Medication Restrictions for Patients Having CAR T-cell Therapy

Pan-UK Pharmacy Working Group for ATMPs

Brijesh Gautama
Lead Pharmacist ATMPs & Genomic Medicine, University Hospitals Bristol & Weston

Sarah Irwin
Consultant Pharmacist ATMP, Cardiff & Vale, UHB

Version 5, September 2023

The first stop for professional medicines advice

Introduction

The Pan UK Pharmacy Working Group (PWG) for Advanced Therapy Medicinal Products (ATMPs) acts as an expert and informed body to support the activities of UK pharmacies to facilitate ATMP usage. The group consists of pharmacists from across the UK that specialise in the governance, prescribing, administration, and monitoring of ATMPs. The aims of the group are to promote good practice, identify and resolve pharmacy issues to maximise the effectiveness and development of services for hospitals to administer advanced therapies. The Pan UK PWG for ATMPs has a clinical and education subgroup which identified a need for and reviewed consistent clinical advice regarding medicine restrictions for CAR-T patients.

Author Summary

At each stage of the CAR T-cell pathway (apheresis, lymphodepletion, CAR-T infusion and post infusion period), there are numerous restrictions regarding permitted medicines and wash-out periods. This document has been produced to document useful information on these restrictions from CAR T-cell manufacturers, clinical trials, published data and best practice recommendations.

Please consider the source of references provided and the product and disease they are relevant to. They may be from a number of sources, including ongoing trial protocols and occasionally may be contradictory. If the patient is in a trial, please follow the clinical trial protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing, please read guidance in both columns as information may be relevant to both time points.

This document has been updated in May 2023.

For further information/comment, please contact either brijesh.gautama@uhbw.nhs.uk or sarah.irwin@wales.nhs.uk

The Pan UK PWG for ATMPs would like to acknowledge and thank Nia Evans (formerly, Consultant Pharmacist ATMPs & Haematology, Cardiff & Vale, UHB) and Rachel Palmer (Lead Genomics Pharmacist, South West Genomic Medicine Service Alliance) for their valuable work in the production of prior versions of this document and clinical and education subgroup members, Sarah Irwin and Brijesh Gautama for their work in updating the document.

For further information about The Pan UK PWG for ATMPs contact anne.black7@nhs.net

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Leukapheresis	Lymphodepletion	CAR T-cell infusion
Live vaccines	Stop 6 weeks before lymphodepletion [1-4]	Stop 6 weeks before lymphodepletion [1-4]	Avoid until immune recovery post CAR-T [1,2,4]
COVID-19 vaccine	See current BSBMT-CT-VSC, EBMT and ASH-ASTCT COVID-19 vaccine statements due to rapidly changing advice [5-7]	See current BSBMT-CT-VSC, EBMT and ASH-ASTCT COVID-19 vaccine statements due to rapidly changing advice [5-7]	See current BSBMT-CT-VSC, EBMT and ASH-ASTCT COVID-19 vaccine statements due to rapidly changing advice [5-7]
Chemotherapy (including low-dose maintenance therapy and **excluding** those listed below)	Stop 2 weeks [8,9] (or 5 half-lives) [9] before apheresis for tisagenlecleucel, but cytarabine <100mg/m^2 can continue until 7 days prior to apheresis [9] Stop high dose chemotherapy 3-4 weeks prior to apheresis [10]. Recovery from cytopenia is required [10] Stop 2 weeks or 5 half-lives before apheresis (whichever is shorter) for axicabtagene ciloleucel [3] and brexucabtagene autoleucel [12,24]	Stop high dose chemotherapy 3-4 weeks prior to lymphodepletion, to reduce additional toxicity and prolonged cytopenia's [10]. Bridging therapy administered after leukapheresis should have been completed 7 days or 5 half-lives (whichever is shorter) prior to lymphodepletion for brexucabtagene autoleucel [12]	Stop ≥1 week before tisagenlecleucel: 6-mercaptopurine, tioguanine, methotrexate <25 mg/m^2, cytarabine ≤100 mg/m^2 and asparaginase (non-PEGylated) [14,15] they should not be given concomitantly or following lymphodepletion [16] Stop ≥2 weeks before tisagenlecleucel: cytarabine >100 mg/m^2 anthracyclines, cyclophosphamide, and methotrexate ≥25 mg/m^2 [14,15] excluding required lymphodepleting chemotherapy [16]. Stop vincristine 2 weeks before tisagenlecleucel [15]. Stop ≥2 weeks before tisagenlecleucel infusion [8,17]

