****

**Influenza Vaccination Guide**

**2021**

**Revised target groups in light of the COVID-19 pandemic are as follows:**

* It is highly recommended for all health care workers to be vaccinated

      Individuals aged >65 years

      Individuals with cardiovascular disease (including chronic heart disease, hypertension, stroke and diabetes), chronic lung disease (including asthma and chronic obstructive pulmonary disease) and individuals living with HIV and AIDS

     Pregnant women

NB: Influenza vaccinations must be recorded in the patient’s file **and** on the antenatal card, treatment card for HIV-infected persons or road to health card for children.

**Cluster: Communicable Diseases**

**national department of health**

**Background**

To mitigate the effect of seasonal influenza, the Department of Health conducts annual influenza vaccinations, targeting individuals at increased risk for severe influenza disease or complications.

The purpose of this document is to provide health workers with the necessary guidelines and tools to facilitate implementation of the influenza vaccinations.

Influenza vaccinations are expected to commence in April 2021 and continue until all vaccines have been utilized or until the end of the influenza season. The influenza vaccinations will be implemented alongside other public health measures, both pharmaceutical (e.g. promoting appropriate use of antivirals) and non-pharmaceutical (e.g. personal hygiene, in particular hand washing, cough etiquette, ensuring adequate ventilation and use of personal protective equipment).

**Objectives**

In keeping with the recommendations of the World Health Organization(WHO) Strategic Advisory Group of Experts (SAGE) on Immunisation, the objectives of the influenza vaccination strategy are to:

* Reduce influenza-related morbidity and mortality, i.e. protect the vulnerable
* Reduce transmission of the influenza virus within communities, i.e., limit the spread of infection and limit the burden on the healthcare system.

**Coordination**

Influenza vaccinations will be coordinated at provincial level. It is recommended that subcommittees be formed to handle the different aspects of the vaccination campaign i.e., logistics, technical, social mobilisation, etc. Consideration must be given to the COVID-19 vaccine roll-out as well.

**Vaccine composition and characteristics**

**Each year, WHO recommends vaccine formulations for the Southern Hemisphere. In 2021, the recommended vaccine components are as follow:**

**Trivalent influenza vaccine (TIV) include:**

* an A/Victoria/2570/2019 (H1N1)pdm09-like virus;
* an A/Hong Kong/2671/2019 (H3N2)-like virus; and
* a B/Washington/02/2019 (B/Victoria lineage)-like virus.

**Quadrivalent Influenza Vaccine (QIV) include:**

* an A/Victoria/2570/2019 (H1N1)pdm09-like virus;
* an A/Hong Kong/2671/2019 (H3N2)-like virus;
* a B/Washington/02/2019 (B/Victoria lineage)-like virus; and
* a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.
* Vaccines should contain 15μg of each haemagglutinin antigen in each 0.5ml dose
* Vaccine packaging: vaccines are pre-packed in syringes (0.5 ml).
* The vaccine induces immunity to influenza approximately 14 days after vaccination. Therefore, persons infected shortly before (1-3 days) or shortly after immunisation can still get disease.
* Vaccine-induced immunity lasts 6 to 8 months.
* This vaccine does not cause influenza disease.
* People who have received influenza vaccine can later have an illness caused by other common viruses (not influenza), which may be mistaken for flu.

**NB: Influenza vaccine can be given concurrently with other injectable, non-influenza vaccines but must be administered at different injection sites. The only exception regarding co-administration is with regards to COVID-19 vaccines. No vaccine may be co-administered with the COVID-19 vaccines. As per the Centers for Disease Control (CDC), the COVID-19 vaccine must be scheduled with at least a 14-day interval of any other vaccine1. If both COVID-19 and Influenza vaccines are available for administering, the COVID-19 vaccine must be administered, first.**

**Vaccine handling**

* Storage: refrigerated conditions at between 2**˚**C and 8**˚**C.
* Provinces to assess logistics including transport and storage (e.g. fridge space).

