

## **Regional Clinical Advice Response Service 26/03/21**

For any COVID-19 vaccination related queries or to escalate an incident please contact:  
[england.swcovid19-voc@nhs.net](mailto:england.swcovid19-voc@nhs.net)

Please note that going forward and in line with the RVOC and NVOC, RCARS will now operate between the hours of 8am and 6pm over the weekend.

**PLEASE SHARE WITH ALL RELEVANT STAFF INVOLVED WITH THE  
VACCINATION PROGRAMME**

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### **Updated PGDs for AstraZeneca and Pfizer**

Please find updated PGDs at the link below:

[Coronavirus » Patient Group Directions \(PGDs\) for COVID-19 vaccines \(england.nhs.uk\)](#)

### **European Medicines Agency – Statement on AstraZeneca Vaccine**

Read the full statement [here](#).

**COVID-19 Vaccine AstraZeneca: benefits still outweigh the risks despite possible link to rare blood clots with low blood platelets**

EMA's safety committee, PRAC, concluded its preliminary review of a signal of blood clots in people vaccinated with COVID-19 Vaccine AstraZeneca at its extraordinary meeting of 18 March 2021. The Committee confirmed that:

- the benefits of the vaccine in combating the still widespread threat of COVID-19 (which itself results in clotting problems and may be fatal) continue to outweigh the risk of side effects;

NHS England and NHS Improvement



- the vaccine is not associated with an increase in the overall risk of blood clots (thromboembolic events) in those who receive it;
- there is no evidence of a problem related to specific batches of the vaccine or to particular manufacturing sites;
- however, the vaccine may be associated with very rare cases of blood clots associated with thrombocytopenia, i.e. low levels of blood platelets (elements in the blood that help it to clot) with or without bleeding, including rare cases of clots in the vessels draining blood from the brain (CVST).

These are rare cases – around 20 million people in the UK and EEA had received the vaccine as of March 16 and EMA had reviewed only 7 cases of blood clots in multiple blood vessels (disseminated intravascular coagulation, DIC) and 18 cases of CVST. A causal link with the vaccine is not proven but is possible and deserves further analysis.

The PRAC involved experts in blood disorders in its review, and worked closely with other health authorities including the UK's MHRA which has experience with administration of this vaccine to around 11 million people. Overall, the number of thromboembolic events reported after vaccination, both in studies before licensing and in reports after rollout of vaccination campaigns (469 reports, 191 of them from the EEA), was lower than that expected in the general population. This allows the PRAC to confirm that there is no increase in overall risk of blood clots. However, in younger patients there remain some concerns, related in particular to these rare cases.

The Committee's experts looked in extreme detail at records of DIC and CVST reported from Member States, 9 of which resulted in death. Most of these occurred in people under 55 and the majority were women. Because these events are rare, and COVID-19 itself often causes blood clotting disorders in patients, it is difficult to estimate a background rate for these events in people who have not had the vaccine. However, based on pre-COVID figures it was calculated that less than 1 reported case of DIC might have been expected by 16 March among people under 50 within 14 days of receiving the vaccine, whereas 5 cases had been reported. Similarly, on average 1.35 cases of CVST might have been expected among this age group whereas by the same cut-off date there had been 12. A similar imbalance was not visible in the older population given the vaccine.

The Committee was of the opinion that the vaccine's proven efficacy in preventing hospitalisation and death from COVID-19 outweighs the extremely small likelihood of developing DIC or CVST. However, in the light of its findings, patients should be aware of the remote possibility of such syndromes, and if symptoms suggestive of clotting problems occur patients should seek immediate medical attention and inform healthcare professionals of their recent vaccination. Steps are already being taken to update the product information for the vaccine to include more information on these risks.

The PRAC will undertake additional review of these risks, including looking at the risks with other types of COVID-19 vaccines (although no signal has been identified from monitoring so far). Close safety monitoring of reports of blood clotting disorders will continue, and further studies are being instituted to provide more laboratory data as well as real-world evidence. EMA will communicate further as appropriate.