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Leukapheresis	Lymphodepletion	CAR T-cell infusion
Pegylated asparaginase	Stop 4 weeks before apheresis for tisagenlecleucel [9,11] Stop ≥3 weeks before apheresis for brexucabtagene autoleucel [5]		Stop ≥4 weeks before tisagenlecleucel infusion [11, 14-16]
Short-acting drugs used to treat leukaemia or lymphoma (cytotoxic/ antiproliferative drugs)	Stop short-acting drugs such as hydroxycarbamide 3 days before apheresis for tisagenlecleucel [9]. Recovery from cytopenia's is required [10].	Stop ≥ 3 days prior to lymphodepletion avoid additional toxicity [10]	Stop hydroxyurea ≥3 days (>72hrs) before tisagenlecleucel infusion [8,9,14,15]
Intrathecal (IT) chemotherapy	Stop IT Methotrexate 1 week before apheresis. IT cytarabine may be given up to day prior to apheresis for tisagenlecleucel [9] Stop CNS directed therapy 1 week before apheresis [10]	Stop 1 week prior to lymphodepletion to avoid additional toxicity [10]	Central nervous system prophylaxis must be stopped ≥1 week before tisagenlecleucel and brexucabtagene autoleucel [8,14,24]. Stop intrathecal methotrexate 1 week before tisagenlecleucel [15]
Lymphotoxic therapy Bendamustine Fludarabine Cladribine Pentostatin	Avoid bendamustine & fludarabine for ≥12 weeks prior to apheresis for tisagenlecleucel if possible, (based on patient's condition & disease status), due to potential long term effect on T-cells. Stop cladrabine ≥3 months before apheresis for brexucabtagene autoleucel [24] Washout of 5 half-lives is adequate for drug clearance, but may not apply to the effect on T cells. Note evidence limited in this area [9] Avoid lymphotoxic therapy (e.g. bendamustine, fludarabine, cladribine, pentostatin) prior to apheresis [13]	If bendamustine & rituximab used as bridging therapy, complete ≥ 2 weeks before lymphodepletion for axicabtagene ciloleucel [3] The addition of polatuzumab to bendamustine and rituximab does not change the recommendation for axicabtagene ciloleucel [18] Complete bridging therapy ≥7 days or 5 half lives (whichever is shorter) before lymphodepletion for brexucabtagene autoleucel [24]	