**Vaccine safety**

* Flu vaccines are safe in pregnancy and in children ≥6 months of age.
* General immunisation safety practice applies, as with other EPI vaccines. Contraindications: the flu vaccine should **not** be administered to:
  + People with history of anaphylaxis (severe allergic/hypersensitive reactions) following receipt of any vaccine component including: eggs, neomycin or polymyxin antibiotics
  + People with a history of severe reaction to previous influenza vaccination
  + People who developed Guillain-Barré syndrome (GBS) within 6 weeks of receiving an influenza vaccine
  + Children < 6 months

**The product package insert must be referred to for more information regarding contraindications.**

**Target population**

Not everyone is at risk for severe disease, and due to limited availability of the vaccine in the public sector, not everyone can be vaccinated against influenza. Therefore, priority groups in the public sector include:

* It is highly recommended for all health care workers to be vaccinated
* Individuals aged >65 years
* Individuals with cardiovascular disease (including chronic heart disease, hypertension, stroke and diabetes), chronic lung disease (including asthma and chronic obstructive pulmonary disease) and individuals living with HIV and AIDS
* Pregnant women

Ensure that all socio-economic groups, especially the least privileged, are given equal access to the influenza vaccines.

The strategy will be revised annually in accordance with availability of vaccines and updated risk group assessment by the National Advisory Group on Immunization (NAGI).

Kindly note that whilst QIV is preferred for high risk patients, in the event of a shortage of stock of QIV it is acceptable to use TIV2.

**When and where?**

Influenza vaccinations will be conducted in public health facilities from April 2021 (or as soon as the vaccines become available in provinces) and will continue until all vaccines have been utilized or until the end of the influenza season. Vaccines should be provided to target groups on a first-come, first-served basis; healthcare workers should strive to deliver all vaccines prior to the start of the influenza season or by 31 May 2021.

Vaccinations should begin before the start of the influenza season i.e. preferably before May-June so that vaccine recipients do not associate other viral infections with vaccination. Also, vaccinating earlier in the season provides protection to the individual throughout the period of influenza virus circulation. But patients may still benefit from influenza vaccination as long as flu viruses are circulating. *Bottom line: EARLIER IS BETTER, BUT LATE IS BETTER THAN NEVER.*

Community mobilization should take place at local levels and in consideration of available vaccines.

**Administering the vaccine (TIV and QIV)**

* The influenza vaccine must be administered intramuscularly (IM) as follows:
  + Injection into the upper arm (deltoid) for most people
  + For infants and younger children, inject the antero-lateral thigh
* **Vaccine dosage for TIV:**

|  |  |  |
| --- | --- | --- |
| **Age Group** | **Dose** | **Number of doses** |
| Adults and children from 9 years of age | Adult dose (0.5ml) IM | Single dose |
| Children 3 years to 8 years | Adult dose (0.5ml) IM | 1 or 2 doses\* |
| Children 6 - 35 months | 0.25ml (half an adult dose) IM | 1 or 2 doses\* |
| \* if receiving the vaccine for the **first time**, 2 doses should be administered at least 4 weeks apart | | |

**Vaccine dose for QIV:**

|  |  |  |
| --- | --- | --- |
| **Age Group** | **Dose** | **Number of doses** |
| 6 months to < 9 years | Adult dose (0.5ml) IM | 1 or 2 doses\* |
| 9 years and above | Adult dose (0.5ml) IM | 1 dose |
| \* if receiving the vaccine for the **first time**, 2 doses should be administered at least 4 weeks apart | | |

**NB: INFLUENZA VACCINATIONS MUST BE RECORED IN THE PATIENT’S FILE AND ON THE ANTENATAL CARD, TREATMENT CARD FOR HIV-INFECTED PERSONS OR ROAD TO HEALTH CARD FOR CHILDREN.**

**Disclaimer: In the event a child < 9 years old, at risk of severe influenza disease who has not received an influenza vaccine in previous years and has received the 1st dose of QIV and there is a subsequent shortage of stock of QIV, it is acceptable to use TIV for the 2nd dose. However, kindly note that the child may not be adequately primed for the additional B strain that is not included in TIV.**

