ROYAL COLLEGE OF PHYSICIANS OF IRELAND

28 June 2021

Dr. Tony Holohan
Chief Medical Officer
Department of Health,
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Dear Dr. Holohan

Thank you for your letter of 22 June 2021 requesting a review of "the potential role of heterologous vaccination and the potential ongoing role of viral vector vaccines as part of the COVID-19 vaccination programme in Ireland" in the context of the Delta variant and the ongoing reopening of society.

The National Immunisation Advisory Committee (NIAC) has held several full and subcommittee meetings in recent days to fully consider this request. This reply is based on the need for a rapid response.

NIAC reviewed the current COVID-19 national and international age-related incidence, the evidence of the rapid displacement of the Alpha strain by the highly transmissible Delta strain, the probable increased associated virulence, and the impact on the effectiveness of partial and full vaccination, and heterologous vaccination. NIAC has been informed by briefings from the NPHET modelling team and updated regarding projected HSE vaccine supplies.

1. Heterologous vaccination

NIAC issued recommendations in the updated Chapter 5a on 25 June 2021 that a heterologous vaccination schedule may be used when there is a contraindication to completing the schedule with the same vaccine e.g., anaphylaxis after the first dose, Capillary Leak Syndrome or Thrombosis with Thrombocytopenia Syndrome (TTS) following a Vaxzevria®.

Preliminary studies indicate that heterologous vaccination results in robust antibody and cellular responses with variable but acceptable reactogenicity. Data from a randomised trial of heterologous vaccination (ComCov) is expected shortly. This should add to the existing evidence to enable appropriate recommendations to be made by NIAC. Those scheduled for

a second dose of Vaxezvria® are strongly recommended to complete the course with this vaccine to ensure the earliest protection against severe COVID-19.

2. Potential role of adenoviral vector vaccines

On 13 May 2021, NIAC stated that, when COVID-19 rates are high or increasing and/or the availability of mRNA vaccines is limited, adenoviral vector vaccines may be recommended for those aged 18-49 years to provide early protection.

Vaccine safety is paramount. TTS is a very rare potentially serious side effect of adenoviral vector vaccines with a case fatality rate of 17 – 20% and a higher reporting rate after the first dose and in adults aged under 50 years. The risk after the first dose is estimated to be 1 per 100,000 for those 50 years and older and 2 per 100,000 for adults under 50 years.

Vaxzevria® is authorised as a two-dose schedule with a 4 – 12 week interval. An interval of 8-12 weeks was advised to because of enhanced immunogenicity afforded by that schedule. That advantage is now counterbalanced by the urgent need to optimise early protection.

In light of the increasing rates of the Delta strain, the likelihood of increasing hospitalisation and the risk of long COVID in younger people, there is an urgency to complete vaccination of as many people as soon as possible. Current levels of infection do not support a change to existing recommendations regarding use of adenoviral vector vaccines in younger age cohorts. Similarly, taking into account the projections for case numbers and hospitalisations based on 40% increase in transmission rate of the Delta strain, mRNA vaccines remain preferrable. If the rise in case numbers is more in line with the higher estimates of 60% increase transmissibility, the benefit of all vaccines will be favourable to all age groups including those aged 18-50 years.

NIAC recommends that:

- All vaccines are highly effective in protecting against COVID-19 related hospitalisation.
- Any person over 50 years of age and those in at-risk groups who are not fully vaccinated should complete vaccination as scheduled.
- Vaxzevria® is authorised as a two-dose schedule with a 4 – 12 week interval. The interval should be reduced to 4 weeks where practicable to enable early completion of vaccination.
- Those scheduled for a second dose of Vaxezvria® are strongly recommended to complete the course with this vaccine to ensure the earliest protection against severe COVID-19.
- Currently, an mRNA vaccine is preferable for those under 50 years of age.
- The data from the ComCov study* is awaited to inform any further recommendations regarding heterologous vaccination.

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- Those aged 16 – 49 years should be offered an mRNA vaccine as previously recommended according to their age. Those aged 18-49 years who wish to opt for earlier vaccination can be offered an adenoviral vector vaccine.
- As with all vaccinations, information on the benefits and risks of vaccination should be widely available for informed consent. This could include the use of infographics, such as those developed by the EMA representing differing benefit-risk scenarios.

The evidence underpinning these recommendations will follow. These recommendations reflect a dynamic vaccination programme strategy. Scientific evidence about COVID-19 vaccines is continuously evolving and being refined. Recommendations will be updated when more information becomes available.

Yours sincerely,

Karina Butler
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Karina Butler
Chair NIAC

*** Issued pre-publication of ComCov study**