food, insect venoms as well as asthma, allergic rhinitis and eczema are not contraindications for BioNTech. Patients with a history of severe allergic reactions after foods, unrelated drugs or vaccines can receive BioNTech with a longer observation of 30 minutes post-vaccination.

Key words Adolescent; Allergy; Contraindication; COVID-19; mRNA vaccine

Background

The COVID-19 pandemic has struck the world for 18 months now. Although COVID-19 mainly affects the elderly and those with chronic medical conditions, children can also suffer physically from this viral infection. Furthermore, children and adolescents are disproportionally affected by the adverse psychosocial effects of prolonged school closure, denial of play opportunities in playgrounds, social restriction, isolation in quarantine facilities and rising rates of domestic violence and child abuse.[1]

Meticulous infection control practice, social distancing and mass COVID-19 vaccination are the key strategies to contain the present pandemic and minimise its public health and societal impact. The first COVID-19 vaccines approved in Hong Kong include BioNTech BNT162b2 mRNA vaccine (Comirnaty) and inactivated virus vaccine (CoronaVac). As of 15 June 2021, Hong Kong has administered a total of 2,964,805 vaccine doses, including 1,203,222 (17.7%) with the second vaccine dose, out of its 7,510,000 population (as of 2019).[2,3] This suboptimal vaccine uptake raises concerns about our inability to establish sufficient herd immunity in our community to halt or mitigate the COVID-19 pandemic. Our College has recently issued an appeal to adults in stable health to receive COVID-19 vaccines as an effective and safe method to protect themselves and their children from being infected.[4]

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The FDA expanded the emergency use authorisation of the BioNTech vaccine to include adolescents aged 12-15 years on 10 May 2021, in addition to its existing licensure for subjects aged 16 years and older.[5] In Hong Kong, the Secretary for Food and Health announced on 3 June 2021 to lower the age limit for the BioNTech vaccination programme from 16 to 12 years. Despite the large numbers of adults and adolescents who have already received mRNA vaccines worldwide, adverse events have only rarely been reported. Nevertheless, there have been reports of severe allergic reactions to these vaccines which, in view of the high prevalence of allergic diseases in adolescents, have led to growing concerns amongst parents about whether youngsters with allergic diseases are fit to receive this vaccine.

This Position Statement encourages adolescents aged 12-17 years old to receive the BioNTech vaccine and includes a fact sheet on this vaccine[6-8] (Appendix 1) and recommendations about when to consider referral to a paediatric allergy clinic for evaluation.

Position Statement on the Relevance of Allergies to BioNTech Vaccination

The personal and societal benefits of BioNTech vaccination outweigh the risk of non-severe adverse vaccine reactions in adolescents. In particular, a very recent study showed that this vaccine was highly effective against COVID-19 and safe when administered to 12-to-15-year-old recipients.[9]

At this time, the BioNTech vaccination is ***contraindicated only*** under the following condition: individuals with a history of anaphylaxis[10] (Appendix 2) to this vaccine or its components (e.g., PEG) as confirmed by appropriate allergy testing.

Subjects require ***paediatric allergy referral and evaluation*** of their fitness to receive the BioNTech vaccine if they have:

- History of *immediate* and *severe* allergic reactions to *drugs or vaccines containing PEG* (Appendix 3); or
- History of *immediate* allergic reaction to the first dose of BioNTech vaccine

"*Severe*" refers to occurrence of any non-cutaneous adverse reactions (e.g., respiratory, cardiovascular or severe gastrointestinal [Appendix 2]); "*immediate*" means within 4 hours.

Allergy to unrelated drugs, food, insect venoms or inhalant allergens (e.g., house dust mites, pollens, animal dander, moulds) as well as asthma, allergic rhinitis and eczema are ***not contraindications*** for BioNTech vaccination. Individuals with these allergic conditions can receive the BioNTech vaccine.

