|  |
| --- |
| **Haematopoietic Stem Cell Transplantation and Cellular Therapies Training Passport for Pharmacists** |
| **Allogeneic, Autologous Stem Cell Transplantation and CAR-T Cell Therapies for Adult Patients** |
| **Record of Training for:**  Name:…………………………………………………………….  Designation:…………………………………………………...  The above pharmacist has completed the Haematopoietic Stem Cell Transplantation and Cellular Therapies Training.  **Trainer:**  Name:………………………………………………………….....  Designation:……………………………………………………  Date:………………………………………………………………. |

Version 2.0. December 2020

Revision Date: December 2021

**Preface**

Haematopoietic Stem Cell Transplantation (HSCT) has become a well-established treatment strategy for many patients with haematological malignancies and certain non-malignant conditions. The number of HSCT procedures has expanded over the last decade and continues to increase. In the United Kingdom (UK) and Republic of Ireland (ROI) there are 46 transplant centres performing allogeneic and/or autologous transplantation in adult patients; in the year 2019, there were 4176 adult transplant procedures performed in the UK and ROI.

The rapid developments in the field, the prevalence of polypharmacy and the increasing treatment complexities, including the recent approval of chimeric antigen receptor T cell (CAR-T) therapies as advanced therapy medicinal products (ATMPs), require skilled clinical pharmacists with specialist HSCT knowledge and experience to ensure provision of safe and effective pharmaceutical care in this high-risk patient population.

The role of the pharmacist as an integral member of the HSCT multidisciplinary team is well-established by the FACT-JACIE accreditation standards. Pharmacists are well positioned to provide a range of clinical pharmacy and medicines optimisation services and take leadership in staff and patient education, service design and the development and implementation of treatment guidelines.

Historically, there have been many different training and competency assessment methods for pharmacists working across UK transplant centres. The aim of this passport is to provide a standardised and consistent approach to documenting core training for clinical pharmacists involved in the care of patients undergoing HSCT. We hope that this will give pharmacists the confidence in their skill-set to ensure that patients benefit from high-quality pharmaceutical care that is evidence-based, up to date and tailored to their individual needs.

We would like to express our gratitude to all pharmacists within the UK BMT Pharmacists’ Group for their contributions and engagement throughout the planning and development of this resource. We are indebted to Nadjoua Maouche for leading the content development process and we particularly acknowledge Vivek Soni, who developed the training passport concept at the Royal Marsden, and whose work provided the backbone upon which this current passport was built. We would like to encourage and invite all pharmacists who undertake training using this passport to feedback on any element of this document to allow us to continue to update and improve on this resource. Please provide feedback by emailing any of the listed contributors.

**Contents**

[Contributors 3](#_Toc22307763)

[Abbreviations 4](#_Toc22307764)

[Scope 5](#_Toc22307765)

**CHANGES SINCE VERSION 1.0…………………………………………………………………………………………………6**

[PART I: Introduction 7](#_Toc22307766)

[1. JACIE standards for pharmacists (B3.8) 7](#_Toc22307767)

[2. Introduction to HSCT and to the HSCT unit 8](#_Toc22307768)

[3. Indications for HSCT 9](#_Toc22307769)

[PART II: Autologous Haematopoietic Stem Cell transplant (Auto-HSCT) 11](#_Toc22307770)

[4. Bone marrow harvesting and mobilisation of haematopoietic stem cells 11](#_Toc22307771)

[5. Auto-HSCT conditioning regimens 12](#_Toc22307772)

[PART III: Allogeneic Haematopoietic Stem Cell transplant (Allo-HSCT) 13](#_Toc22307773)

[6. Donor selection principles in allo-HSCT 13](#_Toc22307774)

[7. Allo-HSCT Conditioning Regimens 13](#_Toc22307775)

[8. Immunosuppression 14](#_Toc22307776)

[PART IV: Prevention and Management of common complications of HSCT 15](#_Toc22307777)

[9. Prevention and management of acute (aGvHD) and chronic graft versus host disease (cGvHD) 15](#_Toc22307778)

[10. Management of veno-occlusive Disease (VOD)/sinusoidal obstruction syndrome (SOS) 16](#_Toc22307779)

[11. Management of Epstein-Barr (EBV) infections 17](#_Toc22307780)

[12. Prevention and treatment of fungal disease 18](#_Toc22307781)

[13. Prophylaxis and treatment of cytomegalovirus (CMV) infection 19](#_Toc22307782)

[14. Prevention and management of Pneumocystis Jirovecii Pneumonia (PJP) infections 19](#_Toc22307783)

[15. Other HSCT complications and general management 21](#_Toc22307784)

[PART V: Chimeric Antigen Receptor T-cell (CAR-T) Therapies 22](#_Toc22307785)

[PART VI: Verification of conditioning chemotherapy 24](#_Toc22307786)

[APPENDIX 1: HSCT Conditioning and CAR-T cell lymphodepletion prescription (re)validation logs 27](#_Toc22307787)

[APPENDIX 2: HSCT Conditioning and CAR-T cell lymphodepletion prescription (re)validation final accreditation sign-off 30](#_Toc22307789)

[APPENDIX 3: Record of Continuing Education 31](#_Toc22307790)

[APPENDIX 4: Annual accreditation for the designated HSCT Pharmacist 35](#_Toc22307791)

[Appendix 5: Test Your Understanding Questions and Activities 36](#_Toc22307792)

[PART I: Indications for HSCT 36](#_Toc22307793)

[PART II: Autologous Haematopoietic Stem Cell Transplant (Auto-HSCT) 36](#_Toc22307794)

[PART III: Allogeneic Haematopoietic Stem Cell Transplant (Allo-HSCT) 39](#_Toc22307795)

[Part IV: Prevention and Management of common complications of HSCT 48](#_Toc22307796)

[PART V: Chimeric Antigen Receptor T-cell (CAR-T) Therapies 58](#_Toc22307797)

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We would also like to thank the following pharmacists who reviewed the draft passport prior to its publication:

Jackie Chappell, King's College Hospital NHS Foundation Trust.

Liz Davies, Manchester University NHS Foundation Trust.

Sumantha Gabriel, Newcastle Upon Tyne Hospitals NHS Foundation Trust.

# Abbreviations

|  |  |
| --- | --- |
| aGvHD | Acute Graft versus Host Disease |
| Allo-HSCT | Allogeneic Haematopoietic Stem Cell Transplant |
| ATG | Anti-Thymocyte Globulin |
| ATMP | Advanced Therapy Medicinal Product |
| ATIMP | Advanced Therapy Investigational Medicinal Product |
| Auto-HSCT | Autologous Haematopoietic Stem Cell Transplant |
| BM | Bone Marrow |
| BMT | Blood and Marrow Transplant |
| BOOP | Bronchiolitis Obliterans Organizing Pneumonia |
| BOPA | British Oncology Pharmacy Association |
| BOS | Bronchiolitis Obliterans Syndrome |
| CAR-T | Chimeric Antigen Receptor T Cell |
| cGvHD | Chronic Graft versus Host Disease |
| CMV | Cytomegalovirus |
| CRS | Cytokine Release Syndrome |
| CSA | Ciclosporin |
| DLI | Donor Lymphocyte Infusion |
| EBMT | European Society for Blood and Marrow Transplantation |
| EBV | Epstein-Barr Virus |
| FACT- JACIE | Foundation for the Accreditation of Cellular Therapy- Joint Accreditation Committee ISCT/EBMT |
| GCP | Good Clinical Practice |
| GCSF | Granulocyte-colony Stimulating factor |
| GvHD | Graft versus Host Disease |
| Haplo | Haploidentical |
| HSC | Haematopoietic Stem Cell |
| HSCT | Haematopoietic Stem Cell Transplant |
| ICANS | Immune Effector Cell-Associated Neurotoxicity Syndrome |
| IFD | Invasive Fungal Disease |
| MAC | Myeloablative Conditioning |
| MDT | Multidisciplinary |
| MSD | Matched Sibling Donor |
| MUD | Matched Unrelated Donor |
| PJP | Pneumocystis jirovecii pneumonia |
| PTLD | Post-transplant lymphoproliferative disorder |
| RIC | Reduced Intensity Conditioning |
| SOP | Standard Operating Procedure |
| SOS | Sinusoidal Obstruction Syndrome |
| TDM | Therapeutic Drug Monitoring |
| VOD | Veno-Occlusive Disease |

# Scope

In line with the FACT-JACIE International Standards for Haematopoietic Cellular therapy (currently 7th edition, 2018); all designated pharmacists providing a service to haematopoietic stem cell transplant (HSCT) patients must demonstrate the minimum JACIE requirements for continuing accreditation.

