CLINICAL GUIDELINES ON COVID-19 VACCINATION IN MALAYSIA

Ministry of Health, Malaysia

2nd Edition

FOREWORD FROM THE DIRECTOR GENERAL OF HEALTH MALAYSIA

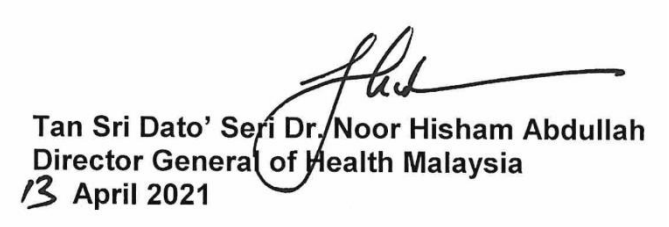
COVID-19 vaccine has brought a new light and hope globally after our challenging struggle with COVID-19 pandemic for more than a year. In order to achieve herd immunity, Malaysia aims to vaccinate at least 70% of the population in less than a year. Immunisation is essential to protect the population from COVID-19 infection, particularly the high risk group of having severe COVID-19 infection such as elderly and those with medical illness. Despite our aim to have extensive coverage of vaccination in a short duration, patient safety and vaccine efficacy need to be considered.

Hence, this Clinical Guidelines On COVID-19 Vaccination In Malaysia is intended to:

1) Provide pertinent information on COVID-19 vaccine.
2) Explain contraindications and precautions of specific vaccine.
3) Guide the healthcare provider in making decision to vaccinate individuals especially those who are at risk of receiving vaccination.
4) Describe various process involves, namely pre-vaccination assessment, vaccination and post-vaccination.
5) Share frequently asked questions related to – vaccine safety, vaccine eligibility and medical conditions.
6) Provide information on specific clinical condition in relation to immunisation.

This guidelines can also be used to assist healthcare providers in conducting "Pre-Vaccination Assessment". I am confident that this revised version of Clinical Guidelines on COVID-19 Vaccination 2nd Edition will be very useful to the healthcare providers and those interested in gaining more knowledge on clinical aspect of COVID-19 immunisation.

I would like to congratulate COVID-19 Immunisation Task Force of Medical Development Division MoH, Disease Control Division of MoH and all the contributors from various medical fraternity and organisations for their commitment and hard work in producing this comprehensive guidelines. "Lindung Diri Lindung Semua". Thank you.



Tan Sri Dato' Seri Dr. Noor Hisham Abdullah
Director General of Health Malaysia
13 April 2021

ACKNOWLEDGEMENT

Advisors

Tan Sri Dato' Seri Dr Noor Hisham bin Abdullah
Director General of Health
Ministry of Health, Malaysia

Dato' Dr Norhizan Ismail
Deputy Director General of Health (Medical)
Ministry of Health, Malaysia

Dato' Dr Chong Chee Kheong
Deputy Director General of Health (Public Health)
Ministry of Health, Malaysia

Datuk Dr Hishamshah bin Mohd Ibrahim
Deputy Director General of Health (Research & Technical Support)
Ministry of Health, Malaysia

Dr Ahmad Razid bin Salleh
Director Medical Development Division
Ministry of Health, Malaysia

Datuk Dr Norhayati Bt Rusli
Director Disease Control Division
Ministry of Health, Malaysia

Dato' Dr Mahiran Bt Mustafa
Senior Consultant Infectious Disease Physician
National Head Infectious Disease Service -
Hospital Raja Perempuan Zainab II, Kelantan

Dato' Dr. Suresh Kumar Chidambaram
Senior Consultant Infectious Disease Physician &
Head of the Medical Department
Hospital Sungai Buloh

Dr Kalaiarasu Peariasamy
Director Institute for Clinical Research
National Institutes for Health, Malaysia

Coordinators & Contributors

Dr Nor'Aishah Bt Abu Bakar	Public Health Physician @ Head of COVID-19 Immunisation Task Force, Medical Development Division, Ministry of Health Deputy Director Medical Care Quality Section, Medical Development Division, MoH
Dr Benedict Sim Lim Heng	Infectious Disease Physician Hospital Sg Buloh

Contributors *(In alphabetical order)*

Dr Asmah Bt Mohd	Consultant Physician and Rheumatologist Hospital Tuanku Ja'afar, Seremban
Datin Dr Asmahan Bt Md Ismail	Consultant Physician and Rheumatologist Hospital Raja Perempuan Zainab II
Dato' Dr Azmillah Bt Rosman	Consultant Physician and Rheumatologist Hospital Selayang
Abby Ang Shoon Yeun	Pharmacist Hospital Sg Buloh
Dr Anilawati Bt Mat Jelani	Infectious Disease Physician Hospital Raja Perempuan Zainab II
Dr Azma Haryaty Bt Ahmad	Emergency Physician Hospital Raja Permaisuri Bainun
Dr Chong Hwee Cheng	Consultant Physician and Rheumatologist Hospital Melaka
Dr Elizabeth Chong Gar Mit	Consultant Geriatrician Hospital Kuala Lumpur
Dr Eznal Izwadi bin Mohd Mahidin	Clinical Oncologist Hospital Kuala Lumpur
Dr Flora Chong Li Tze	Clinical Oncologist Hospital Wanita & Kanak-Kanak Likas, Sabah
Dr Fong Chin Heng	Clinical Oncologist Hospital Pulau Pinang
Dr Gan Chye Lee	Acute Internal Medicine Physician Hospital Melaka
Prof. Dr. Gan Gin Gin	Professor of Internal Medicine and Clinical Haematology Department of Medicine University Malaya Medical Center
Dr Giri Shan Rajahram	Infectious Disease Physician Hospital Queen Elizabeth II

Dr Goh Ai Sim	Consultant Haematologist National Head of Haematology Service Hospital Pulau Pinang
Dato Dr Gun Suk Chyn	Senior Consultant Physician and Rheumatologist Head Department of Internal Medicine Hospital Tuanku Ja'afar
Dr Habibah Bt Mohd Yusoof	Consultant Physician and Rheumatologist Head Department of Internal Medicine Hospital Selayang
Dr Harris Njoo Suharjono	Senior Consultant and State Advisor Obstetrics & Gynaecology Services Hospital Umum Sarawak
Dr Hazlyna Bt Baharuddin	Consultant Physician and Rheumatologist UiTM Medical Specialist Centre
Dr Ina Shaliny a/p Duraisamy	Clinical Oncologist Hospital Sultan Ismail, Johor Bahru
Dr Jameela Bt Sathar	Consultant Haematologist & President of Malaysian Society Haematology Hospital Ampang
Dr Lim Chun Sen	Clinical Oncologist Hospital Sultan Ismail, Johor Bahru
Dr Liza Md Isa	Consultant Physician and Rheumatologist Head of Department Internal Medicine Hospital Putrajaya
Loh Siao Ching	Pharmacist Hospital Sungai Buloh
Dr Low Lee Lee	Infectious Disease Physician Hospital Sultanah Bahiyah
Dr Mohammed Faizal bin Bakhtiar	Allergist (Physician Scientist with expertise in Drug Hypersensitivities) Institute of Medical Research
Dr Mollyza Bt Md Zain	Senior Consultant Physician and Rheumatologist National Head of Rheumatology Services Hospital Selayang
Dr Muniswaran Ganeshan	Maternal Fetal Medicine Specialist Women & Children's Hospital Kuala Lumpur
Dr Nahjatul Kursyiah Bt Abd. Ghafar	Clinical Oncologist Hospital Wanita & Kanak-Kanak Likas, Sabah
Dr Ng Soo Chin	Consultant Haematologist Subang Jaya Medical Center
Dr. Nor Farah Bt Bakhtiar	Senior Principal Assistant Director Medical Care Quality Section Medical Development Division

Dr. Noryati Bt Abu Amin	Transfusion Medicine Specialist Director of National Blood Centre
Dr Nor Shuhaila Bt Shahril	Consultant Physician and Rheumatologist Hospital Putrajaya
Dr Nor Zaila Bt Zaidan	Infectious Disease Physician Hospital Melaka
Dr Norzaihan Bt Hassan	Family Medicine Specialist Klinik Kesihatan Bandar Kota Bharu
Dato' Dr Ong Loke Meng	Consultant Physician & Nephrologist National Head of Nephrology Service Head Department of Internal Medicine Hospital Pulau Pinang
Dr Richard Lim Boon Leong	Palliative Medicine Physician Hospital Selayang
Dr Ravichandran Jeganathan	Senior Consultant Obstetrician & Gynaecologist National Head of O&G Service Head Department of Obstetrician & Gynaecologist Hospital Sultanah Aminah, Johor Bahru
Dr. Rizah Mazzuin Bt Razali	Consultant Geriatrician Hospital Kuala Lumpur
Dr Ros Suzanna Bt Ahmad Bustamam	Senior Consultant Clinical Oncologist National Head of Radiotherapy & Oncology Service Head Department of Radiotherapy & Oncology Hospital Kuala Lumpur.
Professor Sargunan Sockalingam	Professor of Internal Medicine and Rheumatology Department of Medicine University Malaya Medical Center
Prof. Dr. S Fadilah Bt Abdul Wahid	Professor of Clinical Haematology and Transplant Physician Head of Pusat Terapi Sel UKM Medical Center
Assoc. Prof. Dr. Sharifah Faridah Bt Syed Omar	Infectious Disease Physician UM Medical Center
Dr Shereen Ch'ng Suyin	Consultant Physician and Rheumatologist Hospital Selayang
Datin Dr Shaemini Sivasampu	Public Health Physician Head of Centre for Clinical Outcome Research Institute of Clinical Research
Dr Soo Hoo Hwoei Fen	Clinical Oncologist Hospital Pulau Pinang
Dr Soo Kok Foong	Emergency physician Hospital Sungai Buloh

Datuk Dr Soon Ruey	Senior Consultant Obstetrics & Gynaecology State Advisor Obstetrics & Gynaecology Services Hospital Wanita & Kanak-kanak Likas, Sabah
Dr Suhana Bt Yusak	Clinical Oncologist Institut Kanser Negara
Dr Suraya Bt Amir Husin	Senior Principal Assistant Director Medical Care Quality Section Medical Development Division, MoH
Dr Syadwa Bt Abdul Shukor	Clinical Oncologist Hospital Umum Sarawak
Dr Tan Boon Seang	Clinical Oncologist Hospital Pulau Pinang
Dr Tang Min Moon	Dermatologist. Hospital Kuala Lumpur
Dr Teh Cheng Lay	Consultant Physician and Rheumatologist Hospital Umum Sarawak
Dato' Dr. Tunku Muzafar Shah bin Tunku Jaafar	Consultant Geriatrician Hospital Selayang
Dr Vijaya Sangkar Jaganathan	Consultant Haematologist Pantai Medical Center
Dr Voon Hian Yan	Maternal Fetal Medicine Specialist Hospital Umum Sarawak
Dr Wan Nor Aida Bt Wan Mohd Shukri	Emergency Physician Hospital Kuala Lumpur
Dr Wong Yoke Fui	Clinical Oncologist Institut Kanser Negara
Dr Yau Weng Keong	Consultant Geriatrician National Head of Geriatric Service Hospital Kuala Lumput
Dr Yeat Choi Ling	Consultant Palliative Medicine Physician Hospital Raja Permaisuri Bainun, Ipoh

Table of Contents

List of Abbreviations

ABC	:	airway, breathing, circulation
ACEI	:	angiotensin converting enzyme inhibitor
ADEM	:	acute disseminated encephalomyelitis
ADR	:	adverse drug reaction
AEFI	:	adverse event following immunization
ANC	:	absolute neutrophil count
anti-TNF	:	antitumor necrosis factor therapy
ART	:	antiretroviral therapy
BMI	:	body mass index
BPD	:	bronchopulmonary dysplasia
CN VII palsy	:	cranial nerve VII palsy
COPD	:	chronic obstructive pulmonary disease
COVID-19	:	coronovirus disease 2019
CSU/A	:	chronic spontaneous urticaria/angioedema
DM	:	diabetes mellitus
DOAC	:	Direct Oral Anticoagulant
DRESS	:	drug reaction with eosinophilia and systemic symptoms
EES	:	erythromycin ethyl succinate
F	:	female
GBFDE	:	Generalized Bullous Fixed Drug Eruption
GBS	:	Guillain Barré Syndrome
HAART	:	Highly Active Antiretroviral Therapy
HIV	:	Human Immunodeficiency Virus
ICU	:	intensive care unit
IgE	:	Immunoglobulin E
IHD	:	ischaemic heart disease
IM	:	intramuscular
INR	:	International Normalised Ratio
IRIS	:	Immune Reconstitution Syndrome
ISRR	:	Immunization Stress Related Response
IV	:	intravenous
LMA	:	laryngeal mask airway
LMWH	:	Low Molecular Weight Heparin
M	:	male
MDI	:	metered-dose inhaler
MMF	:	mycophenolate mofetil
MPE	:	maculopapular eruption
NPRA	:	national pharmaceutical regulatory agency
NSAIDs	:	non-steroidal anti-inflammatory drugs
Ois	:	opportunistic infections
PEF	:	peak expiratory flow
PEG	:	polyethylene glycol
PhIS	:	pharmacy information system
PLHIV	:	people living with HIV
PVA	:	pre-vaccination assessment

RA	:	Rheumatoid Arthritis
SBP	:	systolic blood pressure
SCARs	:	severe cutaneous adverse drug reactions
SJS	:	Stevens-Johnson Syndrome
SLE	:	Systemic Lupus Erythematosus
SOB	:	shortness of breath
TEN	:	Toxic Epidermal Necrolysis
TIA	:	Transient Ischaemic Attack

1. COVID-19 Vaccine

1.1. Type of vaccines available in Malaysia

Malaysia has secured 66.7 million doses of COVID-19 vaccine through the COVAX Facility and direct purchase form five vaccine manufacturers. Malaysia received the supply of vaccines in stages and subject to approval from the Drug Control Authority (DCA) and the National Pharmaceutical Regulatory Agency (NPRA).

Supply of COVID-19 vaccines that have been acquired by Malaysia

Vaccine	Pfizer	AstraZeneca (Including COVAX Facility purchases)	sinovac	康希诺生物 CanSinoBIO	Sputnik V
Type of Vaccines	mRNA	Viral vector	Inactivated virus	Viral vector	Viral vector
Manufacturer's Country	The United States of America	United Kingdom	China	China	Russia
Number of doses	2	2	2	1	2
Efficacy	95%	62% - 90%	50.4% - 91.25%	65.7%	91.6%
Storage Temperature	-75°C	2-8°C	2-8°C	2-8°C	-20°C
Number of doses (Million)	32	12.8	12	3.5	6.4
% of Populations	50%	20%	18.75%	10.9%	10%
Countries that have used the vaccine	United States of America, Singapore, UK, Bahrain, Canada, Mexico, Switzerland, the European Union	UK, South Africa, Ukraine, Brazil, the European Union, Canada, India	China, Indonesia, Turkey, Chile, Hong Kong, Brazil, Cambodia	China; Mexico; Pakistan	Russia, Argentina, Brazil, South Korea, Belarus

* The vaccine supply is subject to periodic negotiations
* This information is valid as of 16 February 2021 and will be updated from time to time

Source: JKJAV

Overall number of doses: **66.7 million** covering **109.65%** of those in the country

Efficacy of COVID-19 vaccine and why is it different?

The efficacy of a vaccine, or how well the vaccine works, is seen through its ability to protect individuals from the symptoms of COVID-19 through vaccination. The efficacy level varies according to the way clinical studies are conducted, the type of vaccine, the risk of disease in volunteers and various other factors. Although the efficacy level varies, WHO has prescribed that the minimum level of efficacy for the COVID-19 vaccine is 50%. All vaccines approved by NPRA are safe and efficacious for use in Malaysia.

Source: Jawatankuasa Khas Jaminan Akses Vaksin COVID-19 (JKJAV)

What are the types of vaccines?

Types of vaccines	mRNA	Viral vector	Inactivated virus
Primary content and how it reacts 	mRNA sequence which enters the individual cell to produce the specific virus protein	Contains modified (vector) virus to transport the antigen genetic code. The human cell will produce the targeted protein	Virus that have been killed using high heat, chemical or radiation
Function 	Uses the mRNA molecule to stimulate the immunity in order to recognise the targeted virus protein	A safe viral vector is used to deliver the genetic material of the targeted virus and stimulating the human immune response	Virus that has been killed and used to stimulate the human immune response
Advantages 	• Simple and quick to produce • Does not require living component and synthetically produced. • Triggers an adaptive immune response	• Proven technology • Triggers an adaptive reaction for a more effective immune response	• Proven technology • Suitable for those who have a weak immune system • Easy to produce
Challenges 	• Some mRNA vaccines require extremely cold storage conditions • Used as a vaccine for the first time in medical history	• Complex manufacturing process • Important to ensure the virus vector is safe to be used	• High manufacturing cost
Example	None	Ebola, Vaccines for livestock	Polio, Japanese Encephalitis & Rabies
Vaccine candidate	• Moderna • Pfizer/BioNTech	• AstraZeneca • CanSino Biologics • Johnson & Johnson • Sputnik V	• Sinovac

Source: Jawatankuasa Khas Jaminan Akses Vaksin COVID-19 (JKJAV)

1.1.1. Pfizer-BioNTech (*Comirnaty*®)

	Description
Type of vaccine	mRNA
Constituents	• Polyethyleneglycol/macrogol(PEG)aspartofALC-0159. • ALC-0315=(4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), • ALC-0159=2-[(polyethyleneglycol)-2000]-N,N-ditetradecylacetamide • 1,2-Distearoyl-sn-glycero-3-phosphocholine • Cholesterol • Potassiumchloride • Potassiumdihydrogenphosphate • Sodiumchloride • Disodiumhydrogenphosphatedihydrate • Sucrose • Waterforinjection This vaccine contains potassium, less than 1mmol (39mg) per dose, i.e., essentially 'potassium free'. This vaccine contains less than 1mmol sodium (23mg) per dose, i.e., essentially 'sodium free'.
Presentation	The vaccine is a white to off-white frozen dispersion. It is contained in a multi-dose clear glass vial.
Number of doses in each vial	6 doses If more than six 0.3ml doses can be safely and accurately withdrawn from a diluted vial, they can be used as valid doses
Dilution	Yes, with 0.9% Sodium Chloride (supplied separately) *For detailed instructions of use, please refer to package insert*
Latex	No,the vial has a rubber (bromobutyl) stopper, aluminium seal and a flip-off plastic cap. *Bromobutyl is a synthetic rubber*
Preservatives	No
Dosage	0.3ml
Number of doses required	2 doses per person
Interval between doses	The recommended interval between doses is 21days and maximum 41 days
Storage	• **Unopened** vial: Store in a freezer at -90°C to -60°C. • Once **removed** from the freezer, the unopened vaccine can be stored for up to 5 days at 2°C to 8°C, and up to 2 hours at temperatures up to 30°C, prior to use. • Once **diluted**, vaccine is stable for 6 hours at 2°C to 30°C

<table>
<tr><td>Contraindications</td><td colspan="2">Person who had history of an allergic reaction to a previous dose of the Pfizer-BioNTech COVID-19 Vaccine or any of its components
Person with a history of anaphylaxis which include severe angioedema, bronchospasm and/or hypotension, to other drugs, vaccines, food, insect stings, or unknown trigger (idiopathic)
Acute febrile illness</td></tr>
<tr><td rowspan="4">Possible events (by frequency)</td><td>Very Common (≥1/10)</td><td>Local:
Injection site swelling and erythema

General:
arthralgia, fatigue, fever, headache, myalgia</td></tr>
<tr><td>Common (≥ 1/100 to <1/10)</td><td>Local: injection site pain, erythema

General: nausea</td></tr>
<tr><td>Uncommon
(≥ 1/1,000 to <1/100)</td><td>Local: injection site pruritus

General: insomnia, lymphadenopathy, malaise, extremity pain</td></tr>
<tr><td>Rare
(≥ 1/10,000 to <1/1,000)</td><td>Local: -

General: acute peripheral facial paralysis / Bell’s Palsy</td></tr>
</table>

1.1.2. Sinovac *(CoronaVac®)*

	Description	
Type of vaccine	Inactivated (Vero Cell)	
Constituents	• Aluminium hydroxide • Disodium hydrogen phosphate • Monosodium dihydrogen phosphate • Sodium chloride • Sodium hydroxide • Water for injection	
Presentation	Milky-white (opalescent) suspension. Stratified precipitate may form (dispersed by shaking)	
Number of doses in each vial	1 dose	
Dilution	Not applicable	
Latex	No	
Preservatives	No	
Dosage	0.5ml	
Number of doses required	2 doses per person	
Interval between doses	The recommended interval between doses is 21 - 28 days	
Storage	Store between +2ºC to +8ºC and protect from light. Do not freeze. Use immediately.	
***Contraindications**	• Person who are hypersensitive or known to be allergic to any components (active ingredients or excipients or any material used in process) of the vaccine or similar vaccines • Person with a previous history of severe allergic reactions to the vaccine (e.g. acute anaphylaxis, angioedema, dyspnea) • Person with severe neurological conditions (e.g. transverse myelitis, Guillain-Barre syndrome, demyelinating diseases) • Individuals with uncontrolled severe chronic diseases • Pregnant and lactating women	
***Precautions**	• Person with acute diseases, acute exacerbation of chronic diseases, severe chronic diseases, allergies and fever	
Possi ble ev ents (by frequency)	Very Common (≥1/10)	Local: injection site pain General: fatigue, headache
	Common (≥ 1/100 to <1/10)	Local: injection site erythema, injection site urticaria, injection site swelling, injection site

		itchiness, redness, hardening General: Muscle pain, nausea, diarrhea, joint pain, cough, shivering, itchiness, loss of appetite, runny nose, sore throat, stuffy nose, stomachache
	Uncommon (≥ 1/1,000 to <1/100)	Local: injection site burning sensation General: Vomiting, hypersensitivity, abnormal skin and mucous membrane condition, fever. Trembling, flushing, swelling, dizziness, drowsiness
	Rare (≥ 1/10,000 to <1/1,000)	Local: - General: muscle cramp, swelling of eyelids, nose bleeds, bloating, constipation, diminished sense of smell, pink eye, hot flashes, hiccups, eye redness

**Source: Training module on COVID-19 Vaccine CoronaVac by Corporate Communications Department Pharmaniaga*

2. Vaccine Priority Groups

Priority groups - Underlying medical conditions that increase the risk of severe illness from COVID-19 *(adapted from Green Book, Public Health England, Chapter 14a, Covid-19)* **Conditions listed here are in no order of priority**		
1	**Immunocompromised due to disease or treatment**	Bone marrow or stem cell transplant recipients
		Solid organ transplant recipients
		Haematological malignancies
		People with cancers undergoing active chemotherapy, immunotherapy, radiotherapy or other targeted therapy that result in immunosuppression
		Genetic disorders affecting the immune system
		Autoimmune diseases like SLE, RA and psoriasis who require long term immunosuppressive treatment
		Those who are receiving systemic steroids for > 1 month at a daily dose equivalent to prednisolone 20mg or more (for adults)
		Individuals who are receiving immunosuppressive or immunomodulating biological therapy such as anti-TNF, rituximab
2	**HIV infection**	Those with CD4 count $\leq$350cells/mm^2 or with additional underlying conditions that increase the risk of severe illness from COVID-19 are to be considered as priority groups for vaccination
3	**Asplenia or dysfunction of the spleen**	Those who have undergone splenectomy and those with conditions that may lead to splenic dysfunction, such as thalassemia major and coeliac syndrome
4	**Chronic heart disease and vascular disease**	Congenital heart disease, hypertension with cardiac complications, chronic heart failure, ischaemic heart disease, individuals with atrial fibrillation, peripheral vascular disease or a history of venous thromboembolism
5	**Chronic kidney disease**	Chronic kidney disease at stage 3, 4 or 5, chronic kidney failure, nephrotic syndrome, kidney transplantation

6	**Chronic liver disease**	Cirrhosis, biliary atresia
7	**Chronic neurological disease**	Stroke, TIA Individuals with cerebral palsy, severe or profound learning disabilities, Down's Syndrome, multiple sclerosis, epilepsy, dementia, Parkinson's disease, motor neurone disease and related or similar conditions; or hereditary and degenerative disease of the nervous system or muscles; or severe neurological disability. Conditions in which respiratory function may be compromised due to neurological disease
8	**Chronic respiratory disease**	Individuals with a severe lung condition, including those with asthma that requires continuous or repeated use of systemic steroids or with previous exacerbations requiring hospital admission, and COPD, including chronic bronchitis and emphysema; bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and BPD
9	**Diabetes mellitus**	Type 1 or 2 DM
10	**Obesity**	Adults with a BMI ≥ 30 kg/m²
11	**Severe mental illness**	Individuals with schizophrenia or bipolar disorder, or any mental illness that causes severe functional impairment

3. Pre-Vaccination

3.1. Pre-vaccination assessment is an assessment conducted by the treating doctor (i.e medical officer or clinical specialist) to determine the suitability of individual to receive vaccine, timing to receive vaccine and suitable facilitiy for the individual to receive vaccination (i.e hospital or other vaccination centre).

