Immunisation Clinical Advice Response Service 09/09/21

For any COVID-19 vaccination related queries or to escalate an incident please contact: england.swicars@nhs.net

Please note that since Monday 2nd August CARS has now become ICARS and will operate from 9am - 5pm Monday to Friday.

PLEASE SHARE WITH ALL RELEVANT STAFF INVOLVED WITH THE VACCINATION PROGRAMME

Contents:

1. Mixing of Pfizer Vaccine from Different Vials
2. Joint Committee on Vaccination and Immunisation (JCVI) advice on third primary dose vaccination
3. JCVI Advice on Expansion of Vaccination to Children Aged 12-15 Years with Underlying Health Conditions
4. Social Media Cards to Reach Specific Communities and Language Speakers

Mixing of Pfizer Vaccine from Different Vials

As a result of learning from recent incidents, we would like to clarify the guidance about mixing of vaccine from two different vials to make up a single dose of vaccine. Whilst maximising the use of vaccine is important, the Specialist Pharmacy Service Standard Operating Procedure for the preparation of Pfizer vaccine (PVH3) prohibits the mixing of vaccines from different vials.

Joint Committee on Vaccination and Immunisation (JCVI) advice on third primary dose vaccination

The advice can also be read in full at the link below:

Third primary COVID-19 vaccine dose for people who are immunosuppressed: JCVI advice - GOV.UK (www.gov.uk)

On 5 and 19 August 2021 the Joint Committee on Vaccination and Immunisation (JCVI) considered whether some individuals may benefit from a third vaccine dose as part of their primary schedule of COVID-19 vaccination (described henceforth in this document as 'third primary dose').

Third primary dose vaccination

Some individuals who are immunosuppressed due to underlying health conditions or medical treatment may not mount a full immune response to COVID-19 vaccination. Most of the currently available data comes from immunogenicity studies that have measured binding or neutralising antibody levels. Some studies have also measured cellular responses. Interpretation of both types of evidence is hampered by the lack of agreed correlates of protection. It is further recognised that the correlates of protection against infection, symptomatic disease and severe COVID-19 (hospitalisation and deaths) may differ both in the short and longer term. Comparison across studies is affected by the use of different assays with different test characteristics. Some studies indicate that the profile of antibody responses do not necessarily match those of cellular responses. Most of the data relates to the Pfizer-BNT162b2 vaccine.

Preliminary results from UK studies of real-world vaccine effectiveness (VE) in persons who are immunosuppressed suggest only a modest reduction in VE against symptomatic COVID-19, but confidence intervals are wide and overlap with VE estimates for persons who are not immunosuppressed.[footnote 1] Furthermore, as immunosuppression is a heterologous condition that varies widely in severity and in duration, any potential reductions in protection in specific subgroups of the immunosuppressed would be missed by the use of a broader grouping. Clinical effectiveness studies examining more homogeneous sub-groups of persons with specific types of immunosuppression are ongoing. These studies are difficult to conduct due to the relatively small numbers of persons within each sub-group.

A few published studies describing the effect of a third dose of mRNA vaccine in persons who are immunosuppressed report increased immune responses in varying proportions of persons. [footnote 2] [footnote 3] [footnote 4] The OCTAVE-DUO trial is a phase 3 multicentre trial randomising patients in the UK to a third dose of Pfizer-BNT162b2 or Moderna mRNA-1273 with immunogenicity outcomes. The trial is expected to report early results in mid to late September and will probably not have sufficient granularity to inform the management of all types of immunosuppression. mRNA vaccines are being used based on consistent evidence of higher antibody levels, even though some studies suggest that cellular responses with AstraZeneca Vaxzevria vaccine are as good or better than after mRNA vaccines.[footnote 5] Emerging evidence suggests that both antibody and cellular immune responses to the primary course are enhanced with heterologous schedules, and therefore a third primary dose with a different vaccine format may be beneficial.[footnote 6]

Based on experience with other vaccines, it is expected that some persons who are immunosuppressed may not generate a good immune response regardless of the number of vaccine doses administrated. However, data is not currently available to reliably identify who might, or might not, benefit from a third primary dose of a COVID-19 vaccine. A few studies have suggested that timing of vaccine administration in relation to the underlying disease process or therapy is important in determining the level of immune response. For example, responses were higher in those who had completed treatment for clinically aggressive lymphomas more than 6 months earlier compared to those who had had more recent treatment.[footnote 7] Similarly, responses to the first dose of vaccine were higher for patients with solid cancers who had not received chemotherapy within 15 days of vaccination compared to those who had.[footnote 8] This data suggests that a third dose given at an appropriate interval from a period of immunosuppression is likely to provide a better vaccine response.