The training passport is designed for all pharmacists providing pharmaceutical care to HSCT patients including those undergoing autologous and allogeneic transplant, patients admitted to the HSCT unit with post-transplant complications and patients attending post-transplant out-patient clinics. For rotational pharmacists, it is expected that training will be supervised by HSCT-trained and the designated Lead Pharmacist for the HSCT unit and it is accepted that not all aspects of the package may be completed during an individual’s rotation. It is suggested that the designated Lead Pharmacist for the HSCT unit completes all components of this training pertinent to the services provided within their unit and has their competency assessed by the Clinical Programme Lead for the unit.

It is not the intention of this document to be a complete training programme for pharmacists working in the field, but rather to provide a template (focused on the current JACIE standards for pharmacists) which individual centres can build their own training programmes around. The field is rapidly evolving and users are encouraged to link this passport with other resources for further continuing professional development to build on their knowledge, skills and expert practice in the field. In terms of clinical content, we refer the trainees to a list of suggested reading based on national/international reference sources and key guidelines and local protocols, alongside a pool of appendices and assessment questions – note: there is an accompanying document containing example answers to the assessment questions that can be used to support the training. Individual centres can add local guidelines and protocols applicable to their service onto the reading list. In addition, a series of eLearning modules are currently being produced by members of the BOPA Education and Training sub-committee in collaboration with the UK BMT Pharmacists’ Group, to help facilitate pharmacist training in this area.

A distinction is made between “mandatory” and “recommended” reading. It is suggested that all “mandatory” reading including local clinical guidelines should be completed by the pharmacist as soon as possible after the start of the specialist rotation or substantive role in the HSCT team. Pharmacists are encouraged to also complete the “recommended” reading and assessment questions during the course of their specialist rotation.

Once pharmacists complete their training passport, they can use it to evidence their competency as part of their professional portfolio. It is recognised that some pharmacists will only be able to cover a limited range of conditioning regimens, types of transplants or advanced therapies within their individual centres. On transfer to another HSCT unit, the designated lead HSCT pharmacist for the new unit will be able to review the presented passport, assess accuracy of answers and use their professional discretion to determine what additional training is required in the new employment setting.

# Changes since version 1.0

The following content changes have been made in version 2.0 of the passport:

Part I section 2: Addition of the following to the recommended course list:

* BOPA BMT e-learning course – modules 1 and 2

Part I section 3: Addition of the following to the recommended reading list:

* New indication for transplant recommendations from EBMT (2019) and ASTCT (2020).
* Haematopoietic Stem Cell Transplantation (HSCT) for Adults. Welsh Health Specialised Services Committee Specialised Services Policy.
* Clinical Commissioning Policy: Allogeneic Haematopoietic Stem Cell Transplantation for adults with sickle cell disease. NHS England

Part II section 4: Update of the following on the mandatory reading list:

* Updated NHS England Plerixafor Commissioning Policy

Part II section 5: Addition of the following to recommended reading list:

* Shah N et al. Hematopoietic Stem Cell Transplantation for Multiple Myeloma: Guidelines from the American Society for Blood and Marrow Transplantation

Part IV section 9: Addition of the following to the mandatory reading list:

* Updated eBMT consensus recommendations for the prophylaxis and management of GvHD..
* NHSE Rapid policy statement: Ruxolitinib for acute graft versus host disease.
* NHSE Rapid policy statement: Ruxolitinib for chronic graft versus host disease.

Part IV section 10: Update of the following on the mandatory reading list:

* Updated version of the clinical commissioning policy for defibrotide. (Please note, this does not come into effect until the next financial year therefore, both policies have been listed).

Part IV section 10: Addition of the following to the recommended course list:

* EBMT Veno-occlusive disease (VOD) learning program

Part IV section 12: Update of the following on the recommended reading list:

* Revised Definitions of Invasive Fungal Disease from the EORTC and the Mycoses Study Group

Part IV section 13: Addition of the following to the recommended reading list:

* Einsele H et al. How I treat CMV reactivation after allogeneic stem cell transplantation.

PART IV section 15. Addition of the following to the mandatory reading list:

* MASCC/ISOO Clinical Practice Guidelines for the Management of Mucositis Secondary to Cancer Therapy (2020)
* Antiemetics: ASCO Guideline Update (2020)

Part V: Update of the following on the mandatory reading list:

* Pharmacy Institutional Readiness for Marketed CAR-T therapy: Pharmacy Services Checklists

Part V: Addition of the following to the mandatory reading list:

* Practical Guidance on Pharmacy Oversight and Pharmacist Supervision of licensed ATMPs requiring a preparation/reconstitution step
* Medication Restrictions for Patients Having CAR-T Cell Therapy
* Out of Specification Advanced Therapy Medicinal Products - Guidance for Healthcare Organisations
* Diagnosis and Medical Management of Acute CAR-T Cell Toxicities in Adults

Part V: Addition of the following to the recommended course list:

* EBMT CAR-T cell e-course

# PART I: Introduction

## JACIE standards for pharmacists (B3.8)

Refer to FACT-JACIE international standards for Haematopoietic Cellular Therapy – SEVENTH edition <https://www.ebmt.org/sites/default/files/2018-06/FACT-JACIE%207th%20Edition%20Standards.pdf> and FACT-JACIE accreditation manual <https://www.ebmt.org/sites/default/files/2018-06/FACT-JACIE%207th%20Edition%20Manual.pdf> for further details on the most up to date standards.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **FACT- JACIE Standards- 7th Edition** | | **Evidenced by** | **Date** | **Signature** |
| **B3.8.1** | Pharmacists shall be licensed to practice in the jurisdiction of the Clinical Program and shall be limited to a scope of practice within the parameters of their training and licensure | GPhC Registration number\*………………… |  |  |
| **B3.8.2** | Training and knowledge of designated transplant pharmacists shall include: |  | | |
| B3.8.2.1 | Haemato-oncology patient care, including the process of cellular therapy |  |  |  |
| B.3.8.2.2 | Adverse events including, but not limited to, cytokine release syndrome and neurological toxicities |  |  |  |
| B3.8.2.3 | Therapeutic drug monitoring, including, but not limited to, anti-infective agents, immunosuppressive agents, anti-seizure medications, and anticoagulants |  |  |  |
| B3.8.2.4 | Monitoring for and recognition of drug/drug and drug/food interactions and necessary dose modifications |  |  |  |
| B3.8.2.5 | Recognition of medications that require adjustment for organ dysfunction |  |  |  |
| **B3.8.3** | Designated pharmacists shall be involved in the development and implementation of controlled documents related to the pharmaceutical management of cellular related therapy recipients | See Appendix 3,  part B |  |  |
| **B3.8.4** | Designated pharmacists shall participate in a minimum of ten (10) hours of educational activities related to cellular therapy annually |  |  |  |
| B3.8.4.1 | Continuing education shall include, but not be limited to, activities related to the field of haematopoietic stem cell transplantation and cytokine release syndrome and neurological toxicities resulting from cellular therapies. | See Appendix 3,  parts A, C |  |  |
| **B7.4.3** | The pharmacist verifying or preparing the drug shall check and document the doses against the protocol or standardised regimen listed on the orders. | Completion of verification accreditation – see Appendix 1 and 2 |  |  |

\* All pharmacists who practise in the UK are required to be registered with the GPhC and registration is renewed annually. Please visit [www.pharmacyregulation.org.registers/pharmacists](http://www.pharmacyregulation.org.registers/pharmacists) to confirm registration status

## Introduction to HSCT and to the HSCT unit

This section is intended to guide pharmacists’ orientation within the HSCT service. We recognise that there will inevitably be variability between centres in terms of facilities and ancillary services. Pharmacists are encouraged to find out about the patient pathways, team and service structure within their individual centre.

