

COVID-19 Vaccine in patients with haematological disorders British Society for Haematology

This statement has been produced by the British Society for Haematology and has been reviewed by the Intercollegiate Committee on Haematology, on behalf of the Royal College of Physicians of London and the Royal College of Pathologists. Specialist haematology groups have also contributed.

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Information on the new COVID-19 vaccine

The Pfizer/BioNTech COVID-19 vaccine has been authorised for use by the Medicines and Healthcare products Regulatory Authority (MHRA), it was introduced into use in the UK on 8th Dec 2020. This is not a 'live' vaccine so should be safe for most patients with blood cancer. It is likely that other vaccines will be authorised and be available over the coming weeks.

Patients with haematological conditions will be invited for the vaccination over the next weeks and months and many will fall within the priority groups for vaccination.

Patients who are receiving chemotherapy or immunosuppression should discuss with their hospital clinicians if they can safely receive the vaccine and optimal timing of administration. There is no current evidence that the vaccine might be a risk to the immunosuppressed patient. This document aims to support medical staff in providing this advice and has been collated from information currently available and from expert opinion. It will be updated as more information becomes available.

Many patients with haematological conditions are on therapy that will induce immunosuppression or will be immunocompromised as a consequence of their underlying disease and they may have a reduced response to the vaccine. In addition, it is not yet known how effective the immune response to vaccination will be in the older population although there is evidence that the Pfizer vaccine generates responses and gives protection in the elderly. Patients should therefore not presume they are immune after receiving the vaccine (and booster) and should still follow government advice on use of face masks, social distancing and hand hygiene to reduce their exposure to the virus

Whether or not an immunocompromised patient is known to have been infected with COVID-19 should not affect the decision regarding whether to vaccinate. Evidence about the need for and timing of repeated vaccination and monitoring of response to COVID-19 vaccination is not yet available.

Immunocompromised patients and their household contacts should also receive other recommended vaccinations, including influenza as per national recommendations.
<https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book>

Who will receive the vaccine first?

The Joint Committee of Vaccination and Immunisation (JCVI) have set out prioritisation for persons at risk. This advice is available here (as of December 2nd, 2020) and will be regularly updated by the JCVI.

<https://www.gov.uk/government/publications/priority-groups-for-coronavirus-covid-19-vaccination-advice-from-the-jcvi-2-december-2020>

Priority groups for vaccination are based on clinical need with older patients, clinically extremely vulnerable patients and those with underlying health conditions all being ranked as high priority. Patients will be called by the NHS for vaccination when they become eligible.

The priority groups for the first phase of vaccination are ranked as follows:

- 1: residents in a care home for older adults; staff working in care homes for older adults
- 2: all those 80 years of age and over; frontline health and social care workers
- 3: all those 75 years of age and over
- 4: all those 70 years of age and over, clinically extremely vulnerable Individuals (not including pregnant women and those under 16 years of age)
- 5: all those 65 years of age and over
- 6: adults aged 16-65 years who are in a risk group
- 7: all those 60 years of age and over
- 8: all those 55 years and over
- 9: all those 50 years and over.

Clinically extremely vulnerable patients

Patients with haematological conditions who are deemed clinically extremely vulnerable will have previously been advised to shield. They should seek advice from their haematology clinicians on the safety and timing of vaccination.

Further advice on which patients are clinically extremely vulnerable is available here: <https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19>

Underlying health conditions.

Patients from 16-65 years with underlying health conditions will be offered vaccination in group 6. For patients with haematology conditions this includes:

- Bone marrow and stem cell transplant recipients
- People with specific cancers
- Immunosuppression due to disease or treatment
- Asplenia and splenic dysfunction

Are there any groups of patients who should NOT receive the vaccine?

There is very limited data on safety and efficacy of vaccination in children and young people and COVID-19 vaccines are not routinely recommended for children and young people under 16 years of age.

Given the lack of evidence, it is recommended that COVID-19 vaccine is not given during pregnancy or if women are planning a pregnancy within three months of the first dose and that women who are breastfeeding should not be vaccinated until they have finished breastfeeding.

People with a history of immediate-onset anaphylaxis to a vaccine, medicine or food should not have the Pfizer/BioNTech COVID-19 vaccine

Disclaimer

Information in this statement is likely to change rapidly. Advice should be based on updated guidance as it becomes available and will depend on the individual clinical situation.

While the advice and information in this guidance is believed to be true and accurate at the time of going to press, neither the authors, the BSH nor the publishers accept any legal responsibility for the content of this guidance.

Further advice can be found here:

<https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14>.