## Information for patients

- COVID-19 Vaccine AstraZeneca is not associated with an increased overall risk of blood clotting disorders.
- There have been very rare cases of unusual blood clots accompanied by low levels of blood platelets (components that help blood to clot) after vaccination. The reported cases were almost all in women under 55.
- Because COVID-19 can be so serious and is so widespread, the benefits of the vaccine in preventing it outweigh the risks of side effects.
- However, if you get any of the following after receiving the COVID-19 Vaccine AstraZeneca:
  - breathlessness,
  - pain in the chest or stomach,
  - swelling or coldness in a leg,
  - severe or worsening headache or blurred vision after vaccination,
  - persistent bleeding,
  - multiple small bruises, reddish or purplish spots, or blood blisters under the skin,

**please seek prompt medical assistance and mention your recent vaccination.**

## Information for healthcare professionals

- Cases of thrombosis and thrombocytopenia, some presenting as mesenteric vein or cerebral vein/cerebral venous sinus thrombosis, have been reported in persons who had recently received COVID-19 Vaccine AstraZeneca, mostly occurring within 14 days after vaccination. The majority of reports involved women under 55, although some of this may reflect greater exposure of such individuals due to targeting of particular populations for vaccine campaigns in different Member States.
- The number of reported events exceeds those expected, and causality although not confirmed, cannot therefore be excluded. However, given the rarity of the events, and the difficulty of establishing baseline incidence since COVID-19 itself is resulting in hospitalisations with thromboembolic complications, the strength of any association is uncertain.
- EMA considers that the benefit-risk balance of the medicine remains positive, and there is no association with thromboembolic disorders overall. However, steps will be taken to update the SmPC and package leaflet with information on cases of DIC and CVST that have occurred.
- Healthcare professionals are urged to be alert for possible cases of thromboembolism, DIC or CVST occurring in vaccinated individuals.
- Recipients should be warned to seek immediate medical attention for symptoms of thromboembolism, and especially signs of thrombocytopenia and cerebral blood clots such as easy bruising or bleeding, and persistent or severe headache, particularly beyond 3 days after vaccination.

A direct healthcare professional communication (DHPC) will be sent to healthcare professionals prescribing, dispensing or administering the medicine. The DHPC will also be published on a [dedicated page](#) on the EMA website.

## **Prioritisation of B.1.351 (VOC 20DEC-02) for Health Protection Activities**

**24 March 2021**

### **Event Prioritisation of B.1.351 (VOC 20DEC-02) for health protection activities**

**Notified by** Meng Khaw, PHE Incident Director, Meera Chand, PHE Incident Director

**Authorised by** Susan Hopkins, Strategic Director; Sue Ibbotson, Regional Director

**Contact** [ncrc.spoc@dhsc.gov.uk](mailto:ncrc.spoc@dhsc.gov.uk)

### **Background and Interpretation**

The variant B.1.351 (VOC 20DEC-02), first detected in South Africa, was declared a Variant of Concern in December 2020 on the basis of multiple spike mutations and preliminary evidence supporting some degree of escape from immunity.

In subsequent weeks, the epidemiology of this variant has changed, and the results of new studies have become available:

- B.1.351 is now widespread internationally, including causing large outbreaks in Europe
- It is regularly detected in imports to the UK from multiple countries, but the overall UK prevalence remains low at present.
- There is laboratory evidence that antibodies generated by vaccination work less well on B.1.351, compared to the main circulating virus in the UK (B.1.1.7). Of the variants studied so far, B.1.351 shows the largest drop in effect in these studies, including when compared to P.1, the variant first detected in Manaus, Brazil.
- There is clinical trial evidence that vaccines have decreased efficacy in preventing mild to moderate infections with B.1.351, although there is insufficient evidence to know whether they may still protect from severe disease and death after B.1.351 infection.
- There is still insufficient data to judge whether B.1.351 has altered transmissibility or severity.

