

Updated BSBMTCT recommendations for the management of paediatric patients and allogeneic donors during the COVID-19 (causative agent the SARS-CoV-2 virus) outbreak

Beki James, Giovanna Lucchini, Caroline Furness, Sara Ghorashian, Josu De La Fuente, Persis Amrolia and Kanchan Rao on behalf of the Paediatric BSBMTCT COVID-19 Guidelines Group

General status of SARS-CoV-2 in the UK

The waves of the SARS-CoV-2 pandemic have been characterised by Variants of Concern (VOC), most recently dominated by the Omicron variant, the precise impact of which remains uncertain in HSCT, haemato-oncology and other immunocompromised patients, despite being associated with milder illness in the general population. The published data and national experience continue to support the view that the risk of severe COVID-19 infection in paediatric SCT and CAR-T patients (in contrast to adults) is low.¹

Highly effective vaccines against SARS-CoV-2 are widely available with the vast majority of the adult UK population having received at least a two-dose primary course of vaccination, with 68% of the population over the age of 11 now also receiving a third booster. In addition, 53% of pupils aged 12 to 15 years and 70% of pupils aged 16 to 17 years in England have received at least one dose of a COVID-19 vaccine, while 6% and 46% respectively have received two doses (vaccine uptake in this age group is higher in Scotland). Vaccination for 5-11 year olds became available in April 2022.

Despite this success, we now know that the current SARS-CoV-2 vaccines are significantly less immunogenic in patients who have undergone an allogeneic and autologous stem cell transplant leading to the continued vulnerability of such patients to serious life-threatening complications following SARS-CoV-2 infection, even after vaccination. A range of factors can affect response to vaccination, including disease type, time from transplant and immunosuppressive therapy, especially previous treatment with targeted lympho-depleting therapy. Data in CAR-T cell are more limited, but similar principles are expected to apply. The current position of the BSBMTCT is regularly updated by the Vaccination Sub-Committee in our vaccination guidelines available at www.bsbtct.org/bsbtct-and-covid.

Transplant teams must continue to remind patients aged 12-17 that they remain at risk even after receiving a course of vaccination. Transplant teams must also continue to advise patients and their families on social distancing behaviour to minimise exposure to the virus. Vaccination for immunocompromised children in the 5-11 year cohort has now also been recommended in the Green Book Chapter 14a and transplant centres are encouraged to roll out this information to this age group (links are provided at the end of this document).

The efficient rollout of the SARS-CoV-2 vaccination programme in the wider population was hoped to be the key factor that would finally control the pandemic and convert the virus into an endemic state, but the emergence of the new VOCs has significantly challenged this outlook. The enhanced immune-evasive properties of the Omicron variant further reduce the effectiveness of the current generation of anti-spike SARS-CoV-2 vaccines, even in

immunocompetent individuals, and a booster vaccine dose is required to restore most, but not all, of their effectiveness.

While hospitals are much better prepared when compared to the start of the pandemic, most healthcare facilities remain under great pressure as they continue to struggle with accommodating emergency and elective activity alongside the care of increasing numbers of patients admitted with severe COVID-19. Many transplant programmes are again coming under pressure with staff reallocation, illness or isolation due to contact with COVID-19 cases. The impact on transplant activity due to the waves of COVID-19 is varied with some centres able to continue activity and others more negatively affected. However, all centres and staff have experienced increased levels of stress and workload and there is no immediate sign of this pressure easing. The potentially more transmissible BA.2 Omicron variant is likely to further add to this pressure.

With statutory infection control measures within the wider population being removed at pace, transplant teams need to continuously address ongoing risks while maintaining necessary transplant activity through prioritisation and quality measures.

These BSBMTCT recommendations have been produced and updated to provide support to Paediatric BMT teams in the UK. Advice may change as COVID-19 prevalence changes in the UK. They are closely linked with the current NICE Guideline NG164, which links in updates from BSBMTCT and guidance from several sources including the EBMT, ASTCT, WMDA, Anthony Nolan and NHSBT. Individual centres should use these recommendations for general guidance only, as such circumstances will vary between centres and localities over time, and institutional and regional pathways procedures should be followed.