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Leukapheresis	Lymphodepletion	CAR T-cell infusion
Clofarabine	Avoid [11] or stop 8 weeks before apheresis for tisagenlecleucel [9] Stop ≥3 months before apheresis for brexucabtagene autoleucel [24]		Stop ≥2 weeks before tisagenlecleucel infusion [14-16]
Alemtuzumab, ATG	Avoid for ≥6 months before apheresis for tisagenlecleucel and brexucabtagene autoleucel due to potential prolonged effects on T-cells if patient's condition and disease allow [9,24] (previous recommendation was to stop 8 weeks pre-apheresis for tisagenlecleucel [11])	Avoid, may interfere with expansion & persistence of CAR-T [10] Not recommended as bridging therapy due to prolonged half-life and inhibitory effect on T cells [15].	Avoid, may interfere with expansion & persistence of CAR-T [10]
Tyrosine kinase inhibitors (TKI)	Stop imatinib, dasatinib and ponatinib 14 days before apheresis for tisagenlecleucel [9] Stop Nilotinib 5 days before apheresis for tisagenlecleucel [9] Stop TKI's for Philadelphia chromosome positive (Ph+) ≥ 7 days or 5 half-lives (whichever is shorter) before apheresis for brexucabtagene autoleucel [24].	Stop TKIs 3 days prior to lymphodepletion to avoid additional toxicity [10]	Stop TKIs ≥3 days (>72hrs) before tisagenlecleucel infusion [8,14,15] Stop TKIs for Ph+ ALL ≥7 days before brexucabtagene autoleucel infusion [24]
Bruton's tyrosine kinase (BTK) inhibitor (ibrutinib or acalabrutinib)	≥ 2 weeks or 5 half-lives (whichever is shorter) must have elapsed prior to apheresis for brexucabtagene autoleucel [12,24]	Administer after leukapheresis and complete ≥ 5 days prior to initiating lymphodepletion for brexucabtagene autoleucel [12]	
Idelalisib (PI3K inhibitor)	Washout of 5 half-lives is adequate pre-apheresis for tisagenlecleucel. Note limited data [9]		

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Leukapheresis	Lymphodepletion	CAR T-cell infusion
Ruxolitinib (JAK1/2 inhibitor)	Limited data. Washout of 5 half-lives adequate for drug clearance, but if patient's condition & disease status allow, avoid use for ≥14 days prior to apheresis for tisagenlecleucel [9]		
Venetoclax (BCL2 inhibitor)	Washout of 5 half-lives is adequate drug clearance prior to apheresis for tisagenlecleucel. Limited data [9]		
Immunomodulatory drugs (general rule also see specific sections below)	Stop 2 weeks before apheresis for tisagenlecleucel [11] Stop any prior systemic therapy ≥ 2 weeks or 5 half-lives, whichever is shorter, before apheresis for axicabtagene ciloleucel [3] and brexucabtagene autoleucel [12]		

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Leukapheresis	Lymphodepletion	CAR T-cell infusion
Checkpoint inhibitors	Stop inhibitory/stimulatory immune checkpoint molecule therapy (e.g. ipilimumab, nivolumab, pembrolizumab, atezolizumab, OX40 agonists, 4-1BB agonists) ≥ 2 weeks or 3 half lives, whatever is shorter for axicabtagene ciloleucel [3] and ≥3 half-lives before brexucabtagene autoleucel [12,24] Pembrolizumab and durvalumab: No washout is required prior to apheresis for tisagenlecleucel. Half-life is too long to wait for 5 half-lives of washout in most patients. Note limited data [9]		Stop checkpoint inhibitors ≥2 weeks before tisagenlecleucel [15,17]. Longer wash out required for pegylated agents based on pharmacokinetics of each agent [15]
Lenalidomide	Stop 7 days pre-apheresis for tisagenlecleucel [9]	Based on pre-clinical data, stop one week prior to lymphodepletion for diffuse large B cell lymphoma indications, to allow count recovery [13]	Stop 3 days (>72hrs) before tisagenlecleucel infusion [15]

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Leukapheresis	Lymphodepletion	CAR T-cell infusion
Polatuzumab	When used as per licensed indication, in combination with bendamustine and rituximab, the washout for bendamustine must take priority pre-apheresis for tisagenlecleucel (see lymphotoxic therapy section) [9] Washout of 5 half-lives is not required prior to apheresis for tisagenlecleucel if polatuzumab **used as single agent** and patient's condition and disease status do not allow. Adequate absolute lymphoctyte count (ALC) and/or CD3+ count in peripheral blood (PB) required. Note limited data [9]	If bendamustine & rituximab used as bridging therapy, complete ≥ 2 weeks before lymphodepletion for axicabtagene ciloleucel [3] The addition of polatuzumab to bendamustine & rituximab does not change the recommendation for axicabtagene ciloleucel [18]	