Not all patients with co-morbidities require PVA. Furthermore, not all patients in hospitals require PVA.

Generally, the patients that require PVA can be divided into **3 groups**. Most patients that require PVA are under hospital follow up:

1. **Immunocompromised patients** - Patients with diseases or on medications that can compromise or suppress their immune system. These patients include those with cancers, those who had organ transplants, those with chronic HIV infection or those on immune-suppressing medications. Not all of these patients will require to go to their respective hospitals for vaccination. Further details are in the following table.

2. **Patients with bleeding tendency - Patient** or on medications that can cause bleeding or interfere with the body's ability to stop bleeding. These include patients with hemophilia, those being followed up due to very low platelet levels and are on high doses of anticoagulants.

3. **Patients with history of severe allergy** (eg: anaphylaxis) - to vaccine or multiple medications or unknown causes.

Following PVA, the medical officer/clinical specialist will decide whether:

1. Patient can receive vaccination at any time
2. Patient can receive vaccination but at later time (deferred)
3. Patient cannot receive vaccination at any time (absolute contraindication)

*For further details on **"Conditions and Optimal Timing For Vaccination" - Refer Table 3.1**

*For further details related to **allergy- Refer Tables & Flow Charts 3.2 to 3.8**

If the patient can receive vaccination, the doctor needs to decide whether he/she can receive vaccination in the hospital or at any Vaccination Centre in the community. The doctor need to document result of PVA on the "Slip "Penilaian Kesesuaian Menerima Vaksin COVID-19 Bagi Pesakit Dengan Masalah Kesihatan Tertentu" *(Refer example below)*.

PVA is conducted by assessing the patient current health condition, reviewing relevant result of investigation, revieweing past medical history, medication history and allergy history. Hence, it is best conducted by the doctor who regularly treat the patient. This can be done in hospital or clinic.

KEMENTERIAN KESIHATAN MALAYSIA

Slip "Penilaian Kesesuaian Menerima Vaksin COVID-19 Bagi Pesakit Dengan Masalah Kesihatan Tertentu"

Hospital/Institusi/ Klinik: _____

Nama Pesakit: _____

No. Kad Pengenalan: _____

No. Telefon: _____

Wad / Klinik Pakar: _____

1. Penilaian telah dilakukan kepada pesakit seperti butiran di atas dan mendapati pesakit *(sila tandakan √ pada ruang yang berkenaan)*:

	Boleh menerima vaksin COVID-19 pada masa ini.
	Pemberian vaksin COVID-19 perlu ditangguhkan. Namun boleh menerima vaksin COVID-19 pada tarikh akan datang iaitu selepas (masukkan tarikh) _____
	Tidak boleh menerima vaksin COVID-19 (*absolute contraindication*)

2. Bagi pesakit yang boleh menerima vaksin COVID-19, pesakit ini disarankan untuk menerima vaksin di *(sila tandakan √ pada ruang yang berkenaan)*:

	Hospital / Institusi _____
	Fasiliti kesihatan/ pusat imunisasi yang berhampiran dengan tempat tinggal

3. Langkah tambahan (cth: Pesakit perlu pemantauan lebih panjang setelah menerima imunisasi)

   _____

4. Hasil penilaian ini sah sehingga; _____

Pakar / Pegawai Perubatan yang menjalankan penilaian:

Tandatangan:

Nama dan Cop:

Tarikh penilaian:

Sila bawa bersama Slip ini ke Pusat Pemberian Vaksin untuk ditunjukkan kepada pegawai bertugas di Stesen 3.

3.2. Condition and optimal timing for vaccination:

Conditions	Optimal timing for vaccination	Comments
Acute illnesses that require admission to hospital.	Vaccination can be given once the **person recovers** from the acute illness and can perform his/her usual daily baseline activities is deemed clinically stable by the treating clinician. *Patients with acute neurological conditions (e.g. transverse myelitis, GBS, demyelinating diseases, others;) can receive the vaccine after stabilization and deemed suitable by the treating clinician.*	
Persons who previously had SARS-CoV-2 infection and belong to the priority group for vaccination	Vaccination should be deferred until the person has recovered from the acute illness (if symptomatic) and they have met criteria to discontinue isolation. However, current evidence suggests that natural infection with SARS-CoV2 results in good protection against reinfection for at least 3 months. Hence, to prioritise those with no immunity, it is recommended to defer the vaccination by 3 months from onset of covid-19 symptoms or date of covid-19 results (in asymptomatics).	
Persons being quarantined at quarantine centre or under HSO for being a **close contact**.	Vaccination must be given once the persons have completed 10 days of quarantine/self-isolation and no new symptoms to suspect active COVID-19 infection.	
Recent immunisation with any other vaccines.	Vaccination to be deferred or postponed for at least after **2 weeks**.	
Terminally ill with life expectancy less than 1 month	Not for vaccination.	

<table>
<tr><td>Very frail elderly</td><td>Those with Clinical Frailty Score 8:
Vaccination should still be encouraged if patient is not actively dying and there are no acute medical issues.
*Refer to Table 1 in Appendix 1 for further details</td><td></td></tr>
<tr><td>Obstetric & Gynaecology</td><td>Refer to Appendix 2</td><td></td></tr>
<tr><td>Solid organ cancers on active chemotherapy, radiotherapy, or immunotherapy (excluding hormonal treatment) in remission or a cancer survivor</td><td>Discuss with patient’s health care provider regarding the optimal spacing for vaccination and the cancer therapy.
(Refer to Appendix 3)</td><td rowspan="5">COVID-19 vaccine is not a live vaccine, and hence it is NOT contraindicated for the immunocompromised.

Immunocompromised hosts are at high risk of severe COVID-19 infection.

However, there is insufficient data on the efficacy of vaccine.

In order to balance between optimising efficacy of the vaccine and providing timely protection against COVID-19 infection, optimal timing of vaccination has to be decided after discussion with the health care provider of the patient.</td></tr>
<tr><td>Autoimmune diseases like systemic lupus erythematosus and rheumatoid arthritis, and psoriasis who require long term immunosuppressive treatment</td><td>Discuss with patient’s health care provider regarding the optimal spacing for vaccination and the immunosuppressive treatment.
(Refer Appendix 5)</td></tr>
<tr><td>Patients receiving systemic steroids with a dose ≥20mg of prednisone or equivalent for ≥14days</td><td rowspan="2">Discuss with patient’s health care provider regarding the optimal spacing for vaccination and the immunomodulating agents.
(Refer Appendix 5)</td></tr>
<tr><td>Individuals who are receiving immunosuppressive or immunomodulating
biological therapy such as anti-TNF, rituximab</td></tr>
<tr><td>Transplant recipients:
Solid organ
Bone marrow / stem cell</td><td>At least 3 months after transplantation.</td></tr>
</table>

Hematological malignancies	In those receiving intensive cytotoxic chemotherapy, it is advised to delay until ANC recovery. However, for those on long term therapy or those who are expected to have limited or no recovery of marrow failure, vaccination is recommended as soon as vaccine is available. (*Refer Appendix 4*)	*Please refer to COVID-19 Vaccination For Patients With Haematological Disorders (Appendix 4) and Vaccination for Patients with Rheumatic and Musculoskeletal diseases (RMD) and Autoimmune and Inflammatory Rheumatic Diseases (AIIRD) (Appendix 5) and COVID-19 Vaccination for Cancer Patients with Solid Tumours (Appendix 3) for detailed information.*
Haemophilia	There are no specific contraindications to vaccination related to complications of haemophilia and other bleeding disorders or their therapies. For patients with severe/moderate haemophilia A or B, the vaccine injection should be given after a prophylactic dose of Factor VIII (FVIII) or Factor IX (FIX). For patients with a basal FVIII or FIX level above 10%, no haemostatic precautions are required.	The bleeding risk can be reduced by application of firm pressure at the injection site for **5 to 10 minutes** afterwards. Use a **25- or 27-gauge needle** to reduce the pressure gradient as it causes less trauma to the tissue. The vaccine should be injected slowly (≥5 seconds) to reduce the risk of tissue damage. Stabilisation of the limb will reduce the risk of a haematoma.The site should not be rubbed or massaged.
Patients on anticoagulant (e.g. warfarin) and antiplatelet agents	Patients with stable anticoagulation with INR < 4 on their last scheduled visit can receive IM vaccination without stopping the drug. Patients on concomitant warfarin and anti-platelet therapy, should be managed on an individual basis in consultation with their primary physician. On the day of vaccination, warfarin should be taken **AFTER** the vaccine injection.	
Patients with known thrombocytopenia (platelet count <50,000)	Should defer the vaccination till their platelet counts recover, if possible.	

	For those with chronically low platelet counts, vaccination should be performed in consultation with their primary haematologist.	Inspect the injected limb after several minutes and 4-6 hours later and to report any concerns to the vaccination centre. *Please refer COVID-19 Vaccination For Patients With Haematological Disorders for detailed information (Appendix 4)*
Patients taking DOAC or LMWH or fondaparinux	Can delay the dose on the day of vaccination until after the intramuscular injection but do not need to miss any doses.	
Patients with thrombocytopenia	Patients with platelet counts ≥ 50,000 can proceed with vaccination without additional haemostatic support.	
Patients with rare bleeding disorder (including platelet function disorders)	Should be vaccinated in consultation with their primary haematologists.	
HIV not on ARTs **and** CD4 count ≤350cells/mm^2	Optimal timing of vaccination has to be decided after discussion with the health care provider of the patient.	
History of anaphylaxis to vaccines or medications	*Please refer to Section 3.2, 3.3*	

3.3. Guidance on the Indications and contraindications to COVID-19 vaccinations for selected hypersensitive population.

Types of hypersensitivity	Vaccination decision
Drug Hypersensitivities	
• Persons with a history of immediate type of penicillin allergy • Persons with a history of immediate type of antibiotics allergy other than penicillin	**Can receive** COVID-19 vaccines
Persons with a history of anaphylaxis to penicillin or other types of antibiotics	**Can receive** COVID-19 vaccines However, should be observed longer in a controlled environment.
Persons with NSAIDs hypersensitivity (urticaria/angioedema not involving the larynx/bronchospasm)	**Can receive** COVID-19 vaccines Many will have multiple chemically unrelated NSAIDs cross-intolerant reactions. About 15-20% of these will have reactions involving two systems (skin/mucosa and bronchospasm) termed **'blended'** reactions[1]**,** with resolution from antihistamines and corticosteroid institution.
Persons with NSAIDs-induced fixed drug eruptions or SCARs	**Can receive** COVID-19 vaccines
Persons with NSAIDs-induced **anaphylaxis**	**Can receive** COVID-19 vaccines However, should be observed longer in a controlled environment. NSAIDs-induced anaphylaxis may be due to an IgE-mediated reaction (skin test positive) and **does not** cross react with other chemically unrelated NSAIDs group. *NSAIDs can be a co-factor for food-induced IgE-mediated anaphylaxis, e.g., wheat component (omega-5-gliadin) sensitization should be ruled out
• Biologics and/or chemotherapy hypersensitivity • PEGylated biologics/chemotherapy hypersensitivity	**Do not give vaccine containing PEG or polysorbate** May consider other type of COVID-19 vaccine **<u>without</u> PEG or polysorbate.** May consider referring for investigations of polysorbate 80 and PEG hypersensitivity.

History of unexplained recurrent anaphylaxis to unidentified injectable medications (e.g., multiple groups of chemically unrelated drugs or idiopathic anaphylaxis)	**Do not give vaccine containing PEG or polysorbate** May consider other type of COVID-19 vaccine **<u>without</u> PEG or polysorbate.** *These individuals should be investigated for the underlying cause *Consider referral for PEG and polysorbate 80 testing If skin test positive for PEG or polysorbate 80, **contraindicated** to receive **vaccine containing PEG or polysorbate**. Consider other types of COVID-19 vaccines **<u>without</u> PEG or polysorbate**. However, should be observed longer in a controlled environment.
Mild allergic reaction (non-generalized urticaria) to an unidentified medication	**Can receive** COVID-19 vaccines
Vaccine hypersensitivity	
• Persons with history of anaphylaxis to other non-COVID-19 vaccines	**Do not give vaccine containing PEG or polysorbate** May consider other type of COVID-19 vaccine **<u>without</u> PEG or polysorbate.** May consider referring for investigations of polysorbate 80 and PEG hypersensitivity. *Many non-COVID-19 vaccines contain polysorbate 20 or polysorbate 80
Contrast media hypersensitivity	
Persons with history of contrast media hypersensitivity reaction (**not anaphylaxis**)	**Can receive** COVID-19 vaccine
Persons with history of contrast media **anaphylaxis**	**Can receive** COVID-19 vaccine However, should be observed longer in a controlled environment
Persons with history gadolinium-based contrast media hypersensitivity reaction during MRI	**Contraindicated to receive the Moderna mRNA vaccine**. **Can receive** the *Cominarty*® (Pfizer) or *ChAdOx1-S*® (Oxford, AstraZeneca) or *Sputnik V*® vaccines **Gadolinium-based contrast media hypersensitivity reaction has been reported to be due to the excipient **TROMETAMOL[2]**, a component contained in the Moderna vaccine.*

Contact Allergy	
Persons with history of reactions or contact allergy with patch test positive to nickel, perfumes, and cosmetics	**Can receive** COVID-19 vaccines
Identified food, environment and latex	
Persons with history of allergic reaction to specific identified foodstuff (e.g., shellfish, wheat, peanut, soy, cow's milk, egg, gelatin), environment (e.g. house dust mites, pollens), latex	**Can receive** COVID-19 vaccines The current COVID-19 vaccines do not contain derivatives from shellfish, wheat, peanut, soy, cow's milk, egg, gelatin. The vial stopper of all COVID-19 vaccines is made from synthetic rubber. Thus, there is no issue concerning latex contamination.
Persons with convincing history of anaphylaxis to specific identified foodstuff (e.g., shellfish, wheat, peanut, soy, cow's milk, egg), environment, (e.g., house dust mites, pollens), latex	**Can receive** COVID-19 vaccines However, should be observed longer in a controlled environment as a precaution. **Vaccines may be manufactured in a manufacturing facility where trace amounts of e.g., shellfish, wheat, peanut, soy, cow's milk, egg may be present*
Venom allergy	
Persons with history of venom anaphylaxis (e.g., insect or bee or wasp stings)	**Can receive** COVID-19 vaccine However, should be observed longer in a controlled environment. **Persons with history of venom anaphylaxis should be investigated for mast cell disorder* **Persons receiving venom immunotherapy (or other allergen immunotherapy) should be timed accordingly (~ 48 hours interval) with the COVID-19 vaccine to avoid confusion (should an allergic reaction occur)*
Urticaria/Angioedema	
Persons with history of CSU/A	**Can receive** COVID-19 vaccine However, these individuals should take their normally prescribed daily antihistamine(s) as usual, even on the day of vaccination. These individuals should be observed longer in a controlled environment. **Persons with CSU/A may experience mild (non-generalized) urticaria after vaccination. Urticaria is often triggered by stressors (for these individuals).*

	**Persons with CSU/A on immunosuppressive therapy such as cyclosporin should be able to receive the currently available COVID-19 vaccines as none are live attenuated vaccines.*
Persons with angiotensin ACEi-induced angioedema	**Can receive** COVID-19 vaccines However, should be observed longer in a controlled environment.
Persons with hereditary angioedema type I, II and III or acquired angioedema	**Can receive** COVID-19 vaccines[3]. However, should be observed longer in a controlled environment.
Atopy	
Persons with underlying asthma on medication	**Can receive** COVID-19 vaccines **Underlying asthma is **NOT a contraindication** to receive the vaccine* **Poorly controlled asthma should be assessed by the treating physician for suitability and timing of the COVID-19 vaccination* **Asthmatic persons on **high dose oral prednisolone (>20 mg/day) should defer vaccination** until oral prednisolone can be stopped* **Atopic or eosinophilic asthmatic persons on omalizumab, benralizumab, dupilumab, mepolizumab, reslizumab **can receive** the mRNA or viral-vector COVID-19 vaccines[4]* For inactivated virus vaccines, vaccinations should be placed approximately midway through the treatment interval (i.e., between two applications of the respective biologics)[4].
Persons with allergic rhinitis	**Can receive** COVID-19 vaccines
Persons with atopic dermatitis	**Can receive** COVID-19 vaccines
Mast cell disorder	
Persons with systemic mastocytosis or mast cell activation disorder	**Can receive** COVID-19 vaccines However, should be observed longer under medical surveillance. **Persons with mast cell disorder with raised mast cell tryptase requiring treatment should continue their antihistamines, mast cell stabilizers, imatinib during vaccination[5].*

3.4. Scheme for contraindications and precautions when considering vaccination for COVID-19

	Proceed with Vaccination	Special Precautions	Vaccination contraindicated
Patient Characteristics	1. Prior history of allergic reaction (of any severity including anaphylaxis) to an identified food or venom or pet or environmental allergens/ medications/ latex 2. Bronchial asthma 3. Atopy (eczema, allergic rhinitis, allergic conjunctivitis) 4. Family history of allergies 5. Local reaction and non-allergic reactions to a previous dose of vaccine 6. Hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs) e.g. aspirin, diclofenac acid, mefenamic acid, ibuprofen, naproxen, paracetamol 7. Chronic spontaneous urticaria 8. Angiotensin converting enzyme inhibitor (ACEi) induced angioedema 9. Severe cutaneous adverse drug reactions (SCARs)* or other non-IgE mediated hypersensitivities[#] to identified medications/agents 10. Patients receiving omalizumab, dupilumab or other specific biologics for allergic diseases	1. History of anaphylaxis to previous vaccines 2. History of anaphylaxis to injectable medicines or substances possibly containing polyethylene glycol (PEG) or polysorbate[¶]. 3. History of anaphylaxis to multiple different drug classes 4. History of idiopathic anaphylaxis 5. Allergic towards any vaccine	1. **Severe allergic reaction** (e.g. anaphylaxis, SCARs) after a previous dose or to any ingredient[§] of the COVID-19 vaccine 2. **Allergic reaction of any severity within 72 hours** after a previous dose or any known (diagnosed) allergy to any ingredient§ of the COVID-19 vaccine.

Actions	• ***Proceed with vaccination*** *according to local guidelines and settings* *Observation period of 15-30 minutes post vaccination*	***For points 1-4: Do not administer Comirnaty®*** **(Pfizer-BioNTech vaccine); *choose a COVID-19 vaccine without PEG or polysorbate*** ***For point 5: Do not administer CoronaVac®*** **(Sinovac)** • *Refer to Hospital vaccination centre*	• ***Do not vaccinate with the same vaccine in question*** • *Choose a different COVID-19 vaccine that is not contraindicated if available* • *Consider referral to allergists/immunologists if no other vaccine available*

*SCARs – severe cutaneous adverse drug reactions include Stevens-Johnson Syndrome (SJS); toxic epidermal necrolysis (TEN); drug reaction with eosinophilia and systemic symptoms (DRESS); acute generalized exanthematous pustulosis (AGEP); generalized bullous fixed drug eruption (GBFDE) and acute erythroderma.

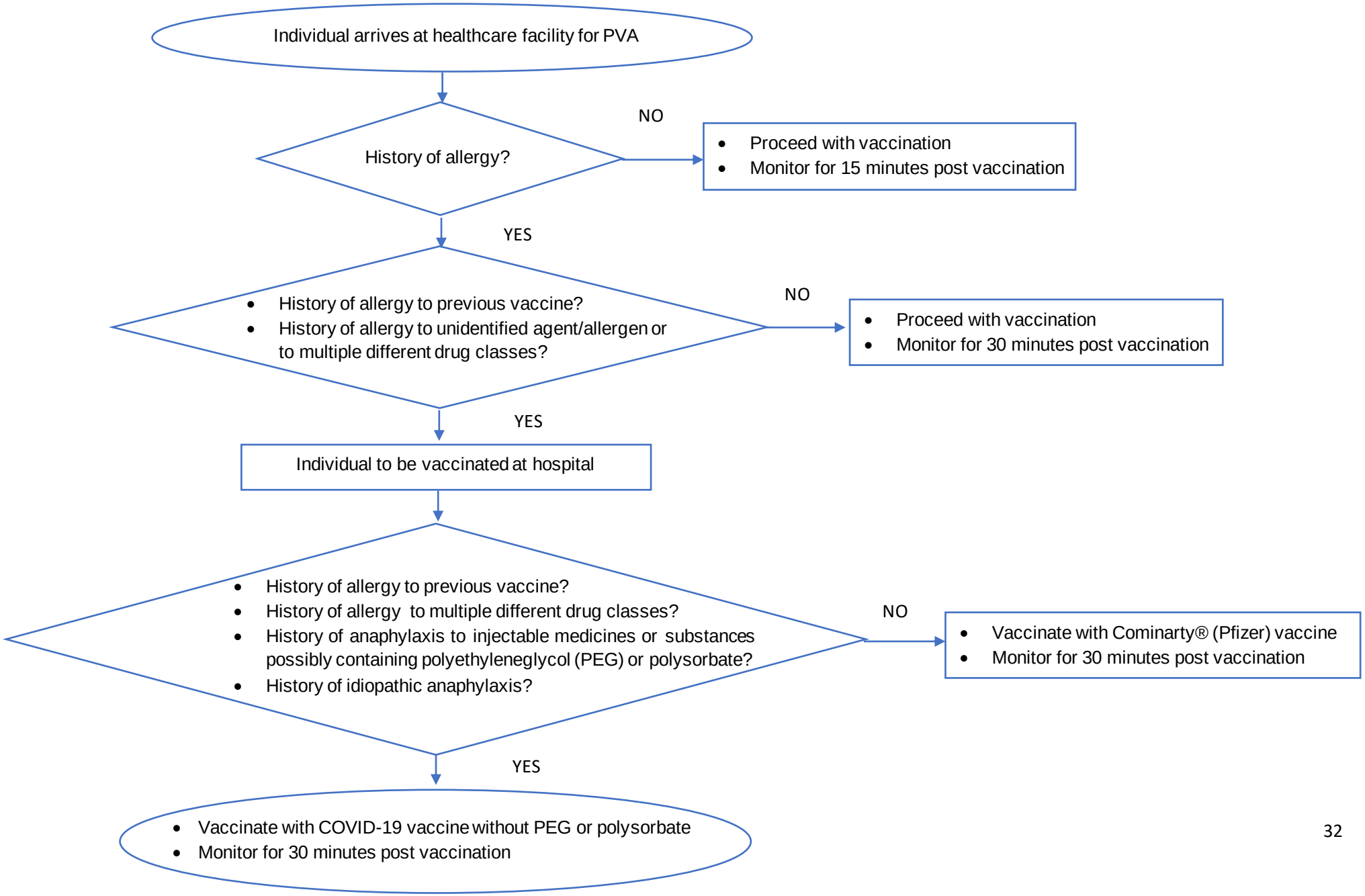
other non-IgE mediated hypersensitivities include vasculitis, maculopapular eruptions, erythema multiforme, fixed drug eruption, symmetrical drug-related intertriginous flexural exanthema

§ ingredient – please refer to Chapter 1 COVID-19 Vaccines

¶Polyethylene glycol (PEG) is an ingredient in *Comirnaty*® (Pfizer-BioNTech); and polysorbate 80 is an ingredient in ChAdOx1-S (Oxford/AstraZeneca; *Covishield*® in India), *Sputnik V*® ((Gamaleya Research Institute) and Janssen COVID-19 Vaccine (Janssen Biotech Inc.). PEG and polysorbate are structurally related, cross-hypersensitivity between these compounds may occur.

For those suspected or confirmed hypersensitivity to PEG or polysorbate, may consider other type of COVID-19 vaccine without PEG or polysorbate e.g.*CoronaVac*®(Sinovac, China) and *BBIBP-CorV*® (Sinopharm, Beijing Institute & Wuhan Inst. of Biological Products).