The above recommendations are supported by authorities and organisations including the US Food and Drug Administration and drug package insert, US Centers for Disease Control and Prevention, American Academy and College of Allergy, Asthma and Immunology, Australasian Society of Clinical Immunology and Allergy, Ministry of Health of Singapore and the Scientific Committee on Vaccine Preventable Diseases of the Centre for Health Protection, Department of Health, the Government of the HK Special Administrative Region.[5,11-15]

COVID-19 vaccine recipients should be observed for at least 15 minutes after vaccination. Patients with a history of severe allergic reactions after foods, unrelated drugs or vaccines can proceed with BioNTech vaccination, but they are advised to be given a longer observation (30 minutes) after vaccination.[16]

Clinicians administering the BioNTech vaccine should be prepared to recognise symptoms of anaphylaxis as early as possible, promptly manage such severe allergic reactions, and activate further emergency medical services while continuing to care for the patient.[16] Patients who develop immediate allergic reaction after the first dose of BioNTech vaccination should be referred to paediatric allergy clinics of the Hospital Authority or College-accredited Paediatric Immunology, Allergy and Infectious Diseases (PIAID) Fellows in private practice who are registered under the Medical Council of Hong Kong for evaluation. *Unless such evaluation excludes BioNTech allergy, these patients should not receive the second dose of this vaccine.*

As COVID-19 vaccines are administered to millions of people globally in the upcoming months, more pharmacovigilance and post-marketing surveillance data will be available to assess the incidence of vaccine allergy and its risk factors as well as the occurrence of rare immune-related adverse events. In case of any change in the licensed age limit for an inactivated virus vaccine and availability of other marketed COVID-19 vaccines and newer generation of vaccines in the future, there will be additional vaccination options and allergy testing strategies.[17] Our College and Society will update this document in due course.

This document was endorsed by the Councils of both organisations on 15 June 2021.

References

1. Tse WY, Kwan MYW. Impacts of the COVID-19 pandemic on the physical and mental health of children. HK Med J 2021; in press.
2. The Government of Hong Kong Special Administrative Region. 2021. Available from https://www.covidvaccine.gov.hk/en/.
3. The Government of Hong Kong Special Administrative Region. Hong Kong - the facts. 2021. Available from https://www.gov.hk/en/about/abouthk/facts.htm.
4. Hong Kong College of Paediatricians, Hong Kong Paediatric Society and Hong Kong Society for Paediatric Immunology, Allergy and Infectious Diseases joint recommendation on appealing to adults to receive COVID-19 vaccination for the psychosocial and physical health of our children. Available from http://www.paediatrician.org.hk/index.php?option=com_content&view=article&id=427&catid=2&Itemid=26.
5. US Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes Pfizer-BioNTech COVID-19 vaccine for emergency use in adolescents in another important action in fight against pandemic, 2021. Available from https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use.
6. United States Centers for Disease Control and Prevention. Allergic reactions including anaphylaxis after receipt of the first dose of Pfizer-BioNTech COVID-19 vaccine - United States, December 14-23, 2020.
7. Anagnostou K, Turner PJ. Myths, facts and controversies in the diagnosis and management of anaphylaxis. Arch Dis Child 2019; 104:83-90.
8. Stone CA, Jr, Liu Y, Relling MV, et al. Immediate hypersensitivity to polyethylene glycols and polysorbates: more common than we have recognized. J Allergy Clin Immunol Pract 2019;7:1533-40. e8.
9. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020; 383: 2603-15.
10. Cardona V, Ansotegui IJ, Ebisawa M, et al. World allergy organization anaphylaxis guidance 2020. World Allergy Organ J 2020;13:100472.
11. American Academy of Allergy, Asthma and Immunology. An update on COVID-19 for the practicing allergist/immunologist. 2021. Available from https://education.aaaai.org/resources-for-a-i-clinicians/Update-for-AI_COVID-19.
12. ACAAI updates to guidance on risk of allergic reactions to COVID-19 vaccines. 2021. Available from https://acaai.org/news/acaai-updates-guidance-risk-allergic-reactions-covid-19-vaccines.
13. Australasian Society of Clinical Immunology and Allergy. Allergy, immunodeficiency, autoimmunity and COVID-19 vaccination frequently asked questions (FAQ). Available from https://www.allergy.org.au/patients/ascia-covid-19-vaccination-faq.
14. Ministry of Health of Singapore. FAQs - safety and efficacy of the COVID-19 vaccine. 2021. Available from https://www.moh.gov.sg/covid-19/vaccination/faqs/faqs---safety-and-efficacy-of-the-covid-19-vaccine.
15. Scientific Committee on Emerging and Zoonotic Diseases and Scientific Committee on Vaccine Preventable Diseases, Centre for Health Protection, Department of Health, the Government of Hong Kong Special Administrative Region. Consensus interim recommendations on the use of COVID-19 vaccines in Hong Kong (as of 9 June 2021). Available from https://www.chp.gov.hk/files/pdf/consensus_interim_recommendations_on_the_use_of_covid19_vaccines_in_hk.pdf.
16. Banerji A, Wickner PG, Saff R, et al. mRNA vaccines to prevent COVID-19 disease and reported allergic reactions: current evidence and suggested approach. J Allergy Clin Immunol Pract 2021;9:1423-37.
17. Banerji A, Wolfson AR, Wickner PG, et al. COVID-19 vaccination in patients with reported allergic reactions: updated evidence and suggested approach. J Allergy Clin Immunol Pract 2021;9: 2135-8.

