



# Blood Clotting following COVID-19 Vaccination

## Information for Health Professionals

**As with all COVID-19 programme resources, this publication is subject to extensive and regular revisions and we recommend linking to the latest version to ensure that you are giving the most up-to-date clinical advice and guidance.**

A range of resources has been developed and updated to support this decision making and are available [on GOV.UK](#).

### 1. What is the condition that has been reported following COVID-19 vaccination?

Since March 2021 there have been reports from the UK and internationally of an extremely rare condition characterised by thromboembolic events (blood clots) accompanied by thrombocytopenia (low platelets) following the first dose of the AstraZeneca (AZ) COVID-19 vaccination. This includes cerebral venous sinus thromboses (CVST) where blood clots develop in the cerebral veins occurring together with low platelet counts. These cases are particularly unusual because despite low platelets, there is progressive thrombosis (formation of blood clots which block blood vessels).

The cases of venous thromboses that have been reported include CVST and portal vein thrombosis, as well as the more usual presentations of deep vein thrombosis and pulmonary embolism. Whilst the cases reported to date have primarily been venous clots, arterial clots have also been reported. Up to 26 May, 348 suspected cases had been reported across the UK through the Regulatory Agency (MHRA) Yellow Card scheme and to date, no confirmed cases have occurred after the second dose of AZ vaccine. For the latest information please see the weekly summary from the [MHRA](#). Typical laboratory features include a low platelet count, very raised D Dimer levels – above the level expected for venous thromboembolism (VTE) and inappropriately low fibrinogen. Antibodies to platelet factor 4 (PF4) have been identified and so this has similarities to heparin-induced thrombocytopenia (HIT), but it is occurring without the patient receiving any heparin treatment. Further information on the investigation and treatment of suspected cases has been

published by the [Expert Haematology Panel of the British Society of Haematology](#).

### 2. What are the risk factors for developing this condition?

This condition is known to occur naturally although the underlying risk factors have not yet been fully established. A detailed review of suspected cases of this condition following COVID-19 vaccination is ongoing by the MHRA, supported by Public Health England (PHE) and other professional groups. This will help us to understand the risk factors for developing this condition. The data reported in the [MHRA weekly report](#) up to 26 May 2021 estimates an overall incidence of around 13.6 per million after first or unknown doses of the AZ vaccine administered in the UK. The incidence after the second dose is 1.3 per million doses and all cases were in patients aged 50 years or older. This data is regularly updated based on the reports received through the Yellow Card reporting scheme. For the latest information please see the weekly summary from the [MHRA](#). Although cases have been reported in all ages and genders, there appears to be a trend for increasing incidence with decreasing age amongst adults, with the highest incidence reported in the younger adult age groups.

### 3. Is this condition only associated with the AZ vaccine?

All suspected cases following vaccination with any of the COVID-19 vaccines being used in the UK are undergoing a detailed review by the MHRA. Up to 26 May 2021, the MHRA received 348 reports of thrombosis events with low platelets of which 128 were cerebral venous sinus thrombosis (CVST). This is out of a total of 24.3 million first doses

and 13.4 million second doses of COVID-19 AZ vaccine given by that date in the UK. For the latest information please see the weekly summary from the [MHRA](#).

There has also been a small number of reports of a similar syndrome following receipt of the Johnson & Johnson/Janssen COVID-19 vaccine (also an adenovirus vector vaccine, although using a different vector) in the US. Following a detailed investigation and temporary pause in the use of the vaccine in the US, the CDC and FDA announced the resumption of the use of the vaccine for all age groups on 23 April 2021. There is currently no evidence to suggest these rare events occur following administration of either the Pfizer/BioNTech or Moderna vaccines which are available in the UK.

Although these extremely rare events have been associated with the AZ vaccine and Johnson & Johnson/Janssen vaccines, further investigations are underway to understand the biological mechanisms and whether the association is related to the vaccine platform (the way in which the vaccine delivers antigen) or some other immunological mechanism.

#### 4. How many people have developed the condition?

This condition is known to occur naturally and is thought to be extremely rare. The background rate of cerebral venous sinus thromboses (CVSTs) is estimated to be around 5 to 16 per million annually, although there is currently limited data on the background rate of CVSTs occurring with thrombocytopenia.

Based on reports to 26 May 2021, the overall incidence following the AZ vaccine is around 13.6 per million first or unknown doses and 1.3 per million second doses administered. For the latest information please see the weekly summary from the [MHRA](#).