JCVI recognises that many persons who are immunosuppressed remain concerned regarding their risk of COVID-19 despite having received 2 doses of the primary vaccine schedule as currently advised. The potential for additional protection from a third primary dose is unknown

at an individual level. While antibody levels may be measured, without a clear understanding of the correlates of protection against severe disease and the interaction of immune suppression with measured immune responses, clinical inferences based on the measurement of antibody levels in persons who are immunosuppressed are difficult. For instance, low antibody levels may not denote poor protection against severe disease; and conversely, high antibody levels in a person unable to generate a commensurate cellular response may not denote good protection against severe disease.
Until more data is available, any provision of a third primary dose to persons who are immunosuppressed will draw on the assumption that a third dose is unlikely to confer significant harms or disadvantages, but may offer the possibility of benefit. These uncertainties in harms and benefits will need to be communicated as part of informed consent, and expectations regarding the value of a third primary dose taken into account.

Advice

At the current time, JCVI advises that a third primary dose be offered to individuals aged 12 years and over with severe immunosuppression in proximity of their first or second COVID-19 vaccine doses in the primary schedule. Severe immunosuppression at the time of vaccination is defined using the guidance and timings stated below.

1. Individuals with primary or acquired immunodeficiency states at the time of vaccination due to conditions including:

    - acute and chronic leukaemias, and clinically aggressive lymphomas (including Hodgkin's lymphoma) who were under treatment or within 12 months of achieving cure
    - individuals under follow up for chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias (note: this list is not exhaustive)
    - immunosuppression due to HIV/AIDS with a current CD4 count of <200 cells/µl for adults or children
    - primary or acquired cellular and combined immune deficiencies – those with lymphopaenia (<1,000 lymphocytes/ul) or with a functional lymphocyte disorder
    - those who had received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months
    - those who had received a stem cell transplant more than 24 months ago but had ongoing immunosuppression or graft versus host disease (GVHD)
    - persistent agammaglobulinaemia (IgG < 3g/L) due to primary immunodeficiency (for example, common variable immunodeficiency) or secondary to disease/therapy

2. Individuals on immunosuppressive or immunomodulating therapy at the time of vaccination including:

    - those who were receiving or had received immunosuppressive therapy for a solid organ transplant in the previous 6 months
    - those who were receiving or had received in the previous 3 months targeted therapy for autoimmune disease, such as JAK inhibitors or biologic immune modulators including B-cell targeted therapies (including rituximab but in this case the recipient would be considered immunosuppressed for a 6-month period), T-cell co-stimulation modulators, monoclonal tumour necrosis factor inhibitors (TNFi), soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors (note: this list is not exhaustive)

- those who were receiving or had received in the previous 6 months immunosuppressive chemotherapy or radiotherapy for any indication

3. Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination including:

    - high-dose corticosteroids (equivalent to ≥ 20mg prednisolone per day) for more than 10 days in the previous month
    - long-term moderate dose corticosteroids (equivalent to ≥10mg prednisolone per day for more than 4 weeks) in the previous 3 months
    - non-biological oral immune modulating drugs, such as methotrexate >20mg per week (oral and subcutaneous), azathioprine >3.0mg/kg/day, 6-mercaptopurine >1.5mg/kg/day, mycophenolate >1g/day in the previous 3 months
    - certain combination therapies at individual doses lower than above, including those on ≥7.5mg prednisolone per day in combination with other immunosuppressants (other than hydroxychloroquine or sulfasalazine) and those receiving methotrexate (any dose) with leflunomide in the previous 3 months

4. Individuals who had received high-dose steroids (equivalent to >40mg prednisolone per day for more than a week) for any reason in the month before vaccination.

Individuals who had received brief immunosuppression (≤40mg prednisolone per day) for an acute episode (for example, asthma / COPD / COVID-19) and individuals on replacement corticosteroids for adrenal insufficiency are not considered severely immunosuppressed sufficient to have prevented response to the primary vaccination.

For the most up-to-date advice, see COVID-19: the green book, chapter 14a.
For those aged 18 years and over, JCVI advises a preference for mRNA vaccines for the third primary dose, with the option of the AstraZeneca Vaxzevria vaccine for individuals who have received this vaccine previously where this would facilitate delivery. In exceptional circumstances, persons who received a mRNA COVID-19 vaccine previously may be offered a third primary dose of AstraZeneca Vaxzevria vaccine following a decision by a health professional on a case-by-case, individualised basis. For those aged 12 to 17 years the Pfizer-BNT162b2 vaccine remains the preferred choice, as set out in JCVI advice of 4 August 2021.

The specialist involved should advise on whether the patient fulfils the eligibility criteria and on the timing of any third primary dose. In general, vaccines administered during periods of minimum immunosuppression (where possible) are more likely to generate better immune responses. The third primary dose should ideally be given at least 8 weeks after the second dose, with special attention paid to current or planned immunosuppressive therapies guided by the following principles:

- where possible, the third primary dose should be delayed until 2 weeks after the period of immunosuppression, in addition to the time period for clearance of the therapeutic agent
- if not possible, consideration should be given to vaccination during a treatment ‘holiday’ or at a nadir of immunosuppression between doses of treatment

As with current advice in the green book (chapter 14a) JCVI has advised that:
individuals who have received a bone marrow transplant after vaccination should be considered for a re-immunisation programme for all routine vaccinations and for COVID-19.