**Tools for data collection**

* Tally Sheets
* Monitoring (Pre-, intra- and post-vaccination checklist for supervisors)
* Vaccine usage and wastage form (by health facility, sub-district, district and province)
* Adverse Events Following Immunisation (AEFI) investigation form

**Data management**

* All vaccination sites must be identified and recorded to ensure capture of data on DHIS
* Daily facility tally sheets: data captured daily on single sheet
* Weekly health facility, sub-district, district and province influenza vaccination summary sheet: to be used weekly to summarize data and then enter data in DHIS

**Monitoring must focus on the following:**

* Social mobilization and patient service
* Cold chain and vaccines
* Health facility organization
* Data management
* Ensure children receive 2nd dose (where applicable)
* Immunization safety practices
* Adverse events**:** in the event of an adverse event following immunization, the AEFI form must be completed and sent to the EPI/CDC coordinator. All AEFI will be followed-up by the national EPI Unit.

***NB: In the case of an adverse event, the report must be analysed and appropriate measures must be taken to ensure continued safe use of the vaccine.***

**Areas of concern**

* **Concern:** Influenza vaccinations will be conducted at the same time as COVID-19 vaccinations.

**Response:** COVID-19 vaccination roll-out must be carefully considered when planning for influenza vaccinations.

* **Concern:** Influenza vaccinations are taking place at a time that is not normally perceived as the influenza season, so there may be concern regarding the duration of vaccine protection and efficacy

**Response:** Influenza vaccinations are given prior to the influenza season to allow sufficient time for the vaccine to begin working. The vaccine should protect for 6 to 8 months so getting the vaccine just prior to the season in March or April should still provide sufficient protection for the season.

* **Concern:** Limited availability of the vaccines

**Response:** A limited number of vaccines are available for distribution in the public sector. These vaccines should be prioritized as follows:

* + Health care workers;
  + Individuals over the age of 65 years;
  + People with cardiovascular disease (including chronic heart disease, hypertension and stroke), diabetes and chronic lung disease (including asthma, TB and chronic obstructive pulmonary disease); and people living with HIV and AIDS
  + Pregnant women (irrespective of stage of pregnancy)
* **Concern:** Historical low uptake and utilization of seasonal influenza vaccines

**Response:** In 2020, approximately 84% of influenza vaccines purchased by provinces were administered to patients. This may be due to poor reporting of vaccination statistics or because they were not utilised. Given that the number of people who fall in a risk groups far outnumbers the doses available, all vaccines should be utilised as quickly as possible and preferably before the start of the influenza season (i.e. before May-June).

**Areas for urgent focus for provinces and districts**

* Micro-planning should be completed as soon as possible to improve vaccine distribution to target groups.
* Provinces and districts should organise pre-vaccination training:
  + Training should include clinicians at designated health facilities and priority clinics (including ANC, ARV, TB, chronic diseases)
  + Provinces should work with districts to ensure training is cascaded to appropriate staff to improve vaccination, documentation and reporting
* Communication messages prepared by the National Department of Health should be disseminated by provinces to districts, sub-districts, facilities etc.
* Due to the limited supply of influenza vaccines, other preventive measures should also be prioritized including hand washing, cough hygiene, and social distancing.

**Considerations in micro-planning**

* **COVID-19 vaccine roll-out**
* Number and location of HCWs
* ANC, TB, ARV and other specialist clinics
  + Identify patients that attend these specialist clinics
* Name and location of all vaccination sites
* Assess capacity for data management
  + Capacity for entry of data on DHIS
* Assess capacity to deliver vaccines (strengths & gaps, what’s needed)
  + Training needs
  + Cold chain capacity
  + Transport facilities for distribution of vaccines
  + Other logistics and supplies e.g. sharps containers, swabs etc.

**References:**

1. https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html
2. Montomoli E, Torelli A, Manini I, Gianchecchi E. Immunogenicity and safety of the new inactivated quadrivalent influenza vaccine vaxigrip tetra: preliminary results in children≥ 6 months and older adults. Vaccines. 2018 Mar;6(1):14.