It is also important to note that thromboses (blood clots) have been reported with natural COVID-19 infection and more than a fifth of hospitalised patients with COVID-19 have evidence of blood clots. A recent [preprint of a study](#) based on analysis of US data showed that CVST was a complication of COVID-19 infection, with a higher incidence (42.8 per million) compared to a matched cohort of patients with influenza (RR=3.83, 95% CI 1.56 to 9.41, P<0.001) and people who had received an mRNA vaccine (RR=6.67, 95% CI 1.98 to 22.43, P<0.001).

#### 5. How many of those affected die?

A detailed review of all suspected cases is ongoing and based on the reports received by the MHRA as of 26 May, there were 61 fatal cases from the 348 events reviewed with an estimated overall case fatality rate of 18%. This compares with the clear demonstrable benefits from the COVID-19 vaccination programme. For the latest information please see the weekly summary from the [MHRA](#). From the 4 January to 26 May 2021 24.3 million first doses and 13.4 million second doses of the AZ vaccine were administered across the UK. It has been estimated that the vaccine programme had prevented 13,000 deaths in adults aged 60 years and older up to the 9 May with a vaccine effectiveness of a single dose against hospitalisation estimated at 80% for both the Pfizer/BioNTech and the AZ vaccines.

#### 6. What is the UK's current advice on the use of the AZ vaccine?

Based on a review of cases reported to the Yellow Card Scheme and the evidence of effectiveness of the COVID-19 vaccines used in the UK to prevent serious complications and deaths from COVID-19 infection, the current MHRA advice remains that the overall benefits of the use of the AZ vaccine in the UK vaccine programme outweighs the extremely rare adverse events reported to date.

The Joint Committee on Vaccination and Immunisation (JCVI) has carefully assessed the overall risk benefit of the use of the AZ vaccine in the UK population and continues to keep this under active review. After considering the relative balance of benefits (in terms of deaths, ICU and hospital admissions averted estimated by Public Health England) and risks (based on data presented by the MHRA on reported adverse events through the Yellow Card Scheme), on 7 April 2021, [JCVI advised](#) that, for adults aged under 30 without underlying health conditions that put them at higher risk of severe COVID-19 disease, there should be a preference for an alternative to the AZ vaccine, if available.

The MHRA has continued to review cases of these extremely rare adverse events, including those reported retrospectively, and data on the frequency of these events by age is now more precise. The available data continues to suggest a trend of increasing incidence of this condition with decreasing age amongst adults, with the highest incidence reported in the younger adult age groups. In contrast, the risks of serious disease associated with COVID-19 increases steeply with

age, with the younger adults at the lowest risk of serious disease. Amongst those healthy adults targeted in Phase 2 (those under 50 years), there continues to be an age-related risk of severe complications from COVID-19. For example, the risk of dying in an individual aged 40 to 49 years is 3 times higher than someone aged 30 to 39 years and 12 times higher than someone aged 20 to 29 years.

JCVI has continued to review the available data on the current epidemiology, benefit-risk profile by age, modelling predictions on future disease trends and the current forecast on vaccine supply. Given the risk (albeit extremely rare) of these adverse events associated with the AZ vaccine, the current control of COVID-19 in the UK, model predictions of the potential scale and timing of a future wave, and promising forecasts for the availability of vaccines in the UK, JCVI has issued updated advice.

- in addition to those aged under 30, unvaccinated adults aged 30 to 39 years who are not in a clinical priority group at higher risk of severe COVID-19 disease, should be preferentially offered an alternative to the AZ vaccine, where possible and only where no substantial delay or barrier in access to vaccination would arise.
- for those within this age group who are of older age, male, obese (BMI above 30), from certain ethnic minority backgrounds or experiencing socio-economic deprivation, the risks of acquiring or suffering complications of COVID-19 are higher. Every effort should be made to remove barriers to accessing vaccination in those individuals. These individuals can choose to have the AZ vaccine if they have been provided with information on the risks and benefits of the vaccine.
- for those aged 18 to 29 years the precautionary advice for a vaccine preference is stronger, reflecting a gradient in the benefit-risk balance with age.

This new advice is specific to the current UK context and is based on all of the following remaining favourable: the current low incidence of disease, the availability of alternatives to the AZ vaccine, and the strength of the whole vaccine programme in terms of maintaining speed and uptake. Should there be a deterioration in any of the above factors, JCVI advises that vaccination of adults aged 30 to 39 years with any of the UK authorised vaccines is always better than no vaccination, except where there are specific contraindications.