Based on both epidemiology and virology, at present, B.1.351 is judged to be the variant most likely to impair successful control of COVID-19 by vaccination. The strategic approach chosen is to suppress transmission of this variant within the UK at the current time.

This briefing note contains instructions for the **prioritisation of B.1.351 for all health protection and infection control activities in the community and in healthcare settings.**

### **Implications for PHE Regions**

Regional Health Protection Teams receive daily line-lists of VOCs, VUIs, and E484K mutations, which include notifications of cases of B.1.351 in their area. The list of countries that have reported cases of B.1.351 continues to increase; individuals (except those on the exempt lists) coming to the UK are required to isolate in Managed Quarantine Facilities or at home and perform PCR tests on Day 2 and Day 8.

Cases without a travel history may be an early indicator of community transmission and these cases need to be urgently investigated.

## **Recommendations to PHE Regions**

1. Health Protection Teams should prioritise the investigation of cases of B.1.351 until further notice. This includes:
2. Active follow-up of cases and their contacts as set out in the VOC/VUI manual [**Note:** the link to the manual is only accessible by PHE colleagues)
3. Identify whether cases with travel history have evidence of non-compliance with isolation and take necessary actions to control onward transmission
4. Activate targeted case finding for cases without travel history to contain transmission, including assessing whether settings where cases may have visited require access to testing
5. Through the regional partnership team, work with local authorities to identify additional control measures and public health actions
6. Health Protection Teams to share this briefing note with Local Authority Directors of Public Health through the Regional Partnership Teams, and with NHS Regions for NHS Trusts and primary care providers.

## **Implications and recommendations for Local Authorities**

Local Authority Directors of Public Health should note the concerns about B.1.351 and raise awareness amongst senior officers and elected members.

They should actively engage in multi-agency Incident Management Teams to implement public health actions required to respond to cases of the variant in their communities.

Case detection (through symptomatic and asymptomatic testing) and active contact tracing of cases is the most effective measure to reduce case numbers and drive down transmission in the community.

## **Implications and recommendations for healthcare providers (including hospitals and care homes)**

Healthcare providers should be aware of the guidance on managing suspected or confirmed variant cases. <https://www.gov.uk/government/publications/sars-cov-2-voc-investigating-and-managing-individuals-with-a-possible-or-confirmed-case>.

Patients with a travel history or confirmed B.1.351 infections should be prioritised for isolation over other known or suspected COVID-19 variants.

All PCR positive samples from NHS laboratories should be sent for sequencing at the current prevalence of infection, through their local COG-UK site or PHE; this is particularly important for individuals with re-infection, post vaccine infection and those who are immunocompromised.

## **Information and resources**

**SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing document** [Investigation of novel SARS-CoV-2 variants of concern - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variants-of-concern)

**Variants:** [Variants: distribution of cases data - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/publications/variants-distribution-of-cases-data)

**Advice on the investigation and management of patients who may be infected with a new SARS-CoV-2 Variant of Concern:** [SARS-CoV-2 VOC and VUI: investigating and managing individuals with a possible or confirmed case - GOV.UK \(www.gov.uk\)](https://www.gov.uk/guidance/sars-cov-2-voc-and-vui-investigating-and-managing-individuals-with-a-possible-or-confirmed-case)

**Guidance on how 'surge testing' and genomic sequencing is being used in locations in England where COVID-19 variants have been identified:** [Surge testing for new coronavirus \(COVID-19\) variants - GOV.UK \(www.gov.uk\)](https://www.gov.uk/guidance/surge-testing-for-new-coronavirus-covid-19-variants)

Please also find this full briefing attached.

## **COVID-19 Vaccination Programme: FAQs on Second Doses**

This document is attached but can also be read below.

