health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Enquiries: Prof B Schoub
E-mail: barry.schoub@gmail.com

Date:	15 August 2022		
To:	**Honourable Minister Dr Joe Phaahla, Minister of Health**	From:	**Ministerial Advisory Committee (MAC) on COVID-19 Vaccines**

ADVISORY
THE USE OF COVID-19 PFIZER VACCINE FOR CHILDREN BETWEEN 5 AND 11 YEARS OF AGE WHO ARE AT RISK OF SEVERE COVID-19 INFECTION & COMPLICATIONS

Note: *This is a living document and may be updated as further evidence is available or the context changes*.

Problem Statement

Background

- The primary goal of the South African COVID-19 vaccination programme is to reduce severe disease and death associated with COVID-19 and protect the health system. A motivation was received from the South African Paediatric Association, requesting that the COVID-19 vaccination programme be extended to include a sub-group of children 5 to 11 years of age who are considered at higher risk of severe disease or death.
- Pfizer-BioNTech SARS-CoV-2 vaccine is approved in South Africa for use in people aged 12 years and older, and regulatory authorities and government ministries in many other countries have approved use in children from 5 to 11 years of age and younger.
- In this context, the VMAC considered the need for an updated evidence review on the benefits and risks of vaccination of children aged 5 to 11 years old.

Points considered

- Committee members from the Ministerial Advisory Committee on COVID-19 Vaccines (VMAC) and the National Essential Medicines List Ministerial Advisory Committee on COVID-19 Therapeutics (NEML MAC C-19T) along with reviewers from the South African GRADE Network prepared a rapid systematic review to evaluate the efficacy, safety, and effectiveness of BNT162b2 (Comirnaty®, Pfizer-BioNTech BNT162b2, tozinameran, two-dose, 10µg) vaccine to prevent morbidity and mortality associated with COVID-19 in children aged 5 to 11 years old. This review considered only the evidence for the two-dose primary vaccination series. The rapid review was appraised and signed off by the NEML MAC on COVID-19 Therapeutics and the VMAC to agree upon the final recommendation. (See Annexure A with full review.)

Effectiveness of vaccination

- A comprehensive search of multiple databases was conducted up to 27 June 2022, identifying one clinical trial and 11 observational studies addressing this question. The studies included children 5 to 11 years of age and did not specifically report on those with higher risk of severe COVID-19 disease.
- Generally, the absolute risk of hospitalisation or death with or without vaccination in this age group was very low.
- The trial included 2,285 participants and was conducted in United States, Spain, Finland and Poland. BNT162b2 vaccine compared to placebo results in 19 fewer cases of COVID-19 per 1,000 vaccines given (ranging from 15 to 21 fewer cases). There were very few adverse events reported, there were no deaths or cases of severe disease reported in the trial.
- The 11 observational studies reported that the BNT162b2 vaccine compared to no vaccination likely results in 137 fewer cases of COVID-19 per 1,000 children who are vaccinated (from 15 to 214 fewer cases); and a small reduction of 3 fewer hospitalisations per 10,000 children who are vaccinated (from 2 fewer to 4 fewer hospitalisations). Deaths are rare in this group, there were two deaths reported overall, hence it is not possible to get a reliable estimate of protection against death.
- The review evidence suggests a small absolute benefit in the prevention of incident COVID-19 cases and hospitalisation if a two-dose BNT162b2 vaccine is offered to children aged 5 to 11 years old compared to placebo (low – moderate certainty evidence) with a good safety profile.

Current situation: access, costs and acceptability

- Availability of vaccine, feasibility:
    - There is currently no registered paediatric 10ug dose COVID-19 vaccine in South Africa. The South African Health Products Regulatory Authority (SAHPRA) is reviewing a Pfizer COVID-19 vaccine that has a paediatric formulation.
    - To provide vaccine for children 5 to 11 years of age, it is possible, as an interim measure to do fractional dosing of the adult vaccine, which has been implemented in other countries. This will need to be accompanied by training of the HCWs on the appropriate preparation of the dose.
    - If a paediatric vaccine is registered by SAHPRA, the Department of Health can procure it through the Section 21 mechanism, which would allow for smaller quantities to be procured.
- The cost of the paediatric formulation is not yet known, and other resources required to vaccinate this population is likely to increase programmatic costs overall.
- Research data regarding acceptability of vaccination for 5 to 11 years of age is not known for South Africa, but it is noted that 1) in other countries where this vaccine is available acceptance is generally low due to concerns with side effects and about the overall benefit; 2) in 12 -18 year olds in South Africa, uptake of the COVID-19 vaccine has been low with around 12% of this age group having received the 2 dose schedule.