Healthy adults aged 40 to 50 years who are offered a vaccine as part of Phase 2 of the programme are recommended to receive any of the available COVID-19 vaccines. Those who have received their first dose of the AZ vaccine without suffering this rare side effect, should continue to be offered the second dose to complete the course (see the [Green Book](#) for further information).

The AZ vaccine should also continue to be offered to those in Phase 1 (which includes older adults, those with underlying conditions, health and social care workers over 40 years old) who have not yet been offered the vaccine. Those who have received their first dose of AZ vaccine without suffering this rare side effect, should continue to be offered the second dose to complete the course. This includes individuals aged 18 to 39 years who have received their first dose of AZ vaccine as part of the Phase 1 programme such as health and social care workers, unpaid carers and family members of those who are immunosuppressed.

Due to its storage and transport requirements, the AZ vaccine is much more easily delivered in some settings, and in these settings may be the only vaccine it is practical to offer. In such circumstances JCVI advises that the benefits of receiving the AZ vaccine outweigh the risks, and individuals in this event should be offered the AZ vaccine.

JCVI considers that there continue to be no safety concerns for this extremely rare adverse event following receipt of a second dose of the AZ vaccine. All those who have received a first dose of the AZ vaccine should continue to be offered a second dose of the AZ vaccine, irrespective of age. The second dose will be important for longer lasting protection against COVID-19.

## 7. Can COVID-19 infection cause the same problem?

Thrombotic events are known to occur in individuals with natural COVID-19 infection and more than a fifth of hospitalised patients with COVID-19 have evidence of blood clots. A [preprint of a study](#) based on analysis of US data showed that CVST was a complication of COVID-19 infection, with a higher incidence (42.8 per million) compared to a matched cohort of patients with influenza (RR=3.83, 95% CI 1.56 to 9.41, P<0.001) and people who had received an mRNA vaccine (RR=6.67, 95% CI 1.98 to 22.43, P<0.001). However, this particular combination of thrombotic

events and thrombocytopenia is extremely rare and not known to be a common feature of COVID-19 infection. Based on cases reported to MHRA as of 26 May 2021, the overall incidence following the AZ vaccine is estimated at 13.6 per million first or unknown doses and 1.3 per million second doses administered. For the latest information please see the weekly summary from the [MHRA](#).

#### 8. Has this condition been reported after both the first and second dose of COVID-19 vaccine?

As of 26 May 2021, of the 348 suspected cases reported to the MHRA following the AZ vaccine, 18 suspected cases have been reported after the second dose all in those aged 50 or older. None of these cases have been confirmed. The JCVI concluded that there continue to be no safety concerns following the second dose of vaccine. As the number of second doses administered has increased, the much lower rate of reported cases and absence of confirmed cases after the second dose is reassuring. The JCVI advises that those who have received their first dose of the AZ vaccine should continue to be offered the second dose unless they have developed this specific syndrome of thrombosis and thrombocytopenia following the first dose or have had an anaphylactic reaction. The [Green Book](#) has further information on contraindications to COVID-19 vaccines.

#### 9. Is it affecting both men and women?

Suspected cases have been reported in patients of all ages in men and women. Whilst reports from some countries have suggested a substantially higher number of cases amongst females, based on the events reported to the MHRA in the UK, such a distinctive gender difference has not been observed. Although the reported incidence rate is higher in females compared to men, this is not seen across all age groups and the difference remains small. It is worth noting that more females were vaccinated early on in the programme, which may partly explain the slight excess of cases reported amongst females.

#### 10. Is it affecting any particular community?

Suspected cases have been reported in patients of all ages and genders and currently, no specific predisposing factors have been identified. There appears to be a trend of increasing incidence of this condition with decreasing age amongst adults, with the highest incidence reported in the younger adult age groups.

#### 11. What are the signs and symptoms?

While the detailed case review is ongoing, it is important to ensure all health professionals are alert to relevant symptoms which require further clinical review and investigation.

Advise patients to seek urgent medical advice if they experience any of the following symptoms more than 4 days and within 28 days of coronavirus vaccination:

- new onset of severe headache, which is getting worse and does not respond to simple painkillers
- an unusual headache which seems worse when lying down or bending over, or may be accompanied by blurred vision, nausea and vomiting, difficulty with speech, weakness, drowsiness or seizures
- new unexplained pinprick bruising or bleeding
- shortness of breath, chest pain, leg swelling or persistent abdominal pain

If you have clinical concerns, patients should be urgently referred to hospital and to appropriate specialist services for further assessment, particularly if the symptoms are unexplained and present in combination with thrombocytopenia. Further guidance for [secondary care](#) is available with specific guidance produced for [Emergency Departments and Acute Medical Units](#) and [primary care](#).