3.5. Flowchart on Pre-vaccination Assessment Process For Individual with History of Allergy



3.6. List of vaccines and medications containing polyethylene glycol (PEG) and polysorbate

a. Common VACCINES containing POLYSORBATE and PEG

Excipient	Vaccine type	Vaccine	Amount per dose
Polysorbate 20	Influenza	Flublok&Flublock quad	≤ 27.5 µg (Tween 20)
Polysorbate 20	Hepatitis A	Havrix	0.05 mg/ml
Polysorbate 20	Hepatitis A & B	Twinrix	Unknown
Polysorbate 20	SARS-COv-2 (Sanofi)		
Polysorbate 80	Tdap	Boostrix	≤ 100 µg (Tween 80)
Polysorbate 80	Influenza	Fluad	1.175 mg
Polysorbate 80	Influenza	Fluarix quad	≤ 0.055 mg (Tween 80)
Polysorbate 80	Influenza	Flucelvax quad	≤ 1500 µg (Tween 80)
Polysorbate 80	Influenza	Flulaval quad	≤ 887 µg
Polysorbate 80	HPV	Gardasil & Gardasil-9	50 µg
Polysorbate 80	Hepatitis B	Heplisav-B	0.1 mg/mL
Polysorbate 80	DTaP	Infanrix	≤ 100 µg (Tween 80)
Polysorbate 80	Japanese encephalitis	JE-Vax	<0.0007%
Polysorbate 80	DTaP + IPV	Kinrix	≤ 100 µg (Tween 80)
Polysorbate 80	DTaP + HepB + IPV	Pediarix	≤ 100 µg (Tween 80)
Polysorbate 80	Pneumococcal 13-valent	Prevnar-13	100 µg
Polysorbate 80	DTaP + IPV	Quadracel	10 ppm
Polysorbate 80	Rotavirus	RotaTeq	?
Polysorbate 80	Zoster	Shingrix	0.08 mg
Polysorbate 80	Meningococcal group B	Trumenba	0.018 mg
Polysorbate 80	DTaP+IPV+HepB+Hib	Vaxelis	<0.0056%
Polysorbate 80	SARS-CoV-2 (Astrazeneca) SARS-CoV-2 (Johnson & Johnson) Sputnik V (Gamaleya)		
PEG2000	SARS-CoV-2 (Moderna) SARS-CoV-2 (Pfizer)		

b. Common PEG containing DRUGS

Generic name (brand name)	Molecular weight	General description
Methylprednisolone acetate (Depo-medrol)	PEG 3350	Anti-inflammatory glucocorticoid for intramuscular, intra-articular, soft tissue or intralesional injection
Methoxy polyethylene glycol-epoeitin beta (Micera)	30-kD methoxy PEG butanoic acid	Used to treat anemia in adults with chronic kidney disease
Pegfilgrastim (Neulasta)	20-kD monomethoxy PEG	Used to help reduce the chance of infection due to low white blood cell count in people with certain types of cancer (nonmyeloid), who receive anticancer medicines (chemotherapy) that can cause fever and low blood cell count
Peginterferon alfa-2b (PEG-Intron)	12000 daltons	Treatment of HCV in combination with other antiviral drugs in patients over 5 years of age with compensated liver disease
Medroxyprogesterone acetate (Depo-provera)	PEG 3350	Contraceptive and adjunctive therapy and palliative treatment of inoperable, recurrent, and metastatic endometrial or renal carcinoma
Brilliant Blue G Ophthalmic Solution (TissueBlue)	PEG 3350	Disclosing agent indicated to selectively stain the internal limiting membrane
Sulfur hexafluoride (Lumason)	PEG 4000	Ultrasound contrast agent
Biomatoprost implant (Durysta)	PEG, (unspecified)	Reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension
Transtuzumab (Herceptin, Herzuma, Kanjinti, Ogivri, Ontruzan)	PEG 3350	Adjuvant treatment of HER2 overexpressing node-positive or node-negative breast cancer
Rilonacept (Arcalyst)	PEG 3350	IL-1 blocker for treatment of cryopyrin-associated periodic syndromes
Perflutren lipid microsphere (Definity)	PEG 5000	Contrast agent used to brighten and clarify images of the heart during echocardiograms

c. Common POLYSORBATE containing DRUGS

Drug class	Generic name (brand name)	Polysorbate
Antiarrhythmic	Amiodarone hydrochloride (generics only)	Polysorbate 80
Antidiabetic	Exanatide (BydureonBcise)	Polysorbate 20
	Insulin glargine (Lantus, Semglee)	Polysorbate 20
	Insulin glulisine (Apidra)	Polysorbate 20
	Dulaglutide (Trulicity)	Polysorbate 80
Antidote	Hyaluronidase (Hylenex Recombinant)	Polysorbate 80
Antifungal	Anidulafungin (Eraxis)	Polysorbate 80
Anti-inflammatory	Interferon beta 1b (Avonex, Plegridy)	Polysorbate 20
	Omalizumab (Xolair)	Polysorbate 20
Antineoplastic	Ofatumumab (Kesimpta)	Polysorbate 80
	Siltuximab (Sylvant)	Polysorbate 80
Antipsychotic	Paliperidone palmitate (Invega Trinza, Invega Sustenna)	Polysorbate 20
	Aripiprazole lauroxil (Aristada)	Polysorbate 20
Antiretroviral	Ibalizumab (Trogarzo)	Polysorbate 80
Antipsoriatic	Adalimumab (Humira, Imraldi)	Polysorbate 20 (Imraldi) polysorbate 80 (humira)
	Golimumab (Simponi)	Polysorbate 80
	Guselkumab (Tremfya)	Polysorbate 80
	Infliximab – dyyb (Inflectra, Remicade, Renflexis)	Polysorbate 80
	Ustekinumab (Stelara)	Polysorbate 80
Antiviral	Interferon-alfa-2b (Intron A)	Polysorbate 80
Biological response modifier	Interferon-gamma-1b (Actimmune)	Polysorbate 20

Drug class	Generic name (brand name)	Polysorbate
Cancer treatment	Ado-trastuzumab (Kadcyla)	Polysorbate 20
	Atezolizumab (Tecentriq)	Polysorbate 20
	Avelumab (Bavencio)	Polysorbate 20
	Bevacizumab (Avastin, Zirabev)	Polysorbate 20
	Daratumumab/hyaluronidase (DarzalexFaspro)	Polysorbate 20
	Denosumab (Prolia, Xgeva)	Polysorbate 20
	Dinutuximab (Unituxin)	Polysorbate 20
	Enfortumab (Padcev)	Polysorbate 20
	Olaratumab (Lartruvo)	Polysorbate 20
	Palifermin (Kepivance)	Polysorbate 20
	Pertuzumab/trastuzumab/hyaluronidase (Phesgo)	Polysorbate 20
	Polatuzumabvedotin (Polivy)	Polysorbate 20
	Tafasitamab (Monjuvi)	Polysorbate 20
	Trastuzumab (Herceptin, Herceptin Hylecta, Herzuma, Kanjinti, Ontruzant, Trazimera)	Polysorbate 20
	Belantamab (Blenrep)	Polysorbate 80
	Brentuximab vedotin (Adcetris)	Polysorbate 80
	Cemiplimab (Libtayo)	Polysorbate 80
	Docetaxel (Taxotere)	Polysorbate 80
	Durvalumab (Imfinzi)	Polysorbate 80
	Elotuzumab (Empliciti)	Polysorbate 80
	Etoposide (Toposar, VePesid)	Polysorbate 80
	Fam-trastuzumab deruxtecan (Enhertu)	Polysorbate 80
	Fosaprepitantdimeglumine (EMEND, Fosaprepitant)	Polysorbate 80
	Inotuzumabozogamicin (Besponsa)	Polysorbate 80
	Ipilimumab (Yervoy)	Polysorbate 80
	Isatuximab (Sarclisa)	Polysorbate 80
	Mogamulizumab (Poteligeo)	Polysorbate 80
	Moxetumomabpasudotox (Lumoxiti)	Polysorbate 80
	Nivolumab (Opdivo)	Polysorbate 80
	Ofatumumab (Arzerra)	Polysorbate 80

Drug class	Generic name (brand name)	Polysorbate
	Pembrolizumab (Keytruda)	Polysorbate 80
	Ramucirumab (Cyranza)	Polysorbate 80
	Rituximab (Truxima, Rituxan, Ruxience)	Polysorbate 80
	Temsirolimus (Torisel)	Polysorbate 80
	Temozolomide (Temodar)	Polysorbate 80
Contraceptive	Medroxyprogesterone acetate (depo-provera, depo-provera CI, Depo-subQprovera 104)	Polysorbate 80
Corticosteroid	Methylprednisolone acetate (Depo-medrol)	Polysorbate 80
	Triamcinolone acetonide (Aristocort forte, Aristopan, Kenalog-40, Kenalog-10, Protherix, Triesence, TriloanSuik, Triloan II Suik, Ziretta)	Polysorbate 80
	Sincalide (Kinevac)	Polysorbate 20
	Tuberculin purified protein derivative (Aplisol, Tubersol)	Polysorbate 80
Disease-modifying antirheumatic drug	Anakinra (Kinert)	Polysorbate 80
	Tocilizumab (Actemra)	Polysorbate 80
Enzyme	Velaglucerase alfa (Vpriv)	Polysorbate 20
	Imiglucerase (Cerezyme)	Polysorbate 80
	Taliglucerase alfa (Elelyso)	Polysorbate 80
		Polysorbate 80
Erythoid maturation agent	Luspatercept (Reblozyl)	Polysorbate 80
Factor Xa inhibitor antidote	Coagulation factor Xa (recombinant), inactivated-zhzo (Adexxa)	Polysorbate 80
Gonadotropin	Follitropin (Menopur, Follistim)	Polysorbate 20
Growth hormone analog	Somatotropin (Nutropin AQ Nuspin 5)	Polysorbate 20
Hematopoietic growth factor	Erythropoeitin (Retacrit)	Polysorbate 20
	Pegfilrastim (Fulphila, Neulasta, Nyvepria, Udenyca)	Polysorbate 20
	Romiplostim (Nplate)	Polysorbate 20
	Darbepoetin alfa (Aranesp)	Polysorbate 80
	Filgrastim (Neupogen, Nivestym, Granix, Zarxio)	Polysorbate 80
Hepatitis B/Hepatitis C agent	Peginterferon (Pegays, Pegintron)	Polysorbate 80

Drug class	Generic name (brand name)	Polysorbate
Hemostatic	Vitamin k (Phytonadione)	Polysorbate 80
Immune globulin	Hepatitis B Immune globulin (HepaGam B, Nabi-HB)	Polysorbate 80
	Rho (d) immune globulin (WinRho)	Polysorbate 80
Immunomodulator	Intereron beta-1a (Avonex, Avonex Pen)	Polysorbate 20
	Emapalumab (Gamifant)	Polysorbate 80
Immunosuppressant	Mycophenolate mofetil (Cellcept IV)	Polysorbate 80
Inflammatory bowel disease agent	Vedolizumab (Entyvio)	Polysorbate 80
Interleukin inhibitor	Sarilumab (Kevzara)	Polysorbate 20
	Dupilumab (Dupixent)	Polysorbate 80
	Mepolizumab (Nucala)	Polysorbate 20
	Secukinumab (Cosentyx)	Polysorbate 80
	Tildrakizumab – asmn (Ilumya)	Polysorbate 80
Kallikrein inhibitor	Lanadelumab (Takhzyro)	Polysorbate 80
Leptin analog	Metreliptin (Myalept)	Polysorbate 20
Macular degeneration agent	Aflibercept (Eylea)	Polysorbate 20
	Ranibizumab (Lucentis)	Polysorbate 20
	Brolucizumab (Beovu)	Polysorbate 80
mAb treatment	Ocrelizumab (Ocrevus)	Polysorbate 20
	Remdesivir (Veklury)	Polysorbate 20
	Romosozumab (Evenity)	Polysorbate 20
	Teprotumumab (Tepezza)	Polysorbate 20
	Atoltivimab/maftivimab/odesivimab-ebgn (Inmazeb)	Polysorbate 80
	Banlanivimab	Polysorbate 80
	Burosumab (Crysvita)	Polysorbate 80
	Canakimumab (Iliris)	Polysorbate 80

Drug class	Generic name (brand name)	Polysorbate
	Casirivimab/Imdevimab	Polysorbate 80
	Eptinezumab (Vyepti)	Polysorbate 80
	Fremanezumab (Ajovy)	Polysorbate 80
	Inebilizumab (Uplizna)	Polysorbate 80
	Raxibacumab	Polysorbate 80
	Natalizumab (Tysabri)	Polysorbate 80
	Dantrolene sodium (Dantrium, Ryanodex)	Polysorbate 80
	Crizanlizumab	Polysorbate 80
	Alirocumab (Praluent)	Polysorbate 20
	Evolocumab (Repaha)	Polysorbate 80
	Belimumab (Benlysta)	Polysorbate 80
	Tenecleptase (Tnkase)	Polysorbate 20
	Alteplase (CathfloActivase)	Polysorbate 80
	Reteplase (Retavase)	Polysorbate 80
	Calcitriol (Calcijex, Rocaltrol)	Polysorbate 20
	Doxercalciferol (Hectorol)	Polysorbate 20
	Vitamins A, B1, B2, B6, C, D3, E, K (Infuvite)	Polysorbate 80

3.7. Case scenarios for allergy assessment BEFORE the first dose of COVID-19 vaccine

Allergy details	Vaccination decision	Precaution
50/M with urticaria, lips swelling and shortness of breath (SOB) to penicillin 30 years ago.	**Can vaccinate** Anaphylaxis to penicillin	Observe for **30 minutes** after vaccination
35/F with history of wheals and angioedema to paracetamol, oral naproxen and IM diclofenac (*Voltaren*®). Given adrenaline injection x1, hydrocortisone and chlorpheniramine at casualty when she had angioedema and SOB due to IM diclofenac (*Voltaren*®).	**Can vaccinate** NSAIDs hypersensitivity	Observe for **30 minutes** after vaccination
45/F with chronic spontaneous urticaria. She had history of angioedema and throat swelling to paracetamol, ibuprofen (*Brufen*®) and mefenamic acid (*Ponstan*®*).* Her symptoms currently controlled with oral cetirizine 20mg bd.	**Can vaccinate** **Continue antihistamines as usual.** NSAIDs hypersensitivity	Observe for **30 minutes** after vaccination
20/M with history of lips swelling and wheals after eating shellfish (prawn and crab). His symptoms resolved spontaneously within 24 hours.	**Can vaccinate** Allergy or intolerance to seafood	Observe for **30 minutes** after vaccination
75/F with DRESS to allopurinol 15 years ago. She has eczema after resolution of DRESS under dermatology follow up.	**Can vaccinate** DRESS to drugs other than vaccine is not a contraindication	Observe for **30 minutes** after vaccination
45/M with HIV, history of maculopapular rash to sulfamethoxazole and trimethoprim (*Bactrim*®*)*, CD4 = 240, viral load undetectable. No throat swelling, no shortness of breath.	**Can vaccinate** MPE (type IV hypersensitivity) to sulfamethoxazole and trimethoprim (*Bactrim*®*)*	Observe for **30 minutes** after vaccination

Allergy details	Vaccination decision	Precaution
43/F with generalized rash after flu vaccine last year. No throat swelling, no shortness of breath, no angioedema, no syncopal attack.	**Do not give vaccine with PEG or polysorbate** Allergic to previous influenza vaccine. Most influenza vaccines contain polysorbate.*	May consider other type of COVID-19 vaccine **without PEG* or polysorbate**. May refer to immunologist for assessment.
67/M flushing and generalized wheals after alcohol and certain preserved/fermented food (sausages, cheese). No angioedema.	**Can vaccinate** Histamine intolerance to alcohol/food that contain high histamine	Observe for **30 minutes** after vaccination
30/M SJS/TEN overlap to carbamazepine 5 years ago.	**Can vaccinate** SJS/TEN to drugs other than vaccine is not a contraindication	Observe for **30 minutes** after vaccination
66/M holding an allergy card GBFDE to celecoxib.	**Can vaccinate** GBFDE to drugs other than vaccine is not a contraindication	Observe for **30 minutes** after vaccination
58/F had angioedema and wheals associated with SOB after taken Forlax® (Macrogol 4000) for constipation	**Do not give vaccine with PEG or polysorbate** Immediate hypersensitivity to Forlax® (Macrogol 4000). Forlax® contains PEG*.	May consider other type of COVID-19 vaccine **without PEG* or polysorbate**. May refer to immunologist for assessment.
70/F with DM, IHD, hypertension and perindopril induced angioedema.	**Can vaccinate** ACE inhibitor induced angioedema	Observe for 30 minutes after vaccination
18/M poorly control bronchial asthma. He is wheezing.	**Defer vaccination**	To get assessment by physician and optimize the bronchial asthma control.

Allergy details	Vaccination decision	Precaution
50/F with chronic spontaneous urticaria (CSU) has an allergy card labelling "multiple drug allergies *to Augmentin*®, cefuroxime, EES, doxycycline, ciprofloxacin, clindamycin, prednisolone and *Piriton*®." Most of her drug reactions were wheals, itch and angioedema. Her CSU is controlled with oral levocetirizine 10mg bd.	**Can vaccinate** Continue antihistamines as usual.	Observe for **30 minutes** after vaccination
33/M DM taking regular metformin and aspirin, had 5 episodes of anaphylaxis occurred during jogging. He took bread an hour before jogging when he had the anaphylaxis. He has an adrenaline autoinjector.	**Can vaccinate** Wheat-dependent exercise-induced anaphylaxis enhanced by aspirin (NSAIDs)	Observe for 30 minutes after vaccination
40/M multiple episodes of angioedema, fullness of throat and near syncopal attacks to various food and drink. He had received IM adrenaline, IV hydrocortisone and IV chlorpheniramine a few times at casualty. He was labelled as idiopathic anaphylaxis and is still under assessment at allergy clinic. He has an adrenaline autoinjector.	**Do not give vaccine with PEG or polysorbate** PEG* could be the culprit in idiopathic anaphylaxis.	May consider other type of COVID-19 vaccine **without PEG* or polysorbate**. May refer to immunologist for assessment.

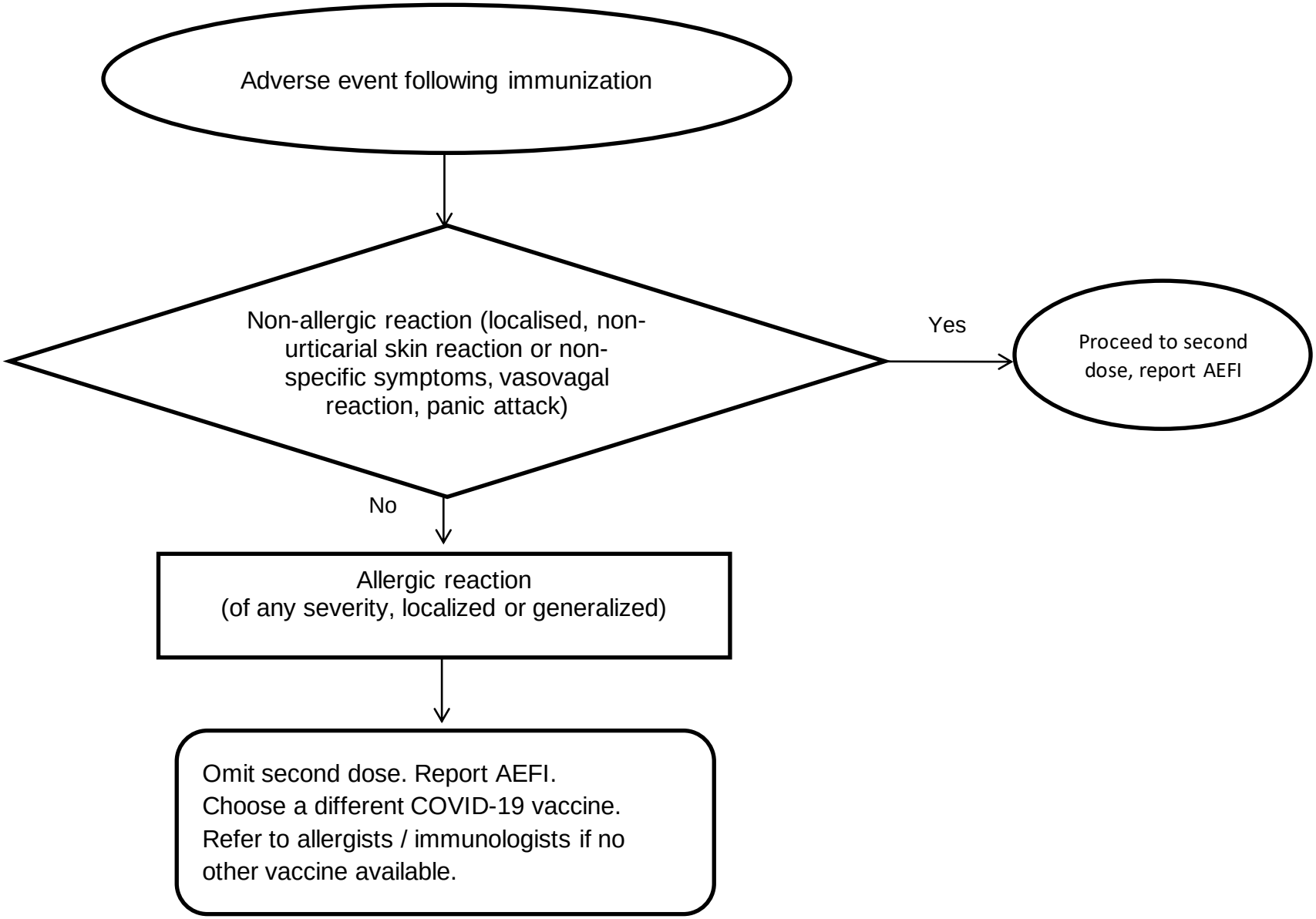
***** *Polyethylene glycol (PEG) is an ingredient in Comirnaty® (Pfizer-BioNTech); and polysorbate 80 is an ingredient in ChAdOx1 (Oxford/AstraZeneca;Covishield in India), Sputnik V (Gamaleya Research Inst) and Janssen COVID-19 Vaccine (Janssen Biotech Inc.). PEG and polysorbate are structurally related, cross-hypersensitivity between these compounds may occur.*

3.8. Case scenarios for reactions developed AFTER the first dose of COVID-19 vaccine

Allergy details	Vaccination decision	Precaution
35/M with generalized wheals that started 6 hours after the first dose of mRNA-COVID-19 vaccine. No throat swelling, no shortness of breath, no syncopal attack. Rash took 2 days to resolve with antihistamines.	**Do not give second dose of vaccine, report AEFI** Allergic reaction (type I reaction, non anapylaxis) to mRNA vaccine	May consider other type of COVID-19 vaccine.
35/F with transient fever for a day and painful swelling at injection site after the first dose of COVID-19 vaccine. Injection site erythema and swelling lasted 3 days. She took paracetamol for the fever and pain.	**Can vaccinate, report AEFI** Non-allergic localized side effect.	Observe for **30 minutes** after vaccination.
26/M with generalized hives, facial swelling and loss of consciousness 15 minutes after first dose of mRNA-COVID-19 vaccine. Documented tachycardia and hypotension. Given IM adrenaline x2, IV hydrocortisone and IV chlorpheniramine and observed overnight at ICU. Discharge well after that.	**Do not give second dose of vaccine, report AEFI** Anaphylaxis to mRNA vaccine	May consider other type of COVID-19 vaccine.
28/M developed bronchospasm within 15 minutes after first dose of mRNA-COVID-19 vaccine. He has well controlled bronchial asthma. His last asthmatic attack was a year ago and was managed at ICU.	**Do not give second dose of vaccine, report AEFI** Bronchospasm to mRNA-COVID-19 vaccine	May consider other type of COVID-19 vaccine.
40/M with history of anaphylaxis due to bee sting. Developed generalized urticaria on day-2 post first dose of mRNA-COVID-19 vaccine. No angioedema	**Do not give second dose of vaccine, report AEFI** Delayed generalized urticaria to mRNA-COVID-19 vaccine	May consider other type of COVID-19 vaccine.