The latest guidance from NICE, EBMT and other specific groups, and for donor issues, the Anthony Nolan, NHSBT and WMDA, is available on their websites:

- NICE Guideline NG164, updated July 2021, COVID-19 rapid guideline: haematopoietic stem cell transplantation www.nice.org.uk/guidance/ng164
- NICE Guideline NG191, updated Dec 2021, COVID-19 rapid guideline: managing COVID-19 www.nice.org.uk/guidance/ng191/chapter/Recommendations
- BSBMTCT www.bsbmtct.org/bsbmtct-and-covid/
- EBMT guidance (regularly updated): www.ebmt.org/sites/default/files/2021-06/EBMT%20COVID-19%20guidelines%20v.%2016.03.pdf
- ASTCT guidance (regularly updated): www.astct.org/communities/community-home/librarydocuments?communitykey=d3949d84-3440-45f4-8142-90ea05adb0e5&tab
- WMDA: <https://share.wmda.info/pages/viewpage.action?pageId=344866320>
- Anthony Nolan COVID-19 information for patients (regularly updated): www.anthonynolan.org/patients-and-families/understanding-stem-cell-transplants/coronavirus-and-your-stem-cell-transplant
- NHSBT: www.nhsbt.nhs.uk/news/coronavirus-update/

Changes to this guidance since the last set of recommendations:

- 1) Update of recommendations for maintaining transplant activity.
- 2) Updated links to other HSCT organisations.
- 3) Updated advice on cryopreservation of donor cells.

- 4) SARS-CoV-2 vaccination.
- 5) SARS-CoV-2 therapeutics.

Maintaining transplant activity

The NHS is now generally better prepared for dealing with the fluctuating incidence of infection in the population but as the Omicron wave continues, transplant teams may experience periods of staff shortages, reduced capacity, and heightened levels of anxiety in their patients and staff. It is expected that transplant programmes continue to follow the NICE Rapid Guideline NG164 which provides advice on establishing and maintaining 'COVID-19 safe' treatment pathways. As the incidence of infection is rising rapidly and pressure on capacity and staff increases, teams must now address the prioritisation of transplant activity.

The main patient groups that have been affected by the deferral of transplantation in previous waves of the pandemic were those requiring HSCT for haemoglobinopathies and non-urgent metabolic and primary immunodeficiency disorders. So far, in the current Omicron wave, we have not seen the pressure on adult ICU facilities as in the previous wave, hence until now, paediatric transplant centres have been able to operate as per normal. However, staff shortages are still a problem at some centres and transplant centres may have to prioritise patients, balancing the risk of transplant in a sub-optimal setting against the risk of delay.

Capacity

It is essential that centres are able to confirm sufficient capacity to manage planned activity. This includes:

- Bed capacity in the transplant unit and in ICU.
- Staffing on the HSCT unit.
- Stem cell laboratory capacity to manage donor cells for cryopreservation.
- Associated services, for example, pharmacy.
- Laboratory testing for SARS-CoV-2 in patients and staff.
- Safe access to critical investigations such as endoscopy, bronchoscopy, and radiology.
- Having 'COVID-19 safe' patient treatment pathways, from clinics, during in-patient stay and post-transplant care.
- Optimising the use of telephone or video clinics to reduce visits.

SARS-CoV-2 surveillance

It will be important to continue to maintain robust policies and procedures to protect HSCT patients from SARS-CoV-2. These should be incorporated into existing Quality Management plans and become routine practice. The virus will remain within the community and will continue to be a major risk to patients. Programmes must work with their local infectious diseases and infection control teams to create safe operational environments for patients. How this will be achieved will have to be determined at a local level but policies that include regular staff screening by symptom awareness and viral swab tests will be required.

The emergence of more infectious variants underlines the need to maintain 'COVID-19 safe' pathways, such as:

- Screening protocols – symptoms, naso-pharyngeal and throat swabs.
- Screening of in-patients with viral swabs on a weekly basis at a minimum.
- Screening of parents/carers as per local policy.

- Pre-admission screening by symptoms checks and viral swabs, ideally within 72hrs of planned admission prior to the start of conditioning.
- Patient triage and quarantine policies in clinics, hospitals, and ambulatory treatment pathways.

EBMT continue to recommend a nucleic acid-based test such as a PCR rather than the antigen rapid test due to the relatively lower sensitivity of the latter (EBMT COVID-19 guidelines, version 16, May 2021: www.ebmt.org/sites/default/files/2021-06/EBMT%20COVID-19%20guidelines%20v.%2016.03.pdf). The role of serological testing is unclear but may be available in some centres.