Mild flu-like symptoms, including headache, chills and fever remain one of the most common side effects of any COVID-19 vaccine. These generally appear within a few hours and resolve within a day or two.

#### 12. What should I do if I suspect a case?

If you have clinical concerns, patients should be urgently referred to hospital and to appropriate specialist services for further assessment, particularly if the symptoms are unexplained and present in combination with thrombocytopenia. Further guidance for [secondary care](#) is available with specific guidance produced for [Emergency Departments and Acute Medical Units](#) and [primary care](#).

In the UK, the MHRA are reviewing all reported cases to the [COVID-19 Yellow Card scheme](#). In order to support the case reporting, clinical review and investigation, PHE has established an electronic clinical reporting scheme collecting patient identifiable information on all suspected cases. It is very important that all suspected cases are also reported to the PHE clinical reporting scheme at [https://cutt.ly/haem\\_AE](https://cutt.ly/haem_AE) with details of the clinical presentation, dates of vaccination, vaccine product received and any underlying conditions.

In order to minimise burden on reporters, for cases reported on the PHE clinical reporting scheme first, the last page of the survey allows all the inputted answers to be copied, and relevant information can then be directly pasted into the COVID-19 Yellow Card form.

#### 13. How should I report suspected cases?

It is very important that all suspected cases are reported to both the MHRA on the [COVID-19 Yellow Card scheme](#) and to PHE's clinical reporting scheme at [https://cutt.ly/haem\\_AE](https://cutt.ly/haem_AE). The PHE clinical reporting scheme collects patient identifiable information with details of the clinical presentation, dates of vaccination, vaccine product received and any underlying conditions. In order to minimise burden on reporters, for cases reported on the PHE clinical reporting scheme first, the last page of the survey allows all the inputted answers to be copied, and relevant information can then be directly pasted into the COVID-19 Yellow Card form.

#### 14. Are there any contraindications or cautions to receiving the AZ vaccine?

The contraindications to vaccination with the AZ vaccine include individuals who have a history of heparin-induced thrombocytopenia and thrombosis (HITT or HIT type 2). These individuals may be offered vaccination with an alternative COVID-19 vaccine. A history of thromboses on its own is not a contraindication to the vaccine. Individuals who experience thrombosis with thrombocytopenia following the first dose of the AZ vaccine should be properly assessed and if they are considered to have the reported condition, vaccination should be delayed until their clotting has completely stabilised and they should be considered for a second dose of an alternative COVID-19 vaccine. There is no evidence that those with a prior history of thrombosis or known risk factors for thrombosis, including antiphospholipid syndrome, are more at risk of developing this immune-mediated condition of thrombosis in combination with thrombocytopenia after the AZ vaccine. The [Green Book](#) has further information on contraindications and cautions to receiving the AZ vaccine.

Individuals aged 40 years or older with past clotting episodes and those diagnosed with thrombophilia, whether or not they are on long term anti-coagulation, remain at risk of COVID-19 disease and should be vaccinated with any of the available vaccines (provided they are not otherwise contraindicated). The same consideration applies

to those who experience common clotting episodes, without concomitant thrombocytopenia, after the first dose of the AZ vaccine. The [Expert Haematology Panel](#) advises that there is no evidence that individuals with a prior history of thrombosis or known risk factors for thrombosis are more at risk of developing the immune complication reported after the AZ vaccine. Furthermore, for the majority of individuals, the risk of recurrent thrombosis due to COVID-19 infection is far greater than the risk of this syndrome.

#### 15. Should we still give people their second dose?

Yes, because of the high risk of complications and death from COVID-19, the MHRA, the World Health Organization and the European Medicines Agency have concluded that the balance is very much in favour of vaccination. There are currently no safety concerns following receipt of the second dose of vaccine. There are no known risk factors for this extremely rare condition, which appears to be an idiosyncratic reaction on first exposure to the AZ vaccine. The [JCVI](#) advises that those who have received their first dose of the AZ vaccine without suffering this rare side effect should continue to be offered the second dose to complete the course.

#### 16. Can my patient receive the AZ vaccine if they have previously had a blood clot?

Importantly, a history of thromboses on its own is not a contraindication to the vaccine and individuals should be reassured that they can still receive the AZ vaccine when offered. The contraindications to vaccination with the AZ vaccine include individuals who have a history of heparin-induced thrombocytopenia and thrombosis (HITT or HIT type 2).