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Apheresis	Lymphodepletion	CAR-T infusion
Immunomodulatory drugs Anti-CD20 therapy	Rituximab, obinutuzumab, ofatumumab: Elimination half-life is long and limited data available. Washout of 5 half lives pre-apheresis is not required if patient's condition and disease status do not allow (information applies to tisagenlecleucel) [9]	If bendamustine & rituximab used as bridging therapy complete ≥ 2 weeks before lymphodepletion for axicabtagene ciloleucel [3] If methylprednisolone & rituximab used as bridging therapy complete ≥ 1 week before lymphodepletion for axicabtagene ciloleucel [3]	Stop antibodies including anti-CD20 therapy e.g. rituximab 4 weeks (or 5 half-lives whichever is greater) - 4 weeks for rituximab before tisagenlecleucel infusion [15,17]
Anti-CD19 therapy	There is limited experience with axicabtagene ciloleucel & tisagenlecleucel in patients exposed to prior CD19-directed therapy [1,2]. Axicabtagene ciloleucel, tisagenlecleucel and brexucabtagene autoleucel are not recommended if the patient has relapsed with CD19-negative disease after prior anti-CD19 therapy [1,2,4] Stop blinatumomab 1-2 weeks before apheresis for tisagenlecleucel and brexucabtagene autoleucel despite short half life [9,24]	Blinatumomab (and other CD19-targeting agents) not recommended as bridging therapy due to potential risk of CD19 antigen escape [11,15]	
Inotuzumab	Note limited data. Half-life too long to wait for 5 half-lives in most patients - washout not required pre-apheresis for tisagenlecleucel if patient's condition does not allow [9]. Adequate lymphocyte and/or CD3+ count prior to apheresis is recommended to avoid failure of T-cell collection [9]		Stop inotuzumab 4 weeks before infusion to allow B-cell/CD-19 antigen recovery for tisagenlecleucel [15]

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Apheresis	Lymphodepletion	CAR-T infusion
Radiation therapy (see separate sections on CNS directed and palliative radiation)	Stop ≥2 weeks or 5 half-lives prior to apheresis (whichever is shorter) for brexucabtagene autoleucel [12,24] For tisagenlecleucel, proceed with apheresis if adequate lymphocyte and/or CD3+ count as no washout for radiotherapy [9] Stop radiation to target index lesion or non-CNS site, 2 weeks before apheresis for axicabtagene ciloleucel [3]	Radiation must be completed > 2 weeks before CAR-T infusion for tisagenlecleucel [16]. Stop ≥ 1 week (2 weeks for lung sites) prior to lymphodepletion to reduce additional toxicity [10] Can be continued until day prior to lymphodepletion provided no cytopenia (expert panel opinion in relation to diffuse large B cell lymphoma indication) [13]	Radiation must be completed > 2 weeks before CAR-T infusion for tisagenlecleucel [8,15,16]
CNS directed radiation	Stop 8 weeks before apheresis for tisagenlecleucel [11]		Completed >8 weeks before CAR-T infusion for tisagenlecleucel [11,15,16]
Palliative radiation to non-target lesion	Allowed up to day of apheresis for axicabtagene ciloleucel [3]	Allowed at discretion of CAR-T consultant for axicabtagene ciloleucel [3] Can be continued until day prior to lymphodepletion provided no cytopenia [13]	Allowed at discretion of CAR-T consultant for axicabtagene ciloleucel [3] Radiation must be completed > 2 weeks before CAR-T infusion for tisagenlecleucel [8,15,16]