**Questions and Answers**

***Question***

*Benefit in current COVID-19 environment*: Has there been a review of the effectiveness and population impact (e.g. mortality benefit) of influenza vaccination in the current setting of the COVID-19 pandemic where generalised masking and other transmission precautions have impacted influenza incidence.

***Answer***

It is evident that the NPIs (non-pharmaceutical interventions) helped to reduce the burden of viral respiratory illness in 2020. In South Africa, similar to other temperate countries in the Southern Hemisphere, there was little or no influenza transmission in 2020. Measures put in place, including travel bans, in response to COVID-19 limited importation and transmission of influenza into South Africa. However, it is not possible to predict with any certainty that this will be the case in 2021 as restrictions continue to be relaxed, or to predict the level of compliance to NPIs or sustained/ continued use of these in 2021, especially with the roll-out of COVID-19 vaccination which may increase the public’s perception of being protected from COVID-19 by the vaccine. It is also possible that following a year with no influenza transmission, South Africa could experience increased transmission.

Preventing influenza by vaccination will reduce the risk of influenza illness and visits to healthcare facilities and hospital admissions especially among those at risk of severe influenza illness, who also happen to be at increased risk of severe COVID-19 disease and outcomes. Influenza vaccination remains the best form of prevention against influenza disease.

There are no data on the impact of influenza vaccination in the current COVID-19 pandemic. A modelling paper by Li et al (1), assessed the effect of mass influenza vaccination on the spread of COVID-19 and other respiratory pathogens in the case of a coincidence of the outbreak with the influenza season. They concluded that increasing influenza vaccine uptake or enhancing the public health interventions (i.e., the use of NPIs) would facilitate the management of respiratory outbreaks coinciding with the peak flu season, and especially ameliorate the shortage of diagnostic kits. Influenza vaccination prior to the onset of the peak influenza season would significantly decrease the number of influenza-like illness (ILI) cases among the general population and specifically the elderly, with fewer persons with ILIs seeking medical care, particularly those in high-risk settings, with frailty, underlying co-morbidities or disabilities. This would minimise the probability of not quickly and accurately identifying circulating respiratory pathogens as well as the possibility of ongoing nosocomial transmission.

1. Li Q, Tang B, Bragazzi NL, Xiao Y, Wu J. Modeling the impact of mass influenza vaccination and public health interventions on COVID-19 epidemics with limited detection capability. *Math Biosci* 2020;325: doi: 10.1016/j.mbs.2020.108378. Epub 2020 May 16.

***Question***

Target population: With the roll-out of the COVID-19 vaccination programme, should healthcare workers still be considered a priority, or should other risk categories be prioritised?

***Answer***

Yes, healthcare workers are an important resource and an integral part of the COVID-19 response, thus vaccinating them will minimise absenteeism due to influenza illness and prevent transmission of influenza from them to patients at risk of severe influenza illness or complications. Hence HCWs should be the top priority group for vaccination in accordance with WHO guidance for influenza vaccination in the COVID-19 pandemic.

***Question***

*Quadrivalent influenza vaccine:* Has an evidence review been done by NAGI for this product, noting the supply challenges?

***Answer***

Quadrivalent influenza vaccines (QIV) offer improved protection during co-circulation of both type-B lineages or when there is a mismatch between the B lineage in the trivalent influenza vaccines (TIV) and circulating B lineage. The main benefit is expected to be experienced by children. Healthy children are not a priority group in South Africa, however children with underlying illnesses may experience some benefit from receiving QIV preferentially over TIV.

The recommendation is that either TIV or QIV can be used depending on cost and availability considerations. There are published data to support that in seasons with high influenza B activity QIV provided more protection (lower odds for hospitalisation, mortality and ILI (Influenza-like illness).

Cost effectiveness studies, including data from South Africa, report that using QIV is cost effective (references below).