These individuals may be offered vaccination with an alternative COVID-19 vaccine. Individuals who experience thrombosis with thrombocytopenia following the first dose of the AZ vaccine should be properly assessed and if they are considered to have the reported condition, vaccination should be delayed until their clotting has completely stabilised and they should be considered for a second dose of an alternative COVID-19 vaccine.

There is no evidence that those with a prior history of thrombosis or known risk factors for thrombosis, including antiphospholipid syndrome, are more at risk of developing this immune-mediated condition of thrombosis in combination

with thrombocytopenia after the AZ vaccine. The [Green Book](#) has further information on contraindications and cautions to receiving the AZ vaccine.

Individuals over 40 years or older with past clotting episodes and those diagnosed with thrombophilia, whether or not they are on long term anti-coagulation, remain at risk of COVID-19 disease and should be vaccinated with any of the available vaccines (provided they are not otherwise contraindicated). The same consideration applies to those who experience common clotting episodes, without concomitant thrombocytopenia, after the first dose of the AZ vaccine.

The [Expert Haematology Panel advises](#) that there is no evidence that individuals with a prior history of thrombosis or known risk factors for thrombosis are more at risk of developing the immune complication reported after the AZ vaccine. Furthermore, for the majority of individuals, the risk of recurrent thrombosis due to COVID-19 infection is far greater than the risk of this syndrome. If a patient has a history of, for example, a deep venous thrombosis (DVT) or pulmonary embolus (PE) without concurrent thrombocytopenia, then they can receive the AZ vaccine. Likewise, if they have had an arterial thrombosis, for example myocardial infarction without thrombocytopenia, then they can receive the AZ vaccine.

Many patients who have had a history of blood clots may be concerned as to whether they also had low platelets at the same time. This is likely to have been communicated at the time of diagnosis of the blood clot and be recorded in the patient's medical records. In the absence of this being recorded in the patient's medical records, such individuals can be offered the AZ vaccine.

A revision to the COVID-19 [Green Book](#) chapter is available with updated information on cautions and contraindications for the AZ vaccine.

#### **17. Can a patient with antiphospholipid syndrome have the vaccine?**

Antiphospholipid syndrome increases the risk of thrombosis but there is no evidence that individuals with a prior history of thrombosis or known risk factors for thrombosis are more at risk of developing the immune complication reported after the AZ vaccine. If an individual with antiphospholipid syndrome is aged 40 years or older and has no contraindications to the AZ vaccine, then they can receive the AZ vaccine.

This information is consistent with the JCVI's advice. The MHRA's current advice is that the AZ vaccine should be considered in individuals with antiphospholipid syndrome when the benefits of the vaccine outweigh the risk for that individual. The JCVI has reviewed the evidence on risks and benefits and has provided advice to the UK population on who should continue to be offered the AZ vaccine and this is the advice, as outlined in the [Green Book](#), that should be followed for vaccination decisions.

For the majority of individuals, the risk of recurrent thrombosis due to COVID-19 infection is far greater than the risk of this syndrome following vaccination with AZ. Individuals who experience a clotting episode with concomitant thrombocytopenia following the first dose of the AZ vaccine should be properly assessed; if they are considered to have the reported condition, further vaccination should be deferred until their clotting has completely stabilised and should then be boosted with an alternative product. The contraindications to vaccination with the AZ vaccine include individuals who have a history of heparin-induced thrombocytopenia and thrombosis (HITT or HIT type 2). These individuals may be offered vaccination with an alternative COVID-19 vaccine. Please see the [Green Book](#) for further advice on cautions and contraindications to vaccination.

#### **18. Can my patient receive the AZ vaccine if they have been or are currently thrombocytopenic?**

Thrombocytopenia on its own is not a contraindication to receiving the AZ vaccine.

The contraindications to vaccination with the AZ vaccine include individuals who have a history of heparin-induced thrombocytopenia and thrombosis (HITT or HIT type 2). These individuals may be offered vaccination with an alternative COVID-19 vaccine. Individuals who experience thrombosis with thrombocytopenia following the first dose of the AZ vaccine should be properly assessed and if they are considered to have the reported condition, vaccination should be delayed until their clotting has completely stabilised and they should be considered for a second dose of an alternative COVID-19 vaccine.

The [Green Book](#) has further information on contraindications and cautions to receiving the AZ vaccine. Individuals with bleeding disorders can still be vaccinated and further information is available in the [Green Book](#).

#### 19. What if someone has had a cerebral or major blot clot with low levels of platelets following the first dose of the AZ vaccine?