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Apheresis	Lymphodepletion	CAR-T infusion
Allogeneic cell therapy: Stem cell transplant	≥12 weeks before apheresis for tisagenlecleucel [2,9,11]. However, note washout periods for ATG and alemtuzumab. Advised that patients should be off immunosuppression & GvHD free for a minimum of 1 month [10] Not a contraindication, but may be associated with increased risk of CAR-T toxicity in ALL patients [10]		A gap of ≥ 4 months is required between allogeneic stem cell transplant and tisagenlecleucel infusion because potential risk of worsening GvHD [2]
Donor lymphocyte infusions (DLI)	Stop ≥4 weeks before apheresis, [9-11,24] 6-8 weeks may be safer to rule out GvHD [10]		DLI must be completed >6 weeks before tisagenlecleucel [14,16]
Graft-vs-host disease (GvHD) therapies (e.g. calcineurin inhibitors)	Stop 2 weeks before apheresis for tisagenlecleucel [9,11] Any systemic drug used to prevent or treat grade 2-4 acute GvHD or extensive chronic GvHD (e.g. calcineurin inhibitors, methotrexate or other chemotherapy drugs, mycophenolate, rapamycin, thalidomide, or immunosuppressive antibodies, such as antitumor necrosis factor α, anti–interleukin6, or anti–interleukin-6 receptor) should be stopped ≥2 weeks before apheresis for tisagenlecleucel and ≥4 weeks for brexucabtagene autoleucel [12]. If grade 2-4 acute GvHD or extensive chronic GvHD develops after leukapheresis collection, the leukapheresis material cannot be used [9]		Stop > 4 weeks before tisagenlecleucel to confirm that GvHD recurrence is not observed e.g. calcineurin inhibitors, methotrexate, or other chemotherapy, mycophenolate mofetil, rapamycin, thalidomide, immunosuppressive antibodies (e.g. anti-CD20 [rituximab], anti-TNF, anti-IL6, or anti-IL6R), systemic steroids for GvHD [15,16] T-cell directed systemic GvHD therapy administered after CAR-T infusion will likely terminate CAR-T therapeutic effect [11]

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Apheresis	Lymphodepletion	CAR-T infusion
Corticosteroid therapy at a pharmacologic dose ≥5 mg/day of prednisone or equivalent doses of other corticosteroids for axicabtagene ciloleucel [3] or brexucabtagene autoleucel [12] >40mg/day hydrocortisone or equivalent in adult patients or >12mg/m^2/day of hydrocortisone or equivalent in paediatric patients for tisagenlecleucel [9]	Stop 7 days prior to apheresis for tisagenlecleucel [9] axicabtagene ciloleucel [3] and brexucabtagene autoleucel [12,24] Ideally stop 7 days (minimum 2-3 days) prior to minimise effect on lymphocyte collection [10,11,13] An absolute lymphocyte count (ALC) ≥0.2x10^9 /L is preferable [10]	See **immunomodulatory drugs** section above if methylprednisolone is used as part of bridging therapy combination. If dexamethasone used as bridging therapy it must be completed ≥ 5 days before start of axicabtagene ciloleucel [3]. If corticosteroid used as bridging therapy it must be administered after leukapheresis and completed ≥ 5 days prior to initiating lymphodepletion for brexucabtagene autoleucel [12] Corticosteroid bridging may be continued until day prior to lymphodepletion (expert panel opinion in diffuse large B cell lymphoma indications) [13]	Prophylactic use of steroids is not recommended e.g. for pre-medication [1,2,10] . They should be avoided prior to or around time of infusion except in case of life-threatening emergency [2,10] or for management of CAR-T adverse reactions [19]. In ZUMA-1 study, steroids were avoided, unless for management of CAR-T adverse effects, until 3 months after axicabtagene ciloleucel administration, unless no reasonable alternatives existed [20] Stop 5-7 days before axicabtagene ciloleucel [3] and brexucabtagene autoleucel (unless used as bridging where it must be stopped 5 days before starting lymphodepletion for brexucabtagene autoleucel) [12,24] Stop therapeutic dose steroids 3 days (>72hrs) prior to tisagenlecleucel infusion [8,15,16]
Topical or inhaled steroids	Topical or inhaled steroids for localised treatment of GvHD permitted for tisagenlecleucel [9] Intermittent topical inhaled or intranasal corticosteroids are allowed [10]		