### **LOCATION OF SECOND DOSE**

#### **Does second dose vaccination need to happen at the same place as the first dose?**

- People using the National Booking Service (booking into a vaccination centre or designated community pharmacy) are given their closest available appointment locations. While we expect most people will book both appointments at the same location, there is an option for the second dose appointment to be booked at a different location. This applies to the COVID-19 AstraZeneca vaccine only.
- People who had their first dose through a GP service should be invited for their second dose through the same GP service.
- People who had their first dose at a Hospital Hub site should be invited or be able to book their second dose at the same location.
- There are other circumstances in which it may be appropriate for a patient to receive their second dose in a different location to their first dose, for example, discharged outpatients, students, doctors in training on rotation to hospitals, people who have become housebound or moved into a care home since their first dose, or patients who have moved to a new house to somewhere a long way away from where they had their first dose.
- Local systems should take a common-sense approach to these cases, eg trying to reduce extensive travel for elderly patients where possible.

### **SECOND DOSE INTERVAL PERIOD**

#### **What is the second dose interval period?**

- The agreed dose interval period is set at 77-84 days as outlined in the [Chief Medical Officer's letter](#). Vaccine will be supplied for second dose clinics to take place 11 weeks post first dose clinics, so that the 12-week time period between doses is achieved.

#### **Can clinics be scheduled early to vaccinate outside of the interval period?**

- Clinics should not schedule second dose appointments earlier than 77 days post the first dose, unless there are exceptional circumstances, as this is not in line with the agreed dose interval.

## **Are there any circumstances when individual patients can receive their second dose outside of the standard interval period?**

- The [Green Book](#) states that second dose should in almost all cases be given between 77 and 84 days after the first dose. However, there are a small number of circumstances when the second dose can be given at a different time interval, for example:

### **Some patients with planned immunosuppressive therapy**

- There are a small number of patients who are about to receive planned immunosuppressive therapy and, where clinically appropriate, should be considered for vaccination prior to commencing therapy (ideally at least two weeks before), when their immune system is better able to make a response.
- Where possible, it would also be preferable for the two-dose-schedule to be completed prior to commencing immunosuppression.
- This would entail offering the second dose at the recommended minimum for that vaccine (three or four weeks from the first dose) to provide maximum benefit that may not be received if the second dose was given during the period of immunosuppression.

### **Homeless people and rough sleepers**

- Given the vulnerabilities of homeless people and rough sleepers, local teams should exercise operational judgement and consider a universal offer, where those experiencing homelessness or rough sleeping are vaccinated alongside priority group 6 (as far as local teams consider appropriate).
- To maximise coverage in this group, JCVI also advise a first vaccine dose should be given, even if follow up for a second dose is likely to be uncertain, and that the dosing schedule can be compressed if that makes delivery of a second dose more certain.
- If an interval longer than the recommended interval is left between doses, the second dose should still be given. The course does not need to be restarted.

## **Can patients be vaccinated sooner than 77-84 days if it is operationally convenient?**

- Second doses should be offered within 77-84 days. The clinical evidence for the COVID-19 AstraZeneca vaccine shows better efficacy following a 12-week gap, which is the basis of the JCVI recommendation.
- However local areas should agree a pragmatic approach to giving doses earlier than this following a clinical assessment and weighing up risks and benefits.

## **SCHEDULING AND ADMINISTERING SECOND DOSES**

### **Can different vaccines be used for first and second doses?**

- The [Green Book](#) states that the same vaccine used for the first dose must be used for the second, except in very exceptional circumstances. These exceptional circumstances are:
  - If the first product received is unknown or if they received a brand that is not available in the UK. In these circumstances every effort should be made to determine which vaccine the individual received for their first dose and to complete the two-dose course with the same vaccine.

- If the patient initially had the Pfizer Vaccine in an LVC or HH clinic and has since become housebound. In these circumstances as the COVID-19 vaccine AstraZeneca can be transported, a second dose with this vaccine can be given.
- Those who experienced anaphylaxis reactions with the first dose of one brand of vaccine may be offered another vaccine if advised by an allergy specialist.