Allergy details	Vaccination decision	Precaution
48/F taking regular prednisolone 10mg daily for underlying autoimmune disease. Developed generalized urticaria associated with itchy throat and nose 1 hour after first dose of mRNA-COVID-19 vaccine. The urticaria subsided 3 days later with antihistamines and high dose of oral prednisolone	**Do not give second dose of vaccine, report AEFI** Generalized urticaria to mRNA-COVID-19 vaccine	May consider other type of COVID-19 vaccine.
35/F with history of severe angioedema many years ago to food and NSAIDs, has been asymptomatic for many years. She took chlorpheniramine 4mg immediately after the first dose of mRNA-COVID-19 vaccine. Developed mild periorbital swelling 12 hours later after vaccination.	**Do not give second dose of vaccine, report AEFI** Urticaria to mRNA-COVID-19 vaccine	May consider other type of COVID-19 vaccine.
40/F developed diffuse facial flushing and swelling of both ears 2 hours post vaccination with the first dose of mRNA-COVID-19 vaccine.	**Do not give second dose of vaccine, report AEFI** Angioedema to mRNA-COVID-19 vaccine	May consider other type of COVID-19 vaccine.
40/M developed periorbital swelling without respiratory or systemic manifestations 10 minutes post vaccination with the first dose of mRNA-COVID-19 vaccine.	**Do not give second dose of vaccine, report AEFI** Angioedema to mRNA-COVID-19 vaccine	May consider other type of COVID-19 vaccine.

3.9. Flow chart for considerations in vaccinating selected groups of hypersensitive population (AFTER 1st VACCINATION)



4. Vaccination

4.1. COVID-19 Vaccination Consent *(Borang Persetujuan Suntikan Vaksin COVID-19)*

KEMENTERIAN KESIHATAN MALAYSIA

BORANG PERSETUJUAN SUNTIKAN VAKSIN COVID-19

Vaksin COVID-19 diberi bagi mengawal penularan COVID-19 di negara ini. Apabila semakin ramai orang mendapat vaksinasi, semakin ramai penduduk membentuk antibodi dan seterusnya mengurangkan kebarangkalian kejadian penyakit COVID-19 yang lebih teruk. Secara tidak langsung kita boleh melindungi golongan berisiko yang tidak layak menerima suntikan vaksin.

Majlis Mesyuarat Khas Jawatankuasa Muzakarah Majlis Kebangsaan bagi Hal Ehwal Ugama Islam yang bersidang pada 3 Disember 2020 mengambil ketetapan bahawa hukum penggunaan vaksin Covid-19 adalah harus dan wajib diambil oleh golongan yang ditetapkan oleh Kerajaan.

Suntikan Vaksin COVID-19 ada yang memerlukan satu (1) atau (2) dos bergantung kepada jenis vaksin. Suntikan ini kebiasaannya diberi pada otot bahu kecuali dalam keadaan tertentu. Jenis vaksin yang diberikan bergantung kepada bekalan vaksin semasa.

Pengambilan Vaksin COVID-19 ini juga mungkin akan mengakibatkan kesan sampingan yang ringan dan kesan sampingan lain yang akan dilaporkan dari semasa ke semasa.

SEJARAH KESIHATAN (Sila lengkapkan)

Adakah anda :

a.	Mengalami kesan sampingan teruk (seperti sawan, pengsan dan kemasukan ke hospital) selepas mendapat mana-mana imunisasi sebelum ini?	YA	☐	TIDAK	☐
b.	Pernah mempunyai sejarah alahan teruk?	YA	☐	TIDAK	☐
c.	Adakah anda sedang hamil atau bercadang untuk hamil? (bagi wanita)	YA	☐	TIDAK	☐
d.	Adakah anda sedang menyusukan bayi? (bagi wanita)	YA	☐	TIDAK	☐

Saya telah membaca/ dibacakan tentang maklumat vaksin COVID-19 serta tujuan dan kaedah pemberian suntikan vaksin tersebut seperti mana di helaian Maklumat Vaksin COVID-19 bagi Penerima Vaksin.

Dengan ini, saya memahami bahawa:

1. pengambilan vaksin COVID-19 ini mungkin akan menimbulkan reaksi serta kesan sampingan seperti yang dinyatakan di dalam maklumat vaksin;

2. saya bertanggungjawab ke atas risiko yang mungkin berlaku akibat keputusan / tindakan saya ini kerana manfaat vaksin adalah jauh lebih baik daripada kesan sampingannya;

3. vaksin ini tidak memberi jaminan sepenuhnya kepada saya daripada tidak mendapat jangkitan COVID-19 pada masa akan datang;

4. dengan menandatangani persetujuan menerima vaksin COVID-19 ini, saya bersetuju dengan rela hati untuk melengkapkan jumlah pengambilan dos vaksin seperti yang dijadualkan.

Sila lengkapkan persetujuan di bawah (yang mana berkaitan):

- Saya, …….. No.K.P/Polis/Tentera…….. ***BERSETUJU / TIDAK BERSETUJU** mendapatkan suntikan Vaksin COVID-19 …… untuk ***diri saya.**

- Saya, …….. No.K.P/Polis/Tentera…….. ***BERSETUJU / TIDAK BERSETUJU** mendapatkan suntikan Vaksin COVID-19 …… untuk ***ibu bapa / *orang di bawah jagaan saya** bernama …….. No. K.P/ Polis/ Tentera ……..

Tandatangan penerima / waris		**Tandatangan Saksi**	
Nama	:	Nama	:
No. Kad Pengenalan	:	No.Kad Pengenalan	:
Tarikh	:	Tarikh	:

**potong yang tidak berkenaan*

Nota penting: Rujuk maklumat lanjut mengenai Vaksin COVID-19 di helaian Maklumat Vaksin COVID-19 bagi Penerima Vaksin.

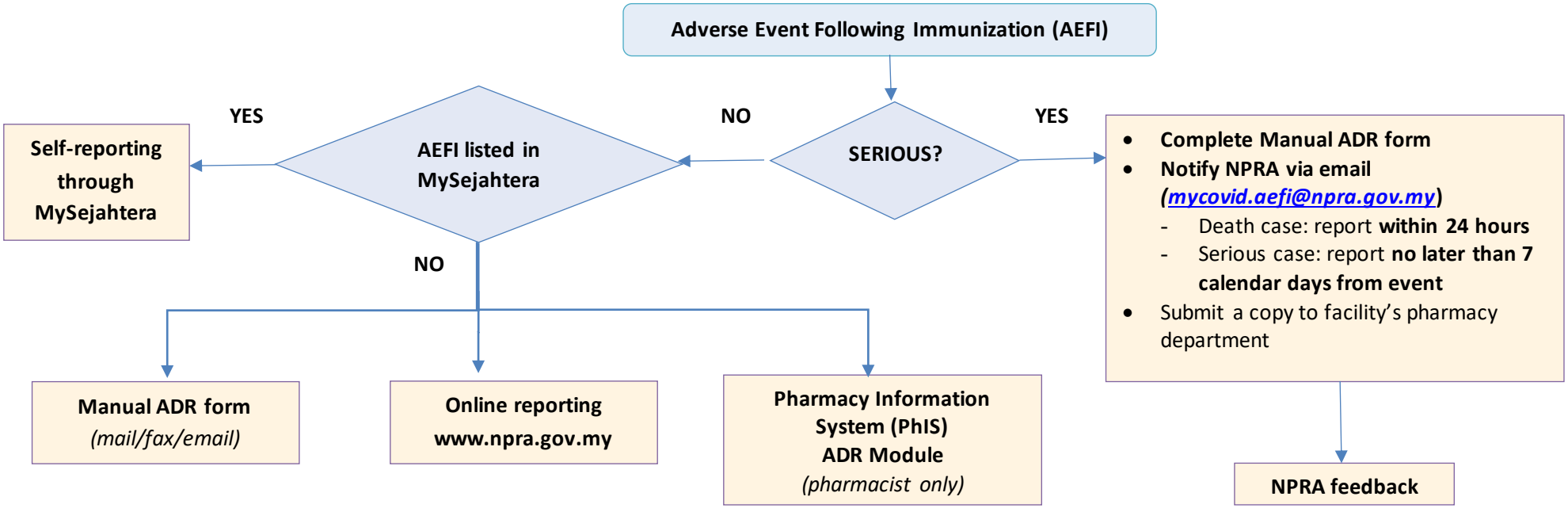
Terima kasih atas kerjasama yang diberi. Sila kembalikan borang ini kepada pihak klinik.

5. Post vaccination

5.1. Post Vaccination Monitoring

a. Following immunization of COVID-19 vaccine the individual **SHOULD** be **monitored on-site**.
b. For those with **history of allergy**, observe for **at least 30 minutes** post vaccination.
c. Otherwise, observe for **at least 15 minutes** post vaccination.
d. Vaccination providers should have appropriate medications and equipment such as **epinephrine, antihistamines, stethoscopes, blood pressure cuffs, and timing devices and access to the emergency trolley** at all COVID-19 vaccination sites.

5.2. Reporting of Adverse Event Following Immunization (AEFI)



An AEFI will be considered **serious**, if it:

- results in death,
- is life-threatening,
- requires in-patient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity,
- is a congenital anomaly/birth defect, or
- requires intervention to prevent permanent impairment or damage.

National Pharmaceutical Regulatory Agency (NPRA). 2021. Reporting ADR. [online] Available at: <https://npra.gov.my/index.php/en/health-professionals/reporting-adr> [Accessed 20 March 2021].

Vaccine-safety-training.org. 2021. MODULE 3 – Classification of AEFIs - WHO Vaccine Safety Basics. [online] Available at: <https://vaccine-safety-training.org/classification-of-aefis.html> [Accessed 20 March 2021]

5.3. COVID-19 vaccine-related anaphylaxis: Definition and management

5.3.1. Introduction

Anaphylaxis is a serious systemic hypersensitivity reaction which is usually acute in onset and may result in death[5]. Severe anaphylaxis is characterised by potentially life-threatening compromise in airway, breathing and/or circulation and may present without the classical skin features or circulatory shock[5]. The incidence of anaphylaxis following COVID-19 vaccination is generally rare[25]. Both Pfizer-BioNTech vaccine and Moderna COVID-19 vaccine have reported an anaphylaxis rate at 4.7 cases and 2.5 cases per million doses administered respectively based on the data through January 2021[21].

5.3.2. Early recognition

Diagnosis of anaphylaxis is made clinically based on signs and symptoms[5]. Failure to recognise and delay in treatment could be catastrophic as it can deteriorate rapidly leading to respiratory and cardiac arrest[24]. Most anaphylaxis cases occur within 15-30 minutes post vaccination though it can sometimes take up to several hours for the first symptoms to develop[8]. Anaphylaxis may present as:

System	Symptoms
Mucocutaneous	● Eyes: Periorbital or conjunctival swelling ● Oral mucosa: Lips, tongue or uvula swelling ● Skin: Generalized urticaria, skin redness, itchiness
Respiratory	● Upper airway: Foreign body sensation, stridor, voice hoarseness, sudden increase/excess in nasal secretions, difficulty in swallowing, hypoxia ● Lower airway: wheezing, breathlessness, chest tightness, coughing, decreased peak expiratory flow (PEF), cyanosis, hypoxia
Cardiovascular	● Early features: syncope, dizziness, tachycardia, hypotension, prolonged capillary refill time ● Late features: bradycardia, shock, altered mental status related to reduced cerebral perfusion/hypoxia, cardiac arrest.
Gastrointestinal	● Persistent abdominal cramp ● Vomiting ● Diarrhea

The clinical diagnosis of anaphylaxis can be challenging in some situations[9]. Anaphylaxis may present as a mild allergic reaction initially and it may be difficult to predict whether a seemingly mild allergy could progress to become an anaphylactic reaction. In addition, individual with communication difficulties such as those with cognitive or neurological deficits may not be able to report their symptoms precisely. Mucocutaneous manifestation such as urticaria and angioedema may be absent in some anaphylaxis cases[5,28].

Criteria listed in the table below aid in the diagnosis of anaphylaxis.

Diagnosis criteria for anaphylaxis Anaphylaxis is highly likely if any **ONE** of the criteria presents:	
Criteria 1	Criteria 2
Acute onset of illness (minutes to several hours) with mucocutaneous involvement (either skin, mucosal or both) **AND** at least one of the following: ● Respiratory symptoms/signs (e.g., dyspnea, wheezing, hypoxia, stridor, reduced PEF) ● Episode of hypotension or with associated manifestations (e.g., hypotonia, syncope, collapse, incontinence ● Severe gastrointestinal symptoms (e.g., crampy abdominal pain, repetitive vomiting)	Acute onset of hypotension[1] **or** bronchospasm[2] **or** laryngeal involvement[3] after exposure to a **known*** or **highly likely*** allergen (minutes or several hours), even in the absence of typical skin involvement.

Adapted from the diagnostic criteria of anaphylaxis (WAO) 2020[5]

Note:

**The term highly likely allergen and known allergen referred to the COVID-19 vaccine in the context with post vaccination anaphylactic reaction.*

[1] Hypotension is defined as systolic BP < 90mmHg or reduction in systolic BP greater than 30% from the individual's baseline.

[2] Excludes lower respiratory symptoms triggered by common inhalant allergens or food allergens perceived to cause "inhalational" reactions.

[3] Laryngeal symptoms include stridor, vocal changes, odynophagia.

On the contrary, not all signs and symptoms mentioned above are necessarily a result of an anaphylaxis reaction. Careful assessment and clinical judgement can differentiate anaphylaxis from other mimicking conditions[4]. Below are some differential diagnoses:

Category	Differential diagnosis
Cardiac	Myocardial infarct, arrhythmias
Pulmonary	Acute exacerbation of asthma, acute exacerbation of chronic obstructive airway disease, pulmonary embolism, foreign body inhalation
Neurology	Seizure, cerebrovascular accident
Histamine	Systemic mastocytosis, leukemia, scombroid fish ingestion
Skin flushes	Carcinoid syndrome, post-menopausal
Hypotensive, shock	Hypovolemic, cardiac, or septic shock
Psychological	Panic attacks, hyperventilation syndrome, psychosomatic episodes
Others	Hereditary angioedema, pheochromocytoma

Vasovagal syncope is not uncommon during vaccination[15]. Vasovagal attack may present with transient hypotension with bradycardia and tend to improve with supine positioning and resolve spontaneously[11,23]. In contrast, syncope due to anaphylaxis tend to have persistent hypotension, weak pulse volume and tachycardia[9]. Hypotension and poor peripheral perfusion in anaphylaxis would persist unless intervention such as adrenaline and IV fluid administration are given[23].

5.3.3. Anticipating and Managing Anaphylaxis in Vaccination Centres

All vaccination centres should have enough staff, medication, and equipment to recognise and treat anaphylaxis. Healthcare workers who are trained to recognise anaphylaxis and deliver intramuscular adrenaline injection should be readily available at site. Transport should be available to send patients to specialist centres if anaphylaxis is diagnosed. The following equipment should be accessible during anaphylaxis:

Equipment	Drugs
1. Transport Stretcher 2. Emergency Cart or Bag 3. Wheelchair 4. Cardiac monitor or Defibrillator 5. Oxygen regulator 6. Portable Oxygen Source 7. Laryngoscope size 3,4 8. Endotracheal tube size 7, 7.5 & 8 9. Laryngeal mask airway (LMA) size 3 and 4 10. Bag Valve Mask 11. Medications Chart 12. Portable Suction 13. Glucometer 14. Stethoscope 15. Large Bore cannula (16G,18G and 20G)	1. Adrenaline 2. Normal Saline 3. Salbutamol 4. Chlorpheniramine 5. Hydrocortisone 6. Ranitidine

5.3.4. Management

If anaphylaxis reaction or anaphylactic shock is suspected, the following steps are critical as part of the initial emergency management:

Acute management

- Get additional help immediately.
- Lie patient in recumbent position with leg raised. In patients who are vomiting or having breathlessness, allow patients to be in the position of comfort[22]. Pregnant patients can be put on the left lateral position.
- The first and most critical treatment in anaphylaxis is adrenaline[5,22]. There is **NO** absolute contraindication for adrenaline administration in anaphylaxis. Administer IM injection of adrenaline 1:1000 0.5ml (0.5mg) preferably over the mid-lateral thigh as soon as possible. This can be repeated every 5-10 minutes, as necessary. If more than three IM injections of adrenaline are required, consider giving intravenous (IV) injection for refractory anaphylaxis.
- Give 100% oxygen supplementation via high flow mask[22].
- Immediate intubation in impending airway obstruction from angioedema.
- Consider nebulized/ MDI salbutamol with persistent bronchospasm.

Treatment for refractory anaphylaxis*

Give IV adrenaline infusion for refractory symptoms despite 3 doses of IM adrenaline and IV fluid boluses. The preferred method of adrenaline infusion will be using an infusion pump[5].

- IV adrenaline infusion can be prepared by adding 3mg adrenaline 1:1000 in 47ml of normal saline in a 50ml syringe. Initial dose can be set at 0.1mcg/kg/min using an infusion pump (e.g. in a 50kg patient, to start infusion adrenaline at 5ml/hour). Titrate the infusion rate according to the blood pressure and heart rate.
- Alternatively, IV adrenaline infusion can be prepared by diluting 0.5ml 1:1000 (0.5mg) adrenaline in 500ml normal saline if the infusion pump is not available. The initial dose can be set at 2ml per minute (equivalent to 2mcg per minute). This can be gradually increased up to 10mcg/min (10ml/min) titrating the infusion rate according to the blood pressure and heart rate[5].

Patients on beta blocker may not respond adequately to adrenaline[22]. Consider administering IV glucagon 1-5mg over 5 minutes followed by infusion 5-15mcg/min in patients resistant to adrenaline[19]. Rapid administration of glucagon may trigger vomiting[19].

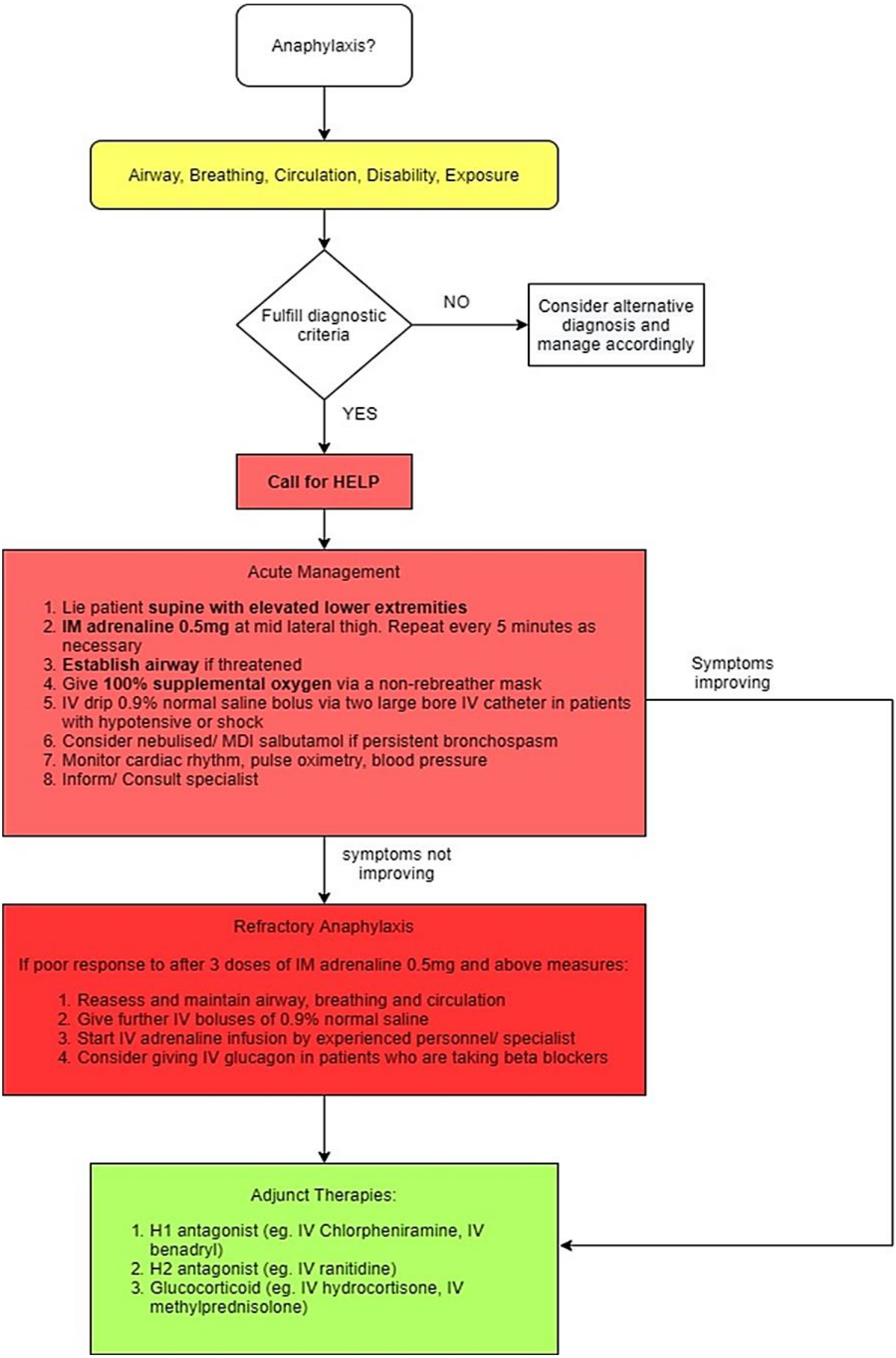
Adjunct therapies[5]

- H1 antagonist: IV chlorpheniramine 10mg
- H2 antagonist: IV ranitidine 50mg
- Glucocorticoid: IV hydrocortisone 200mg
- Monitoring: Pulse oximetry, cardiac monitoring, blood pressure and urine output charting

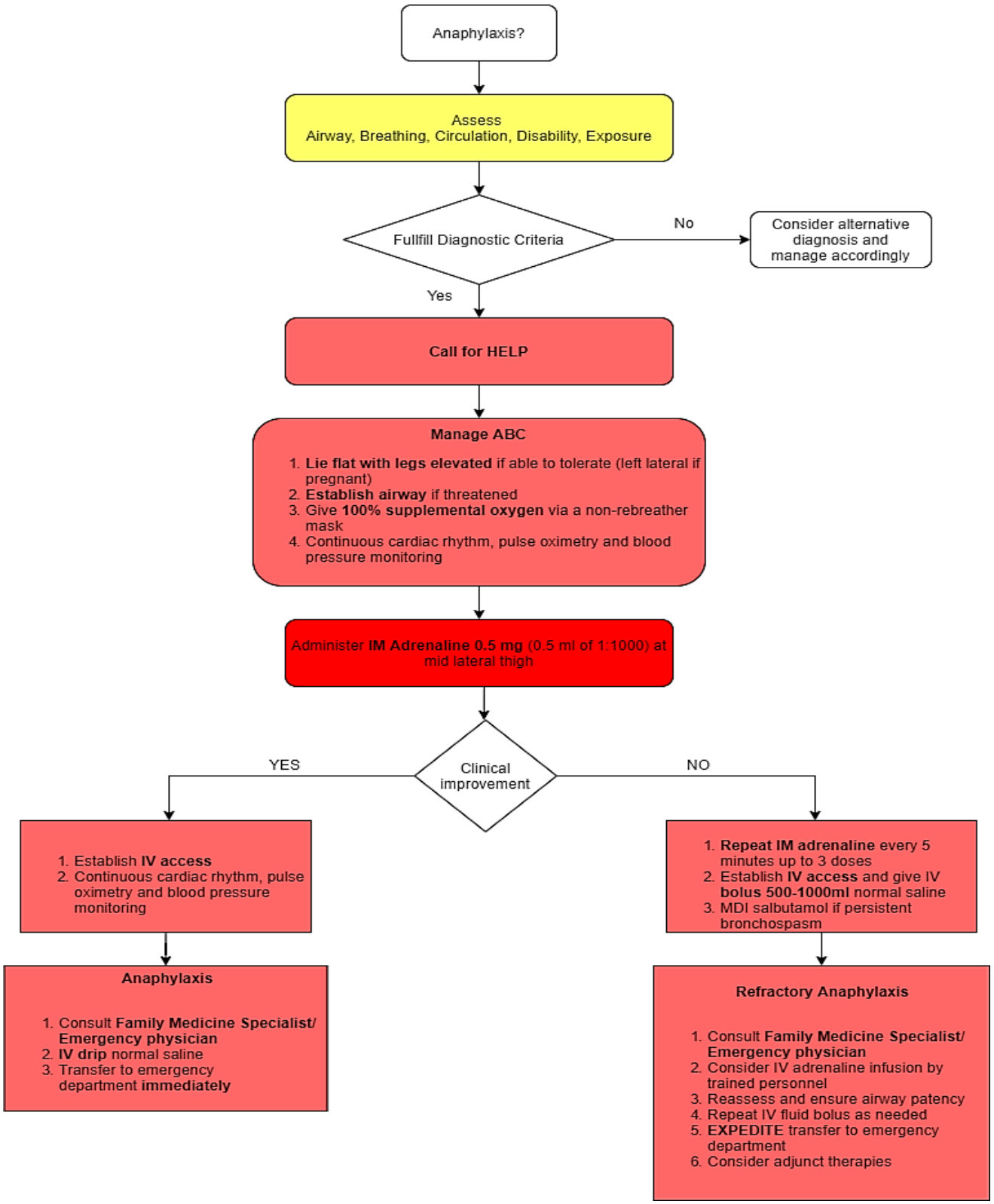
**It is important to consult specialists when encounter refractory anaphylaxis. IV adrenaline should be used only by trained personnel or with guidance from specialists. Glucagon is mostly available in the tertiary hospitals setting.*

Note: **Prioritize** on **adrenaline** administration first over adjunct treatments[11]. While antihistamine and glucocorticoid can relieve symptoms, they do not immediately reverse life threatening airway obstruction or hypotension.