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Drug	Apheresis	Lymphodepletion	CAR-T infusion
Immunosuppressive therapy	Stop 1 week before apheresis for axicabtagene ciloleucel and brexucabtagene autoleucel [3,12] Stop 2 weeks before apheresis for tisagenlecleucel [8] Allow wash out of 4-5 half lives pre-apheresis if possible [13]		Any systemic immunosuppressant may impair CAR-T efficacy [10] Stop ≥2 weeks before for tisagenlecleucel [8] ≥5 days prior to brexucabtagene autoleucel administration [12,24]
Growth factors: Long-acting growth factors (e.g. pegfilgrastim)	Stop 14 days before apheresis for tisagenlecleucel [9,11]		Stop 10 days before infusion for tisagenlecleucel [15]
Short-acting growth factors (e.g. granulocyte colony-stimulating factor/filgrastim)	Stop 5 days before the apheresis for tisagenlecleucel [9,11]		Stop short acting growth factors 3 days (>72hrs) before infusion and avoid GM-CSF for tisagenlecleucel [15]. Avoid for 3 weeks or until CRS resolved as may worsen CRS for tisagenlecleucel [2] Stop short acting growth factors ≥7 days before infusion for brexucabtagene autoleucel [24] G-CSF from 2 weeks post infusion may be considered to reduce neutropenia but avoid if patient has CRS or ICANS [10]. Conflicting evidence regarding earlier use in small retrospective studies [21,22]
Alternative medications e.g. herbal medicines	Stop as long as possible before (≥ 5 half-lives if that information is available or 2 weeks[23]). Not enough information available for interaction check and safety to be assured. Effect on cell collection cannot be ruled out.	Stop as long as possible before (≥ 5 half-lives if that information is available or 2 weeks[23]). Not enough information available for interaction check and safety to be assured.	Stop as long as possible before (≥ 5 half-lives if that information is available or 2 weeks [23]). Not enough information available for interaction check and safety to be assured. Effect on CAR-T treatment cannot be ruled out.

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

Medications not listed in the table	Stop any prior systemic therapy ≥ 2 weeks or 5 half-lives, whichever is shorter, before apheresis for axicabtagene ciloleucel [3] and brexucabtagene autoleucel [12] Consider pharmacokinetics (including half-life) and pharmacodynamics of the drug, impact of the drug on T-cells and/or CD19 and potential for lymphopenia [9]. Washout of 5 half-lives is adequate for drug clearance, but effects of some drugs on T cells may persist after drug clearance [9]	Consider pharmacokinetics (including half-life) and pharmacodynamics of the drug, impact of the drug on T-cells and/or CD19 and potential for lymphopenia [9]. Washout of 5 half-lives is adequate for drug clearance, but effects of some drugs on T-cells may persist after drug clearance [9]	Consider pharmacokinetics (including half-life) and pharmacodynamics of the drug, impact of the drug on T-cells and/or CD19 and potential for lymphopenia [9]. Washout of 5 half-lives is adequate for drug clearance, but effects of some drugs on T cells may persist after drug clearance [9] The co-administration of agents known to stimulate T-cell function has not been investigated and the effects are unknown [2]

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.