Appendix 1. Fact sheet related to allergies and the BioNTech vaccine

- This vaccine is packaged in multi-dose vials and must be diluted before use. There are no added adjuvants or preservatives, while lipids, sucrose and salts are added as excipients to stabilise the active vaccine substance (mRNA encoding SARS-CoV-2 spike glycoprotein).
- This mRNA vaccine does not contain any live virus, so it can be safely given to patients with impaired immune response. However, it is possible that the vaccine immunogenicity and efficacy are lower in such patients.
- Most adverse events (e.g., injection site pain and redness, fatigue, headache, fever, chills, myalgia, arthralgia, regional lymphadenopathy) following immunization are a result of the vaccine stimulating a protective immune response instead of being allergic in nature.
- Allergic reactions after BioNTech vaccine have been reported to occur in 11.1 cases per one million doses, including anaphylaxis in 5 cases per one million doses.[6] Other allergic reactions include skin rash, urticaria and lip/face angioedema. Seventy-one percent of these allergic reactions occurred within 15 minutes of vaccination. To date, there has not been any confirmed anaphylactic death due to this vaccine.
- Anaphylaxis can happen to anyone, anywhere and anytime. There is no correlation with age, sex, asthma, atopic status or previous non-severe reactions.[7]
- Polyethylene glycol (PEG), also known as macrogol, is a polyether compound widely used as an additive in cosmetics, pharmaceutical products and foods. For this vaccine, a PEG with a molecular weight of 2,000 g/mol (PEG 2000) is used to improve the aqueous solubility of the lipid nanoparticle.[7]
- IgE-mediated allergic reactions and anaphylaxis to PEGs of different molecular weights have previously been reported.[8] However, PEG allergy and anaphylaxis following mRNA vaccination are rare.

Appendix 2. Anaphylaxis defining criteria

Anaphylaxis is ***highly likely*** when one of the following two criteria is fulfilled:

1. Acute onset of an illness (minutes to several hours) with mucocutaneous features such as generalised hives, pruritus or flushing, and swollen lips, tongue and uvula **AND** one of the following three non-cutaneous manifestations:
   (a) Airway/breathing (e.g., dyspnoea, stridor, wheeze, reduced peak expiratory flow, hypoxaemia)
   (b) Cardiovascular (e.g., hypotension, syncope, incontinence)
   (c) Severe gastrointestinal (e.g., severe abdominal pain, repetitive vomiting)
2. Acute onset of hypotension or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), **even in the absence of typical skin involvement as detailed under point 1**.