<https://www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19/information-for-healthcare-professionals-on-pfizerbiontech-covid-19-vaccine>

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/943589/COVID-19_vaccination_programme_guidance_for_healthcare_workers_December_2020_V2.1.pdf

Appendix: COVID-19 Vaccination in patients with haematological disorders

Advice from haematology groups on specific haematological conditions Bleeding Disorders

BSH Haemostasis and Thrombosis taskforce

Heritable bleeding disorders do not increase the risk of acquiring COVID-19 and so patients with these conditions may be vaccinated according to the published schedule. The vaccine itself does not present any additional safety concerns for these patients but the intra-muscular route of administration may increase the risk of bleeding at the injection site. As yet there is no evidence that the vaccine can be given efficaciously by the sub-cutaneous route.

- Patients with severe haemophilia on prophylaxis with factor concentrate should have their normal prophylactic dose prior to the injection.
- Patients with mild bleeding disorders can generally have an intra-muscular injection without any haemostatic treatment. If there is any uncertainty, advice should be sought from the patient's haemophilia centre.
- Those on emicizumab can have the vaccination without any additional treatment if they are at steady state because this is effectively a similar status to mild haemophilia.
- Other patients not falling into these categories should be managed on an individual basis.

Patients on Anticoagulation or Anti-platelet therapy

BSH Haemostasis and Thrombosis taskforce

The previous advice from Public Health England for immunisations by the intra-muscular route continues to apply. As for patients with bleeding disorders there is a slightly increased risk of bleeding due to the intra-muscular route of administration.

- Patients on standard intensity anticoagulation with warfarin (target INR 2.0 – 3.0) can receive intra-muscular injections as long as the most recent INR is <3.0. There is no need for an extra INR check prior to vaccination.
- Patients on maintenance therapy with Direct Oral Anticoagulants, therapeutic low-molecular weight heparin or fondaparinux can delay the dose on the day of vaccination until after the intra-muscular injection but do not need to miss any doses.
- Patients on single agent anti-platelet therapy (e.g., aspirin or clopidogrel) can continue on these medications without any adjustment.
- Patients with higher intensity anti-thrombotic treatment, for example warfarin with a target INR > 3.0 or dual antithrombotic medications, should be managed on an individual basis. For higher range patients we suggest ensuring the INR is <4.0. The risk of haematoma formation should be reduced by application of firm pressure at the injection site for at least 5 minutes afterwards.

Further information is available at <https://thrombosisuk.org/>

Auto-immune haematological conditions on immunosuppression

BSH General Haematology taskforce

Adults who are receiving immunosuppressive agents including but not restricted to rituximab, cyclophosphamide, mycophenolate or steroids (20mg/day for over a month) are deemed as clinically extremely vulnerable and should be encouraged to receive the vaccine in group 4.

COVID-19 Vaccination in patients with Haemoglobinopathies and Rare Inherited Anaemias

UK Forum on Haemoglobin Disorders/National Haemoglobinopathy Panel

People who were previously asked to shield due to being deemed “clinically extremely vulnerable” will be offered the vaccine in **Group 4**.

This includes all adults with sickle cell disease, small numbers of children with very severe complications of sickle cell disease and some patients with thalassaemia and inherited rare anaemias who have severe iron overload.

Patients aged 16-65 years with underlying health conditions will be offered vaccination in **Group 6**.

This group includes people who receive the flu jab every year because they have problems with their spleen or have had their spleen removed. This group will include thalassaemia and rare inherited anaemia patients who have had their spleen removed.

Further information is available on the National Haemoglobinopathy Panel website. <https://www.nationalhaempanel-nhs.net/covid19>

Haematopoietic stem cell transplantation (HSCT)

British Society of Blood and Marrow Transplantation & Cellular Therapy

Detailed information on COVID-19 vaccination has been prepared by the BSBMT&CT and is available here:

https://bsbmtct.org/wp-content/uploads/2020/12/BSBMTCT-COVID-19-Guidelines-5.0-Dec-2020_final.pdf

In summary, taking into consideration evidence for established vaccines and expert opinion from this group:

- Consider vaccination with a COVID-19 vaccine from 3-6 months following allogeneic HSCT, except if patient remains on immunosuppression (ciclosporin, tacrolimus etc)
- Consider vaccination with a COVID-19 vaccine from 3-6 months following autologous HSCT
- Consider vaccination of patients with mild chronic GvHD and/or receiving ≤ 0.5 mg/kg prednisolone (or equivalent).
- For patients with moderate/severe cGvHD or on more intensive immunosuppressive therapy (high dose steroids >0.5 mg/kg) assess the potential benefits of COVID-19 vaccination on a case-by-case basis.