## **CONSENT**

### **Does consent need to be obtained for the second dose, in particular in the case of care home residents?**

- [The Standard Operating Procedure for Covid vaccination in community settings](#) states that “the giving and obtaining of consent is viewed as a process, not a one-off event. Consent should still be sought on the occasion of each immunisation visit. Consent must be given voluntarily and freely”. It is not necessary for care home staff to obtain a second consent form. The original consent forms include the second dose, as they describe consent for the full course. However, patients should have the opportunity to refuse the second dose – this may occur in the rare case of a side effect. Further details are available on NHS Futures web platform issued by the clinical workstream.
- If care home residents do not have capacity and the decision to vaccinate has been made on best interests or through an attorney, this would have been for the full course, so would not necessarily require a second process. However, at the time of the vaccination, there should be the opportunity for an individual or advocate to refuse consent. We expect this to be unlikely in most cases.

## **DATA AND RECORDING**

### **How are first and second dose vaccination events recorded?**

- First and second dose vaccinations are to be recorded in the points of care system in an accurate and timely manner in order to start the allocation calculations. This is important for Pfizer in particular, as its supply is finite.
- Outcomes4Health differentiates between first and second doses.
- Once a first dose event has been recorded on the system this will trigger a second dose allocation requirement 11 weeks later.
- It is important that doses are recorded onto the points of care system at the point of vaccination to ensure clinical safety, eg ensuring that a patient receives the correct second dose.

## **VACCINE ALLOCATIONS AND SUPPLY**

### **How do we manage any surplus doses?**

- Where there is surplus vaccine following second dose clinics, this should be used for first doses in the prevailing priority cohorts, for those patients who have been vaccinated prior to starting immunosuppression and who need a shorter interval between doses.
- For LVS in particular, every effort is being made to right-size Pfizer supply with the use of pack down in order to minimise surplus.



### **How will we separate first and second dose vaccines on site?**

- Vaccine deliveries will not be separated into first and second doses. This will need to be done on site on arrival, informed by the allocation planning process. Sites will receive their regular weekly allocation information which will include first and second dose summaries in order to do this.
- Care must be taken to ensure that volume allocated for second dose activity is appropriately identified and directed to second dose clinics.
- HHs' and VCs' Immform accounts will show total allocation per site – there is no differentiation between first and second dose on Immform.

### **When will second dose allocations be available?**

We are trying to provide visibility of four weeks' worth of allocations ahead of time, to be finalised about two weeks in advance of delivery to Local Vaccination Services, or availability to order in the case of Vaccination Centres or Hospital Hubs. Exact timelines will be communicated shortly through the usual cascade routes. For Local Vaccination Services and Pfizer vaccine we are making efforts to extend to more than four weeks' worth of allocations **ahead of time**.

### **What if we don't have sufficient supplies to cover patients who didn't have their first dose at that site?**

In the unlikely event that supply is insufficient please urgently escalate through the normal routes.

### **Who do I contact if I have a query around final second dose allocations?**

- If your query is related to final dose allocation, it should follow the standard comms route, ie from SVOC, to RVOC, to NVOC which is then shared with the central team.
- Please do not bypass this process, to ensure your queries and requests are actioned as soon as possible.
- The role of Customer Services remains unchanged, same routes apply for second dose as those for first dose.

### **Vaccine Update – Official Guidance Issues 316-318.**

Please follow the links to each issue of vaccine update:

Issue 316 – Covid-19 Special Edition

<https://www.gov.uk/government/publications/vaccine-update-issue-316-january-2021-covid-19-special-edition>

Issue 317

<https://www.gov.uk/government/publications/vaccine-update-issue-317-february-2021>

Issue 318

<https://www.gov.uk/government/publications/vaccine-update-issue-318-march-2021>

**All COVID-19 vaccination queries and incidents should be directed to:**  
**[england.swcovid19-voc@nhs.net](mailto:england.swcovid19-voc@nhs.net)**