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| The HSCT Unit. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies. 2019. ISBN 978-3-030-02278-5 | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |
| The Role of Unrelated Donor  Registries in HSCT. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |
| Consensus recommendations for the role and competencies of the EBMT clinical pharmacist and clinical pharmacologist involved in hematopoietic stem cell transplantation | Langenbrake C et al. Bone Marrow Transplant 2019;  Available online.  <https://doi.org/10.1038/s41409-019-0538-9> |  |
| **Local guidelines, protocols and SOPs to include: (add other relevant local guidelines and protocols here)** | | |
| Transplant Pathway |  |  |
| HSCT MDT operational Policy |  |  |
|  |  |  |

**Recommended courses**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| BOPA BMT e-learning course (2020) – modules 1 and 2 | <https://www.bopa.org.uk/course-category/haemato-oncology/>  (note – accessible to BOPA members only) |  |

**Activity 1:** Identify key clinical areas within your HSCT service. Visit the areas where applicable, shadow a senior member of the team and discuss the patient and donor pathway:

* The inpatient unit
* The outpatient unit
* The role of unrelated donor registries in HSCT
* Stem cell collection and processing facility
* Referring/referral centres including CAR-T cell centres
* The HSCT multidisciplinary team (MDT) meeting
* The ambulatory unit
* Intensive Care Unit
* The Blood Bank
* Radiotherapy
* Anthony NolanOther:…………………………………………………………………………………………………………………………………

**Activity 2:** Meet key members of the HSCT team where possible and discuss their role within the HSCT service:

* The programme clinical director:…………………………………………………………………………………………
* The HSCT Physicians:……………………………………………………………………………………………………………
* The HSCT specialist nurses:………………………………………………………………………………………………….
* The transplant co-ordinator:………………………………………………………………………………………………..
* The service quality manager:………………………………………………………………………………………………..
* The service data manager:……………………………………………………………………………………………………
* Ancillary medical services:
* Infectious diseases
* Dermatology
* Neurology, Gastroenterology, Renal, Respiratory medicine
* Other:…………………………………………………………………………………………………………………………………

## Indications for HSCT

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| Indications and Results. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies. 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |
| EBMT: Indications for haematopoietic stem cell transplantation for  haematological diseases, solid tumours and immune disorders:  current practice in Europe, 2019 | Rafael F. Duarte et al. Bone Marrow Transplantation (2019) 54:1525–1552. Accessible on PubMed. |  |
| ASTCT: Indications for Hematopoietic Cell Transplantation and Immune  Effector Cell Therapy: Guidelines from the American Society for  Transplantation and Cellular Therapy | Abraham S. Kanate et al. Biol Blood Marrow Transplant 26 (2020) 1247-1256. Accessible on PubMed. |  |
| Clinical commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages). NHS England B04/P/a. 2015. | Available online. <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/b04-haematp-stem-cll-transplt.pdf> |  |
| Haematopoietic Stem Cell Transplantation (HSCT)  for Adults. Welsh Health Specialised Services Committee Specialised Services  Policy Position PP142. 2020 | Available online.  <http://www.whssc.wales.nhs.uk/sitesplus/documents/1119/PP142%20HSCT%20v1.01.pdf> |  |
| Clinical Commissioning Policy: Second allogeneic haematopoietic stem cell transplant for relapsed disease (all ages). NHS England 16068/P. 2017 | Available online. <https://www.england.nhs.uk/wp-content/uploads/2017/02/clin-comms-policy-16068p.pdf> |  |
| Clinical Commissioning Policy: Haematopoietic stem cell transplantation (HSCT) for lymphoplasmacytic lymphoma (adults). NHS England 16067/P. 2016 | Available online.  <https://www.england.nhs.uk/wp-content/uploads/2016/12/clin-comm-pol-16067P.pdf> |  |
| Clinical Commissioning Policy: Allogeneic Haematopoietic Stem Cell Transplant for Primary Immunodeficiencies (all ages) NHS England 170129P. 2019 | Available online.  <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2019/07/Clinical-Commissioning-Policy_Allogeneic-Haematopoietic-Stem-Cell-Transplant-for-Primary-Immunodeficiencies.pdf> |  |
| Clinical Commissioning  Policy: Allogeneic  Haematopoietic Stem Cell  Transplantation for adults  with sickle cell disease. NHS England 190138P. 2019 | Available online.  <https://www.england.nhs.uk/wp-content/uploads/2020/02/clinical-commissioning-policy-allogeneic-haematopoietic-stem-cell-transplantation.pdf> |  |

# PART II: Autologous Haematopoietic Stem Cell transplant (Auto-HSCT)

## Bone marrow harvesting and mobilisation of haematopoietic stem cells

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| Clinical Commissioning Policy Plerixafor for stem cell mobilisation in adults and children. NHS England July 2019. (Publication reference no: 200601P) | Available online <https://www.england.nhs.uk/wp-content/uploads/2020/09/1902_Plerixafor_Clinical_Commissioning_Policy.pdf>  *Note: only applicable to England. Commissioning may vary between England, Scotland, Wales and Northern Ireland* |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| *Include local mobilisation protocols* |  |  |
| *Include local mobilisation protocols* |  |  |
| *Include local mobilisation protocols* |  |  |
| *Include local mobilisation protocols* |  |  |
|  |  |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| EBMT educational presentation. Haematopoietic Stem Cell Mobilisation and Apheresis. | Available online.  <https://www.slideshare.net/EBMT/module1final170212> |  |
| ASBMT Guideline. Peripheral Blood Progenitor Cell Mobilization for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the American Society for Blood and Marrow Transplantation | Duong H.K et al. Biol Blood Marrow Transplant 20 (2014) 1262-1273. Accessible online. https://www.astct.org/asbmt/practice-resources/practice-guidelines |  |
| Mobilization and Collection of HSC. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Section 15.  Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |
| Bone Marrow Harvesting for HSCT. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Section 14.  Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |

## Auto-HSCT conditioning regimens

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| *Include local conditioning protocols for autologous transplants* |  |  |
| *Include local conditioning protocols for autologous transplants* |  |  |
| *Include local conditioning protocols for autologous transplants* |  |  |
| *Include local conditioning protocols for autologous transplants* |  |  |
| *Include local conditioning protocols for autologous transplants* |  |  |
|  |  |  |
|  |  |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| ASBMT Guideline. Hematopoietic Stem Cell Transplantation for Multiple Myeloma: Guidelines from the American Society for Blood and Marrow Transplantation | Shah, N. et al. Biol Blood Marrow Transplant 21 (2015) 1155-1166. Accessible online. https://www.astct.org/asbmt/practice-resources/practice-guidelines |  |

# PART III: Allogeneic Haematopoietic Stem Cell transplant (Allo-HSCT)

## Donor selection principles in allo-HSCT

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| *Include local mobilisation protocol for healthy donors* |  |  |
|  |  |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| The Role of Unrelated Donor Registries in HSCT. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |
| Recommendations for Donor Human Leukocyte Antigen Assessment and Matching for Allogeneic Stem Cell Transplantation: Consensus Opinion of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) | Howard CA, Fernandez-Vina MA, Appelbaum FR, et al. Biol Blood Marrow Transplant. 2015;21(1):4–7. Available online: <https://www.bbmt.org/article/S1083-8791(14)00598-9/pdf> |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| *Include local protocols for related donor pathway* |  |  |
|  |  |  |
|  |  |  |

## Allo-HSCT Conditioning Regimens

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| *Include local conditioning protocols for Reduced Intensity Transplants* |  |  |
| *Include local conditioning protocols for Full Intensity (Myeloablative) transplants* |  |  |
|  |  |  |
|  |  |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| Conditioning. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |

## Immunosuppression

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| Guidelines for the Use of CSA |  |  |
| Tacrolimus for Adult Patients Receiving Allogeneic Blood and Bone Marrow Transplantation |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| Prophylaxis and treatment of GvHD: EBMT–ELN working group recommendations for a standardized practice | Ruutu T et al. Bone Marrow Transplantation volume 49, pages 168–173 (2014).  Available online: <https://www.nature.com/articles/bmt2013107> |  |
| GvHD Prophylaxis (immunosuppression). The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |

# 

# PART IV: Prevention and Management of common complications of HSCT

## Prevention and management of acute (aGvHD) and chronic graft versus host disease (cGvHD)

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| Clinical Commissioning Policy: Treatments for Graft versus Host Disease (GvHD) following Haematopoietic stem cell transplantation. NHS England 16069/P | Available online. <https://www.england.nhs.uk/wp-content/uploads/2017/03/gvhd-heamatopoietic-stem-cell.pdf> |  |
| Prophylaxis and management of graft versus host disease after stem cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation | The Lancet. Haematology , 2020, Vol.7(2), p.e157-e167 |  |
| Ruxolitinib for acute graft versus host disease. Rapid policy statement 2009. NHS England. 2020 | Available online:  <https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/11/C0733-2009RU-aGvHD_PostCP_November-2020-v1.1.pdf> |  |
| Ruxolitinib for chronic graft versus host disease. Rapid policy statement 2010. NHS England. 2020 | Available online:  <https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/11/C0733-2010RU-PostCP-November-2020.pdf> |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| Acute Graft versus Host Disease: Diagnosis and Management |  |  |
| Chronic Graft versus Host Disease: Diagnosis and Management |  |  |
|  |  |  |
|  |  |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| EBMT educational material. eGvHD app | Can be downloaded <https://www.uzleuven.be/egvhd> |  |
| Acute Graft-versus-Host Disease. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |
| Chronic Graft-versus-Host Disease. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |
| EBMT educational material. Graft vs Host Disease - An educational DVD for healthcare Professionals, Part 1 | Available online. <https://www.ebmt.org/ebmt/documents/graft-vs-host-disease-educational-dvd-healthcare-professionals-part-1> |  |
| EBMT educational material. Graft vs Host Disease - An educational DVD for healthcare Professionals, Part 2 | Available online. <https://www.ebmt.org/ebmt/documents/graft-vs-host-disease-educational-dvd-healthcare-professionals-part-2> |  |
| EBMT educational material Graft vs Host Disease - An educational DVD for healthcare Professionals, Part 3 | Available online <https://www.ebmt.org/ebmt/documents/graft-vs-host-disease-educational-dvd-healthcare-professionals-part-3> |  |
| Acute Graft-versus-Host Disease - Biologic Process, Prevention, and Therapy | Zeiser R, Blazar BR. N Engl J Med. 2017 Nov 30; 377 (22):2167-2179. Available online:  <https://www.ncbi.nlm.nih.gov/pubmed/29171820> |  |

## Management of veno-occlusive Disease (VOD)/sinusoidal obstruction syndrome (SOS)

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| **Up to and including 31st March 2021:**  Clinical Commissioning Policy: Use of defibrotide in severe veno-occlusive disease following stem cell transplant. NHS England B04/P/c | Available online.  <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/b04-use-defibrotide.pdf>  *Note: only applicable to England. Commissioning may vary between England, Scotland, Wales and Northern Ireland* |  |
| **From 1st April 2021:**  Clinical Commissioning Policy (Revised): Use of defibrotide in severe veno-occlusive disease following stem cell transplant. NHS England P200804P | Available online.  <https://www.england.nhs.uk/wp-content/uploads/2020/11/Defibrotide-for-severe-veno-occlusive-disease-following-stem-cell-transplant-v2.pdf>  *Note: only applicable to England. Commissioning may vary between England, Scotland, Wales and Northern Ireland* |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| Veno-occlusive Disease: Diagnosis and Management |  |  |
|  |  |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| EBMT Presentations. VOD learning programme modules.  Module 1: Haematopoietic stem cell transplantation  Module 2: Pathophysiology of VOD  Module 3: Diagnosis of VOD  Module 4: Assessment and management of VOD  Module 5: VOD case studies | Available online on EBMT Website Education Section. <https://www.ebmt.org/education> |  |
| EBMT. Revised diagnosis and severity criteria for sinusoidal obstruction syndrome/veno-occlusive disease in adult patients: a new classification from the European Society for Blood and Marrow Transplantation. | Mohty M et al. Bone Marrow Transplant. 2016 Jul; 51(7):906-12. Available online:  <https://www.ncbi.nlm.nih.gov/pubmed/27183098> |  |
| Management of veno‐occlusive disease: the multidisciplinary approach to care | Wallhult E et al. European Journal of Haematology 2017; 98: 322–329. Available online:  <https://onlinelibrary.wiley.com/doi/full/10.1111/ejh.12840> |  |
| BCSH/BSBMT guideline: diagnosis and management of veno‐occlusive disease (sinusoidal obstruction syndrome) following haematopoietic stem cell transplantation | Dignan F L et al. British Journal of Haematology 2013; 163: 444–457. Available online:  <https://www.ncbi.nlm.nih.gov/pubmed/24102514> |  |

**Recommended course**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| EBMT Veno-occlusive disease (VOD) learning program | <https://www.ebmt.org/veno-occlusive-disease-vod-learning-programme> |  |

## Management of Epstein-Barr (EBV) infections

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| ECIL 6 Guidelines. Management of Epstein-Barr Virus infections and post-transplant lymphoproliferative disorders in patients after allogeneic hematopoietic stem cell transplantation | Styczynski J et al. Haematologica. 2016; 101: 803-11. Available online: <https://www.ncbi.nlm.nih.gov/pubmed/27365460> |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| Management and monitoring of EBV Reactivation and PTLD in Allogeneic Blood and Marrow Transplant Recipients |  |  |
|  |  |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| Viral Infections. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |

## Prevention and treatment of fungal disease

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |  |
| --- | --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | | **Date and Signature** |
| ECIL-6 Guidelines. Triazole antifungal therapeutic drug monitoring | ECIL6 Meeting. September 11-12 2015. Available online. <http://www.ecil-leukaemia.com/telechargements2015/ECIL6-Triazole-TDM-07-12-2015-Lewis-R-et-al.pdf> | |  |
| ECIL-6 Guidelines For The Treatment Of Invasive Candidiasis, Aspergillosis and Mucormycosis In Leukaemia And Hematopoietic Stem Cell Transplant Patients | Frederic Tissot et al. Haematologica March 2017 102: 433-444. Available online:  <https://doi.org/10.3324/haematol.2016.152900> | |  |
| ECIL guidelines. European guidelines for primary antifungal prophylaxis in adult haematology patients: summary of the updated recommendations from the European Conference on Infections in Leukaemia. | Maertens JA1 et a. J Antimicrob Chemother. 2018 Dec 1; 73(12):3221-3230. Available online. <https://www.ncbi.nlm.nih.gov/pubmed/30085172> | |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | | |
| Antifungal therapy guidelines |  |  | |
|  |  |  | |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| Revision and Update of the Consensus Definitions of  Invasive Fungal Disease From the European Organization  for Research and Treatment of Cancer and the Mycoses  Study Group Education and Research Consortium | Donnelly JP et al. Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clin Infect Dis. 2020; 71:1367-1376. Available online: <https://doi.org/10.1093/cid/ciz1008> |  |
| Global guideline for the diagnosis and management of  mucormycosis: | Cornelly O et al. Lancet Infect Dis 2019; Nov 4th. Available online:  <https://doi.org/10.1016/S1473-3099(19)30312-3> |  |

## 

## Prophylaxis and treatment of cytomegalovirus (CMV) infection

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| Guidelines for the management of cytomegalovirus infection in patients with haematological malignancies and after stem cell transplantation from the 2017 European Conference on Infections in Leukaemia (ECIL 7**)** | Ljungman P et al. 2019. Lancet Infect Dis 2019; 19 (8): e260-e272. Available online:  <https://www.ncbi.nlm.nih.gov/pubmed/31153807> |  |
| Letermovir for preventing cytomegalovirus disease after a stem cell transplant. NICE TA591. July 2019 | Available online.  <https://www.nice.org.uk/guidance/TA591> |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| Monitoring and Treatment for CMV Infection and Disease |  |  |
|  |  |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| Viral Infections. The EBMT handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |
| How I treat CMV reactivation after allogeneic stem cell transplantation | Einsele H et al. 2020. Blood; 135: 1619-29  Available online:  <https://doi.org/10.1182/blood.2019000956> |  |

## 

## Prevention and management of Pneumocystis Jirovecii Pneumonia (PJP) infections

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| ECIL-6. ECIL guidelines for treatment of Pneumocystis jirovecii pneumonia in non-HIV-infected haematology patients. | Maschmeyer G et al. J Antimicrob Chemother. 2016 Sep; 71(9):2405-13. Available online. <https://www.ncbi.nlm.nih.gov/pubmed/27550993> |  |
| ECIL-5. ECIL guidelines for preventing Pneumocystis jirovecii pneumonia in patients with haematological malignancies and stem cell transplant recipients. | Maertens J et al. J Antimicrob Chemother. 2016 Sep; 71 (9):2397-404. Available online. <https://www.ncbi.nlm.nih.gov/pubmed/27550992> |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| Prophylaxis and Treatment of Pneumocystis Jirovecii Pneumonia |  |  |
| Administration of Pentamidine |  |  |
|  |  |  |

