



MINISTRY OF HEALTH
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To All Medical Practitioners

ADDENDUM: GUIDELINES IN PREPARATION FOR THE MANAGEMENT OF ANAPHYLAXIS AND SEVERE ALLERGIC REACTIONS AFTER COVID-19 VACCINATION IN CHILDREN AGED 5 – 11 YEARS OLD

1. Following the United States (US) Food and Drug Administration (FDA)'s announcement in October 2021 that the Pfizer-BioNTech COVID-19 vaccine has met the safety and efficacy standards for authorisation in children ages 5 through 11 years old, the US Centers for Disease Control (CDC) Advisory Committee on Immunization Practices (ACIP) recommended in November 2021, that children in the above mentioned age group be vaccinated against COVID-19 with this vaccine to prevent COVID-19 infections. Along with other preventive measures, vaccination can protect children from COVID-19 infection, hospitalisation/ severe infection, and death. In Singapore, the Health Sciences Authority (HSA) is evaluating an application from Pfizer for a paediatric formulation of the Pfizer-BioNTech vaccine to be used for children ages 5 through 11 years old. The Expert Committee on COVID-19 Vaccination (EC19V) is concurrently reviewing the available evidence on the clinical efficacy and safety of this vaccine for use in this age group.

2. In anticipation of HSA's regulatory authorisation of the vaccine and EC19V's recommendations to extend vaccination to children of ages 5 through 11 years old under the National Vaccination Programme for COVID-19, this advisory provides guidelines for medical practitioners who will be operating vaccination centres for these children using the Pfizer-BioNTech vaccine, to prepare ahead of time. The guidelines were developed based on public information made available by the US CDC, and in consultation with clinical experts from Kangar Kerbau Hospital (KKH) and National University Hospital (NUH). **The guidelines are provisional and will be adjusted based on HSA's authorisation, EC19V's recommendation, and MOH's final decision on whether to include the vaccine in the National Vaccination Programme, respectively.**

3. Anaphylactic reactions to vaccines (including COVID-19 vaccines) are rare but potentially life-threatening. Under-recognition of anaphylaxis is common, hence rapid identification is vital. These guidelines inform all medical practitioners on the recognition and management of anaphylaxis and severe allergic reactions post-vaccination in children aged 5 -11 years old.

RECOGNITION OF ANAPHYLAXIS

4. All persons who receive COVID-19 vaccines have to be seated and should be observed for 30 minutes after vaccination¹. When anaphylaxis occurs after the administration of vaccine, patients generally develop symptoms within 30 minutes, although the onset may rarely be delayed for up to several hours.
5. Medical practitioners are advised to provide treatment for anaphylaxis in patients **with two** out of three of the following sets of symptoms*:
- Acute onset mucocutaneous symptoms (flushing, pruritus, urticaria, angioedema - look out especially for swelling of lips, tongue and uvula);
 - Respiratory symptoms and signs (wheezing, stridor, hypoxia, shortness of breath, sensation of throat tightness and hoarse voice);
 - Symptoms and signs of hypotension (fainting, dizziness, confusion, elevated heart rate or respiratory rate (see **Annex A** for normal paediatric vital signs by age).

* In some cases, persons may also present with gastrointestinal symptoms (crampy abdominal pain, nausea, vomiting).

6. The later onset anaphylaxis reactions tend to be less severe. Do note that it may be more difficult to recognise symptoms in persons with communication difficulties. Younger children may also present with non-specific signs such as sudden onset of lethargy, voice change/hoarseness, or agitation.

7. As there are other reactions to vaccines that can mimic an anaphylactic reaction, including vasovagal reactions and anxiety-related symptoms, **careful monitoring of vital signs and physical examinations (e.g. skin, oropharynx, lungs) are essential.**

MEDICATIONS, EQUIPMENT AND SUPPLIES USED IN ANAPHYLAXIS MANAGEMENT

8. **Table 1** lists the medications, equipment and supplies used for assessing and managing anaphylaxis. The patient's weight should be recorded on the patient's form at baseline, to facilitate medication titration in accordance to the patient's body weight. Children <25kg require lower dosing of adrenaline for management of anaphylaxis. Vaccination Centres may consider colour-tagging children at point of triage when their weights are taken, to facilitate matching with the appropriate EpiPen that they should receive based on their weight, should they develop post-vaccination anaphylaxis.

9. Facilities providing COVID-19 vaccines for children aged <12 years should ensure they have age and size appropriate emergency supplies on hand, and should

¹ The Center for Disease Control (CDC), United States, found that 71% of persons who experienced anaphylaxis showed symptoms within 15 minutes post-vaccine administration.

stock syrup formulations where available, in the event that the patient is unable to swallow tablets.