Summary on management of anaphylaxis



5.3.5 Flow Chart for Management of Post Vaccination Anaphylaxis at Vaccination Centers



***In the case of confirmed anaphylaxis, adrenaline must be administered as soon as possible. Contact emergency medical services immediately and transfer the patient to a centre with higher medical care** for observation for complications and delayed reaction (biphasic phase).

5.3.6 Considerations for special population/ groups

Pregnant patient

The emergency management of anaphylaxis with pregnancy is essentially the same as non-pregnant patients. Early patient transfer to tertiary centers for both maternal and fetal monitoring should be made. If the patient is in shock, emphasis should be given to establish adequate perfusion by rapid administration of intravenous fluid and positioning the patient on the left lateral position or perform manual left uterine displacement to minimise compression of the inferior vena cava in a gravid uterus[6]. It is important to maintain adequate perfusion (SBP> 90mmHg) in pregnant patients as the utero-placental circulation is devoid of autoregulation mechanism and largely depends on the maternal circulation[6].

Elderly patient

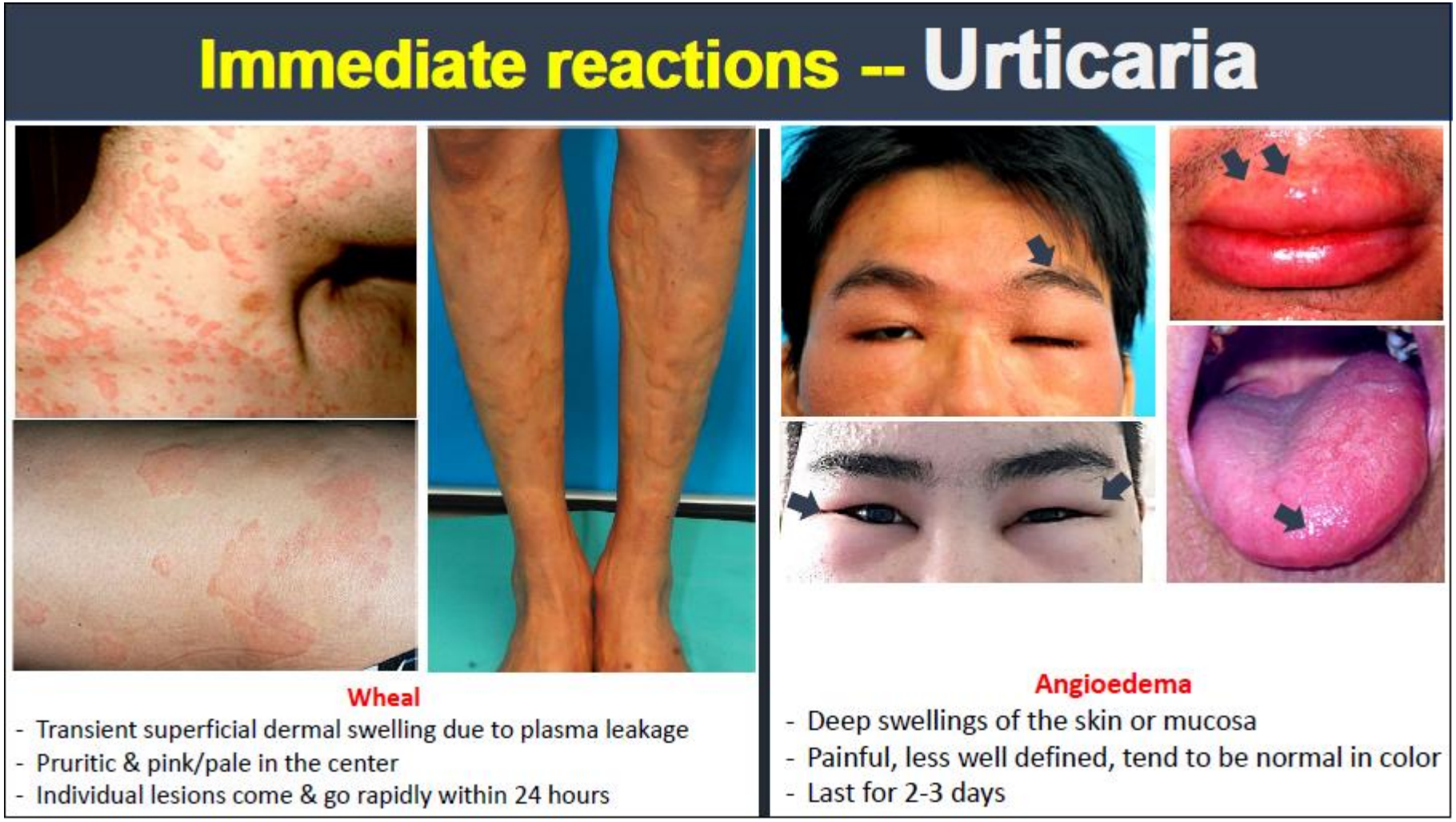
Adrenaline administration is the cornerstone for anaphylaxis treatment and is not contraindicated even in elderly with comorbidities such as ischemic heart disease or hypertension. It is important for the vaccination center to have staff who are trained to recognise and manage anaphylaxis so that appropriate treatment is delivered while minimising unnecessary administration of adrenaline.

5.4. Differences between anaphylaxis, vasovagal reaction and panic attack

Characteristics	Anaphylaxis	Vasovagal reaction	Panic attack
Onset	Usually within 15 minutes after immunization, but can occur within hours	Sudden, occur before, during or after immunization	Sudden, occur before, during or after immunization
Cutaneous	• Urticaria, pruritus with or without rash and angioedema (face and tongue) • Warm skin, progressing to clammy and pallor	Pallor, sweating, clammy skin, pallor	Sweating
Respiratory	Upper airway swelling, bronchospasm, respiratory distress, sensation of throat closure/swelling	Normal or shallow	Hyperventilation, sensations of shortness of breath
Cardiovascular	• Hypotension (systolic pressure <90mmHg) • Tachycardia (rapid, weak, irregular)	• Hypotension • Bradycardia (slow, weak but regular)	Tachycardia
Neurological	Anxiety	Lightheaded, weakness, clonic seizure activities	Anxiety, lightheaded, dizzy, paresthesias in lips and fingertips
Gastrointestinal	Nausea, vomiting, abdominal pain, diarrhoea	Nausea, vomiting	Nausea, abdominal pain

Treatment	See protocol.	• Place patient in a recumbent position and elevate legs above head (or have patient sit with head between their knees) • Ventilate the room well • Give reassurance	Reassurance
Prevention	Avoid in those who had history of anaphylaxis or severe reactions to previous vaccines including the first dose of COVID-19 vaccine or any ingredient in an COVID-19 vaccine.	• Do not vaccinate a standing person • Before vaccinating ask if he/she tends to faint; if so, ask patient to lie down	May consider psychiatry evaluation before vaccination if the level of anxiety is uncontrollable and disturb the functioning.

5.5. Immediate reactions: Clinical photographs of urticaria and definition



6. Frequently Asked Questions

6.1. General

6.1.1 Vaccine Safety	
Can a person get COVID-19 from the vaccine?	No. None of the vaccines approved for use contain live SARS COV-2 virus, so they cannot cause COVID-19 illness. Vaccines prime your immune system to recognize and fight off a disease, but they do not actually cause an infection.
What are the possible side effects of the COVID-19 vaccine? Will a person feel unwell after vaccination?	The side effects may include pain, redness, swelling and itchiness where the vaccine was given. Some people experience local injection site reactions within 1-2 days after the vaccine, but they are usually self-limiting. Other side effects include tiredness, headache, fever, chills, muscle or joint soreness, nausea and vomiting. Most people feel those side effects slightly more after the second dose.
Are vaccine side effects a good sign?	The side effects are part of the immune response to the vaccine. However, everyone's reaction to the vaccine is different, so the absence of side effects after vaccination does not mean the vaccine is not working.
6.1.2 Vaccine eligibility	
Can someone who is a close contact of a confirmed COVID-19 case be vaccinated?	Yes. Once completed 10 days of quarantine/isolation and no new symptoms to suggest acute COVID-19 infection.
How soon after acute illness or surgery can a person be vaccinated?	To defer vaccination until recovery from acute illness or surgical procedure and a person can perform usual / normal activities.
Can a person on immunosuppressive agents be vaccinated? (e.g. SLE, RA)	Yes. To discuss with patient's healthcare provider regarding the optimal timing of vaccination. *Please note that there is insufficient efficacy data in immunocompromised hosts. Individuals with immunosuppression may not make a full immune response to vaccination.*

Can a person with the following underlying conditions receive COVID-19 vaccine? ● DM ● Hypertension ● Dyslipidemia ● Chronic kidney diseases ● Chronic Respiratory diseases: ○ Bronchial asthma * ○ COPD ○ Chronic lung disease e.g., Bronchiectasis ● Chronic heart and vascular diseases ● Obesity, BMI >30 kg/m²	A person with pre-existing chronic illness is more likely to progress to severe disease, hence recommended for COVID-19 vaccination. **Poorly controlled asthma should be assessed by the treating physician for suitability and timing of the COVID-19 vaccination*
Can a person with the following underlying conditions be vaccinated? 1. Solid organ cancers on active chemotherapy, radiotherapy or immunotherapy (excluding hormonal treatment) 2. Patients on long term immunosuppressive treatment who receive : • systemic steroids for > 1 month at a daily dose equivalent to prednisolone ≥ 20mg • immunomodulating therapy 3. Transplant's recipients (solid organ/bone marrow/stem cell)	To discuss with the patient's healthcare provider regarding the optimal timing of COVID-19 vaccination. For transplant's recipients, vaccination can be given at least 3 months after transplantation if patient is stable. *Notes: COVID-19 vaccine is not a live vaccine; hence it is not contraindicated for the immunocompromised.* *Immunocompromised hosts are at high risk of severe COVID-19 infection. However, there is insufficient data on the efficacy of vaccine in immunocompromised hosts.*
Can PLHIV be vaccinated?	Yes, PLHIV should receive vaccination regardless of CD4 or viral load. However; • PLHIV with lower CD4 counts or has just started on ARVs may suffer from opportunistic infections or IRIS. This may be misinterpreted as post-vaccination side effects. Defer vaccination until patients are more stable.

	• PLHIV with lower CD4 count may not mount full level of protection as the immunocompetent hosts. Defer vaccination until at least 3 months after initiation of ART. • PLHIV in older age group (> 60 years old) or with chronic disease should be prioritised compared to those stable on HAART.
Can a person with chronic liver disease including Chronic Hepatitis B/C be vaccinated?	Yes, a person with stable chronic liver disease may receive vaccination. However, if a person is in the decompensated stage, decision may be made on an individual basis, if the benefits outweigh the risks. Consider prioritization for vaccination after discussion with the healthcare provider.
Can a person with underlying mental illness be vaccinated?	Yes. Individuals with schizophrenia or bipolar disorder, or any mental illness that causes severe functional impairment are recommended to be vaccinated.
6.1.3 Neurological conditions	
Can COVID-19 vaccines cause Bell's palsy?	Bell's palsy post-vaccination has been reported, however causal relationship with vaccines has not been determined. Bell's palsy was reported in 6 of 34,000 participants enrolled in clinical trials of Pfizer-BioNTech and Moderna vaccines; this incidence is not higher than in the general population.
Can a person with a previous history of Bell's palsy receive Covid-19 vaccine?	Yes, may proceed for vaccination considering the benefits outweigh risks. There are case reports on persons with recurrent Bell's palsy which developed post vaccination, however the causal association with COVID-19 vaccine was not concluded.

Can a person who developed Bell's palsy after the first dose COVID-19 vaccine, to receive a second dose?	Yes, second dose may be given after assessment by clinician. Assessment should be carried out to rule out other causes of CN VII palsy. Management should be according to standard practice and notified as AEFI. To discuss with a physician/neurologist if necessary. Vaccine recipient should be counselled regarding: ● effect of corticosteroids (equivalent to prednisolone >20mg OD for 14 days) on the safety and efficacy of COVID-19 vaccines is currently unknown. ● to proceed with vaccination while being treated for Bell's palsy versus delaying vaccination until after completion of treatment.
Do COVID-19 vaccines cause GBS or ADEM?	To date, no GBS or ADEM has been reported post-vaccination of Pfizer-BioNtech or other COVID-19 vaccines. GBS and ADEM has been reported with temporal relationship after vaccination for other infection, e.g. influenza vaccines, however causal association is not proven.
6.1.4 Haematological disorders, anticoagulant and antiplatelet therapy	
Can patients with thrombocytopenia be vaccinated?	Patients with **platelet count > 50,000** can be vaccinated without additional haemostatic support. Patients with **platelet count < 50,000** should defer the vaccination till their platelet counts recover, if possible. For those with chronically low platelet counts, vaccination should be performed in consultation with their primary haematologist.
Can a patient with haemophilia and other rare bleeding disorders be vaccinated?	For patients with severe/moderate haemophilia, the vaccine injection should be given after a prophylactic dose of Factor VIII (FVIII) or Factor IX (FIX). For patients with a basal FVIII or FIX level above 10%, no haemostatic precautions are required. Patients with other rare bleeding disorder including platelet function disorders should be vaccinated in consultation with their primary haematologists.

Can patients receiving anticoagulants be vaccinated?	1. Warfarin ● Can be vaccinated if INR < 4.0 ● If INR ≥ 4.0, to discuss with the patient's healthcare provider on the optimal timing of vaccination and precautions to be considered. 2. DOAC (eg. Apixaban, Dabigatran) or LMWH ● Delay the dose on the day of vaccination until after the injection but do not need to miss any dose
If patient has taken warfarin on the day of scheduled vaccination, can patient proceed with vaccination?	Yes. The risk of haematoma formation is reduced by applying firm pressure at the injection site for at least 5 minutes.
Do I need to take another INR before vaccination?	No, unless the patient missed their last scheduled visit.
Can patients with higher intensity anti-thrombotic treatment, for example warfarin with a target INR >4.0 or dual antithrombotic medications be vaccinated?	These patients should be managed on an individual basis and in consultation with their primary physician, to discuss regarding the optimal timing of vaccination.
Are there any special precautions to be taken during vaccination of patients on anticoagulation therapy and bleeding disorder?	Patients receiving anticoagulant therapy or bleeding disorder may develop haematomas in IM injection sites. The risk of haematoma formation is reduced by applying firm pressure at the injection site for at least 5 minutes. Use a 25- or 27-gauge needle to reduce the pressure gradient and cause fewer traumas to the tissue. Vaccine should be injected slowly (≥5 seconds) to reduce the risk of tissue damage. Stabilisation of the limb will reduce risk of haematoma. Bleeding risk can be reduced by application of firm pressure at injection site for at least 10 minutes. The site should not be rubbed or massaged and inspect injected limb after several minutes and 2-4 hours and to report any concerns immediately
Can patients on single antiplatelet therapy (aspirin or clopidogrel) be vaccinated?	Yes. Can continue these medications without any adjustment.

6.1.5 Post COVID-19 infection	
Should a person who already had COVID-19 infection be vaccinated?	Yes. Vaccination should be deferred until the person has recovered from the acute illness (if symptomatic) and they have met criteria to discontinue isolation.
Should a person who is diagnosed with COVID-19 infection after the first dose of vaccine, get the second dose?	Yes, the second dose should be administered once the person has recovered from the acute illness (if symptomatic) and they have met criteria to discontinue isolation.
Can a person who received convalescent plasma or monoclonal antibodies as part of therapy for COVID-19 infection be vaccinated?	Yes. Defer vaccination at least 3 months after recovery from COVID-19 infection.
Should people who are suffering from Long COVID (Post- acute sequelae of COVID-19) get vaccinated?	Yes, there is no evidence of any safety concerns from vaccinating individuals with COVID-19 infection sequelae.
6.1.6 Miscellaneous	
If a person is unable to take the second dose of a vaccine, can a different vaccine brand be given as a second dose?	No, COVID-19 vaccines are not interchangeable. *Currently, there is no data to support the efficacy and safety of using one brand of vaccines for the first dose and another for the second.*
Can a person receive another (non-COVID-19) vaccine at the same time as COVID-19 vaccine?	COVID-19 vaccinations should be separated by at least 14 days from any other vaccine (before or after).
When can a person donate blood after receiving COVID-19 vaccine?	Blood donation to be deferred at least 7 days post vaccination. If any mild side effect occurs post vaccination, to defer until 7 days after symptoms resolution.
6.1.7 Immunization Stress Related Response (ISRR)[1]	
What is ISRR?	ISRR is an AEFI arising from anxiety about immunization. Manifestations include signs and symptoms of vasovagal-mediated, hyperventilation-mediated and/or stress-related neurological and psychiatric reactions after vaccination or even immediately before vaccination.

Should the second dose be administered in a person with ISRR after the first dose?	Yes
What is the management of stress & anxiety post vaccination?	Identify those with needle fear and at risk of having ISRR early. Provide a private and calm space for the vaccination. Communicate clearly, explain & reassure. General principle of managing an acute stress response is with calm, reassuring, positive communication with the vaccine recipient until resolution of symptoms. Patients with vasovagal reaction should be placed in the supine position and practise muscle tension. Once an ISRR is identified, the vaccinator should clearly explain that it was not related to the vaccine product, immunization program or procedure error. The nature of the symptoms which are not harmful and will spontaneously resolve without medication should be explained. More complex presentations such as dissociative neurological symptom reaction with or without non-epileptic seizures warrant multidisciplinary team for medical & psychological assessment.

References:

1. World Health Organization (2019). Immunization stress-related response. *A manual for program managers and health professionals to prevent, identify and respond to stress related responses following immunization.* Geneva. Available at: < https://www.who.int/publications/i/item/978-92-4-151594-8> [Accessed 17 March 2021].

6.2. Pfizer-BioNTech (*Comirnaty®*)

6.2.1 About *Comirnaty®*	
What type of vaccine is *Comirnaty®*?	It is an mRNA vaccine.
What does an mRNA vaccine contain?	The vaccine contains a synthetic, small piece of SARS-CoV-2 genetic material (mRNA) that encodes for a spike protein of SARS-CoV-2 virus. The vaccine also contains water, salts, sugars and lipids. In the vaccine, the mRNA is placed inside a lipid nanoparticle that helps to deliver it to the cell.
How is *Comirnaty®* given?	The vaccine is given via an intramuscular injection at deltoid region
How do mRNA vaccines work?	The mRNA instructs cells to initiate host production of SARS COV-2 spike protein copies, which in turn triggers the immune system to create antibodies in response to the foreign viral protein
How many doses of *Comirnaty®* does a person need?	2 doses at 3 weeks (21 days) apart.
Can the second dose of *Comirnaty®* be administered at less than the recommended interval of 21 days?	The second dose should be administered as close to the recommended interval as possible, but not earlier than recommended. Under unforeseen circumstances a grace period of 4 days earlier than the recommended date is still considered valid.
Can the second vaccine dose be deferred for more than 3 weeks?	The second dose should be given at day 21. Under unforeseen circumstances, the second dose may be deferred up to 6 weeks (42 days) from the first dose. If the second dose is not given within this time frame, it should be given as soon as feasible and vaccine series need not to be restarted.
Are booster doses needed after the series is completed?	The need for and timing of booster doses for mRNA COVID-19 vaccines has not been established. No additional doses beyond the two-dose primary series are recommended at this time.

6.2.2 Vaccine Safety	
Do mRNA vaccines alter DNA?	No, because mRNA does not access the nucleus of cells, so it cannot be incorporated into DNA. mRNA vaccines lack all the basic requirements necessary to alter DNA. The mRNA remains in the cell cytoplasm for just a few days before it is destroyed.
Can a person get COVID-19 from the vaccine?	No. None of the vaccines approved for use contain live SARS COV-2 virus, so they cannot cause COVID-19 illness. Vaccines prime your immune system to recognize and fight off a disease, but they do not actually cause an infection.
6.2.3 COVID-19 Prevention	
Does *Comirnaty*® prevent COVID-19?	In clinical trials *Comirnaty*® was found to be 95% effective in preventing the disease.
Do the vaccines provide long-term protection and immunity?	The vaccine has been designed specifically to give reliable, lasting immunity; however, it is yet to be determined how long it offers protection.
Does the vaccine work against variants?	Study showed *Comirnaty*® effectively neutralized the coronavirus strain first detected in Brazil, as well as the U.K. variant, and had a "robust but lower" effectiveness against the South Africa variant
6.2.4 Pregnancy and breastfeeding	
Can women who are pregnant or plan to get pregnant be vaccinated?	Women who are pregnant, or are planning to get pregnant, should discuss with their health care provider about the vaccine's benefits and risks. Decisions for vaccination may be based on the risk of exposure to COVID-19 infection (e.g., frontliners) and the risk of getting severe disease (e.g., high risk with co-morbidities).
When can a pregnant mother be vaccinated?	Between 14-33 weeks of gestation
Should the second dose be administered to a woman who finds out she is pregnant after getting the first dose?	Yes. However, the second dose should be deferred until 14 weeks of gestation.

Can breastfeeding mothers be vaccinated?	Yes. Vaccination is recommended in breastfeeding mothers where the exposure to COVID-19 infection is high (e.g. frontliners) or those at risk of getting severe disease (e.g. high risk with co-morbidities). There is no need to discontinue breastfeeding for any period after vaccination.
Will the baby of a vaccinated breastfeeding mother get the protection from COVID-19 infection?	There has been some evidence that the baby may also benefit from antibodies that may be introduced through breast milk after the mother is vaccinated via passive immunity.
How soon after completing vaccination series can a person undergo assisted reproductive therapy?	Consider postponing the start of assisted reproductive therapy for up to 2 months after completed vaccination.

6.3. Sinovac (*CoronaVac®)*

6.3.1 About *CoronaVac®*	
What is *CoronaVac®* vaccine used for?	It is a vaccine used to prevent COVID-19 infection caused by coronavirus (SARS CoV-2).
How does *CoronaVac®* work?	The vaccine, which contains (inactivated SARS-CoV-2 viruses) stimulates the immune system (the body's natural defences) to produce antibodies and blood cells that work against the virus. This will help to increase protection against COVID-19.
How is the *CoronaVac®* vaccine given?	It is administered intramuscularly, and the recommended immunisation schedule is 2 doses at 28 days interval.
Are booster doses needed after the series is completed?	No additional doses beyond the two-dose primary series are recommended at this time.
6.3.2 Vaccine Safety	
Can a person get COVID-19 from the vaccine?	No. *CoronaVac®* contains only the killed SARSCoV2 virus, so it will not cause COVID-19 infection to an individual receiving it.

6.3.3 COVID-19 Prevention	
Do the vaccines provide long-term protection and immunity?	The exact duration of protection from vaccination is not known for sure at the moment.
Does the *CoronaVac*® vaccine work against variants?	Further trials are required to confirm the efficacy of *CoronaVac*® to emerging SARSCoV2 variants.
6.3.4 Pregnancy and breastfeeding	
Can pregnant or breastfeeding women receive *CoronaVac*® vaccine?	According to the product information of *CoronaVac*® (at the time of review), it is not recommended in pregnant or breastfeeding women.