Individuals who experience thrombosis with thrombocytopenia following the first dose of the AZ vaccine should be properly assessed and if they are considered to have the reported condition, vaccination should be delayed until their clotting has completely stabilised and they should be considered for a second dose of an alternative COVID-19 vaccine (see the [Green Book](#)).

#### 20. Can my patient still have a second dose of the AZ vaccine if they had a blood clot after the first dose?

Importantly, a history of thromboses on its own (without thrombocytopaenia) following the first dose of the AZ vaccine is not a contraindication to receiving their second dose and individuals should be reassured that they can still receive the AZ vaccine when offered.

The contraindications to vaccination with the AZ vaccine include individuals who have a history of heparin-induced thrombocytopaenia and thrombosis (HITT or HIT type 2). These individuals may be offered vaccination with an alternative COVID-19 vaccine. A history of thromboses on its own is not a contraindication to the vaccine. Individuals who experience thrombosis with thrombocytopenia following the first dose of the AZ vaccine should be properly assessed and if they are considered to have the reported condition, vaccination should be delayed until their clotting has completely stabilised and they should be considered for a second dose of an alternative COVID-19 vaccine. There is no evidence that those with a prior history of thrombosis or known risk factors for thrombosis, including antiphospholipid syndrome, are more at risk of developing this immune-mediated condition of thrombosis in combination with thrombocytopaenia after the AZ vaccine.

The [Green Book](#) has further information on contraindications and cautions to receiving the AZ vaccine.

The [Expert Haematology Panel advises](#) that there is no evidence that individuals with a prior history of thrombosis or known risk factors for thrombosis are more at risk of developing the immune complication reported after the AZ vaccine. Furthermore, for the majority of individuals, the risk of recurrent thrombosis due to COVID-19

infection is far greater than the risk of this syndrome. Individuals who experience a clotting episode with concomitant thrombocytopenia following the first dose of the AZ vaccine should be properly assessed; if they are considered to have the reported condition, further vaccination should be deferred until their clotting has completely stabilised and should then be boosted with an alternative product.

In the UK about 1 in a 1,000 people are affected by venous thrombosis each year. This compares with reports up to 19 May to the MHRA of 332 thrombosis events with low platelets out of a total of 24.2 million first doses of AZ vaccine given by that date. Therefore, by chance, a lot of people will have blood clots after vaccination which are not due to this syndrome.

#### 21. What if somebody under 40 years has had AZ for their first dose – should they have the second?

The AZ vaccine should continue to be offered to those in Phase 1 who have not yet been offered the vaccine. This includes older adults, those with underlying conditions, health and social care workers 40 years or older. There are currently no known risk factors for this extremely rare condition, which appears to be an idiosyncratic reaction on first exposure to the AZ vaccine. Those who have received their first dose of the AZ vaccine and have not suffered this rare side effect should continue to be offered the second dose to complete the course.

Individuals aged 18 to 39 years who have received their first dose of the AZ vaccine, without suffering this rare side effect, should complete their course with the same vaccine. This will include those who are eligible as part of the Phase 1 programme, for example health and social care workers, and this includes unpaid carers and family members of those who are immunosuppressed. There is currently no evidence on the interchangeability of the COVID-19 vaccines although studies are underway. Furthermore, [preliminary data](#) suggests that individuals receiving mixed schedules (a dose of AZ followed by a dose of Pfizer or vice versa) have higher rates of reactions. Therefore, every effort should be made to determine which vaccine the individual received and to complete with the same vaccine.

Please see the [Green Book](#) for further advice on vaccination.

## 22. Should my patient have a second dose of a different vaccine other than the AZ vaccine?

Individuals who experience thrombosis with thrombocytopenia following the first dose of the AZ vaccine should be properly assessed and if they are considered to have the reported condition, vaccination should be delayed until their clotting has completely stabilised and they should be considered for a second dose of an alternative COVID-19 vaccine. There are currently no safety concerns following receipt of the second dose of the AZ vaccine. This extremely rare condition appears to be an idiosyncratic reaction on first exposure to the AZ vaccine and there are no known risk factors for it. The [JCVI advises](#) that those who have received their first dose of the AZ vaccine without suffering this rare side effect should continue to be offered the second dose to complete the course. This includes individuals aged 18 to 39 years who have received their first dose of the AZ vaccine without this rare side effect.