Reference: Cardona V, Ansotegui IJ, Ebisawa M, et al. World Allergy Organization anaphylaxis guidance 2020. *World Allergy Organ J* 2020;13:100472.

Appendix 3. List of PEG-containing drugs*

Generic name (brand name)	Molecular weight	General description
	Locally available injectable medications	
Betamethasone	Macrogols	Corticosteroid
Busulphan	PEG	Chemotherapy
Certolizumab pegol prefilled syringe	PEGylated Fab'	Treatment of autoimmune diseases including Crohn's disease, rheumatoid arthritis, etc.
Cyclofem (medroxyprogesterone acetate and estradiol cypionate)	PEG 3350	Contraceptive therapy
Cyclosporin A	Macrogoglycerol ricinoleate (PEG 35 castor oil)	Immunosuppressant
Doxorubicin HCl (liposomal)	N-(carbonyl-methoxy**polyethylene glycol 2000**)-1,2-distearoyl -SN-glycero-3-phosphoethanolamine sodium salt (MPEG-DSPE)	Chemotherapy
Etoposide	PEG 300	Chemotherapy
Medroxyprogesterone acetate (Depo-Provera)	PEG 3350	Contraceptive therapy and treatment of endometrial and renal carcinoma
Methoxy polyethylene glycol-epoetin beta (Mircera)	30-kD methoxy PEG butanoic acid	Treatment of anaemia in patients with chronic kidney disease
Methylprednisolone acetate (Depo-Medrol)	PEG 3350	Corticosteroid
Nimodipine (Nimotop)	PEG 400	Anti-hypertensive drug
Paclitaxel	Macrogoglycerol ricinoleate (PEG 35 castor oil)	Chemotherapy
Paliperidone palmitate (Invega Trinza) prefilled syringe	PEG 4000	Treatment of schizophrenia
Pegaspargase (Oncaspar)	PEG 345-410	Chemotherapy
Pegfilgrastim (Neulasta, Neulastim)	20-kD monomethoxy PEG	Stimulate the production of white blood cells in patients with chemotherapy-induced neutropaenia
Temsirolimus	PEG 400 (Diluent)	Treatment of renal cell carcinoma
	Locally available oral medications	
Alfacalcidol drops	Macrogolglycerol hydroxystearate (PEG 40 castor oil)	Treatment of hypocalcaemia, osteomalacia, hyperparathyroidism, hypoparathyroidism and renal osteodystrophy
Carbamazepine suspension	PEG 400	Anti-epileptic drug
Cyclosporin A (Teva) solution	Macrogolglycerol hydroxystearate (PEG 40 castor oil)	Immunosuppressant
Macrogol 4000 powder	Macrogol 4000	Laxative
Mylanta suspension (aluminium hydroxide, magnesium hydroxide, simethicone)	Cetomacrogol 1000 (PEG hexadecyl ether)	Antacid
Oxcarbazepine suspension	PEG-400-stearate; Macrogol stearate (PEG stearate)	Anti-epileptic drug
Polyethylene glycol electrolyte powder (Klean-Prep)	PEG 3350	Laxative
	Medications that are available overseas	
Brilliant Blue G Ophthalmic Solution (TissueBlue)	PEG 3350	Disclosing agent indicated to selectively stain the internal limiting membrane
Perflutren lipid microsphere (Definity)	PEG 5000	Contrast agent used to brighten and clarify images during echocardiograms
Rilonacept (Arcalyst)	PEG 3350	IL-1 blocker for treating cryopyrin-associated periodic syndromes
Sulfur hexafluoride (Lumason)	PEG 4000	Ultrasound contrast agent

* This list is not exhaustive and will be revised from time to time based on the best available evidence. Please refer to the College website at http://www.paediatrician.org.hk/ for the most updated version.

Reference: Banerji A, Wickner PG, Saff R, et al. mRNA vaccines to prevent COVID-19 disease and reported allergic reactions: current evidence and suggested approach. *J Allergy Clin Immunol Pract* 2021;9:1423-37.