COVID-19 vaccination in patients with lymphoma

National Cancer Research Institute Lymphoma Research Group

Patients with lymphoma may be immunosuppressed to a varying extent depending on the lymphoma diagnosis and treatment history. This has implications for overall vaccination strategy and treatment decisions.

Safety and efficacy of COVID-19 vaccines in immunocompromised patients. There are no data regarding the safety or efficacy of currently available COVID-19 vaccines in immunosuppressed patients. However, there is no *a priori* reason to believe that replication-deficient vaccines should be unsafe in this setting. Regarding clinical efficacy, it is reasonable to assume that patients with B-cell depletion/dysfunction are likely to have an impaired humoral response to vaccination, while those with T-cell depletion/dysfunction are likely to have an impaired cellular response and possibly also an impaired humoral response due to loss of T helper function.

Overall COVID-19 vaccination strategy. Based on current safety/benefit considerations and in the absence of data or guidance to the contrary, we recommend that all patients with lymphoma should receive a non-replicating COVID vaccine (unless explicitly contraindicated), accepting that this might not achieve full protection if there are pre-existing defects in humoral and/or cellular immunity. For these patients, vaccination of close contacts may be at least as important. It should be emphasised that neither of these measures removes the need for social distancing.

Implications for lymphoma treatment. The predicted effects of specific lymphoma treatments on cellular and humoral responses to COVID-19 vaccination should be considered and discussed with patients in a balanced way alongside other treatment considerations, e.g., the desire to maximise progression-free survival and minimise overall treatment-related toxicity. This is particularly relevant for drugs such as bendamustine and rituximab, which deplete T and B cells, respectively, but may also improve long-term disease control.

Timing of COVID-19 vaccines. COVID-19 vaccination should be timed with the aim of achieving optimal protection at the earliest opportunity without compromising lymphoma outcome. Where possible, vaccination should be completed at least 2 weeks before any immunosuppressive treatment is given. For patients who have already received immunosuppressive treatment, the advantages and disadvantages of interrupting therapy or delaying vaccination to allow immune recovery requires careful consideration and discussion bearing in mind that short interruptions in treatment may not be sufficient for any meaningful improvement of immune function. For patients in clinical trials the timing of vaccination should be discussed with the relevant co-ordinating centre.

Chronic Lymphocytic Leukaemia

CLL Forum

Patients with CLL of all stages (including patients on active monitoring) have degree of immunosuppression. Published trials have not included immunosuppressed patients or those on immunosuppressive treatments, however there are no concerns on safety of currently offered vaccinations. Efficacy of vaccination in all patients with CLL are likely to be significantly compromised. Patients with CLL are advised against receiving live vaccines but attenuated and mRNA-based vaccines can be safely given.

Multiple Myeloma

UK Myeloma Forum

Patient with multiple myeloma (MM) are extremely vulnerable because of age (median age at diagnosis is 70 years), disease and treatment-related immunocompromise. The use of high dose steroids as the back-bone of therapy with the addition of agents known to cause/exacerbate pancytopenia (e.g., daratumumab) increase the vulnerability further. Live vaccines are not generally recommended in MM patients but attenuated and mRNA-based vaccines are. There is currently no specific safety or efficacy data of the Pfizer/BioNTech COVID-19 vaccine in patients with MM or related disorders including Amyloidosis or MGUS. Given the vulnerability of these patients on balance it is advised that they be vaccinated (unless there are specific contraindications) in appropriate priority groups as benefits are likely to significantly outweigh any risks. Patients who have received a stem cell transplant should follow the BSBMTCT guidance.

COVID-19 vaccines and Myelodysplasia

UK MDS Forum

MDS patients are asking about the safety and advisability of the vaccines, on the background of being amongst the highest risk groups for COVID-19.

In the absence of precise information on the safety and efficacy of the current Covid-19 vaccines in patients with blood cancers, the MDS UK Forum (MDS expert group in the UK), have produced the following guidance.

UK MDS Forum guidance:

There is currently only one licensed and available vaccine for Covid-19 – the Pfizer/BioNtech vaccine.

This is a not a 'live' vaccine and therefore should be safe for blood cancer patients, including MDS patients. The Joint Committee of Vaccination and Immunisation (JCVI) have set out a prioritisation for persons at risk, including those who are defined as clinically extremely vulnerable (CEV). This can be found on the government website.

The consensus is that generally, for blood cancer patients, the benefits of the vaccine far outweigh any potential side effects of the vaccine and the risks associated with having COVID-19 infection. Therefore, vaccination is recommended, except in people with a history of severe allergic reactions.