Table 1. Medications, Equipment and Supplies in Anaphylaxis Management

	Mandatory	Optional for non-hospital vaccination sites
Medications	<ol style="list-style-type: none"> 1. Adrenaline vial, pre-filled syringe or autoinjector, 0.15mg and 0.30mg 2. Intravenous (IV) fluids 3. Antihistamines (H1 and H2 antagonists)² 4. IV Hydrocortisone 4-5 mg/kg IV (max 100mg for children) 5. Inhaled bronchodilators e.g. Metered Dose Inhaler (MDI) Salbutamol (10 puffs for body weight 10kg and above) with appropriate delivery devices 	
Equipment and supplies	<ol style="list-style-type: none"> 6. BP cuffs in child size, small adult size and upwards 7. Stethoscope 8. IV drip set 9. IV cannulas (22G / 24G) 10. Paediatric Airway Management Kit <ul style="list-style-type: none"> • Ventilation Bag (450ml) • O₂ Reservoir Bag (2500ml) • Oral Airway² #0 & #1 • Face Mask #2 (Round) 	<ol style="list-style-type: none"> 16. Intubation kit³, including the following core items: <ol style="list-style-type: none"> i. Laryngoscope with blades of different sizes (size 2 and 3 macintosh & upwards⁴) and battery ii. Endotracheal tubes (ETT) of different sizes iii. ETT introducer (stylet) iv. 10cc disposable syringe and other accessories 17. Airway suction device (e.g. portable aspirator). Can be used to assist with intubation

² H1 blockers e.g. IV diphenhydramine 1-2mg/kg (max 50mg/ dose) or IM promethazine 0.25- 0.5mg/kg (max 25mg/dose), If able to tolerate orally, add Cetirizine (2 - 5 years old - 2.5mg stat 6 years and above - 5mg stat). H2 blockers e.g. IV famotidine 0.5-1mg/kg (max 40 mg/dose) or ranitidine 1mg/kg (max 50mg/dose), when refractory to H1 blockade.

² Trace an imaginary line on one side of the face from one corner of child's mouth to the earlobe. Place the device on child's face along this line. The OP airway is the correct length if it reaches from the corner of mouth to the earlobe.

³ Non-hospital sites may opt to provide intubation equipment. Intubation should only be performed by medical personnel who are trained and kept current with the appropriate skills, or possess valid certification e.g. ACLS, FCCS.

⁴ Size 1 macintosh required only if the team plans to intubate children.

	<ul style="list-style-type: none"> • Face Mask #3 11. Pulse oximeter ² 12. Oxygen with delivery devices (e.g. face mask) ² in child size 13. Spacer for children (as needed for point 5 above) 14. Weighing Machine (as patient's weight should be recorded) 15. Glucometer (used during resuscitation efforts for an individual who is unresponsive or has a decreased conscious level, to test for hypoglycaemia)	by clearing secretions or other bodily fluids that may be obstructing the airway.
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10. The mandatory items listed in **Table 1** should be inspected daily before the start of vaccination operations. Staff carrying out the inspection must ensure equipment are in good working order and medication supplies are sufficient and not expired.

EMERGENCY CARE OF A CLINICALLY UNSTABLE PATIENT POST-VACCINATION

11. If anaphylaxis is suspected, emergency care should be administered immediately (see **Table 2** for details).

Table 2: Emergency Care of a Clinically Unstable Paediatric Patient aged 5-11 years old Post-Vaccination

<ul style="list-style-type: none"> • Rapidly assess airway, breathing, circulation, mental activity.
<ul style="list-style-type: none"> • Call 995 for emergency ambulance for conveyance to the nearest Emergency Department (ED)
<ul style="list-style-type: none"> • Place patient in supine position (unless there is an airway obstruction or if the patient is vomiting).
<ul style="list-style-type: none"> • Administer adrenaline early. Adrenaline is the first-line treatment for anaphylactic shock or airway compromise. Because anaphylaxis is acute and life-threatening, there are no contraindications to adrenaline administration. <ul style="list-style-type: none"> ○ Adrenaline 1mg/mL (1:1000 solution) OR ○ 0.15 mg Adrenaline Auto-injectors (EpiPen® Junior)⁵

⁵ The parameters are based on UK-approved weight/ licensing indications: EpiPen® Jr. auto injector 0.15 mg is recommended for children weighing 7.5 – 25 kg. For children weighing more than 25 kg, EpiPen® auto injector 0.3 mg (adult formulation) is recommended. <https://www.medicines.org.uk/emc/product/4290/smpc>