There is currently no evidence on the interchangeability of the COVID-19 vaccines although studies are underway. Therefore, every effort should be made to determine which vaccine the individual received and to complete with the same vaccine. Preliminary data from a [study](#) of 463 people aged 50 to 69 years in evaluating the interchangeability of COVID-19 vaccines suggests that a mixed schedule appears to lead to more systemic side effects after the second dose, such as fever and muscle aches. More individuals who received the AZ vaccine for the first dose and Pfizer for the second dose reported fever compared to those who received the AZ vaccine for both doses (difference 24%, 95% CI 13 to 35%). A similar pattern was seen for those individuals who received the Pfizer vaccine for the first dose and AZ for the second dose compared to those who received the Pfizer vaccine for both doses (difference 21%, 95% CI 8 to 33%). Please see the [Green Book](#) for further advice on vaccination.

## 23. Will taking aspirin before vaccination with the AZ vaccine reduce the clotting risk for my patients?

It is NOT recommended to take aspirin before vaccination with AZ, unless this is already part of your patient's regular medications. Investigations are underway to understand the biological mechanisms behind this extremely rare condition of thromboembolic events with thrombocytopenia and whether the association is related to the vaccine

platform (the way in which the vaccine delivers antigen) or some other immunological mechanism. Whilst aspirin may be used to reduce clotting risk in other conditions, it is not currently thought to have the same effect in this condition and may in fact worsen the outcome by increasing the risk of bleeding. Therefore no one should self-medicate with aspirin to cover the period around and after the vaccination.

## 24. How can I communicate the potential benefits and risks of the AZ vaccine to my patients?

[Resources](#), such as patient information leaflets, have been produced which explain the benefits and risks of the AZ vaccination by different age bands. Older age groups, such as those aged 50 or older or with underlying medical problems, have a higher risk of hospitalisation, intensive care admission or death from COVID-19 infection than younger age groups:

- for those aged 50 and older or with underlying medical problems, the risk of this extremely rare side effect is around 1 in every 100,000 first dose and the benefit of 1 dose of the vaccine is an 80% reduction in deaths, hospitalisation and intensive care admission
- for people aged 40 to 49, the risk of this very extremely side-effect is around 1 in every 100,000 first doses and the benefit of one dose of the vaccine is 60 to 70% reduction in catching and passing on the infection
- for people aged 18 to 39, the risk of this extremely rare side effect is around 1 in every 50,000 first doses and the benefit of 1 dose of the vaccine is 60 to 70 % reduction in catching and passing on the infection

Someone who is vaccinated will continue to accrue benefits from vaccination over their lifetime from being protected against COVID-19, whilst the risk from vaccination occurs only in the few weeks after vaccination.

## 25. What if my patient refuses the AZ vaccine?

To make an informed decision it is important that all individuals are provided with the relevant information, including the benefits and risks, and that they have the opportunity to discuss this with their healthcare provider if they wish. If the patient is under 40 years, an alternative vaccine will become available, but they may need to go to a different vaccination site. [Resources](#), including patient leaflets, are available to support decision making.



#### 26. What if my patient under 40 years old wants to have the AZ vaccine?

Patients under 40 who decide to go ahead after they have considered all the risks and benefits can be vaccinated with the AZ vaccine. You should document that you have had a full conversation with the patient and that you have provided them with sufficient information for them to give informed consent to vaccination. [Resources](#), including patient leaflets, are available to support decision making.

#### 27. Can patients taking the combined oral contraceptive pill have the AZ vaccine?

Yes, patients taking the combined oral contraceptive pill can have the AZ vaccine, if they do not have any of the contraindications or cautions to its use (see the [Green Book](#) for further information).

The JCVI has concluded that for adults under 40 years of age who are not in a clinical risk group, it is preferable to offer an alternative to the AZ vaccine [if available](#). Healthy adults aged 40 to 50 years are recommended to receive any of the available COVID-19 vaccines. Those who have received their first dose of AZ vaccine without suffering this rare side effect should continue to be offered the second dose to complete the course.

Patients who are taking the combined oral contraceptive pill may be concerned that they have an increased risk of thrombosis and should not have the AZ vaccine. The [Expert Haematology Panel advises](#) that there is no evidence that individuals with a prior history of thrombosis or known risk factors for thrombosis are more at risk of developing the immune complication reported after the AZ vaccine. Furthermore, for the majority of individuals, the risk of recurrent thrombosis due to COVID-19 infection is far greater than the risk of this syndrome.

The Faculty of Sexual and Reproductive Healthcare (FSRH) has published a statement on this topic [FSRH CEU statement: Cerebral venous sinus thrombosis AstraZeneca COVID-19 vaccination and CHC](#)

#### 28. What is the current advice for pregnant women?

The [Expert Haematology Panel advises](#) that there is no evidence that individuals with a prior history of thrombosis or known risk factors for thrombosis are more at risk of developing the immune complication reported after the AZ vaccine. Hence, prothrombotic states such as pregnancy and contraception are not likely to confer a higher risk.