Conclusion

- Overall, the Committee considered many factors when making this decision: health benefits and harms; access and equity; cost and likely resource requirements; and uptake/ acceptance.

- The committee considered that broad vaccination of the general 5 to 11 years of age group may not be justified for the relatively small absolute benefit, along with consideration of the high levels of infection-acquired immunity in our context that may further reduce the overall benefit of vaccination. In addition, challenges with implementation were noted due to lack of availability of a paediatric formulation, and the likely high programmatic cost, and possible low uptake and acceptability.

- Benefit of vaccination is likely to be greatest for children at higher risk of severe COVID-19. Vaccination may also be most feasible as these children may be reached by their health care provider. Although no paediatric formulation is yet available, clinicians may decide to vaccinate 5 to 11 years old children off-label for high-risk children, with a fractional adult vaccine dose (10ug dose).

Table 1: List of conditions that result in higher risk of severe COVID-19 for children
This list of indicative, but additional conditions may be identified

Disease state	Comment
Chronic respiratory disease	Including those with poorly controlled asthma[1] that requires continuous or repeated use of systemic steroids or with previous exacerbations requiring hospital admission, cystic fibrosis, ciliary dyskinesias, bronchopulmonary dysplasia, tuberculosis
Chronic heart conditions	Haemodynamically significant congenital and acquired heart disease, or less severe heart disease with other comorbidity. This includes: - Single ventricle patients or those palliated with a Fontan (Total Cavopulmonary Connection) circulation - Those with chronic cyanosis (oxygen saturations <85% persistently) - Patients with cardiomyopathy requiring medication - Patients with congenital heart disease on medication to improve heart function - Patients with pulmonary hypertension (high blood pressure in the lungs) requiring medication
Chronic conditions of the kidney, liver or digestive system	Including those associated with congenital malformations of the organs, metabolic disorders and neoplasms, and conditions such as severe gastro-oesophageal reflux that may predispose to respiratory infection as well as renal and liver failure.
Chronic neurological disease	This includes those with - Neuro-disability and/or neuromuscular disease that may occur as a result of conditions such as cerebral palsy, autism, epilepsy and muscular dystrophy - Hereditary and degenerative disease of the nervous system or muscles, other conditions associated with hypoventilation - Severe or profound multiple learning disabilities (PMLD), Down's syndrome, those on the learning disability register - Neoplasm of the brain
Endocrine disorders	Including diabetes mellitus, Addison's and hypopituitary syndrome
Immunosuppression	Immunosuppression due to disease or treatment, including: - Those undergoing chemotherapy or radiotherapy, solid organ transplant recipients, bone marrow or stem cell transplant recipients - Genetic disorders affecting the immune system (e.g., deficiencies of IRAK-4 or NEML, complement disorder, SCID) - Those with haematological malignancy, including leukaemia and lymphoma

[1] https//www.cdc.gove/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#children

	- Those receiving immunosuppressive or immunomodulating biological therapy including transplant patients - Those treated with or likely to be treated with high or moderate dose corticosteroids - Those receiving any dose of non-biological oral immune modulating drugs e.g., methotrexate, azathioprine, 6-mercaptopurine or mycophenolate - those with auto-immune diseases who may require long term immunosuppressive treatments. - Those living with Human Immunodeficiency Virus infection. Children who are about to receive planned immunosuppressive therapy should be considered for vaccination prior to commencing therapy.
Asplenia or dysfunction on the spleen	Including hereditary spherocytosis, homozygous sickle cell disease and thalassemia major
Serious genetic abnormalities that affect a number of systems	Including mitochondrial disease and chromosomal abnormalities

Recommendations

1. COVID-19 vaccination using Pfizer-BioNTech BNT162b2 may be offered to children aged 5 – 11 years old who are considered at higher risk for severe illness and death*.

2. In the absence of a paediatric formulation, use of a fractional adult dose (two doses of 10ug each), with appropriate training on administration of this, is recommended.

3. At this stage, VMAC is not recommending vaccination for the general children population of 5 to 11 years of age (*i.e., this is not a priority population for vaccination at this stage*).

*High risk children include, but are not limited to, the following: *Chronic respiratory disease; chronic heart conditions; chronic conditions of the kidney, liver or digestive system; chronic neurological disease; endocrine disorders; immunosuppression; asplenia or dysfunction on the spleen; serious genetic abnormalities that affect a number of systems*. (See Table 1 for details)

Thank you for consideration of this request.

Kind regards,

PROFESSOR BARRY SCHOUB
CHAIRPERSON: MINISTERIAL ADVISORY COMMITTEE ON COVID-19 VACCINES
DATE: 15 August 2022

CC:
» **Dr S Buthelezi (Director-General)**
» **Prof P Parish (Chairperson: NEML MAC C-19T)**