- Firstly, administer adrenaline via IM injection into the mid lateral thigh.
 - 0.01 mg/kg if using adrenaline (1:1000) ampoule OR
 - One injection of 0.15mg auto-injector (EpiPen® Junior) for child weighing between 7.5-25kg
 - One injection of 0.30mg auto-injector (EpiPen® Adult) for child weighing greater than 25kg
 - Maximum dose for prepubertal child is 0.3 mg per dose (refer to dosage chart in **Annex B**).
 - Repeat every 5 to 15 minutes (or more frequently) as needed. The number and timing of adrenaline doses should be recorded and communicated to the SCDF paramedic.
 - Second, if patient requires > 2-3 doses of IM adrenaline, establish IV access (with at least 2 large-bore peripheral cannulas). IV adrenaline should only be administered in the hospital setting⁶.
 - Provide IV crystalloid fluid resuscitation for hypotensive patients using intravenous normal saline (0.9% sodium chloride). Dosage of 20mLs/kg (max 500mLs each fluid bolus) to be administered. Be aggressive with fluid resuscitation, as the patient may be intravascularly volume-depleted from vasodilation and massive capillary leak.
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- Third, to consider the following adjuncts:
 - a) Inhaled bronchodilators e.g. Metered Dose Inhaler (MDI) Salbutamol delivered via spacer with facemask / Aerochamber (10 puffs for body weight 10 kg and above)⁷
 - b) Antihistamines do not treat airway obstruction or hypotension, but they can help relieve hives and itching
 - i) H1 blockers e.g.
 - IV/IM diphenhydramine 1-2mg/kg (max 50mg/dose) OR
 - IM promethazine 0.25-0.5mg/kg (max 25mg/dose).
 - If able to tolerate orally, can add a stat dose of Cetirizine 5mg for child 5 - 11 years old.
 - ii) H2 blockers⁸ e.g.
 - IV famotidine 0.5mg/kg (max 20 mg/dose) or, when refractory to H1 blockade
 - c) Glucocorticoids – IV hydrocortisone 4-5 mg/kg IV (max 100mg/dose for children)

⁶ Medical practitioners are urged to exercise extra caution when using IV adrenaline; a clinical pharmacist should be involved whenever possible. Adrenaline is available in two concentrations, 1:1000 and 1:10,000; errors related to concentration and dilution can result in serious adverse events.

⁷ To repeat same dose 10-15 minutes later if patient is assessed to still be in moderate to severe respiratory distress.

⁸H2 blockers with H1 blockers have additive benefit over H1 blockers alone in anaphylaxis. The use of H2 blockers may be considered when available.

COMPETENCY

12. Non-hospital vaccination sites should be staffed with providers competent in the recognition and management of anaphylaxis as outlined above and possess valid BCLS certification⁹.

PATIENT DISPOSITION

13. Admission. All patients presenting with anaphylaxis should be conveyed to the nearest ED post-haste. Patients who are resistant to initial treatments and require IV adrenaline infusion should be admitted to the ICU. Patients with persistent stridor, phonation changes, and tongue or laryngeal swelling should be admitted to the ICU for continued monitoring. Patients who require advanced airway management in the ED should be managed in the ICU. As anaphylaxis may recur after patients begin to recover, monitoring for at least 4 hours is advised, even after complete resolution of symptoms and signs.

FOLLOW-UP

14. Patients who experience anaphylaxis with the first dose of COVID-19 vaccination should be advised NOT to receive any additional doses.

15. All suspected serious adverse events (SAEs) related to COVID-19 vaccination must be reported to the Health Sciences Authority (HSA) and the Ministry of Health (MOH) in the stipulated format and timelines detailed in MOH Circular No. 04/2021 dated 15 January 2021, 'MONITORING SUSPECTED SERIOUS ADVERSE EVENTS OF COVID-19 VACCINES AND INCIDENT REPORTING AT VACCINATION SITES'.



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⁹ Providers who do not possess valid BCLS certification should obtain it within 1 month of release of this Advisory.

ANNEX A

NORMAL VITAL SIGNS FOR AGE OF PAEDIATRIC PATIENTS

Age	Heart rate (bpm)	Respiratory Rate (bpm)	Minimal Systolic Blood Pressure (SBP) ¹ (mmHg)	Diastolic Blood Pressure (DBP)
5 years	65-140	15-25	80	About 2/3 of the SBP
6 years	65-120	12-20	82	
7 years			84	
8 years			86	
9 years			88	
10 years			90	
11 years				

HR and RR values adapted from Silverman BK, *Practical Information (Textbook of Pediatric Emergency Medicine, 2006)*

¹For children aged 5 to 9 years old, the formula used for the lowest acceptable systolic blood pressure would be $70 + (\text{age} \times 2)$ = starting at systolic pressure of 80mmHg for a 5 year old, 82mmHg for a 6 year old, 84mmHg for a 7 year old, 86mmHg for a 8 year old and 88mmHg for a 9 year old.

ANNEX B

IM ADRENALINE DOSAGE CHART

Weight (Kg)	Adrenaline dose (1mg/ml) amp	Auto-injector Dose to Administer
7.5-10	0.1 mg	0.15 mg (EpiPen® Junior)
11-15	0.15 mg	
16-20	0.2 mg	
21-25	0.25 mg	
26-30	0.3 mg	0.3 mg (EpiPen® Adult)
31-35	0.35 mg	
36-40	0.4 mg	
41-45	0.45 mg	
≥46	0.5 mg	