General resources:

1. Cdc.gov. 2021. *Vaccines and Immunizations | CDC*. [online] Available at: <https://www.cdc.gov/vaccines/index.html> [Accessed March 2021].

2. Covid 19 mortality review by the Clinical Audit Unit, Medical Care Quality Section, Medical Development Division, Ministry of Health Malaysia

3. Ireland's Health Services. 2021. *Clinical Guidance for COVID-19 Vaccination* [Version 10.1]. Available at: https://www.hse.ie/eng/health/immunisation/hcpinfo/covid19vaccineinfo4hps/clinicalguidance.pdf

4. Public Health England. 2021. COVID-19: the green book [Chapter 14a]. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/961287/Greenbook_chapter_14a_v7_12Feb2021.pdf

5. Sim, B., Chidambaram, S., Wong, X., Pathmanathan, M., Peariasamy, K., Hor, C., Chua, H. and Goh, P., 2020. Clinical characteristics and risk factors for severe COVID-19 infections in Malaysia: A nationwide observational study. *The Lancet Regional Health - Western Pacific*, 4, p.100055.

6. Singapore Ministry of Health. 2021. *UPDATED GUIDANCE ON THE INDICATIONS AND CONTRAINDICATIONS TO COVID-19 VACCINATION* [MOH Circular No. 29/2021

7. References

1. American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA: American Psychiatric Association

2. Australasian Society of Clinical Immunology and Allergy (ASCIA) (2021). *Allergy, Immunodeficiency, Autoimmunity and COVID-19 Vaccination Position Statement*. [online] Available at: <https://www.allergy.org.au/hp/papers/ascia-hp-position-statement-covid-19-vaccination> [Accessed 17 March 2021].

3. Bakhtiar MF et al. (2018). Non-steroidal anti-inflammatory drugs (NSAIDs) hypersensitivity phenotypes and their common triggering medications. *Clin Transl Allergy*, 8 (Suppl 3), P130.

4. Banerji A, Wickner PG, Saff R, Stone CA Jr, Robinson LB, Long AA et al.(2020, Dec 31). mRNA Vaccines to Prevent COVID-19 Disease and Reported Allergic Reactions: Current Evidence and Suggested Approach. *J Allergy Clin Immunol Pract*.,S2213-2198(20), 31411-2.

5. Cardona V, Ansotegui IJ, Ebisawa M, El-Gamal Y, Fernandez Rivas M, Fineman S, et al. (2020). World allergy organization anaphylaxis guidance 2020. *The World Allergy Organization journal*, 13(10),100472.

6. Cdc.gov. (2008). *Syncope After Vaccination --- United States, January 2005--July 2007.MMWR*, 57(17), 457-460 [online] Available at: <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5717a2.htm> [Accessed 18 March 2021].

7. Centers for Disease Control and Prevention (2021). *COVID-19 Vaccines and Severe Allergic Reactions*. [online] Available at: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/allergic-reaction.html> [Accessed 18 March 2021].

8. COVID C, Team R. (2021). Allergic reactions including anaphylaxis after receipt of the first dose of Moderna COVID-19 Vaccine—United States, December 21, 2020–January 10, 2021. *Morbidity and Mortality Weekly Report*, 70(4),125.

9. De Feo G, Parente R, Triggiani M. (2018). Pitfalls in anaphylaxis. *Current opinion in allergy and clinical immunology*., 18(5), 382-6.

10. HAE International (2021). *HAEi Webinar Brief about HAE and COVID-19 vaccine. HAE International (HAEi)*. [online] Available at: <https://haei.org/haei-webinar-brief-about-hae-and-covid-19-vaccine> [Accessed 17 March 2021]

11. JAMES J. ARNOLD D, and PAMELA M. WILLIAMS.(2011, Nov15). Anaphylaxis: Recognition and Management. *American Family Physician*, 84(10), 1111-1118.

12. Kleine-Tebbe, J., Klimek, L., Hamelmann, E., Pfaar, O., Taube, C., Wagenmann, M., Werfel, T. and Worm, M. (2021). Severe allergic reactions to the COVID-19 vaccine – statement and practical consequences. *Allergologie select*, 5(01), pp.26-28.

13. Lukawska J et al.(2019). Anaphylaxis to trometamol excipient in gadolinium-based contrast agents for clinical imaging. *J Allergy Clin Immunol Pract*., Mar;7(3):1086-1087.

14. *National Pharmaceutical Regulatory Agency (NPRA). 2021. Reporting ADR. [online] Available at: <https://npra.gov.my/index.php/en/health-professionals/reporting-adr> [Accessed 20 March 2021].*

15. Nokleby H. (2006). Vaccination and anaphylaxis. *Current allergy and asthma reports*., 6(1), 9-13

16. Public Health England (2021). *Guidance COVID-19: the green book, chapter 14a Coronavirus (COVID-19) vaccination information for public health professionals.*. [online] Available at: <https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/961287/Greenbook_chapter_14a_v7_12Feb2021.pdf> [Accessed 18 March 2021].

17. Rama, T., Moreira, A. and Castells, M. (2021). mRNA COVID-19 vaccine is well tolerated in patients with cutaneous and systemic mastocytosis with mast cell activation symptoms and anaphylaxis. *Journal of Allergy and Clinical Immunology*, 147(3), pp.877-878.

18. Rcpi.ie. (2021). *Frequently Asked Questions about COVID-19 vaccines for people with pre-existing allergic conditions*. [online] Available at: <https://www.rcpi.ie/news/releases/frequently-asked-questions-about-covid-19-vaccines-for-people-with-pre-existing-allergic-conditions/> [Accessed 17 March 2021].

19. Rukma P.(2019). Glucagon for refractory anaphylaxis. American journal of therapeutics., 26(6), e755-e6.

20. Section of Clinical Immunologists and Allergist College of Physicians Singapore (2021,March). *Consensus Statement COVID-19 Vaccination for Individuals with Allergic/Hypersensitivity Disorders*. [online] Available at: <https://www.ams.edu.sg/view-pdf.aspx?file=media%5c5976_fi_19.pdf&ofile=COVID19+Vaccination+for+Individuals+with+Allergic+or+Hypersensitivity+Disorder+(5+March+2021).pdf> [Accessed 18 March 2021].

21. Shimabukuro TT, Cole M, Su JR. (2021). Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US—December 14, 2020-January 18, 2021. JAMA, 325(11),1101-2.

22. Soar J, Pumphrey R, Cant A, Clarke S, Corbett A, Dawson P, et al.(2008). Emergency treatment of anaphylactic reactions—guidelines for healthcare providers. Resuscitation.,77(2),157-69.

23. Sreevastava DK, Tarneja VK.(2003). Anaphylactic Reaction: An Overview. *Med J Armed Forces India*., 59(1), 53-6.

24. Turner PJ, Jerschow E, Umasunthar T, Lin R, Campbell DE, Boyle RJ. (2017). Fatal anaphylaxis: mortality rate and risk factors. *The Journal of Allergy and Clinical Immunology: In Practice*., 5(5), 1169-78.

25. Turner PJ, Ansotegui IJ, Campbell DE, Cardona V, Ebisawa M, Yehia E-G, et al. (2021). COVID-19 vaccine-associated anaphylaxis: A statement of the World Allergy Organization Anaphylaxis Committee. *World Allergy Organization Journal*, 100517.

26. *Vaccine-safety-training.org. (2021). MODULE 3 – Classification of AEFIs - WHO Vaccine Safety Basics. [online] Available at: <https://vaccine-safety-training.org/classification-of-aefis.html> [Accessed 20 March 2021].*

27. Vanlander, A. and Hoppenbrouwers, K. (2014). Anaphylaxis after vaccination of children: Review of literature and recommendations for vaccination in child and school health services in Belgium. *Vaccine*, 32(26), pp.3147-3154.

28. LM, Lieberman P.(2006). Anaphylaxis: a review of 601 cases. *Annals of Allergy, Asthma & Immunology*. , 97(1), 39-43.

Appendix 1

RECOMMENDATIONS FOR COVID-19 VACCINATION IN THE ELDERLY FRAIL AND TERMINALLY ILL POPULATION - BY THE GERIATRIC MEDICINE AND PALLIATIVE MEDICINE FRATERNITY, MINISTRY OF HEALTH

Based on current evidence and expert opinions from the geriatric and palliative medicine fraternities, recommendations for COVID-19 vaccination in the elderly frail and terminally ill population are as follows:

1. Persons who are elderly and frail should be ENCOURAGED to have COVID-19 vaccination as the benefits still outweigh risks of COVID-19 infection.

2. Persons with incurable illnesses such as metastatic cancer, dementia, congestive cardiac failure etc. COVID-19 vaccination is still RECOMMENDED unless the person is actively deteriorating with an estimated survival of less than 1 month.

3. Patients requiring palliative care **should not be immediately considered terminally ill** and should be ENCOURAGED to have COVID-19 vaccination if their estimated survival is more than 3 months.

4. Clinical Frailty Scores (CFS) should not be used as the sole criteria to exclude or include an elderly person from COVID-19 vaccination. Persons with high CFS should be further assessed clinically to determine if vaccination is appropriate or to be deferred.

5. Persons who are very frail who receive the COVID-19 vaccination should be monitored post vaccination for at least 72 hours for symptoms of fever, poor oral intake, confusion and weakness which may lead to an acute deterioration in condition. If such symptoms arise appropriate supportive measures should be provided till these symptoms resolve.

6. For persons who lack capacity to decide/consent for vaccination due to conditions such as dementia, stroke, brain injuries etc., family members/careers may decide/consent on behalf of the person.

7. When discussing the role and benefits of vaccination for the elderly frail and palliative care population, it should be mentioned that among the benefits of vaccination would also include the following:

    a. Ease of care and subsequent management in the event of hospitalization or acute illness as isolation procedures may be minimized.
    b. Vaccination will enable better social interaction to occur with family and friends.
    c. Care home residents will protect all other members of the home and minimize risk of outbreaks within the care home.
    d. Preferences for end-of-life care may be more easily fulfilled as there will be less risk of COVID-19 infection and the need for public health procedures.

Table 1: Vaccination criteria for frail elderly

Condition	Home *(Family/carer to register person)*	Residential Care *(Responsible carer in home to register person)*	Clinical Assessment *(performed by any clinician reviewing patient at hospital, outpatient or homecare setting)*
Fit to mild frailty *(Clinical Frailty Score 1-5)*	**Vaccination is encouraged** - Consent may be by patient or carer	**Vaccination is encouraged** - Consent may be by patient or carer	Pre-vaccination assessment not required
Moderate to severe frailty *(Clinical Frailty Score 6-7)*	**Vaccination is encouraged** - Consent may be by patient or carer	**Vaccination is encouraged** - Consent may be by patient or carer. - May involve care home management	Patient must be stable in that there are no on-going medical problems such as acute or recurrent/persistent infections or complications where on-going deterioration is anticipated.
Very severely frail *(Clinical Frailty Score 8)*	**Vaccination should still be encouraged if patient is not actively dying and there are no acute medical issues** - If patient unable to consent then family or carer who is informed of risk & benefits to consent	**Vaccination should still be encouraged if patient is not actively dying and there are no acute medical issues** - If patient unable to consent then family or carer who is informed of risk & benefits to consent.	Signs of active dying include declining vital signs and clinical condition in the face of medical complications which are not reversible. (eg. Sepsis not responding to antibiotics or severe AKI not for dialysis)

		- May involve care home management	
Terminally ill / Patients requiring palliative care	**Vaccination is encouraged unless actively deteriorating with an expected prognosis of less than 1 month)**	**Vaccination is encouraged unless actively deteriorating with an expected prognosis of less than 1 month**	The prognosis of patients requiring palliative care can range from more than 6 months to just a few weeks. Patients in this category should therefore not be excluded from vaccination unless they are in the last stages of their disease trajectory where the expected duration of survival is less than 1 month. Signs of active deterioration includes weekly deterioration in performance status (very disabled to bed bound) and progressive decline in oral intake as well as congnitive function.

REFERENCES:

1. Centres for Disease Control and Prevention, Covid-19 Vaccination 2. R.L. Soiza et al, Efficacy and safety of COVID-19 vaccines in older people, Age and Ageing 2021; 50: 279–283

2. Age and frailty in COVID-19 vaccine development. The Lancet, 2020. https://doi.org/10.1016/ S0140-6736(20)32481-8

3. COVID-19 vaccination – COVID-19 vaccination decision guide for frail older people, including those in residential aged care facilities, Melbourne Vaccine Education Centre

4. Torjesen I. Covid-19: Doctors in Norway told to assess severely frail patients for vaccination. BMJ 2021;372: n167 http://dx.doi.org/10.1136/bmj.n167

5. Torjesen I. Covid-19: Norway investigates 23 deaths in frail elderly patients after vaccination. BMJ 2021 ;372: n149. doi: 10.1136/bmj. n149 pmid: 33451975 2 NICE. Clinical Frailty Scale. https://www.nice.org.uk/guidance/ng159/resources/clinical frailtyscale-pdf-8712262765.

6. Guidance on shielding and protecting people who are clinically extremely vulnerable from COVID-19. Downloaded from www.gov.uk on 10th March 2021

7. COVID-19 vaccine and cancer – latest updates. Downloaded from https://scienceblog.cancerresearchuk.org/2021/03/02/covid-19-vaccine-and-cancer-latest-updates/ on 10th March 2021

8. Ribas A. et al. Priority COVID-19 Vaccination for Patients with cancer while Vaccine supply Is Limited. Cancer Discovery 2021

9. Preliminary recommendations of the NCCN COVID-19 Vaccination Advisory Committee. National Comprehensive Cancer Network. January 22, 2021; Accessed: February 25, 2021. https://www.nccn.org/covid- 19/pdf/COVID-19_Vaccination_Guidance_V1.0.pdf.

10. Lim SHB et al. Clinical characteristics and risk factors for severe COVID-19 infections in Malaysia: A nationwide observational study. Lancet Regional Health-Western Pacific, Nov 2020

11. Christina Chu C, White N., Stone P; Prognostication in Palliative Care. Clinical Medicine Jul 2019;19 (4) 306-310; DOI: 10.7861/clinmedicine.19-4-306

Appendix 2

GUIDELINES ON COVID-19 VACCINATION IN OBSTETRICS & GYNAECOLOGY
VERSION 1
Updated 23rd MARCH 2021

1. KEY RECOMMENDATIONS

a. Pregnant mothers are considered a vulnerable cohort susceptible to severe COVID-19 infections, especially in the second and third trimester.

b. Those with underlying medical illnesses are considered to be at a higher risk. Maternal age of ≥ 40 and BMI ≥ 40kg/m^2 are among identifiable risk factors for severe COVID-19 infection in pregnancy.

c. Although most pregnant mothers are asymptomatic, the need for ICU admission and mechanical ventilation are higher, particularly with infection by the newer strains. Severe infections in pregnancy are associated with higher risk of pulmonary embolism, iatrogenic prematurity, stillbirth and maternal mortality.

d. Although evidence with regards to the safety of COVID-19 vaccination continues to evolve, as initial studies did not include pregnant mothers, virology principles and recent data suggest that these vaccines are safe in pregnancy and breastfeeding. Evidence continues to emerge as more pregnant mothers are included in the study cohort.

e. Protecting pregnant mothers who are vulnerable, especially those with identifiable risk factors should remain a health care priority for vaccination. COVID-19 vaccination however, does not provide neonatal immunity. Other routine vaccinations such as Influenza and TDAP can also be safely administered 14 days apart.

f. COVID-19 vaccination should be advocated in pre-pregnancy care, especially for mothers with identifiable risk factors and also those seeking infertility treatment.

g. Routine pregnancy screening with urine pregnancy test prior to vaccination is not recommended. Vaccination of girls below the age of 18 is also not advisable at this moment.

h. High risk gynae-oncological patients are also susceptible and should be prioritized to receive vaccination. Since it is a not a live vaccine, chemotherapy and radiation are not contraindicated.

Note:

Evidence on COVID-19 vaccine continues to evolve as more data is acquired during real-world application. Theoptimal interval between doses remains controversial at the time of writing. Although the authors strive to ensure that information contained within this guideline is accurate at the time of writing, clinicians are responsible to keep abreast with the latest development.

2. OBSTETRICS

2.1. FACTS AND RATIONALE FOR COVID-19 VACCINATION IN PREGNANCY

Pregnant women with Covid-19 infection in pregnancy have an *increased* risk of pneumonia, intensive care admission, invasive ventilation, death and preterm birth.

Pregnant and recently pregnant women with COVID-19 infection are more likely to require intensive care unit admission (1.62, 1.33 to 1.96; I^2=0%; 4 studies; 91606 women) and invasive ventilation (1.88, 1.36 to 2.60; I^2=0%; 4 studies; 91606 women) as compared to non-pregnant women of reproductive age.[1]

These findings were consistent with data from the ongoing prospective COV19Mx cohort in Mexico, where propensity score matching was used to adjust for other risk factors or co-morbidities. Amongst the 5183 pregnant and 5183 non-pregnant matched women, pregnant women had a higher odds of death (odds ratio (OR), 1.84; 95% CI, 1.26–2.69), pneumonia (OR, 1.86; 95% CI, 1.60–2.16) and ICU admission (OR, 1.86; 95% CI, 1.41–2.45) than non-pregnant women. The odds of intubation however, were similar (OR, 0.93; 95% CI, 0.70–1.25).[2]

Severe illness appears to be more common in the second and third trimester. In the UKOSS study, most women were hospitalized in their third trimester or peripartum (n = 342, 81%). The median gestational age at hospital admission was 34+0 weeks of gestation (interquartile range [IQR] 29–38 weeks).[3] A retrospective multicentre study involving 190 women from France and Belgium also showed that women were five times more likely to be admitted to the ICU in the second half, compared to the first half of pregnancy. [4]

The overall rate of preterm birth was 17% (13 to 21%; 30 studies; 1872 women), although the majority were iatrogenic, including to facilitate ventilation. This was a 3-fold increase compared to pregnant women without disease.[1] In another cohort of 64 pregnant women with severe or critical COVID-19 disease, up to 75% of women delivered preterm.[5] Spontaneous preterm birth rate was 6% (3% to 9%; I^2=55%; 10 studies; 870 women).[1]

Thus, vaccinating pregnant mothers with identifiable risk factors not only improves maternal morbidity and mortality but also reduces fetal morbidity from preterm deliveries.

2.2. SAFETY OF COVID-19 VACCINES IN PREGNANCY

Despite the lack of involvement of pregnant women in clinical trials during development of COVID-19 vaccines, contemporary scientific knowledge indicates that COVID-19 vaccinations among pregnant and breastfeeding mothers are likely to be safe. There is no known risk with giving inactivated virus or bacterial vaccines or toxoids during pregnancy or whilst breast-feeding. Furthermore, pregnant women have been receiving vaccines such as tetanus toxoid, influenza and pertussis vaccination (TDaP) without demonstrable harm to the fetus.[6]

Both Pfizer-BioNTech and Moderna are mRNA-based vaccines which builds “spike proteins”, mimicking the surface protein of SARS-COV-2 to trigger an immune response. These vaccines do not contain live SARS-CoV-2 and hence is not infective to the pregnant mother and her fetus.

A developmental and reproductive toxicity (DART) study to assess potential fertility and pre and postnatal development effects of mRNA-1273 (Moderna) in pregnant and lactating female Sprague Dawley rats has been completed. The U.S Food and Drug Administration (FDA) review of this study concluded that mRNA-1273 given prior to mating and during gestation periods at dose of 100 µg did not have any adverse effects on female reproduction, fetal/embryonal development, or postnatal developmental except for skeletal variations which are common and typically resolve postnatally without intervention. Pregnancy-related animal data for the Pfizer-BioNTech vaccine also seem to point toward similar conclusions. [7]

Although the data from women who had inadvertently receive COVID-19 vaccine while pregnant are small, the outcomes are reassuring. 13 pregnancies were reported, 6 in the mRNA-1273 arm and 7 in the placebo arm respectively. 10 out of the 13 pregnancies were on going without complications. Among those in the placebo group, one patient experienced spontaneous miscarriage at 7 weeks of gestation, another had an elective termination at 6 weeks while another patient was lost to follow up while no adverse outcomes were reported in the mRNA-1273 group.[8]

The Centers for Disease Control and Prevention (CDC) has set up a smartphone application called ”v-safe" to solicit reports of side effects from immunized people. About 15,000 pregnant women have enrolled in the registry at the time of writing and this will likely provide more evidence of its safety.[9]

Use of COVID-19 vaccine in pregnancy and lactation is off-label. However, clinicians should reassure women that the benefits outweight risks for emergent use during a pandemic.

2.3. SIDE EFFECTS

Common side effects are arm pain, headache, muscle aches, chills and fatigue which are usually self-limiting and resolves after a few days. Women with severe allergies or previous anaphylaxis, especially to polyethylene glycol (PEG) and polysorbate should avoid COVID-19 vaccination until further data is available.

	Injection Site Reactions	Fatigue	Chills	Muscle Pain	Joint Pain	Headaches
Moderna	91.6%	68.5%	43.4%	59.6%	44.8%	63%
Pfizer-BioNTech	84.10%	62.90%	31.90%	38.30%	23.60%	55.10%

**Fever was the least common side effect reported; see text above for data on frequency of fever*

Table 2: Common side effects of COVID-19 Vaccinations[10]

Women who develop fever after vaccination should be counseled on taking acetaminophen, which is safe in pregnancy and does not alter the immunologic response towards COVID-19 vaccine.[9]

2.4. PRE-PREGNANCY CARE

All women with identifiable risk factors should be advised to complete their vaccination before embarking on a pregnancy.

Routine pregnancy screening using urine pregnancy test prior to vaccination is not recommended. There are concerns that such measures may increase vaccine hesitancy and put off women against vaccination. It is essential to check for prior allergy risk and those declining vaccinations should be given more information on the benefits and safety of COVID-19 vaccination.

Those who are considered vulnerable include:

Age ≥ 40
BMI ≥ 40kg/m^2
Cardiac disease
Significant lung condition eg. Tuberculosis/ Severe asthma
Moderate and severe renal diseases
Connective tissue diseases such as SLE, Sjogren's Syndrome
Severe anemia
HIV patients
Patients with liver diseases – including Hepatitis B patients on antiviral
Patients on immunosuppressive therapy
Organ transplantation (including bone marrow / stem cell)
Currently undergoing cancer treatment
History of splenectomy / Apslenia
Pulmonary embolism or other underlying medical diseases

Table 1: Vulnerable groups in pregnancy

2.5. CRITERIA AND TIMING OF COVID-19 VACCINATION IN THE ANTENATAL PERIOD

Frontline workers, including non-healthcare workers who are at increased risk of repeated exposure to SARS-COV-2 due to the nature of their occupation, should ideally be vaccinated against COVID-19 particularly, if pregnant.

Pregnant frontline workers should receive priority in vaccination, due to the risk of repeated exposure to SARS-COV-2

Appreciating the current shortage of vaccines globally, prioritizing the vaccines for the vulnerable group of patients should remain an important criterion and those who will benefit from vaccinations are listed in Table 1.

Pregnant women who opt for vaccination should receive the first dose between 14 to 33 weeks of gestation

Vaccinating women early in pregnancy in the setting of a pandemic offers increased emergent protection against the virus. However, such a strategy also potentially reduces the rate of protection towards the end of pregnancy. There is still uncertainty about the duration of protection after completion of the 2-dose vaccine.

Vaccinating women in the second half of pregnancy protects women against COVID-19 disease which has been associated with greater morbidity in the third trimester.[4]

On the other hand, the first trimester is also a period of great uncertainty for some women and the risk of complications such as miscarriage is also highest. Despite the lack of evidence of harm on fetal/embryonal development from the developmental and reproductive toxicity (DART),[8] out of an abundance of caution to avoid suspicion of connection, even coincidental, between pregnancy and fetal harm, in our opinion, it is reasonable to begin vaccination after the first trimester.

2.6. CONCEIVING PRIOR TO COMPLETION OF VACCINATION IN PREGNANCY

Pregnant women who conceive after receiving the first dose may choose to delay the second dose until after 14 weeks

While it is possible to continue the second dose of vaccination in women who inadvertently conceive soon after the first dose, some women may be reassured by delaying this until after the first trimester. Based on the manufacturers' advice, the second dose can be delayed up to 6 weeks (Moderna, Pfizer-BioNTech) to 12 weeks (Oxford-Astra Zeneca). [11,12,13] There is currently no data on prolonging interval between vaccinations for other candidate vaccines such as Sinovac and Sputnik V. Single-dose vaccines, when available, may solve this conundrum. Options given to women who conceive or find out they are pregnant after receiving the first of two doses of vaccine is expounded in the appendix (Updated version 23rd March 2021).