## Other HSCT complications and general management

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| MASCC/ISOO Clinical Practice Guidelines for the Management of Mucositis Secondary to Cancer Therapy | Elad et al. Cancer, 2020 Oct 1;126(19):4423-4431. Accessible online on PubMed. <https://pubmed.ncbi.nlm.nih.gov/32786044/> |  |
| Antiemetics: ASCO Guideline Update. 2020 | Paul J. Hesketh et al. Clinical Oncology 38, no. 24 (August 20, 2020) 2782-2797. Available online. |  |
| ECIL-4. Fourth European Conference on Infections in Leukaemia: guidelines for diagnosis and treatment of human RSV, parainfluenza virus, metapneumovirus, rhinovirus, and coronavirus | Hirsch et al. Clin Infect Dis. 2013 Jan; 56(2):258-66.  Available online: <https://www.ncbi.nlm.nih.gov/pubmed/23024295> |  |
| ECIL guidelines for the prevention, diagnosis and treatment of BK polyomavirus -associated haemorrhagic cystitis in HSCT recipients | Cesaro S et al. J Antimicrob Chemother. 2018 ; 73: 12-21. Available online  <https://www.ncbi.nlm.nih.gov/pubmed/29190347> |  |
| ECIL- 7 guidelines for vaccination of haemopoietic stem cell transplant recipients | Cordonnier C et al. Lancet Infect Dis 2019; 19: e200-e212. Available online:  <https://www.ncbi.nlm.nih.gov/pubmed/30744963> |  |
| Important drug interactions in hematopoietic stem cell transplantation: what every physician should know | Glotzbecker B et al. Biol Blood Marrow Transplant. 2012 ;18: 989-1006  Available online:  <https://www.ncbi.nlm.nih.gov/pubmed/22155504> |  |
| Clinically relevant drug interactions in HSCT. The EBMT handbook. HSCT and Cellular Therapies 2019. | Available online. <https://www.ebmt.org/sites/default/files/2019-01/2019_Book_TheEBMTHandbook.pdf> |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| Management of Febrile Neutropenic sepsis |  |  |
| Infection Prevention and Control |  |  |
| Management of Viral Infections other than CMV |  |  |
| Tumour Lysis Syndrome |  |  |
| Antiemetic guidelines |  |  |
| Management of Oral Mucositis |  |  |
| Diagnosis and Management of Haemorrhagic Cystitis Post Transplant |  |  |
| Nutrition |  |  |
| Iron overload |  |  |
| Vaccination guidelines post transplantation |  |  |
| Diagnosis and Management of Transplant Associated Microangiopathy (TAM) – formerly known as TTP |  |  |

# PART V: Chimeric Antigen Receptor T-cell (CAR-T) Therapies

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |  |
| --- | --- | --- | --- |
| **Reference Title** | | **Reference Location/Link/Identifier** | **Date and Signature** |
| Pharmacy Institutional Readiness for Marketed CAR-T Therapy: Checklists for Pharmacy Services | | Anne Black. Version 4.0. January 2020  https://www.sps.nhs.uk/wp-content/uploads/2018/10/Pharmacy-Institutional-Readiness-for-Marketed-CAR-T-Therapy-Guidance-for-Chief-Pharmacists-V4.pdf |  |
| Practical Guidance on Pharmacy Oversight and Pharmacist Supervision of licensed ATMPs requiring a preparation/reconstitution step | | Anne Black. Version 1.0. January 2020.  https://www.sps.nhs.uk/wp-content/uploads/2020/01/Pharmacy-Oversight-and-Supervision-Requirements-for-Preparation-of-Licensed-ATMPs.pdf |  |
| Medication Restrictions for Patients Having CAR-T Cell Therapy | | Nia Evans. Version 2.0. August 2020  https://www.sps.nhs.uk/wp-content/uploads/2020/01/Medication-Restrictions-for-Patients-having-CAR-T-Therapy-Aug-2020.pdf |  |
| Out of Specification Advanced Therapy Medicinal Products - Guidance for Healthcare Organisations | | Anne Black. Version 1.2. March 2020.  https://www.sps.nhs.uk/wp-content/uploads/2020/02/Out-of-Specification-Advanced-Therapy-Medicinal-Products-V1.2-March-2020.pdf |  |
| Diagnosis and Medical Management of Acute CAR-T Cell Toxicities in Adults | | Alice Mason and Sumantha Gabriel. Version 1.0. December 2020.  https://www.sps.nhs.uk/wp-content/uploads/2020/12/Diagnosis-and-medical-management-of-acute-CAR-T-cell-toxicities-in-Adults-V1.pdf |  |
| Evidence for use of siltuximab or anakinra as second line therapies (after failure of tocilizumab) for Cytokine Release Syndrome (CRS) following use of Chimeric Antigen Receptor T-cell (CAR-T) therapy | | Sheena Vithlani. Version 1. April 2019  Available online.  <https://www.sps.nhs.uk/wp-content/uploads/2019/05/SPS_Siltuximab_Anakinra_CRS_postCAR_T_Feb20-1.pdf> |  |
| NHS England Interim Service Specification. Axicabtagene Ciloleucel Chimeric Antigen Receptor T Cell (CAR T) Therapy for the treatment of adult patients with relapsed or refractory large B-cell lymphoma. 170099S (draft interim). | | Available online.  <https://www.england.nhs.uk/wp-content/uploads/2018/12/Axicabtagene-Ciloleucel-Chimeric-Antigen-Receptor-T-Cell-CAR-T-Therapy-for-the-treatment-of-adult-patients-wit.pdf> |  |
| NHS England Interim Service Specification. Tisagenlecleucel Chimeric Antigen Receptor T Cell (CAR T) Therapy for ALL and DLBCL. 170100S (draft interim) | | Available online.  <https://www.england.nhs.uk/wp-content/uploads/2018/12/Tisagenlecleucel-Chimeric-Antigen-Receptor-T-Cell-CAR-T-Therapy-for-ALL-and-DLBCL.pdf> |  |
| Tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people aged up to 25 years. NICE TA554. December 2018 | | Available online.  <https://www.nice.org.uk/guidance/ta554> |  |
| Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more systemic therapies. NICE TA559. January 2019 | | Available online.  <https://www.nice.org.uk/Guidance/TA559> |  |
| Tisagenlecleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies. NICE TA567. March 2019 | | Available online.  <https://www.nice.org.uk/guidance/ta567> |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | | |
| Policy for the Use of Advanced Therapy Medicinal Products (ATMPs) |  | |  |
| Delivery, Receipt, Storage, Issue and Infusion of Advanced Therapy Medicinal Products (ATMPs) |  | |  |
| Lymphodepletion protocols |  | |  |
| Guideline on the management of Cytokine Release Syndrome (CRS) |  | |  |
| Guideline on the management of Immune Effector Cell‐Associated Neurotoxicity Syndrome (ICANS) |  | |  |
| Supportive care guidelines for patients receiving ATMPs |  | |  |
|  |  | |  |
|  |  | |  |
| **Specific training related to each Advanced Therapy Medicinal Product delivered at the centre (add other relevant local guidelines and protocols here)** | | | |
| **Novartis (Kymriah®)** | | | |
| Novartis Kymriah® risk management protocol training |  | |  |
| Cell Chain Portal training |  | |  |
| **Gilead (Yescarta®)** | | | |
| Gilead Yescarta® risk management protocol training |  | |  |
| Kite Konnect Portal training |  | |  |
|  |  | |  |
|  |  | |  |

**Recommended reading**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells | Lee DW et al. Biol Blood Marrow Transplant 25 (2019) 625638. <https://www.bbmt.org/article/S1083-8791(18)31691-4/pdf> |  |
| The why, what, and how of the new FACT standards for immune effector cells | Maus M, Nikiforow S. Journal for Immunotherapy of Cancer (2017) 5:36.  <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5394615/pdf/40425_2017_Article_239.pdf> |  |
| CAR T cell immunotherapy for human cancer. | June, C. H. et al. (2018). Science, 359(6382), 1361–1365. <https://doi.org/10.1126/science.aar6711> |  |
| Chimeric antigen receptor T-cell therapy — assessment and management of toxicities | Neelapu, S. S et al, E. J. (2017). Nature Reviews Clinical Oncology. <https://doi.org/10.1038/nrclinonc.2017.148> |  |
| Severe Cytokine-Release Syndrome after T Cell–Replete Peripheral Blood Haploidentical Donor Transplantation Is Associated with Poor Survival and Anti–IL-6 Therapy Is Safe and Well Tolerated. | Abboud, R.et al (2016). Biology of Blood and Marrow Transplantation, 22(10), 1851–1860. [10.1016/j.bbmt.2016.06.010](https://doi.org/10.1016/j.bbmt.2016.06.010) |  |