1. Yun JW, Choi MJ, Shin GS, Lim JO, Noh JY, Kim YK, Song JY, Kim WJ, Choi SE, Cheong HJ. Cost-effectiveness of influenza vaccine strategies for the elderly in South Korea. *PLoS One* 2019;14:. (1): e0209643.
2. de Boer PT, Kelso JK, Halder N, Nguyen TPL, Moyes J, Cohen C, Barr IG, Postma MJ, Milne GJ. The cost-effectiveness of trivalent and quadrivalent influenza vaccination in communities in South Africa, Vietnam and Australia. *Vaccine* 2018;36:997–1007.
3. Jamotte A, Clay E, Macabeo B, Caicedo A, Lopez JG, Bricks L, Romero Prada M, Marrugo R, Alfonso P, Moreno Arévalo B, Franco D, Garcia Diaz L, Isaza de Molto Y. Public health impact and economic benefits of quadrivalent influenza vaccine in Latin America. *Hum Vaccines Immunother* 2017;13:877–888.
4. Milne GJ, Halder N, Kelso JK, Barr IG, Moyes J, Kahn K, Twine R, Cohen C. Trivalent and quadrivalent influenza vaccination effectiveness in Australia and South Africa: results from a modelling study. *Influenza Other Respi Viruses* 2016;10:324–332.
5. de Boer PT, Crépey P, Pitman RJ, Macabeo B, Chit A, Postma MJ. Cost-Effectiveness of Quadrivalent versus Trivalent Influenza Vaccine in the United States. *Value Heal* 2016;19:964–975.
6. García A, Ortiz de Lejarazu R, Reina J, Callejo D, Cuervo J, Morano Larragueta R. Cost–effectiveness analysis of quadrivalent influenza vaccine in Spain. *Hum Vaccines Immunother* 2016;12:2269–2277.

***Question***

*Double-dosing:* Is there evidence regarding the recommendation for double-dosing amongst children 6 months to 8 years receiving the vaccine for the first time?

***Answer***

There are several published studies confirming benefits of a two-dose strategy in children. A recent study (1), found one dose giving less than half the protection of two doses, even in older children aged 6 to 8 years (2). Previous studies providing supportive evidence recommending two doses for children include references (3) and (4) below.

Currently in South Africa, we continue to recommend two doses for children <9 years of age who have not been immunised previously. However, healthy children are not a recommended priority group.

1. Abraham C, Stockwell MS. The Clinical Importance of a Second Dose of Influenza Vaccination in Young Children. *JAMA Pediatr* 2020;174:643–644.
2. Chua H, Chiu SS, Chan ELY, Feng S, Kwan MYW, Wong JSC, Peiris JSM, Cowling BJ. Effectiveness of Partial and Full Influenza Vaccination among Children Aged <9 Years in Hong Kong, 2011-2019. *J Infect Dis* 2019;220:1568–1576.
3. Neuzil KM, Jackson LA, Nelson J, Klimov A, Cox N, Bridges CB, Dunn J, DeStefano F, Shay D. Immunogenicity and reactogenicity of 1 versus 2 doses of trivalent inactivated influenza vaccine in vaccine-naive 5-8-year-old children. *J Infect Dis* 2006;194:1032–1039.
4. Englund JA, Walter EB, Gbadebo A, Monto AS, Zhu Y, Neuzil KM. Immunization with trivalent inactivated influenza vaccine in partially immunized toddlers. *Pediatrics* 2006;118:e579-85.

***Question***

What is the rationale for the recommendation that COVID-19 vaccination be initiated before influenza vaccination, with a 14-day interval between vaccine administration?

***Answer***

Rationale for administering COVID-19 vaccine first:

"Of the two, the COVID-19 vaccine:

* Is, in general, more effective than the annual flu vaccine,
* Targets a more serious disease,
* Is being given to people less likely to have pre-existing immunity, and
* It is more important that COVID-19 immunity is achieved as soon as possible.

 So, until we can recommend co-administration, when both are available, it is preferable to defer flu vaccination for 2 weeks"

***Question***

Can TIV and QIV be used interchangeably?

***Answer***

TIV and QIV can be used interchangeably, but according to the SA influenza vaccine guidelines, children may benefit most from QIV, then healthcare workers and adults at risk, including pregnant women.