2.7. CONCOMITANT USE OF OTHER VACCINES

There is no contraindication for administration of other essential vaccines in pregnancy such as Tdap and influenza. However, COVID-19 vaccines should not be administered within 14 days of receipt of another vaccine. [10]

2.8. ANTI-D IMMUNOGLOBULINS

Anti-D immunoglobulin (e.g., Rhogam) should not be withheld from women who are planning or have recently received a COVID-19 vaccine as it does not interfere with the immune response to the vaccine.[10]

2.9. NEONATAL PROTECTION

A critical benefit to vaccinating pregnant women against pertussis and to a lesser extent, influenza in the third trimester is that the vaccine protects the infant for several months after birth by the transplacental transfer disease-specific serum immunoglobulin G. In this way, antenatal vaccination helps protect not only the mother but also provides neonatal protection.

In contrast, the transfer of SARS-COV-2 maternal antibodies to the infant is inefficient when compared to vaccine-induced influenza antibodies. Therefore, it is unlikely that COVID-19 vaccination will provide protection to newborns. No vaccines are currently available to infants or young children.[9,14]

2.10. VACCINATION AND BREASTFEEDING

Cessation of breastfeeding is not recommended in lactating women

Many lactating women fall into categories prioritized for vaccination, such as front-line health care workers. Both the WHO Interim Guidance on the use of mRNA-1273 (Moderna) and the Academy of Breastfeeding Medicine do not recommend cessation of breastfeeding for individuals who are vaccinated against COVID-19. Similar to pregnant women who were excluded from COVID-19 vaccine trials, there is currently little data for nursing mothers. However, there is little biological plausibility that the vaccine will cause harm and antibodies to SARS-CoV-2 in milk may protect the breastfeeding child.

The vaccine is made of lipid nanoparticles that contain mRNA for the SARS-CoV-2 spike protein, which stimulate an immune response, protecting the individual from COVID-19 illness. During lactation, it is unlikely that the vaccine lipid would enter the blood stream and reach breast tissue. If it does, it is even less likely that either the intact nanoparticle or mRNA would transfer into milk. In the unlikely event that mRNA is present in milk, it would be expected to be digested by the child and would be unlikely to have any biological effects.

While there is little plausible risk for the child, there is a biologically plausible benefit. Antibodies and T-cells stimulated by the vaccine may passively transfer into milk. Following vaccination against other viruses, IgA antibodies are detectable in milk within 5 to 7 days. Antibodies transferred into milk may therefore protect the infant from infection with SARS-CoV-2.[15]

3. GYNAECOLOGY

3.1. ADOLESCENT & TEENAGE GIRLS

Vaccination is not recommended for those below the age of 18. The rationale for this is because firstly, they are not considered to be a vulnerable cohort and secondly, there is lack of data among this cohort. Furthermore, in view of the global shortage of vaccines at the moment, prioritizing those who need the vaccines are essential.

3.2. VACCINATION AND FERTILITY TREATMENT

Loss of fertility after vaccination is scientifically unlikely and none has been reported amongst trial participants

While fertility was not specifically studied in the clinical trials, no loss of fertility has been reported among trial participants or among the millions who have received the vaccines since their authorization. Furthermore, no signs of infertility appeared in animal studies.[16]

Consider postponing the start of ART treatment for up to 2 months after completion of vaccination

There are different viewpoints with regards to the need to postpone conception after vaccination. The American Society for Reproductive Medicine (ASRM) does not recommend delaying pregnancy attempts because of Covid-19 vaccination, including women undergoing fertility treatment. The European Society of Human Reproduction and Embryology (ESHRE) however, recommends a more cautious approach. It suggests postponing the start of assisted reproduction treatments (sperm collection, ovarian stimulation, embryo transfer) for at least a few days after the completion of vaccination (i.e., after the second dose) to allow time for the immune response to settle. It also adds that in the absence of information on the effect of the COVID-19 vaccine on oocytes and sperm, embryo implantation and early stages of pregnancy, and to allow time for antibody development, a more cautious approach could be considered (i.e., postpone the start of ART treatment for up to 2 months).[17,18]

3.3. WOMEN WITH GYNAECOLOGICAL MALIGNANCIES

Observations on influenza vaccination indicate the likelihood that most women with malignancies are able to mount sufficient immune response

Based on non-comparative retrospective studies, patients with cancer as a group have appear to be at higher risk of severe COVID-19. Patients with solid tumours, including gynaecological malignancies, are at increased risk particularly in the first year after diagnosis and if the disease is active. [19]

There is paucity of data on the immune response to vaccination in women with cancer.

However observational clinical studies on influenza vaccination suggests that cancer patients are able to mount an efficient immune response, based on the lower reported mortality and morbidity rates. The immunological response to vaccination also depends on the type of cancer, with better response reported for women with solid tumours compared to haematological malignancies.[20]

Whenever possible, the administration of the vaccine should be performed before initiation of chemotherapy. In patients who have already initiated chemotherapy, the existing data do not support a specific timing of administration with respect to chemotherapy infusions.

At the time of writing, COVID-19 vaccines available are not developed using live vaccines, which are contraindicated in women with malignancy. [21]

3.4. VACCINATION AFTER COVID-19 INFECTION

Some degree of natural immunity is gained after infection with SARS-COV-2 virus. However, it is uncertain how long this immunity might last, although reinfection appears uncommon within 6 months of a PCR-confirmed SARS-COV-2 infection.[13]

Due to the potentially severe health risks posed by COVID-19 and its widespread extent, women who are at risk should still be considered for vaccination against COVID-19. The timing of vaccination recommended after COVID-19 infection is listed below:

RISK LEVEL	RECOMMENDATION
Frontline workers, especially healthcare workers	Vaccination recommended if recovered from COVID-19 disease ≥ 3 months ago
Clinically vulnerable women	Vaccination recommended if recovered from COVID-19 disease ≥6 months ago
Women who had COVID-19 infection at any gestation in pregnancy	Vaccination is recommended after the puerperium (and ≥6 months post-infection) Frontline workers in this category should be considered for redeployment to an environment with lower risk of occupational exposure

3.5. CARE FOR WOMEN DECLINING VACCINATION

Women who are at risk but decline vaccination should have an opportunity for further discussion with an obstetrician and gynaecologist. This should be documented in their clinical notes. In addition, general measures for prevention of infection such as avoidance of crowds and unnecessary travel, use of a 3-ply mask in public areas, hand hygiene and compliance to standard operating procedures issued by the Ministry of Health should be reinforced.

4. ANNEXES

ANNEX 1: SELECTED INTERNATIONAL RECCOMENDATIONS ON COVID-19 VACCINATION IN PREGNANCY

Pregnancy	Lactation
World Health Organization (WHO)[a]	
• Developmental and toxicology reproductive studies have not shown harmful effects in pregnancy • Vaccination only if benefit outweighs risk, such as pregnant healthcare workers or with comorbidities • Delaying pregnancy following vaccination not recommended	• Vaccine efficacy is expected to be similar in lactating women as in other adults. • No data on the safety of COVID-19 vaccines in lactating women • Biologically and clinically unlikely to pose a risk to the breastfeeding child • Cessation of breastfeeding not recommended
Centers for Disease Control and Prevention (CDC)[b]	
• Pregnant healthcare personnel and those who are part of a group recommended to receive the vaccine may choose to be vaccinated • A conversation with a clinician may be helpful but not required prior to vaccination	• No data on the safety of COVID-19 vaccines in lactating mothers or on the effects of mRNA vaccines on breastfed infant • mRNA vaccines are not thought to be a risk to the breastfeeding infant
Public Health England	
• Pregnant women who are at very high risk of catching the infection or serious complication from Covid-19 infection may choose to have vaccination following a discussion with her doctor or nurse • Pregnant women should be reassured that the vaccine cannot cause COVID-19 infection in her or in her baby • If a woman finds out she is pregnant after she has started a course of vaccine, she should complete her pregnancy before finishing the recommended schedule	
Academy of Breastfeeding Medicine	
	• Cessation of breastfeeding not recommended • Strongly recommends that future research studies routinely include pregnant and lactating participants to protect them through research, not from research

[a]WHO Interim Recommendations on use of Moderna mRNA-1273

[b]CDC Vaccination Considerations for People who are Pregnant or Breastfeeding

[C]Public Health England. The Safety of COVID-19 Vaccines when given in Pregnancy

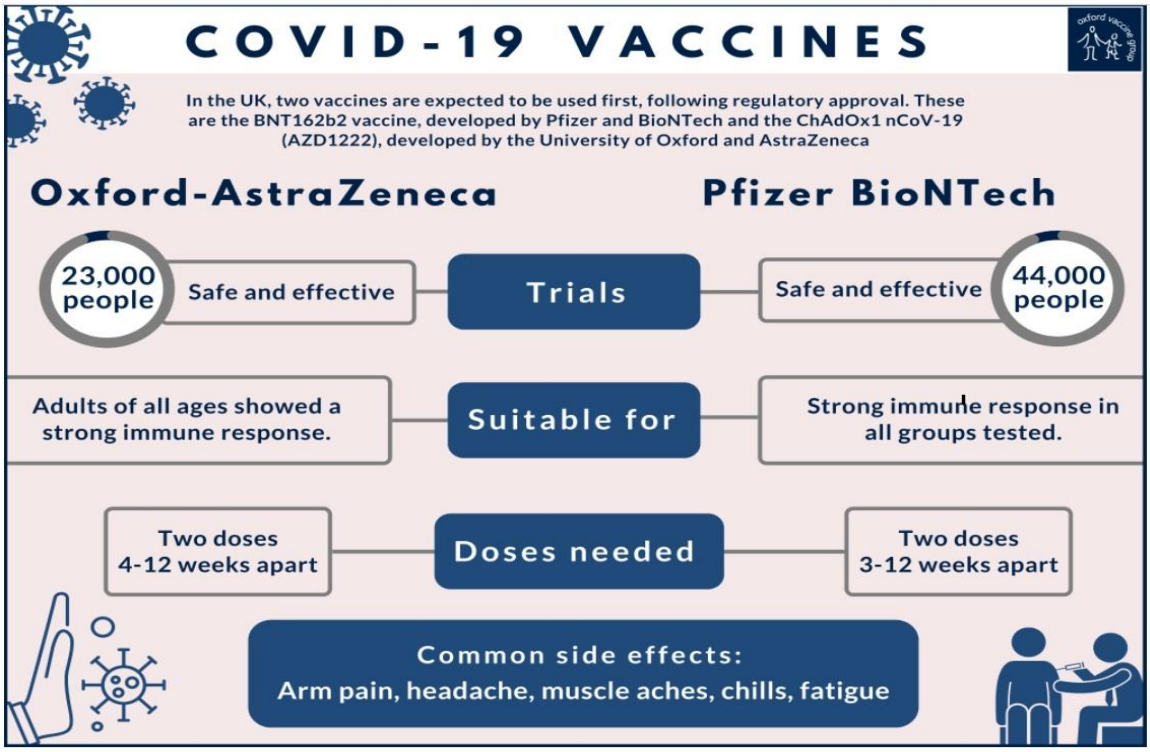
ANNEX 2: OUTCOMES OF PREGNANT WOMEN WHO RECEIVED COVID-19 mRNA-1273 VACCINATION

Treatment Group	Expected Due Date (calculated by LMP)	Previous Pregnancies	Date of First Injection	Date of Second Injection (if Applicable)	Outcome
Placebo	17 Mar 2021	3 previous pregnancies; 2 live births, and 1 abortion	3 Aug 2020	N/A	Ongoing
Placebo	1 Jun 2021	13 previous pregnancies; 11 abortions (all induced), 2 live births	26 Aug 2020	N/A	Spontaneous abortion
Placebo	7 Jun 2021	None reported	28 Aug 2020	N/A	Elective termination
Placebo	2 Jun 2021	1 live birth	24 Aug 2020	N/A	Ongoing
Placebo	26 May 2021	2 live births	4 Aug 2020	1 Sep 2020	Ongoing
Placebo	6 Jun 2021	None reported	9 Sep 2020	7 Oct 2020	Unknown (participant was lost to follow-up)
Placebo	10 Jul 2021	2 previous pregnancies, both induced abortions	24 Aug 2020	21 Sep 2020	Ongoing
mRNA-1273	18 May 2021	1 previous pregnancy	7 Aug 2020	4 Sep 2020	Ongoing
mRNA-1273	1 Apr 2021	None reported	10 Aug 2020	N/A	Ongoing
mRNA-1273	19 May 2021	None reported	14 Aug 2020	N/A	Ongoing
mRNA-1273	7 Jun 2021	2 previous pregnancies; 1 spontaneous abortion & 1 ectopic pregnancy	24 Aug 2020	N/A	Ongoing
mRNA-1273	Unknown	5 previous pregnancies; 2 live births, 2 spontaneous abortions, and 1 elective termination	13 Aug 2020	10 Sep 2020	Ongoing
mRNA-1273	2 Jul 2021	2 live births	9 Aug 2020	11 Sep 2020	Ongoing

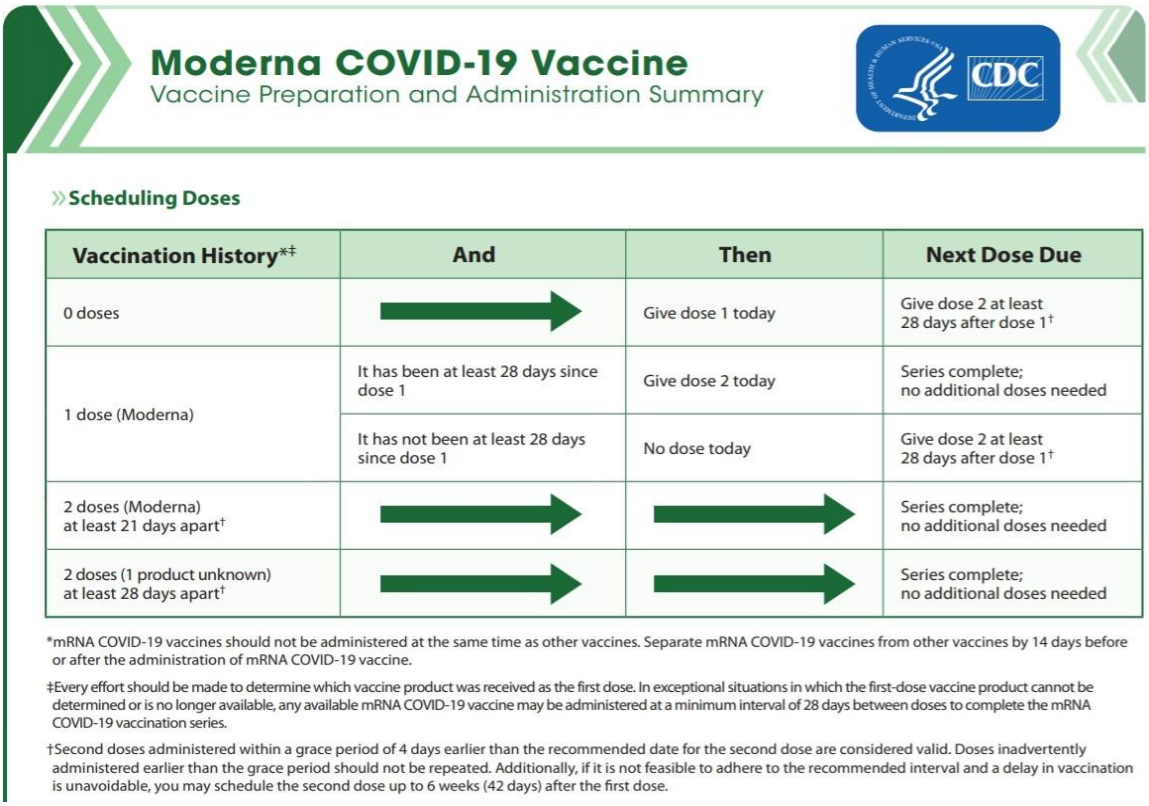
Abbreviations: LMP = last menstrual period; N/A = not applicable.
Note: Pregnancies are only collected in the Pharmacovigilance Global Database

Pregnancies in Female Participants in Study-301 using mRNA-1273 vaccine (Moderna) as of 2nd December 2020[8]

ANNEX 3: INFOGRAPHICS ON VACCINE DOSING INTERVAL



Adopted from Covid-19 Vaccines. Oxford Vaccine Group[11]



Moderna COVID-19 Vaccine
Vaccine Preparation and Administration Summary

CDC

Scheduling Doses

Vaccination History*‡	And	Then	Next Dose Due
0 doses	→	Give dose 1 today	Give dose 2 at least 28 days after dose 1†
1 dose (Moderna)	It has been at least 28 days since dose 1	Give dose 2 today	Series complete; no additional doses needed
	It has not been at least 28 days since dose 1	No dose today	Give dose 2 at least 28 days after dose 1†
2 doses (Moderna) at least 21 days apart†	→	→	Series complete; no additional doses needed
2 doses (1 product unknown) at least 28 days apart†	→	→	Series complete; no additional doses needed

*mRNA COVID-19 vaccines should not be administered at the same time as other vaccines. Separate mRNA COVID-19 vaccines from other vaccines by 14 days before or after the administration of mRNA COVID-19 vaccine.

‡Every effort should be made to determine which vaccine product was received as the first dose. In exceptional situations in which the first-dose vaccine product cannot be determined or is no longer available, any available mRNA COVID-19 vaccine may be administered at a minimum interval of 28 days between doses to complete the mRNA COVID-19 vaccination series.

†Second doses administered within a grace period of 4 days earlier than the recommended date for the second dose are considered valid. Doses inadvertently administered earlier than the grace period should not be repeated. Additionally, if it is not feasible to adhere to the recommended interval and a delay in vaccination is unavoidable, you may schedule the second dose up to 6 weeks (42 days) after the first dose.

Adopted from Moderna Covid-19 vaccine: Vaccine preparation and administration summary. [12]

At the time of writing, Moderna is not expected to be available in Malaysia

COVID-19 VACCINATION IN PREGNANCY

1 **IS IT SAFE IN PREGNANCY?**
Covid-19 vaccination is not contraindicated in pregnancy although its safety continues to evolve.

2 **WHO SHOULD GET VACCINATED?**
Pregnant women with risk factors such as age above 40, BMI >40 or has various underlying medical illness are especially vulnerable in the second and third trimester. They may benefit from vaccination.

3 **WHEN SHOULD I GET MY VACCINE?**
For pregnant women that are high risk, vaccination is recommended between 14 - 33 weeks of pregnancy.

4 **CAN I BREASTFEED MY BABY?**
It is safe to breast feed after receiving the Covid-19 vaccine as it is unlikely to transfer through breast milk. Cessation of the breast feeding is therefore unnecessary.

5 **IS MY BABY IMMUNE IF I GET THE VACCINE?**
The Covid-19 vaccine does not protect your baby from Covid-19 infection.

6 **WHAT ARE THE SIDE EFFECTS?**
Some common side effects of the Covid-19 vaccine include pain at the injection site, headaches, chills, fatigue and muscle ache.

7 **WHAT IF I HAVE ALLERGIES?**
Women with severe allergies or previous anaphylactic reactions should consult a physician prior to receiving the vaccine.

8 **CAN I RECEIVE OTHER VACCINES TOGETHER?**
You still need Influenza and Tdap vaccinations in pregnancy although it is recommended to be taken 14 days apart from the Covid-19 vaccine.

9 **WHAT IF I PREVIOUSLY HAD COVID-19 INFECTION BEFORE PREGNANCY?**
You may still benefit from vaccination as there is a small risk of reinfection.

Source: Guidelines on Covid-19 vaccination in obstetrics

CONSULT YOUR OBSTETRICIAN IF YOU HAVE ANY QUESTIONS REGARDING COVID-19 VACCINATION IN PREGNANCY.

FEBRUARY 2021

ANNEX 4: CONSENT FORM

CONSENT FOR COVID-19 VACCINATION DURING PREGNANCY

Name of proposed intervention

COVID-19 Vaccination during pregnancy (Between 14 to 33 weeks of pregnancy)

Intended benefits

To reduce the risk of severe COVID-19 infection in pregnancy, particularly among high risk mothers
To reduce the risk of COVID-19 infection amongst pregnant frontline workers who are at increased risk of exposure to SARS-COV-2

Frequent Risks associated with COVID-19 Vaccination

i) Pain at the injection site
ii) Headache
iii) Chills
iv) Fatigue
v) Muscle ache

**Your risk may be higher if you are known to have severe allergies or previous anaphylactic reasons. Consult your doctor first.*

Serious Risks

A) Maternal risk

Studies among non-pregnant women has shown that serious risks, including anaphylaxis and death from vaccinations are very rare. While there is a lack of safety data among pregnant mothers at this moment, there are no reasons to believe this would differ.

B) Fetal risk

No safety concerns have been found in experimental animal studies. However, there is no direct or long term safety data on COVID-19 vaccinations to the fetus.

Alternative options

I understand that I have the option to decline vaccination during pregnancy in view of safety concerns but this may increase my risk of having severe COVID-19 infections, especially if I am considered high risk, which includes ICU admissions, need for ventilation, stillbirth, prematurity and death.

Patient information

I have been given information and resources on COVID-19 including the benefits and risk of having vaccinations in pregnancy. I have been given sufficient time to make my informed decision. I also have been counselled on the various type of available vaccines and its benefits.

I hereby consent to have the COVID-19 vaccination during pregnancy.

Signature of Mother:
Name:
Identification No:

Signature of Doctor
Name:
Stamp:

Witness:
Translator (if required):
Date:

ANNEX 5: ADDENDUM ON CONCEIVING PRIOR TO COMPLETION OF VACCINATION IN PREGNANCY

Women who conceive or find out about their pregnancy after the first dose of vaccination (and prior to the second dose) should be reassured about the overall safety of COVID-19 vaccines based on developmental and toxicity studies (DART).[8] In a COVID-19 vaccine safety update by the CDC in early March, more than 30,000 pregnancies have been reported to v-safe, involving the use of Pfizer-BioNTech and Moderna. More than 1800 women have enrolled for the v-safe pregnancy registry as of 18th February with 275 completed pregnancies. Rates of miscarriage, pregnancy complications such as gestational diabetes and preeclampsia, preterm birth, congenital anomalies and neonatal death were no higher than background rates.[22]

Therefore, pregnant women could be given one of these 3 options:

Defer 2nd dose till 14 weeks of gestation	Although the manufacturer recommends an interval of no longer than 6 weeks for Moderna/Pfizer for optimal immune response, the UK Joint Committee on Vaccination and Immunization (JCVI) has recommended delaying the 3-week interval to up to 12 weeks, based on the short-term effectiveness quoted below.[23] This is in part, to facilitate rapid high-level uptake of the vaccine.
Omit 2nd dose	Short term effectiveness of 52-89% has been reported after a single dose of vaccine, although the duration of this protection remains uncertain.[24,25]
Continue 2nd dose as scheduled	If pregnant women are at high risk of severe disease or repeated exposure to SARS-COV-2, they may choose to continue receiving the 2nd dose of vaccine as scheduled, based on the current safety data reported from v-safe.[22]

These options are valid at the time of writing and may change when more evidence is made available. It would be reasonable for women to consult their obstetrician in such instances.

REFERENCES

1. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ 2020;370:m3320.

2. Martinez-Portilla RJ, Sotiriadis A, Chatzakis C, et al. Pregnant women with SARS-CoV-2 infection are at higher risk of death and pneumonia: propensity score matched analysis of a nationwide prospective cohort (COV19Mx). Ultrasound Obstet Gynecol 2021; 57:224-231

3. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. BMJ 2020;369:m2107.

4. Badr DA, Mattern J, Carlin A, et al. Are clinical outcomes worse for pregnant women at ≥20 weeks' gestation infected with coronavirus disease 2019? A multicenter case-control study with propensity score matching. Am J Obstet Gynecol 2020;223(5):764-768.

5. Pierce-Williams RAM, Burd J, Felder L, et al. Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. Am J Obstet Gynecol MFM. 2020 Aug;2(3):100134.

6. ACIP: Guidance for Vaccine Recommendations in Pregnant and Breastfeeding Women. https://www.cdc.gov/vaccines/pregnancy/hcp-toolkit/guidelines.html [Accessed 12th February 2021].