**Recommended course**

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| EBMT CAR-T cell e-course | <https://www.ebmt.org/car-t-cell-e-course> |  |

# PART VI: Verification of conditioning chemotherapy

**Mandatory reading** (includes local guidelines and protocols as appropriate)

|  |  |  |
| --- | --- | --- |
| **Reference Title** | **Reference Location/Link/Identifier** | **Date and Signature** |
| BOPA Standards for Pharmacy Verification of Prescriptions for Cancer Medicines | 3rd edition. October 2018. Available online: <http://www.bopawebsite.org/publications/guidelines-standards>. |  |
| BOPA Verification of chemotherapy prescriptions e-module | Available online <http://www.bopawebsite.org/courses/course/verification-chemotherapy-prescriptions> |  |
| ASBMT Guideline Conditioning Chemotherapy Dose Adjustment in Obese Patients | Bubalo, Joseph et al. 2014. Biology of Blood and Marrow Transplantation, Volume 20, Issue 5, 600 - 616  Available online.  <https://www.bbmt.org/article/S1083-8791(14)00050-0/fulltext> |  |
| Dose recommendations for anticancer drugs in patients with renal or hepatic impairment | Krens SD et al. Lancet Oncol 2019 Apr;20(4):e200-e207  Available online  <https://www.ncbi.nlm.nih.gov/pubmed/30942181> |  |
| **Local guidelines, protocols and SOPs to include (add other relevant local guidelines and protocols here)** | | |
| Screening of high-dose chemotherapy Standard Operating Procedures |  |  |
| Special blood requirements guidelines |  |  |
| Good Clinical Practice training (If involved in clinical trials) |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

Before independently verifying conditioning or lymphodepletion regimens, it is recommended that the pharmacist performs a minimum verification accreditationlogaccording to the transplant programme. A suggested minimum verification would be:

* **5** allo-HSCT prescriptions
* **5** auto-HSCT prescriptions
* **2** lymphodepletion CAR-T prescriptions for each CAR-T product.

For those centres wishing to stipulate a higher number of verifications before accreditation then the table in appendix 1 can be photocopied to provide additional logs.

It is also recommended that:

1. The minimum number of logs required may be adjusted at the discretion of the designated HSCT lead pharmacist.
2. Depending on the transplant activity of the Centre, prescriptions should cover a range of conditioning regimens to include: Autografts, Allogeneic (Reduced Intensity (MUD, Sib), Haplo, Myeloablative, Cord etc.)
3. It is recommended that rotational pharmacists who are not permanent members of the team/rotation will need to complete annual re-accreditation of 2 supervised conditioning or lymphodepletion prescriptions to maintain competency.
4. It is recommended that those permanent pharmacists returning to work after a long period of absence (e.g. maternity leave) will need to complete re-accreditation logs of at least 2 supervised conditioning or lymphodepletion prescription to maintain competency.
5. Those pharmacists joining the team/rotation with previous experience of stem cell transplantation can complete a shortened accreditation at the discretion of the designated HSCT lead pharmacist.
6. Pharmacists can be signed off for a subset of conditioning regimens (e.g. reduced intensity or myeloablative) at the discretion of the designated HSCT lead pharmacist.
7. Final sign-off can only be done by the designated HSCT lead pharmacist.
8. **Appendix 1** can be used as a record of conditioning or lymphodepletion prescription validation logs and competency parameters. Note: the logs must not include patient identifiable information.
9. **Appendix 2** can be used as a record of the final (re)accreditation sign-off for conditioning HSCT and CAR-T cell lymphodepletion prescription validation.
10. **Appendix 3** can be used to record annual (re)accreditation for the designated HSCT Pharmacist.

# APPENDIX 1: HSCT Conditioning and CAR-T cell lymphodepletion prescription (re)validation logs

Trainee Name: ............................................................................................................... (Re)validation logs for Auto-HSCT ⎕ Allo-HSCT ⎕ CAR-T ⎕ ATIMPs ⎕

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Regimen name** | **Date** | **Interventions identified by trainee** | **Competency Parameters evidenced (table below)** | **Trainee signature**  **& Date** | **Topics discussed with assessor** | **Interventions identified by assessor** | **Assessors signature & Date** |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |

## Competency parameters

By completing the validation logs and before final accreditation sign-off, the trainee should demonstrate evidence of competence in the following parameters\*:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **No.** | **Validation Parameter** | **Assessor Comments** | **Date completed** | **Assessors signature** |
| 1 | The trainee confirms the MDT selected conditioning regimen has been correctly selected and prescribed |  |  |  |
| 2 | The trainee confirms patient consent |  |  |  |
| 3 | The trainee utilises clinical notes / transplant work up forms to confirm recipient pre-transplant assessments have been completed |  |  |  |
| 4 | The trainee checks relevant donor investigations and assessments have been completed |  |  |  |
| 5 | The trainee confirms relevant transplant documentation i.e. recipient and donor clearance and make records where appropriate |  |  |  |
| 6 | The trainee confirms special blood requirements have been requested from the blood bank as appropriate |  |  |  |
| 7 | The trainee refers to the correct protocol(s) and checks conditioning schedule and stem cell infusion dates are correct |  |  |  |
| 8 | The trainee checks dose calculations are correct including adjustments for obesity as appropriate |  |  |  |
| 9 | The trainee ensures the correct diluent, volume, infusion times and pump types are annotated on the prescription |  |  |  |
| 10 | The trainee ensures supportive medication including, but not limited to, anti-emetics, anti-infective, anti-viral and immunosuppressive agents, anti-seizure medications are prescribed as appropriate |  |  |  |
| 11 | The trainee understands the monitoring for and recognition of drug/drug and drug/food interactions and the necessary dose modifications |  |  |  |
| 12 | The trainee demonstrates recognition of medications that require adjustment for organ dysfunction |  |  |  |
| 13 | The trainee shows evidence of intervention if there is a lack of clinical information |  |  |  |
| 14 | For clinical trials, the trainee confirms randomisation/enrolment, treatment allocation against the trial protocol and trial specific investigational medicinal product requirements |  |  |  |
| **In addition, for CAR-T Cell Therapies** | | | | |
| 15 | The trainee checks washout of medication, including and not limited to, steroids prior to CAR-T infusion |  |  |  |
| 16 | The trainee confirms that steroids are not prescribed during lymphodepletion or available on the chart as required for infusion/allergic reactions |  |  |  |
| 17 | The trainee confirms CAR-T cell product manufacture has been successful prior to commencing lymphodepletion chemotherapy |  |  |  |
| 18 | The trainee ensures 4 doses of tocilizumab are available prior to CAR-T administration (depending on local standard operating procedure ensures that doses have been prescribed, pharmacy verified and dispensed prior to starting CAR-T infusion. |  |  |  |

**\* Note: some of the parameters listed above may not always apply depending on agreed local MDT practice and agreed processes for recipient work up and donor clearance.**

# APPENDIX 2: HSCT Conditioning and CAR-T cell lymphodepletion prescription (re)validation final accreditation sign-off

**The trainee** ………………………………………………………………………. (Enter name), has

1. completed all relevant mandatory and recommended reading as directed in the HSCT competency passport for pharmacists
2. successfully completed verification screening logs

The trainee is accredited to independently verify the following HSCT regimens (tick, sign and date as appropriate):

Auto-HSCT conditioning prescriptions

**Signature of the HSCT lead pharmacist** ………………………………..……...Date:…………………..

**Responsibility accepted by trainee**………………………………………………Date:………………..…

Allo-HSCT conditioning prescriptions:

* Reduced Intensity/Non-myeloablative
* Myeloablative (Full intensity)
* Haplo-identical

**Signature of the HSCT lead pharmacist:** ………………………………..…….Date:…………..………

**Responsibility accepted by trainee**………………………………………………Date:…………..………

CAR-T cells therapies prescriptions for the following products:

* Tisagenlecleucel (Kymriah®)
* Axicabtagene cileucel (Yescarta®)
* Advanced Therapy Investigational

Medicinal Products (ATIMPs)

**Signature of the HSCT lead pharmacist** ……………………………………....Date:…………………..

**Responsibility accepted by trainee**……………………………….……………..Date:…………………..

# APPENDIX 3: Record of Continuing Education

**B3.8.4 Designated transplant pharmacists shall participate in ten (10) hours of educational activities related to cellular therapy annually at a minimum.1**

B3.8.4.1 Continuing education shall include, but is not limited to, activities related to the field of HPC transplantation and cytokine release syndrome and neurological toxicities resulting from cellular therapies.