Guidance for HSCT recipients before SCT

- Each individual indication for transplant should be reviewed at a local MDT to assess the urgency and local capacity. Transplantation for any non-urgent indications should be deferred if there are concerns about capacity and safety. If the transplant is urgent, but there are local capacity issues then 'mutual aid' should be sought.
- As a preventive measure, recipients should be advised to avoid crowded places, public transport, use good hand hygiene measures and remain in self-isolation for 14 days prior to the start of conditioning.
- Face masks should be worn by recipients to provide protection when outside of the home.
- Siblings may attend school during work up; but this should be reviewed locally, and some centres may advise that siblings stay at home for 10-14 days before admission; similarly, parents should then work from home if possible.
- All parents and siblings should be reminded of hygiene measures.
- There should be regular careful history taking to determine whether the patient has had recent contact with an individual proven to have COVID-19 or symptoms suggestive of COVID-19 (as per government guidance).
- If close contact with a COVID-19 individual has occurred immediately prior to transplant, defer transplant for 14 days, if possible (EBMT guidelines), test if symptomatic, following local infection control guidelines.
- Asymptomatic recipients, and those with no history of a contact, should be screened for respiratory viruses and SARs-CoV-2 at least once 72 hours before the donor starts GCSF, where the cells are being collected and cryopreserved, before the recipient starts conditioning. The recipient should have also completed pre-transplant assessments and be deemed fit to proceed to transplant.
- Asymptomatic recipients, and those with no history of a contact, should be screened for respiratory viruses and SARs-CoV-2 at least once 72 hrs before the recipient starts conditioning. The recipient should have also completed pre-transplant assessments and be deemed fit to proceed to transplant.
- Testing should be repeated at least twice, ideally 1 week apart or as a minimum >24 hours apart, but practice and availability of testing may vary between institutions. It is strongly advised to use PCR tests rather than an antigen-based testing method.
- Patients who test positive for SARS-CoV-2 pre-SCT should be managed as detailed in the section 'SARS-CoV-2 positive patients pre-transplant'.

Guidance for allogeneic stem cell donors

- Sibling/paediatric family donors stay off nursery/school/work for 10-14 days prior to donation. Adult family donors are strongly advised to work from home, if possible, to avoid crowded public places and to practise good hygiene for 10-14 days prior to donation.
- If the donor develops any symptoms suggestive of SARS-CoV-2 infection, then they need viral swabs (asymptomatic screening indicated below).

The situation regarding the cryopreservation of allogeneic donor HSC grafts, either prior to or after transport to the receiving transplant centre, is complex and changing. Recent data from BSBMTCT-CTC/AN/UK (mostly adult transplants), is reassuring about HSCT outcomes following the use of cryopreserved products. There is still concern from international data on the use of cryopreserved products in some diseases at a high risk of graft failure (cases to be discussed on an individual basis at MDTs). The BSBMTCT strongly encourages transplant centres to return data on transplant outcomes following the use of cryopreserved allogeneic donor stem cells to the Anthony Nolan and BSBMTCT survey.

The decision on whether to use fresh or cryopreserved HSC from allogeneic donors **must** be made on a case-by-case basis as several factors need to be considered. These include disease indication for transplant (some indications have a higher risk of graft failure), donor age, stem cells source (BM may be at greater risk of stem cell attrition), country of origin (incidence of SARS-CoV-2, risk of late donation failure, time from cell collection to cryopreservation, possible disruption to local/international transport networks).

The current rise in the incidence of the Omicron variant of SARS-CoV-2 in the UK and Europe has now once again swung the balance of risk in favour of cryopreservation for donor cells from countries with high COVID-19 cases. At this time, the incidence of infection in the UK and internationally is high and routine collection, transportation and cryopreservation of allogeneic stem cells are strongly recommended to avoid serious disruption and prevent late failure of cell donation after commencing patient conditioning (for example, the donor testing positive for SARS-CoV-2 late in donation pathway and/or needing to isolate due to close/household contact with Omicron variant of SARS-CoV-2).

In individual cases where there is a clinical requirement for fresh stem cell or bone marrow infusion, this should be carefully discussed at the local BMT MDT before proceeding. If fresh cells are to be used, it is strongly advised that 'back-up' donors including alternative unrelated donors, haplo-identical donors or cord blood units are identified ahead of the start of conditioning and are worked up to a point where they could be activated very rapidly (ideally with donation <1 week from the original date). Anthony Nolan can support with identification and work up of backup donors.

Internationally, registries have varying policies surrounding both testing and backup donor workups. The situation is extremely dynamic so advice may change, and some national registries will check whether cryopreservation is planned. For the recommendations in specific countries, check the WMDA webpage: <https://share.wmda.info/display/LP/COVID-19+-+Impact+on+Registry+Operations> (regularly updated). Where possible, we recommend identifying a UK backup donor or cord blood unit. Anthony Nolan, DKMS UK, NHSBT and the Welsh Bone Marrow Donor Registry can each bring a backup donor to medical and clearance if requested.