7. CDC. Understanding mRNA Covid-19 vaccines. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html [Accessed 12th February 2021]

8. mRNA-1273 Vaccines and Related Biological Products Advisory Committee . https://www.fda.gov/media/144452/download [Accessed 12th February 2021]

9. COVID-19 Vaccines and Pregnancy: Conversation Guide for Clinicians. https://www.acog.org/covid-19/covid-19-vaccines-and-pregnancy-conversation-guide-for-c linicians [Accessed 12th February 2021]

10. ACOG Practice Advisory: Vaccinating Pregnant and Lactating Patients Against COVID-19 December 2020 (Updated 4th Feb 2021)

11. Oxford Vaccine Group, University of Oxford. Covid-19 vaccines. https://vk.ovg.ox.ac.uk/vk/covid-19-vaccines [Accessed 12th February 2021]

12. Moderna Covid-19 vaccine: Vaccine Preparation and Administration Summary https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/downloads/prep-and-ad min-summary.pdf [Accessed 14th February 2021]

13. World Health Organization. Interim guidance. Interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing, 8 January 2021.https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_ recommendation-BNT162b2-2021.1 [Accessed 14th February 2021]

14. Edlow AG, Li JZ, Collier AY, et al. Assessment of maternal and neonatal SARS-CoV-2 viral load, transplacental antibody transfer, and placental pathology in pregnancies during the COVID-19 pandemic. JAMA Netw Open 2020;3(12): e2030455.

15. Academy of Breastfeeding Medicine. Considerations for Covid-19 Vaccination in Lactation. https://abm.memberclicks.net/abm-statement-considerations-for-covid-19-vaccination-in-lactation [Accessed 14th February 2021]

16. ASRM Bulletin. ASRM, ACOG and sMFM Joint Statement: Medical Experts Continue to Assert that COVID Vaccines do not Impact Fertility. 5th February 2021. https://www.asrm.org/news-and-publications/news-and-research/press-releases-and-bulle tins [Accessed 14th February 2021]

17. ASRM Patient Management and Clinical Recommendations during the Coronavirus-19 Pandemic; Update No.11.Covid-19 Vaccination. 16th December 2021. https://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/covid-19/c ovidtaskforceupdate11.pdf [Accessed 14th February 2021]

18. ESHRE:Covid-19 Vaccination and Assisted Reproduction.https://www.eshre.eu/ Europe/Position-statements/COVID19/ vaccination [Accessed 14th February 2021]

19. Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet 2020; 395:1907-1918.

20. European Society for Medical Oncology. ESMO Statements for Vaccination against Covid-19 in Patients with Cancer. https://www.esmo.org/ covid-19-and-cancer/ covid-19-vaccination [Accessed 14th February 2021]

21. Rubin LG, Levin MJ, Ljungman P, et al. Infectious Diseases Society of America. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014; 58:309-318.

22. Shimabukuro T. Covid-19 Vaccine Safety Update. CDC Covid-19 Vaccine Task Force. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covi d-Shimabukuro.pdf [Accessed 22nd March 2021]

23. Department of Health and Social Care. Optimising the covid-19 vaccination programme for maximum short-term impact. 2021. https://www.gov.uk/government/publications/prioritising-the-first-covid-19-vaccine-dose-jcvi-statement/optimising-the-covid-19-vaccination-programme-for-maximum-short-t erm-impact [Accessed 22nd March 2021]

24. Pimenta D, Yates C, Pagel C, et al. Delaying the second dose of covid-19 vaccines. BMJ 2021;372:n710

25. Iacobucci G, Mahase E. Covid-19 vaccination: What's the evidence for extending the dosing interval? BMJ 2021;372:n18

Appendix 3

COVID-19 VACCINATION FOR CANCER PATIENTS WITH SOLID TUMOURS

Introduction

This consensus statement is based on reviews of international guidelines on COVID-19 vaccination. Currently none of the authorized COVID-19 vaccines are live virus vaccines. Although data on safety for cancer patients is limited, there are many examples of vaccination for vulnerable patients including cancer patients in countries which rolled out COVID vaccine much earlier than Malaysia and proven that the benefit continues to outweigh the possible adverse effects. It is hence considered beneficial for patients with underlying cancers to receive vaccination against COVID-19. There is interim data indicating lower seroconversion of cancer patients on active treatment. This does not change the benefit derived from vaccination although indicating timing of vaccination could be adjusted for better efficacy. Family members and caregivers are encouraged to have the vaccination for protection of the vulnerable group who are not able to have the vaccination.

DISCLAIMER

This statement is current as of 30th March 2021, and recommendations may change as more data becomes available. Please consult the treating oncologists before vaccination. For further update and information, please refer to the Guidelines for Covid-19 vaccination from MOH Malaysia.

RECOMMENDATIONS

A. Patients on active cancer treatment

The patients who are on active cancer treatment are classified as the patients who are due for the treatment below:

Type of treatment	Status	Recommended timing
Chemotherapy neoadjuvant/ adjuvant/ palliative)	ongoing treatment	Vaccination 3 months after completed chemotherapy OR earlier up to the discretion of oncologist.
	due to start chemotherapy	Complete vaccination before and/ or after surgery prior to oncology treatment For urgent chemotherapy e.g. germ cell tumor or metastatic patients in visceral crisis, chemotherapy should be proceeded WITH NO delay.

		If vaccination was not given before initiation of oncology treatment, to delay until after completion of treatment OR at the discretion of oncologist.
	completed the last cycle	For vaccination 3 months after completed chemotherapy OR earlier up to the discretion of oncologist.
Hormonal / targeted therapies/ Immunotherapy **e.g., Imatinib/ Pazopanib/ Sunitinib/ Lenvatinib/ Herceptin/ Pertuzumab**	at any treatment time	For vaccination once it is available. The vaccine is relatively safe and recommended; However discussion with treating physician/ oncologist is recommended before the injection.
Checkpoint inhibitors	at any treatment time	For vaccination once blood count recovers and up to the discretion of oncologist.
Radical/ palliative radiotherapy	at any treatment time	For vaccination 3 months after completed concurrent chemoradiotherapy OR earlier up to the discretion of oncologist. For palliative radiotherapy, vaccination once completed treatment and up to the discretion of oncologist.

B. Patients in remission or cancer survivors

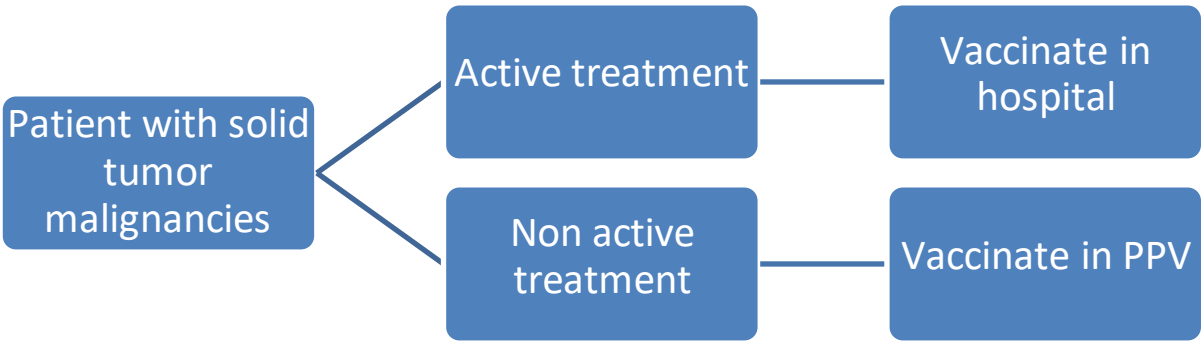
All cancer patients who have completed their treatment for at least three months and are in remission, along with cancer survivors could be vaccinated anytime according to national vaccine guideline.

Patient groups recommended to be vaccinated in hospital. The timing for vaccination is up to the discretion of oncologist.

a. Patient with potential allergy to components in the vaccine e.g. PEG
b. Patients with metastatic disease
c. Thoracic malignancy
d. Patients aged 60 years and above
e. Patient under clinical trials

C. Vaccination Sites for Cancer Patients

a. 6 MOH Oncology Centres – Hospital Kuala Lumpur, Institut Kanser Negara, Hospital Sultan Ismail, Hospital Wanita dan Kanak-kanak Likas, Hospital Umum Sarawak and Hospital Pulau Pinang.
b. Peripheral hospitals – state and major hospitals with specialists providing chemotherapy and palliative care.
c. Pusat Pemberian Vaksin (PPV) - for stable, not on active treatment patients.



References:

1. Desai, A. et al. Mortality in hospitalized patients with cancer and coronavirus disease 2019: a systematic review and meta-analysis of cohort studies. *Cancer* https://doi.org/10.1002/cncr.33386 (2020)

2. Desai, A., Sachdeva, S., Parekh, T. & Desai, R. COVID-19 and cancer: lessons from a pooled meta-analysis. *JCO Glob. Oncol.* **6**, 557–559 (2020).

3. Covid-19: Doctors in Norway told to assess severely frail patients for vaccination Ingrid Torjesen, BMJ 2021;372:n167, Published: 19 January 2021

4. COVID-19 vaccine guidance for patients with cancer participating in oncology clinical trials Aakash Desai et all, *Nature Reviews Clinical Oncology* (2021), Published: 15 March 2021

5. Interim results of the safety and immune-efficacy of 1 versus 2 doses of COVID-19 vaccine BNT162b2 for cancer patients in the context of the UK vaccine priority guidelines

6. Baden LR, El Sahly HM, Essink B et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. NEJM 2020. doi: 10.1056/NEJMoa2035389.

7. Bielicki JA, Duval X, Gobat N, et al. Monitoring approaches for health-care workers during the COVID-19 pandemic. Lancet Infect Dis. 2020 Oct;20(10):e261-e267. doi: 10.1016/S1473-3099(20)30458-8

Appendix 4

CONSENSUS STATEMENT FROM MALAYSIAN SOCIETY OF HAEMATOLOGY

COVID-19 VACCINATION FOR PATIENTS WITH HAEMATOLOGICAL DISORDERS

CONSENSUS STATEMENT

Malaysian Society of Haematology

March 2021

BACKGROUND

This consensus statement is based on reviews of international guidelines on COVID-19 vaccination. There is also no preference to the types of vaccine available currently. None of the authorized COVID-19 vaccines are live virus vaccines, hence they are considered safe for patients with underlying haematological cancers or those on immunosuppressive drugs. Family members/ caregivers are encouraged to have the vaccination for protection of the vulnerable group who are not able to have the vaccination. It is crucial that all ought to practice the recommended precaution even after vaccination.

DISCLAIMER

This statement is current as of 22 March 2021, and recommendations may change as more data becomes available. The society and authors will not accept any legal responsibility. Please consult the treating hematologists before vaccination. For further update and information, please refer to the KKM guidelines at covid-19.moh.gov.my.

RECOMMENDATION

A. Patients with Haematological Cancers

- Patients who are undergoing active therapy such as chemotherapy are advised to discuss the risks and benefits of the vaccines prior to considering vaccination.

- Patients who are on long term or maintenance therapy (other than B-cell depleting agents) or have completed treatment can have their COVID-19 vaccination. These include patients with chronic myeloid leukemia, multiple myeloma, lymphomas, chronic lymphocytic leukemia, myelodysplastic syndrome and myeloproliferative neoplasms.

- In patients who are receiving B-cell depleting agents such as anti-CD20 monoclonal antibodies e.g. Rituximab, the vaccine should be administered preferably 6 months after the last dose; if this is not possible, we recommend completing the full course of vaccination at least 4 weeks prior to the next dose of Rituximab.

- Patients who are currently receiving other types of cancer treatment are advised to wait for normalization of blood counts before vaccination.

B. Patients who received Haematopoeitic Stem Cell Transplantation (HSCT) and/or Cellular Therapy

i. Patients can have their vaccination as early as 3 months after autologous HSCT.

ii. Patients can have their vaccination starting from 3 - 6 months after allogeneic HSCT if the risk of community transmission is high. Otherwise, we would recommend deferral beyond 6 months after HSCT.

iii. Patients who have severe, uncontrolled grades III - IV acute graft versus host disease are recommended to defer vaccination until it is controlled.

iv. Consider vaccination in patients with mild chronic graft versus host disease and receiving
    i. ≤ 0.5 mg/kg prednisolone (or equivalent).

v. Consider vaccination in patients who have received Chimeric Antigen Receptor - T cells (CAR-T) 3 - 6 months after completion of treatment.

C. Patients with Bleeding Disorders

i. People with bleeding disorders are not at greater risk of contracting COVID-19 or developing a severe form of the disease.

ii. The vaccine itself does not present any additional safety concerns for these patients but the intramuscular route of administration may increase the risk of bleeding at the injection site.

iii. Patients with a history of allergic reactions to extended half-life clotting factor concentrates containing polyethylene glycol (PEG) should discuss vaccine choice with their physician because some COVID-19 vaccines (e.g. Pfizer-BioNTech vaccine) contain PEG as an excipient.

iv. For patients with severe or moderate haemophilia A or B, the vaccine injection should be given after a prophylactic dose of Factor VIII (FVIII) or Factor IX (FIX). For patients with a basal FVIII or FIX level above 10%, no haemostatic therapies are required.

v. For patients with inhibitors, the vaccine injection should be given after a prophylactic dose of bypassing agent.

vi. Patients on Emicizumab (with or without an inhibitor) can be vaccinated by intramuscular injection at any time without haemostatic precautions and without receiving a dose of FVIII or bypassing agent.

vii. Patients with Type 1 or 2 Willebrand disease (VWD), depending on their baseline von Willebrand factor (VWF) activity levels, should use haemostatic therapies [i.e. tranexamic acid, desmopressin (DDAVP) or VWF concentrate] in consultation with their haematologists. Patients with Type 3 VWD should be given a prophylactic dose of VWF concentrate prior to the intramuscular COVID-19 vaccination.

viii. Patients with platelet counts of 50 x 10^9/L and above can proceed with vaccination without additional haemostatic support. Patients with platelet counts below 50 x 10^9/L should defer the vaccination till their platelet counts recover, if possible. For those patients with chronically low platelet counts, vaccination should be performed in consultation with their primary haematologist.

ix. Patients with other rare bleeding disorders including platelet function disorders should be vaccinated in consultation with their primary haematologists.

x. The currently available COVID-19 vaccines should be administered intramuscularly. There are no data for the subcutaneous route and this should not be done. The smallest gauge needle available (25 to 27 gauge) should be used. Pressure should be applied to the site for 5 to 10 minutes post-injection to reduce bleeding and swelling. Additionally, self-inspection and palpation of the injection area several minutes and 4 to 6 hours later is recommended to ensure that there is no delayed haematoma. Discomfort in the arm felt for 1 to 2 days after injection should not be alarming unless it progressively worsens and is accompanied by swelling. Any adverse events (e.g., haematoma, allergic reaction) should be reported to the haematology clinic or emergency department

D. Patients on Anti-Coagulation and Anti-Platelet Agents

i. Warfarin

- Patients on warfarin can receive intramuscular vaccination if their most recent international normalized ratio (INR) is below 4, without stopping the drug.
- On the day of vaccination, warfarin should be taken after the vaccine injection. The risk of haematoma formation is reduced by applying firm pressure at the injection site for at least 5 minutes.
- Patients on concomitant warfarin and anti-platelet therapy should be managed on an individual basis in consultation with their primary physician.

ii. Direct Oral Anticoagulants (DOAC) and Low Molecular Weight Heparins (LMWH)

- Patients on maintenance therapy with DOAC, LMWH or fondaparinux can delay the dose on the day of vaccination until after the intramuscular injection but do not need to miss any doses.

iii. Anti-platelet agents

- Patients on single agent anti-platelet therapy (e.g. aspirin or clopidogrel) can continue on these medications without any adjustment.

- Patients on dual antiplatelet agents should be managed on an individual basis and in consultation with their primary physician.

E. Patients with Haemoglobinopathies, Enzymopathies and Rare Inherited Anaemias

i. This includes all adults with transfusion-dependent thalassaemia, G6PD (Glucose-6- phosphate dehydrogenase) deficiency and rare inherited anaemias. These patients can receive COVID-19 vaccination.

ii. In patients with splenectomy or functional asplenia, all routine vaccines are likely to be effective and therefore these patients should receive COVID-19 vaccination.

F. Patient with Autoimmune Haematological Conditions on Immunisuppression

i. There are no clinical trials of COVID-19 vaccine which enrolled immunocompromised patients. Thus, the efficacy and safety of a COVID-19 vaccine have not been established in the different categories of immunocompromised patients.

ii. The following categories of immunocompromised patients may have attenuated or absent responses to COVID-19 vaccines:

- Primary and secondary immunodeficiencies involving adaptive immunity
- B-cell depleting agents [e.g. anti-CD20 monoclonal antibody like Rituximab]
- T-cell depleting agents [e.g. calcineurin inhibitors, anti-thymocyte globulin]
- Daily corticosteroid therapy with a dose ≥20 mg (or >2 mg/kg/day for patients who weigh <10 kg) of prednisone or equivalent for ≥14 days

iii. The risks and benefits of immunocompromised patients receiving the vaccine should be weighed on a case-by-case basis. If plans to proceed with the vaccination are made, we recommend completing the full course of vaccination at least 2 weeks before the initiation of the planned immunosuppressive therapy or splenectomy. If the patient is receiving or has received immunosuppressive therapy, consider vaccination 6 months after the patient has been taken off immunosuppressive therapy to increase the likelihood of mounting an effective immune response.

REFERENCES:

1. https://b-s-h.org.uk/media/19195/haematology-covid-19-v10-vaccination-statement-231220.pdf
2. https://www.ebmt.org/covid-19-and-bmt. EBMT COVID-19 recommendations update; February 17, 2021
3. https://ehaweb.org/covid-19/eha-statement-on-covid-19-vaccines/recommendations-for-covid-19-vaccination-in-patients-with-hematologic-cancer/
4. https://www.hematology.org/covid-19/ash-astct-covid-19-and-vaccines
5. https://www.mskcc.org/coronavirus/covid-19-vaccine
6. http://www.stjames.ie/services/hope/nationalcoagulationcentre
7. https://www.wfh.org/en/covid-19-communications. COVID-19 World Federation of Hemophilia (WFH) Announcements and Statements 2021
8. Consensus statement by Singapore Society of Haematology 2021

IF YOU HAVE ANY QUESTIONS OR QUERIES, PLEASE CONTACT YOUR HAEMATOLOGIST

Appendix 5

MALAYSIAN CONSENSUS ON COVID-19 VACCINATION FOR PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES (RMD) AND AUTOIMMUNE AND INFLAMMATORY RHEUMATIC DISEASES (AIIRD)

Version 1, 3rd March 2021

GENERAL GUIDANCE

1. There should be a shared decision between the clinician and patient regarding COVID-19 vaccination.

2. Patients with AIIRD should be prioritised to receive COVID-19 vaccination. This is because they are at higher risk of severe COVID-19 infection with a worse outcome compared to the general population.

3. The expected response to COVID-19 vaccination for patients on immunomodulatory treatment is likely to be blunted in its magnitude and duration compared to the general population.

4. A theoretical risk for flare or disease worsening exists following vaccination. However, the benefit of COVID-19 vaccination outweighs the potential risk of new onset autoimmunity.

DISCLAIMER

This consensus was adapted from various international guidelines including the American College of Rheumatology (ACR) COVID-19 Vaccine clinical guidance summary, European Alliance of Associations for Rheumatology (EULAR) view points on SARS-COV-2 vaccination in patients with RMDs and Arthritis and Musculoskeletal Alliance Principles for COVID-19 vaccination in musculoskeletal and rheumatology for clinicians.

RECOMMENDATIONS:

1. RMD and AIIRD patients age 18 years and above should receive vaccination if there are no contraindications.

2. There is no preference for one vaccine over another.*

3. Vaccination should preferably be given when disease is under control.

4. Vaccination should preferably be given before planned immunosuppression if feasible.

5. For patients who are already on immunosuppression, appropriate timing of vaccination may need to be considered. For guidance on timing of vaccination and immunomodulatory therapy, refer to Table 1.

** unless there is contraindication for a particular vaccine; Of note certolizumab pegol contains polyethylene glycol (PEG) so patients who have had an allergic reaction to certolizumab pegol should not receive the Pfizer/BioNTech vaccine (as it contains PEG) or any other vaccine that uses PEG as an excipient*.

Table 1: Guidance regarding use and timing of COVID-19 vaccination and immunomodulatory therapies

Medication	Action
DMARDs	
Methotrexate	Hold for 1 week after each vaccine dose*; no modifications to vaccination timing
Leflunomide, Sulphasalazine, Hydroxychloroquine	No modifications to either immunomodulatory therapy or vaccination timing
tsDMARDs	
Tofacitinib, Baricitinib, Upadacitinib	Hold for 1 week after each vaccine dose*; no modification to vaccination timing
bDMARDs	
Infliximab, Etanercept, Adalimumab, Golimumab, Tocilizumab, Secukinumab, Ixekizumab, Ustekinumab Guselkumab	No modifications to either immunomodulatory therapy or vaccination timing
IV Belimumab IV Immunoglobulin SC Denosumab	No modifications to either immunomodulatory therapy or vaccination timing
Immunosuppressives (oral)	
Azathioprine, Mycophenolate, Cyclosporin, cyclophosphamide	No modifications to either immunomodulatory therapy or vaccination timing
Corticosteroids**	No modifications to either immunomodulatory therapy or vaccination timing
IV Cyclophosphamide	Schedule infusion 1 week after each vaccine dose, when feasible
IV Rituximab	vaccinate 4 weeks prior to next scheduled infusion; delay next infusion 2-4 weeks after 2nd vaccine dose if disease activity allows
DMARDs = disease modifying anti-rheumatic drugs; tsDMARDs = targeted synthetic DMARDs; bDMARDs = biologic DMARDs; IV = intravenous; SC = subcutaneous	

**provided disease is well controlled enough to allow for a temporary interruption; otherwise to consider on a case-by-case basis considering circumstances involved*

*** prednisolone-equivalent dose ≥20mg/day, to consider on a case-by-case basis considering circumstances involved*

REFERENCES

1. COVID-19 Vaccine Clinical Guidance Summary for Patients with Rheumatic and Musculoskeletal Diseases; Developed by the ACR COVID-19 Vaccine Clinical Guidance Task Force; 8 February 2021; https://www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf

2. EULAR View-points on SARS-CoV-2 vaccination in patients with RMDs; December 2020; https://www.eular.org/eular_sars_cov_2_vaccination_rmd_patients.cfm

3. Principles for COVID-19 Vaccination in Musculoskeletal and Rheumatology for Clinicians; 27 January 2021; http://arma.uk.net/covid-19-vaccination-and-msk/

4. Hyrich KL and Machado PM. Rheumatic disease and COVID-19: epidemiology and outcomes. Nature reviews Rheumatology 17, 71-72 (2021)

Appendix 6

GENERAL GUIDE - BLOOD DONATION IN RELATION TO COVID-19 IMMUNIZATION

1. Individual who intends to donate blood and have received vaccine COVID-19 (from the category of non-live vaccine) needs to **defer blood donation process for 7(seven) days after receiving vaccine.**

2. Individual who intends to donate blood, has received vaccine COVID-19 and experienced **mild reaction** needs to **defer blood donation process for 7(seven) days following complete recovery of the reaction.**

3. Individual who intends to donate blood, has received vaccine COVID-19 and experienced **severe reaction** such as anaphylaxis is **not allowed to donate blood (permanent deferral).**

4. Volunteers of COVID-19 **vaccine clinical study** needs to **defer blood donation process for 12 (twelve) months** after completing vaccination (i.e. full doses).

Appendix 7

GENERAL GUIDE – HEMODIALYSIS PATIENT AND VACCINATION

1. Dialysis patients should be given priority for COVID-19 vaccination due to the high risk of mortality and to reduce the risk of cross infection in the Dialysis Unit.

2. The timing and place of vaccination should be discussed with the patients in consultation with the nephrologist in charge and/or the registered medical practitioner in charge of the Dialysis Unit.

3. Refer to the guideline on the need for pre-vaccination assessment (PVA).

4. For patient's convenience, vaccination can be given before or towards the end haemodialysis session;

    4.1. If feasible, vaccination should be given before the start of hemodialysis session

    4.2. If the vaccination is administered at the end of the hemodialysis session, the session can be shortened by 30 minutes to allow time for observation after the vaccination. The arteriovenous (AV) fistula needle is removed after the end of the observation period.

5. The risk of haematoma at the site of injection is low. The adjustment of heparin dose should be decided by the nephrologist in charge.