Evidence of continuing education may include either formal or informal study. Examples of appropriate continuing education activities include 1:

* The annual meeting of several professional societies that includes information directly related to the field.
* Grand Rounds, if specifically related to cellular therapy or diseases for which transplantation is a therapeutic option. The continuing education log must include the title, subject, and date of the presentation.
* Presentation of continuing education lectures.
* Presentation of a paper at a scientific meeting.
* Publication of a manuscript related to cellular therapy,
* Participation in a webinar or on-line tutorial.
* Review of an article in the medical literature related to cellular therapy; including those where the journal offers CME credits.
* Local or regional journal club, potentially including the preparation time.
* Morbidity and mortality, governance and quality meetings attendance.

To assess the appropriateness of the amount and type of continuing education in which the designated transplant pharmacists participated, the following information must be submitted for each of the completed continuing education activities within each accreditation cycle 1:

* Title of activity.
* Type of activity (e.g., webinar, meeting, grand round).
* Topic of activity (e.g., haematology, cell transplantation).
* Date of activity.
* Approximate number of hours of activity.

The requirements listed above may be provided in a variety of formats, including reports or listings submitted to professional organisations to obtain related credentials. Content must reflect regular education in cellular therapy and/or diseases in which cellular therapy is a therapeutic option 1. Note: GPhC CPD and peer-review revalidation records may be printed out and attached to the training file.

1FACT-JACIE international standards and Accreditation Manual – SEVENTH edition

### Record of Continuing Professional Development

Designated transplant pharmacists must demonstrate continuing education that shall include, but is not limited to, activities related to the field of HPC transplantation and cytokine release syndrome and neurological toxicities resulting from cellular therapies.

\* GPhC CPD records may be printed out and attached to training file

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Activity Title** | **Type** | **Topic/Delivered by** | **Date** | **Number of CPD Hours** | **Impact on Practice** |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

**Signature of designated HSCT pharmacist ………………………………………………....................................…………. Date …………………**

**Signature of [Insert Role]……………. …………………………………………………………………………………………………. Date …………………**

### Record of evidence of the development & implementation of guidelines or SOPs

Pharmacists shall be involved in the development and implementation of guidelines or SOPs related to the pharmaceutical management of cellular therapy recipients

|  |  |  |
| --- | --- | --- |
| **Guideline or SOP Title** | **Impact on Practice** | **Date** |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

**Signature of designated HSCT pharmacist………………………………………………....................................…… …… Date …………………..**

**Signature of [insert role].………………………………………………………………………………………………………………… Date …………………..**

### Record of written publications or teaching and training delivered

|  |  |  |
| --- | --- | --- |
| **Publication / Speaker / Teaching or training** | **Summary** | **Date** |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

**Signature of designated HSCT pharmacist ………………………………………………....................................………… Date …………………..**

**Signature of [insert Role] ………………………………………………………………………………………………………………... Date ………………….**

# APPENDIX 4: Annual accreditation for the designated HSCT Pharmacist

**The designated pharmacist** …………………………………………………………………. (Enter name), has maintained competence to verify HSCT regimens by:

1. completing all reading of updated guidelines and SOPs related to the pharmaceutical management of cellular therapy recipients
2. completing a minimum of 10 hours of continuing professional education within the last year. This includes, but is not limited to, activities related to the field of HPC transplantation and cytokine release syndrome and neurological toxicities resulting from cellular therapies.
3. being involved in the development and implementation of guidelines or SOPs related to the pharmaceutical management of cellular therapy recipients

The designated HSCT pharmacist is accredited to continue verifying the following HSCT regimens (tick, sign and date as appropriate):

Auto-HSCT conditioning prescriptions

**Signature of [insert role]**……………………………………………………………………………..…...Date:……………...

**Responsibility accepted by designated HSCT pharmacist** …………… …………………Date:………………

Allo-HSCT conditioning prescriptions:

* Reduced Intensity/Non-myeloablative
* Myeloablative (Full intensity)
* Haplo-identical

**Signature of [insert role]** ……………………………….………………………...…………………………Date:………………

**Responsibility accepted by designated HSCT pharmacist** …………………………………Date:………………

CAR-T cells therapies prescriptions for the following products:

* Tisagenlecleucel (Kymriah®)
* Axicabtagene cileucel (Yescarta®)
* Advanced Therapy Investigational

Medicinal Products (ATIMPs)

**Signature of [insert role]**………………………….…….……………………………………………….....Date:……………..

**Responsibility accepted by designated HSCT pharmacist**………………………………...Date:……………..

# Appendix 5: Test Your Understanding Questions and Activities)

## PART I: Indications for HSCT

**Question:** What are the most common haematological indications for allogeneic and/or autologous HSCT?

|  |
| --- |
| **Answer** |

**Question:** List other solid tumour and non-malignant disorders for which allogeneic and/or autologous HSCT is indicated.

|  |
| --- |
| **Answer** |

## PART II: Autologous Haematopoietic Stem Cell Transplant (Auto-HSCT)

### Bone marrow harvesting and mobilisation of Haematopoietic Stem Cells

**Question:** What are the strategies to mobilise HSC from the bone marrow to the peripheral blood in auto-HSCT? Discuss the advantages and disadvantages of those strategies.

|  |
| --- |
| **Answer** |

**Question:**  What are the most common harvesting regimens used in auto-HSCT by your centre?

|  |
| --- |
| **Answer** |

**Question:** What is the GCSF dosing schedule when used with chemotherapy and without chemotherapy?

|  |
| --- |
| **Answer** |

**Question:** What is the minimum CD34+ cell harvest yield required to proceed to auto-HSCT transplantation? What are the factors predictive of poor mobilisation?

|  |
| --- |
| **Answer** |

**Question:** Discuss the use of plerixafor for peripheral blood stem cell mobilisation, in relation to: indications, patient eligibility (pre-emptive vs rescue), dosing and dose adjustments, maximum number of doses and funding requirements.

|  |
| --- |
| **Answer** |

**Question**: What are the most commonly employed auto-HSCT conditioning regimes? List the chemotherapy agents, the most common toxicities associated with each agent and the supportive measures used to minimise such toxicities.

|  |
| --- |
| **Answer** |

## PART III: Allogeneic Haematopoietic Stem Cell Transplant (Allo-HSCT)

### Donor selection principles in allo-HSCT

**Question:** List the different types of donor and their considerations in donor selection.

|  |
| --- |
| **Answer** |

**Question:** What are the donor-recipient histocompatibility genes most relevant for transplantation? Discuss permissive and non-permissive mismatches and their implications on transplant outcomes.

|  |
| --- |
| **Answer** |

**Question:** What are the different graft sources for allo-HSCT? Discuss the advantages and disadvantages for the different sources.

|  |
| --- |
| **Answer** |

**Question:** Besides donor-recipient histocompatibility, what are the other donor and recipient characteristics relevant to donor selection and transplant outcomes?

|  |
| --- |
| **Answer** |

**Activity:** Attend HSCT MDT meeting, choose one patient and discuss with the transplant physicians donor selection strategies. You can make notes here.

|  |
| --- |
| **Notes** |

**Question:** What is the GCSF dosing schedule for healthy donors in allo-HSCT? And what is the minimum CD34+ve cells target yield.

|  |
| --- |
| **Answer** |

**Question:** In which situations a BM may be selected as preferred source of HSC to peripheral mobilised blood?

|  |
| --- |
| **Answer** |

### 

### Allo-HSCT conditioning regimes

**Question:** What are the different types of allo-HSCT conditioning regimens used?

|  |
| --- |
| **Answer** |

**Question**: What are the factors taken into consideration when selecting the optimal conditioning regimen for a specific patient?

|  |
| --- |
| **Answer** |

**Question**: What are the chemotherapy agents (or other modalities) commonly employed in allo- conditioning regimens? List the most common toxicities associated with each agent and the supportive measures used to minimise such toxicities.