Transplant centres should liaise closely with their local stem cell processing laboratories to warn them of each donation and whether to cryopreserve or not. Anthony Nolan and NHSBT can help identify cryopreservation facilities if local cryopreservation capacity is limited.

Other allogeneic donor issues

Anthony Nolan and some other registries will arrange SARS-CoV-2 testing of unrelated donors at medical, prior to starting GCSF (for cryopreserved products), prior to patient starting conditioning (for fresh products), and prior to attending for apheresis. Results should be available by the time product is cryopreserved. If not, the processing laboratory may need to quarantine cryopreserved cells until results are available.

Donors should be screened twice for SARS-CoV-2 testing prior to donation; once at the medical (or within 72 hours) and prior to starting GCSF (for cryopreserved products) or prior to the patient starting conditioning therapy (for fresh products). Donors may also be screened prior to attending the local apheresis centre although timings may vary. Transplant centres should liaise with their local units.

Donors with confirmed or suspected COVID-19 should be excluded from donation for 28 days, from:

- a) The *resolution of symptoms* if they had confirmed COVID-19 by PCR for SARS-CoV-2 **and** history of one or more symptoms of COVID-19 infection.
- b) The *date of the positive diagnostic test* if they had confirmed SARS-CoV-2 by PCR **but no history of symptoms of COVID-19 infection**.
- c) The *resolution of symptoms* if they had *suspected* COVID-19 due to one or more symptoms of COVID-19 **but had not been tested for SARS-CoV-2**.

If there are no suitable alternative donors and the HSCT is urgent, the centre should perform a risk assessment and liaise with the registry to confirm the lack of alternate donors. A decision may be made to accept a donation less than 28 days from the positive result. In this situation, the recipient should be involved in the discussion and be informed of the donor's situation.

Donors should be deferred for 10 days if in close contact with a COVID-19 case and should have at least 2 negative swabs prior to starting the harvesting procedure. The latest information on donor eligibility criteria due to SARS-CoV-2 infection can be found on JPAC guidelines: www.transfusionguidelines.org/dsg/bm/guidelines/coronavirus-infection.

Donors who have received a COVID-19 vaccine under the UK vaccination programme must not donate if:

- a) Less than 14 days after the last immunisation has passed if the vaccine given was a nucleic acid (mRNA) vaccine.
- b) Less than 28 days after the last immunisation has passed if the vaccine given was a virus-vector-based (non-replicating virus) vaccine.
- c) Donor felt unwell due to unexpected complications (other than common side effects) after any vaccination. In this case, refer to the donor medical team for an individual risk assessment.

Donors who have received a COVID-19 vaccine outside the UK vaccination programme, including participants in clinical trials of donors vaccinated outside of the UK, should be

referred to the donor medical team for individual risk assessment. The latest information on donor eligibility criteria due to SARS-CoV-2 vaccination can be found on JPAC guidelines: www.transfusionguidelines.org/dsg/bm/guidelines/coronavirus-vaccination.

There have been concerns that SARS-CoV-2 may be passed via blood products. Although viral RNA has been detected in blood samples of patients with COVID-19 there have been no reports of transmission of infection by blood products.

Donors should be contacted approximately 14 days post-harvest to determine if they have experienced any symptoms suggestive of COVID-19. If they have, then testing is recommended.

Management of SARS-CoV-2 positive patients pre transplant

There are two considerations regarding the decision to proceed to transplant in patients who develop SARS-CoV-2 infections prior to the start of transplant conditioning:

- 1) The risk from the underlying haematological/immunological or oncological condition.
- 2) The severity of the SARS-CoV-2 infection.

In patients with a high-risk disease indication for transplant, HSCT should be deferred until the patient is asymptomatic and has achieved three virus PCR negative tests at least one week apart (i.e. a deferral of 14 days minimum). This differs from the EBMT guidance but in practice assumes that after two negative tests patients would start pre-transplant assessments including organ function with a final test immediately prior to the start of conditioning. There is growing evidence that some patients may remain PCR positive for many weeks following infection with SARS-CoV-2, possibly because of a limited immune response due to their treatment or disease. Patients that remain PCR positive for SARS-CoV-2 but who are otherwise well will need to be carefully assessed on the risk versus benefit of proceeding to transplant or for any transplant-related procedure such as autologous stem cell harvest.