However, because of more extensive experience and available safety data for Pfizer and Moderna vaccines from the US, these vaccines are preferred in pregnancy. Further information is available in the [Green Book](#).

#### 29. What investigations do I need to organise for cases?

Guidance for [secondary care](#), including which investigations should be organised, are available and specific guidance has been produced for [Emergency Departments and Acute Medical Units](#) and [primary care](#).

If a case is confirmed positive for PF4 antibodies by ELISA, then treatment should continue as described in the above guidance. Further samples should also be collected:

- (1) Serum samples should be sent to PHE Colindale for COVID-19 antibody testing and storage. Please use the [E59 sample submission form](#) and use the code VATTs (Vaccine-associated Thrombosis and Thrombocytopaenia Syndrome) for easy identification.

For the attention of Dr Kevin Brown  
Consultant Medical Virologist  
Virus Reference Department  
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- (2) EDTA for whole genome sequencing – email [gel@liverpoolft.nhs.uk](mailto:gel@liverpoolft.nhs.uk) with patient name, dob, gender, NHS number and location, to receive a barcode for the EDTA tube and a document pack with patient information and consent form.

Consent is obtained using 100,000 Genomes Project approved Patient Information Leaflets (PILs) and consent forms and there are options for deceased and patients lacking capacity.

The Research Ethics Opinion for this study is in line with a Research Tissue Bank approval therefore individual Trust approval is not required. However if needed, Genomics England Limited (GEL) will liaise with the referring Trust's Research and Development and provide the Genomics England Research Library letter to notify the department of the recruitment activity. This ethics covers England, Wales and Northern Ireland. Separate arrangements are made for Scotland.

## Blood Clotting following COVID-19 Vaccination

### Information for Health Professionals

#### Sources

[Guidance produced from the Expert Haematology Panel \(EHP\) focussed on syndrome of Thrombosis and Thrombocytopenia occurring after coronavirus vaccination | British Society for Haematology \(b-s-h.org.uk\)](#)

COVID-19: the green book, chapter 14a

Use of the AstraZeneca COVID-19 vaccine: JCVI statement [www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement](http://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement)

MHRA issues new advice, concluding a possible link between COVID-19 vaccine AstraZeneca and extremely rare, unlikely to occur blood clots [www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots](http://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots)

Coronavirus Yellow Card reporting site [Official MHRA side effect and adverse incident reporting site for coronavirus treatments and vaccines | Coronavirus \(COVID-19\)](#)

Public Health England – reporting thrombotic events with thrombocytopenia following immunisation to COVID-19 [https://cutt.ly/haem\\_AE](https://cutt.ly/haem_AE)

COVID-19 vaccination and blood clotting resources [www.gov.uk/government/collections/covid-19-vaccination-and-blood-clotting](http://www.gov.uk/government/collections/covid-19-vaccination-and-blood-clotting)

Expert Haematology Panel: <https://b-s-h.org.uk/media/19537/letter-to-mhra-from-expert-haematology-group-endorsed-by-thrombosis-uk-1300-8th-april-2021.pdf>

PHE monitoring of the effectiveness of COVID-19 vaccination: [www.gov.uk/government/publications/phe-monitoring-of-the-effectiveness-of-covid-19-vaccination](http://www.gov.uk/government/publications/phe-monitoring-of-the-effectiveness-of-covid-19-vaccination)

RCEM: Management of patients presenting to the Emergency Department/Acute Medicine with symptoms [ED-AM Vaccine pathway concerns – RCP – SAM – RCEM.pdf](#)

JCVI final statement on phase 2 of the COVID-19 vaccination programme: 13 April 2021: [www.gov.uk/government/publications/priority-groups-for-phase-2-of-the-coronavirus-covid-19-vaccination-programme-advice-from-the-jcvi](http://www.gov.uk/government/publications/priority-groups-for-phase-2-of-the-coronavirus-covid-19-vaccination-programme-advice-from-the-jcvi)

MHRA: Coronavirus vaccine – weekly summary of Yellow Card reporting [Coronavirus vaccine – weekly summary of Yellow Card reporting – GOV.UK \(www.gov.uk\)](#)

RCGP Primary Care Management of Suspected Thromboembolism with Thrombocytopenia after COVID-19 Vaccination Headaches after AZ, April 2021 ([rcgp.org.uk](http://rcgp.org.uk))

**Vaccination, helping to protect those most vulnerable.**