|  |
| --- |
| **Answer** |

**Question**: List the most commonly employed conditioning regimens for: MSD, MUD, Haplo and cord HSCT in your centre. Note the differences in dosing, schedule (days of administration), doses.

|  |
| --- |
| **Answer** |

### Immunosuppression

**Question:** What is the most commonly employed immunosuppression after MAC, RIC, MUD, and haplo HSCT?

|  |
| --- |
| **Answer** |

**Question:** what is the dosing schedule and dose taper for ciclosporin, methotrexate and mycophenolate in the setting of HSCT conditioning regimes?

|  |
| --- |
| **Answer** |

**Question:** Name the common and the serious side effects associated with both rabbit ATG (Genzyme®) and alemtuzumab administration? How are these managed?

|  |
| --- |
| **Answer** |

**Question:** Discuss infusion administration requirements with rabbit ATG (Genzyme®)?

|  |
| --- |
| **Answer** |

**Question:** How often and on which days should ciclosporin (CSA) levels be measured on inpatients and outpatients?

|  |
| --- |
| **Answer** |

**Question:** What brands of CSA are being used in the trust for oral and IV use? What is the dosing conversion from oral to IV?

|  |
| --- |
| **Answer** |

**Question:** Is the ciclosporin level taken as a trough or peak level? What is the target therapeutic level in HSCT patients?

|  |
| --- |
| **Answer** |

**Question:** List four common side effects patients can experience with CSA. How can ciclosporin-associated side effects be managed?

|  |
| --- |
| **Answer** |

**Question:** List common clinically relevant drug/drug and drug/food interactions interaction with ciclosporin and tacrolimus.

|  |
| --- |
| **Answer** |

**Question**: How often and when should tacrolimus levels be measured for inpatients and outpatients? What is the target trough level for a patient on oral tacrolimus?

|  |
| --- |
| **Answer** |

**Question:** List four common side effects patients can experience with tacrolimus.

|  |
| --- |
| **Answer** |

### 

## Part IV: Prevention and Management of common complications of HSCT

### Prevention and management of acute (aGvHD) and chronic graft versus host disease (cGvHD)

**Question:** List the organs most commonly affected by aGvHD. What is their typical time of onset?

|  |
| --- |
| **Answer** |

**Question**: What is the first line therapy for aGvHD? Discuss the dose, duration and dose/response optimisation.

|  |
| --- |
| **Answer** |

**Question**: What second line treatment options are available in the case of steroid refractory aGvHD?

|  |
| --- |
| **Answer** |

**Question**: List 5 risk factors for patients developing cGvHD.

|  |
| --- |
| **Answer** |

**Question**: List the most commonly affected organs by cGvHD manifestation

|  |
| --- |
| **Answer** |

**Question**: What is the first line treatment strategy in mild and moderate/severe cGvHD?

|  |
| --- |
| **Answer** |

**Question:** what other treatment options are available for unresponsive or steroid-refractory cGvHD?

|  |
| --- |
| **Answer** |

### 

### Management of veno-occlusive disease (VOD)/sinusoidal obstruction syndrome (SOS)

**Question:** List 5 risk factors for the development of VOD post HSCT. What prophylaxis should be administered to patients at risk of VOD?

|  |
| --- |
| **Answer** |

**Question:** How is the diagnosis of VOD made?

|  |
| --- |
| **Answer** |

**Question:** What supportive care measures and drugs are used in the treatment of VOD?

|  |
| --- |
| **Answer** |

### Management of Epstein-Barr (EBV) infections

**Question**: What are the risk factors for EBV disease after allo-HSCT? Discuss the recommendations for prevention of EBV disease after HSCT?

|  |
| --- |
| **Answer** |

**Question**: What are the recommendations for pre-emptive therapy and treatment of EBV disease?

|  |
| --- |
| **Answer** |

### Prevention and treatment of fungal disease

**Question:** List 4 factors that make a patient at high risk of invasive fungal disease.

|  |
| --- |
| **Answer** |

**Question**: What the first line mould active antifungal prophylaxis agent recommended in your trust guideline?

|  |
| --- |
| **Answer** |

**Question**: Discuss the bioavailability and dose equivalence of oral vs intravenous voriconazole. What advice would you give about administration of voriconazole in relation to food?

|  |
| --- |
| **Answer:** |

**Question**: List 4 side effects of voriconazole. Are there any risks associated with long term therapy >6 months.

|  |
| --- |
| **Answer** |

**Question**: What is the therapeutic and safety target level for voriconazole? When should the first and subsequent TDM be performed? What dose adjustments should be made in the case of sub-therapeutic and toxic levels?

|  |
| --- |
| **Answer** |

**Question:** Discuss bioavailability of the posaconazole tablet vs oral solution formulation. What advice would you give about administration of posaconazole in relation to food and other drugs?

|  |
| --- |
| **Answer** |

**Question:** What is the plasma posaconazole target level for prophylaxis and treatment**?** What is the preferred formulation to maximise achieving target level? Is TDM performed routinely?

|  |
| --- |
| **Answer** |

**Question**: Discuss the oral bioavailability of oral itraconazole when given in tablet and liquid formulation. What is the advice in relation to co-administration with food and other medication?

|  |
| --- |
| **Answer** |

**Question**: What is the target itraconazole level for therapeutic effect and safety when used in prophylaxis and treatment of IFD.

|  |
| --- |
| **Answer** |

**Question:** What is the recommended first line antifungal agent in the case of invasive candidiasis and mucormycosis?

|  |
| --- |
| **Answer** |

**Question**: How should liposomal amphotericin B be safely prescribed? List common side effects associated with liposomal amphotericin B therapy and any monitoring required.

|  |
| --- |
| **Answer** |

**Question:** List common drug/drug interactions associated with azoles in HSCT setting

|  |
| --- |
| **Answer** |

### Prophylaxis and treatment of cytomegalovirus (CMV) infection

**Question**: Discuss choice of donor based on cytomegalovirus serological status of recipient.

|  |
| --- |
| **Answer** |

**Question**: Discuss prophylaxis with letermovir including dosing, duration and drug interactions?

|  |
| --- |
| **Answer** |

**Question**: What is the frequency of CMV monitoring post allo-HSCT.

|  |
| --- |
| **Answer** |

**Question**: Discuss the available options for the pre-emptive treatment of CMV disease. What are the common side effects associated with ganciclovir, valganciclovir, foscarnet and cidofovir?

|  |
| --- |
| **Answer** |

### 

### Prevention and management of Pneumocystis Jirovecii Pneumonia (PJP) infections

**Question**: What are the dosing schedule and main side effects of co-trimoxazole and pentamidine for PJP prophylaxis? What routes of administration can pentamidine be administered by for this indication?

|  |
| --- |
| **Answer** |

**Question**: What other second line agents can be used in the prophylaxis of PJP infections?

|  |
| --- |
| **Answer** |

**Question**: Which agent indicated for the prevention and treatment of PJP is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency?

|  |
| --- |
| **Answer** |

## PART V: Chimeric Antigen Receptor T-cell (CAR-T) Therapies

**Question:** What are the currently commissioned CAR-T products? Describe the pathway for patient access to treatment

|  |
| --- |
| **Answer** |

**Question:** Describe the Blueteq applications available for CAR-T products and when they should be completed.

|  |
| --- |
| **Answer** |

**Question:** When should the patient NOT receive CAR-T infusion?

|  |
| --- |
| **Answer** |

**Question:** Explain why steroids should be avoided during lymphodepletion, CAR-T infusion and post-infusion.

|  |
| --- |
| **Answer** |

**Question:** What are the serious medical complications that can arise post CAR-T cell infusion?

|  |
| --- |
| **Answer** |

**Question:** What are the common symptoms of cytokine release syndrome (CRS)?

|  |
| --- |
| **Answer** |

**Question:** Which toxicity is most likely to occur within 24-48 hours post CAR-T infusion?

|  |
| --- |
| **Answer** |

**Question:** How does tocilizumab have an effect on CRS?

|  |
| --- |
| **Answer** |

**Question:** Describe the dose, frequency and duration of tocilizumab for CRS management? How would you ensure tocilizumab was available for a patient due CAR-T cell therapy during and outside of working hours?

|  |
| --- |
| **Answer** |

**Question:** Name two long term toxicities of CAR-T cell therapies

|  |
| --- |
| **Answer** |

The End!