In patients with low-risk haematological disease, a three-month HSCT deferral is recommended if they experienced moderate to severe COVID-19 symptoms, with negative SARS-CoV-2 PCR tests and critical organ function tests and performance status similar to pre-COVID-19 levels.

Patients that experienced moderate to severe COVID-19 symptoms should have sufficient time to allow recovery of critical organ function and general performance status to those similar to pre-COVID-19 infection levels. In cases of asymptomatic or mildly symptomatic infection, a deferral of a minimum of 14 days, preferably 21 days, with three negative swab test results is recommended, similar to EBMT guidance.

SARS-CoV-2 positive patients detected in the pre-transplant period may be eligible for specific newer therapies (detailed later). Each such positive case should be discussed with the hospital infectious disease team for further advice on management.

During and after transplant

In order to protect the recipient when they are at their most vulnerable, we recommend that:

- The resident carer is shown a good hand-washing technique, and this is reviewed by the admitting team.

- The admitting team take time to explain the ways to reduce any potential infective contacts.
- The recipient is managed in strict protective isolation; risk assess the need for any investigations and procedures that remove the patient from their isolation room (there may be a greater risk from exposure to SARS-CoV-2 than from not having the investigation).
- Patients who are known to be SARS-CoV-2 positive should be isolated in negative pressure cubicles wherever possible, or, if this is not available, in a neutral pressure cubicle. When seeing such patients, healthcare professionals should wear full PPE including gowns, FFP3 masks, gloves, and visors.

There is evidence of prolonged viral PCR positivity in patients post-transplant. It is possible that these patients may be shedding viable virus. Such patients may remain relatively well but should be managed in ways to minimise the transfer of virus to other patients and staff with strict viral isolation policies.

Management of COVID-19 cases should involve a multidisciplinary team. In order to establish COVID-19 free environments and the evidence of asymptomatic carriage and possible transmission, programmes should work with their Infection Control and Infectious Disease teams to develop routine procedures for in-patient, parent/carer and staff screening.

After discharge

This will be the time of greatest risk to transplant recipients due to high levels of COVID-19 in the community. The risk of severe COVID-19 appears to be greatest in patients with neutrophils $<0.5 \times 10^9/l$ and/or lymphocytes $<0.2 \times 10^9/l$, or with co-morbid conditions or with poor performance status irrespective of transplant type (3,4).

Although evidence from EBMT and international studies suggested that paediatric HSCT recipients did not experience increased mortality due to post-transplant COVID infection, we still do not know the effect of the Omicron variant and need to ensure reasonable caution.

We recommend that:

- The need for sensible isolation of the transplant recipient is re-iterated for all at discharge. In practice, this will be similar to what would have been advised in general after HSCT before the pandemic.
- If there is lymphopenia (lymphocytes **$<0.2 \times 10^9/l$**) and/or neutropenia (neutrophils **$<0.5 \times 10^9/l$**) **then** strict isolation of transplant recipient and if possible, the immediate carer(s) should be recommended.
- Telephone or video follow-up clinics should be used when possible.
- Blood tests should be arranged in a place where there is the smallest risk of exposure to other people.
- Medicines should be delivered in a way which reduces the risk of exposure to other people, for example, using home delivery services.
- Strategies should be developed to minimise risks to patients attending the hospital for essential face to face visits.
- Vitamin D3 levels are monitored regularly and be replaced if low, in line with EBMT recommendations, as there is some evidence that individuals with low vitamin D3 levels may develop more severe COVID-19 disease.

Staff

Healthcare professionals with cough, SOB, fever, other cold-like symptoms or loss of taste and smell should not come to work. Symptoms with the recent Omicron variant have been more coryza like. They should follow local pathways and/or specialist advice for staff on HSCT programmes, including obtaining a SARS-CoV-2 swab test for PCR.

Be aware of the less frequent symptoms that have been associated with SARS-CoV-2 infection; staff education and self-reporting procedures must be in place to increase awareness of these symptoms.

HCP who are coryzal without fever should consult local policies which could include testing to exclude SARS-CoV-2 before caring for immunocompromised patients. They should be screened for respiratory viruses (if local arrangements allow) and SARS-CoV-2. These recommendations need to be discussed with your local Infection Control Team.