Re-vaccination with a 2-dose schedule should be considered 3 to 6 months post autologous and allogeneic human stem cell transplant or CAR-T therapy. A third primary dose of vaccine should be administered at least 8 weeks after the second dose (in line with the advice above).

Most individuals whose immunosuppression commenced at least 2 weeks after the second dose of vaccination do not require a third primary dose at this stage. Alongside those with lower levels of immunosuppression, they are likely to become eligible for a booster dose as part of a routine booster programme from around 6 months after the second dose, pending further advice.
It is expected that severely immunosuppressed inviduals will become eligible for a booster dose as part of a routine booster programme from around 6 months after their third primary dose, pending further advice.

Implementation

To optimise vaccine use, specialists should take responsibility for providing clear advice to the patient's general practitioner about the need for a third primary dose of vaccine and the optimal timing. Organisational support within deployment teams to enable vaccination of these persons within the optimal timing window for them should be considered a priority.

1. Whitaker HJ et al. Pfizer-BioNTech and Oxford AstraZeneca COVID-19 vaccine effectiveness and immune response among individuals in clinical risk groups (2021, preprint).
2. Hall VG et al. Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. N Engl J Med. 2021 Aug 11. doi: 10.1056/NEJMc2111462.
3. Kamar, N et al. Three Doses of an mRNA COVID-19 Vaccine in Solid-Organ Transplant Recipients. N Engl J Med 2021 Aug 12;385(7):661 to 662. doi: 10.1056/NEJMc2108861.
4. Werbel, WA et al. Safety and Immunogenicity of a Third Dose of SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series. Ann Intern Med 2021 Jun 15;L21-0282. doi: 10.7326/L21-0282.
5. Parry H et al. Immunogenicity of single vaccination with BNT162b2 or ChAdOx1 nCoV-19 at 5 to 6 weeks post vaccine in participants aged 80 years or older: an exploratory analysis. Lancet Healthy Longev 2021 Aug 12. doi: 10.1016/S2666-7568(21)00169-0.
6. Liu X et al. Safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV): a single-blind, randomised, non-inferiority trial. Lancet. 2021 Aug 6:S0140-6736(21)01694-9. doi: 10.1016/S0140-6736(21)01694-9.
7. Lim SH et al. Antibody responses after SARS-CoV-2 vaccination in patients with lymphoma. Lancet Haematol 2021 Aug;8(8):e542 to e544. doi: 10.1016/S2352-3026(21)00199-X.
8. Monin L et al. Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study. Lancet Oncol. 2021 Jun; 22(6): 765 to 778. doi: 10.1016/S1470-2045(21)00213-8.

JCVI Advice on Expansion of Vaccination to Children Aged 12-15 Years with Underlying Health Conditions

The Joint Committee on Vaccination and Immunisation (JCVI) published updated advice last Friday in relation to COVID-19 vaccinations for children and young people which expanded the eligibility criteria for those at risk aged 12-15s.

Their guidance can be found at this link:

https://www.gov.uk/government/publications/jcvi-statement-september-2021-covid-19-vaccination-of-children-aged-12-to-15-years/jcvi-statement-on-covid-19-vaccination-of-children-aged-12-to-15-years-3-september-2021#annex-a-jcvi-advice-on-vaccination-of-children-aged-12-to-15-years-with-underlying-health-conditions-31-august-2021

To note, the existing National Protocol and Patient Group Direction (PGD) for the Pfizer BioNTech COVID-19 vaccine includes reference to “children and those aged 12 years and over with specific underlying health conditions that put them at risk of serious COVID-19” and refers to the relevant chapter of the Green Book which has been updated to reflect the expanded definition.

Social Media Cards to Reach Specific Communities and Language Speakers

Five media cards have been published and are for using in digital campaigns nationally, and to reach communities and speakers of specific languages.
https://www.healthpublications.gov.uk/ViewArticle.html?sp=Scovid19vaccinationsocialmediacards2021national

National social media graphics include multiple translations across 25 languages: Albanian, Arabic, Bengali, Brazilian Portuguese, Bulgarian, Chinese, Estonian, Farsi, Greek, Gujarati, Hindi, Latvian, Lithuanian, Panjabi, Polish, Romanian, Russian, Spanish, Somali, Tagalog, Turkish, Twi, Ukrainian, Urdu and Yiddish.

These cards can be downloaded directly from the Health Publications website (you only need to register on the site with your name and address if you want copies sent to you of other resource).

Here is the link to the Health Publications website – Please register at the website here: https://www.healthpublications.gov.uk/Home.html

You can order free copies of many of the publications including the COVID-19 leaflets and posters such as Easy Read, braille, large print, translated versions and BSL videos.

Example Media Card:

All COVID-19 vaccination queries and incidents should be directed to: england.swicars@nhs.net