For now, we are only looking at the Pfizer/BioNtech vaccine.

Which MDS patients should get the Pfizer/BioNtech vaccine?

The MAJORITY of MDS patient should be receiving the Pfizer/BioNtech vaccine.

This will include:

- ✓ All MDS subtypes regardless of age
- ✓ All IPSS & IPSS-R risk groups
- ✓ MDS patients on watch & wait or treatment, now or in the past
- ✓ MDS Patients on clinical trials

Which MDS patients should exercise caution regarding the vaccine, and speak to their haematologist before receiving the vaccine?

- ✗ patients with a known severe allergy
- ✗ patients who carry an EPI-PEN
- ✗ Patients who have a low platelet count who may bleed or bruise at the injection site. To reduce this risk, we recommend the platelet count should be $30 \times 10^9/l$ or above and that prolonged pressure at the injection site should be applied for 5 minutes. Those receiving regular platelet transfusions should have their vaccine after a platelet transfusion. If the platelet count is less than $30 \times 10^9/l$ and the patient is not receiving regular platelet transfusions, they should discuss with their haematologist.

Post-transplant haematology patients should follow the up-to-date advice from BSBMTCT

What remains to be decided?

Whether it will be the hospital or GP who will administer the Pfizer/BioNtech vaccine to blood cancer patients.

Whether the vaccine will offer a sufficient level of protection against COVID-19 in immune-compromised and blood cancer patients.

What will patients need to do post vaccination?

As the effectiveness of the Pfizer/BioNtech vaccine may not be guaranteed in immune-compromised patients, it will be necessary for all vaccinated patients to maintain social distancing and follow the currently recommended government precautions against COVID-19. These precautions are updated regularly on www.gov.uk/coronavirus.

Myeloproliferative Disorders

MPN Voice

Having an MPN and any MPN treatment is not a contraindication to receiving the vaccine.

If you are taking an anticoagulant, e.g., warfarin, rivaroxaban, apixaban etc, you will be asked about bleeding.

Allergic reactions to the vaccine. You should not have the vaccine if you've ever had a serious (anaphylaxis) allergic reaction to medicines, vaccines or food. You will be asked by staff before you are vaccinated if you ever had anaphylaxis and need to carry an epi pen. Facilities will be available to deal with reactions. Read the latest COVID-19 vaccine advice if you have a history of allergies on Gov.UK

How safe is the COVID-19 vaccine? The vaccine approved for use in the UK was developed by Pfizer/BioNTech. It has met strict standards of safety, quality and effectiveness set out by the independent Medicines and Healthcare products Regulatory Agency (MHRA). Any Coronavirus vaccine that is approved must go through all the clinical trials and safety checks all other licensed medicines go through. The MHRA follows international standards of safety. Other vaccines are being developed, they will be available on the NHS once they have been thoroughly tested to make sure they are safe and effective. So far, thousands of people have been given a COVID-19 vaccine and reports of serious side effects, such as allergic reactions, have been very rare. No long-term complications have been reported. Read about the approved Pfizer/BioNTech vaccine for COVID-19 by MHRA on Gov.UK.

More information is available on www.mpnvoice.org.uk

Aplastic Anaemia

BSH Aplastic Anaemia Guideline Group.

There are case reports of AA developing post-vaccination, and of recovered AA patients relapsing following vaccine administration. The evidence is limited and based also on an appreciation that a viral insult is likely to be an important trigger in the pathogenesis of AA.

In the setting of the COVID-19 pandemic, current ASH COVID-19 and AA guidance (<https://www.hematology.org/covid-19/covid-19-and-aplastic-anemia>) is that the risk versus benefit would favour vaccine administration, particularly in those with additional risks for severe COVID-19 disease (age, obesity, other comorbidities associated with increased risk). No data on efficacy in immunosuppressed patients has been made available to date for any of the SARS-CoV-2 vaccines in development.

Those patients within 6 months of ATG/CSA initiation are unlikely to mount an appropriate immune response to a vaccine. Those AA patients remaining on CSA more than 6-12 months post-ATG treatment may respond to a vaccine. Vaccinations may be given after thoroughly considering and balancing risk versus benefit.

Post-transplantation AA patients should follow standard post-transplantation guidelines for vaccine administration. These will be updated regarding SARS-CoV-2 vaccines when they become available, extrapolating from recommendations for other vaccines (<https://www.hematology.org/covid-19/ash-astct-covid-19-and-vaccines>).

Acknowledgements and contacts

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