There is evidence that healthy individuals can continue to shed virus for up to 12 days from the onset of symptoms. Therefore, staff should be *free of fever for 7 days* **and** have a *negative viral swab by PCR* before working directly with transplant patients. If a PCR test is not available, then a negative lateral flow test may be acceptable in lieu of a PCR. It is recognised that a positive PCR test beyond 10 days from the start of symptoms in an individual recovered from symptoms may not correlate with infectiousness and return to work should be based on local policies. This recognises that some people continue to have cough and taste/smell disturbance for several weeks.

Contact of staff with household or other exposure should follow current government guidelines, which are linked with vaccination status and other criteria, plus individual risk assessment of staff depending on their role within the organisation and HSCT programme. The impact of staffing on units/departments is a consideration at a local level to maintain services and staff can be instructed to work from home, be deployed or directly support the service depending on individual and local factors.

During times of acute increase in SARS-CoV-2 cases, meetings should switch to being virtual as much as possible and splitting the workforce may be considered to mitigate the risk of a large proportion of the team being affected at the same time. At other times, there has been a trend to normalisation of travel to national/ international meetings, but care should be taken to minimise the risk of an entire workforce being affected and measures such as splitting staff may be considered. Additionally, avoid teams de-masking at the same time by, for example, splitting lunch breaks. Be aware of the additional psychological and emotional stress that staff will experience and identify measures to provide support.

CAR-T therapy

Depending on prior allo-SCT and time from lymphodepletion/CAR-T infusion, patients may have a similar degree of increased risk as allo-HSCT recipients. Delays in patients having MNC collection, or receiving immune-depletion therapy, prior to infusion of CAR-Ts increases the risk of progression of the underlying disease (Ghorasian et al, 2021). In a period of an acute increase in local SARS-CoV-2 infection rates, this risk must be balanced against the risk of the patient proceeding when capacity is stretched and the risk of acquiring SARS-CoV-2 infection after CAR-T infusion when it may be more severe. As such, individualised decisions

should be made taking into all these considerations, with discussion at the National CAR-T Panel as needed.

In relation to harvesting patients who remain SARS-CoV-2 PCR positive, pharmaceutical companies involved in the manufacture of CAR-T should be contacted directly for up-to-date information, as this has not been a barrier to accepting a leucapheresis product for manufacture under certain circumstances.

Vaccination against SARS-CoV-2

The vaccination sub-committee of the BSBMTCT has produced detailed guidance relating to vaccination of transplant patients against SARS-CoV-2 here: www.bsbmtct.org/bsbmtct-and-covid/. The relevant guidance in the Green Book, ch14a, is found here: www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a.

COVID-19 therapeutics

A number of therapeutics in the management of COVID-19 have been developed and are now in routine use in the UK. Transplant teams are strongly recommended to work with multidisciplinary teams including specialists from infectious disease, infection control, respiratory medicine and intensive care when managing transplant patients who develop COVID-19.

Specific treatment, if needed, will depend on the age of the patient, if there is a need for hospitalisation, genotyping of the virus, vaccination status, presence of additional co-morbidities and COVID-19 antibody status. In general, children with COVID-19 infection post HSCT have had far milder disease than that described in adults.

Hospitalised patients should have urgent serology and genotyping to aid decision making. In most cases, RCPCH guidelines for management should be followed:

www.rcpch.ac.uk/resources/covid-19-management-children-hospital-and-non-hospitalised

The national criteria for monoclonal antibody treatment are summarised here:

www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103191

www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103192

These treatment guidelines are updated very frequently, so it is advisable to look for the latest alert here: www.cas.mhra.gov.uk/Home.aspx

References

- 1) Lucchini G, Furness C, Lawson S, Gibson B, Wynn R, Slatter M, Shillitoe B, James B, Carpenter B, Hough R, Amrolia P, de la Fuente J; UK and Ireland Paediatric BMT Group. COVID-19 infection in paediatric recipients of allogeneic stem cell transplantation: the UK experience. *Br J Haematol*. 2021 Aug;194(4):e74-e77. doi: 10.1111/bjh.17547. Epub 2021 Jun 20. PMID: 34132400; PMCID: PMC8444814.
- 2) Ghorashian S, Malard F, Yüksel MK, Mauff K, Hoogenboom JD, Urbano-Ispizua A, Kuball J, de la Camara R, Ljungman P, Ruggeri A, Chabannon C. Defining the impact of SARS-COV-2 on delivery of CAR T-cell therapy in Europe: a retrospective survey from the CTIWP of the EBMT. *Bone Marrow Transplant*. 2021 Nov 20:1–3. doi: 10.1038/s41409-021-01483-8. Epub ahead of print. PMID: 34802048; PMCID: PMC8605455.