References

1. Yescarta summary of product characteristics. Dec 2022. Accessed via https://www.medicines.org.uk/emc/product/9439 on 12 May 2023.
2. Kymriah summary of product characteristics. August 2022. Accessed via https://www.medicines.org.uk/emc/product/9456 on 12 May 2023.
3. Data on file, Kite Pharma. Yescarta cessation of prior therapies document approved. 15 Nov 2022
4. Tecartus summary of product characteristics. Feb 2023. Accessed via https://www.medicines.org.uk/emc/product/11987 on 12 May 2023
5. EBMT COVID-19 vaccine information: COVID-19 vaccines. Version 8. 03 Jan 2022. Accessed via https://www.ebmt.org/sites/default/files/2022-01/COVID%20vaccines%20version%208.3%20-%202022-01-03.pdf on 15 Mar 2022.
6. ASH-ASTCT COVID-19 vaccination for HCT and CAR T cell recipients: FAQ (v5.0; updated Mar 22, 2022). Accessed via https://www.hematology.org/covid-19/ash-astct-covid-19-vaccination-for-hct-and-car-t-cell-recipients on 15 Mar 2022.
7. SARS-CoV-2 vaccination following haematopoietic stem cell transplant (HSCT) and chimeric antigen receptor T-cell (CAR-T) therapy. British Society of Blood and Marrow Transplantation and Cellular Therapy Vaccination Sub-Committee (BSBMTCT-VSC); updated 31 Oct 2022. Accessed https://bsbmtct.org/wp-content/uploads/2021/11/BSBMTCT-SARS-CoV-2-vaccination-statement_30Nov2021_FINAL.pdf on 07 Jul 2023.
8. Supplementary appendix to: Schuster SJ., Bishop MR., Tam CS., et al. Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma. N Engl J Med 2019; 380: 45-56.
9. Novartis leukapheresis reference manual CAR-T version G3. May 2022. Published by Novartis, Novartis Technical Operations.
10. Hayden PJ., Roddie C., Bader P., Basak GW., Bonig H., Bonini C., et al. Management of adults and children receiving CAR T-cell therapy: 2021 best practice recommendations of the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE) and the European Haematology Association (EHA). Ann Oncol. 2022; 33(3): 259-275.
11. Kansagra AJ., Frey NV., Bar M., Laetsch TW., Carpenter PA., Savani BN., et al. Clinical utilization of Chimeric Antigen Receptor T-cells (CAR-T) in B-cell acute lymphoblastic leukemia (ALL)-an expert opinion from the European Society for Blood and Marrow Transplantation (EBMT) and the American Society for Blood and Marrow Transplantation (ASBMT). Bone Marrow Transplant. 2019; 54(11): 1868-80.
12. Tecartus cessation of prior therapies for adult B-ALL. 5 Oct 2022. Kite Pharma, Gilead Sciences Inc.

13. Jain T., Bar M., Kansagra AJ., Chong EA., Hashmi SK., Neelapu SS., et al. Use of chimeric antigen receptor T cell therapy in clinical practice for relapsed/refractory aggressive B cell non-Hodgkin lymphoma: an expert panel opinion from the American Society for Transplantation and Cellular Therapy. Biol Blood Marrow Transplant. 2019; 25(12): 2305-21.
14. Mahadeo KM., Khazal SJ., Abdel-Azim H., Fitzgerald JC., Taraseviciute A., Bollard CM., et al. Expert consensus document management guidelines for paediatric patients receiving chimeric antigen receptor T cell therapy. Nat Rev Clin Oncol. 2019; 16:45-63.
15. Bridging therapy: recommended washout time prior to tisagenlecleucel infusion. Novartis slide received Jan 2021.
16. Information regarding ELIANA trial received from Novartis Pharmaceuticals UK on 6 Nov 2019.
17. Information regarding JULIET trial received from Novartis Pharmaceuticals UK on 6 Nov 2019.
18. Personal communication with Matt Yates, Kite Pharma on 2 Mar 2021.
19. Kymriah healthcare professional training material ONC20-C076. Aug 2020. Accessed via https://www.medicines.org.uk/emc/rmm/1287/Document on 15 Mar 2022.
20. Personal communication with Alison Levoguer, Kite Pharma on 4 Nov 2019.
21. Gaut D., Tang K., Shin Sim M., Duong T., Young P., Sasine J., et al. Filgrastim associations with CAR T-cell therapy. Int J Cancer. 2021; 148(5): 1192-96. Available from: https://onlinelibrary.wiley.com/doi/10.1002/ijc.33356
22. Galli E., Allain V., Di Blasi R., Bernard S., Vercellino L., Morin F., et al. G-CSF does not worsen toxicities and efficacy of CAR-T cells in refractory/relapsed B-cell lymphoma. Bone Marrow Transplant. 2020; 55(12), 2347–49. https://www.nature.com/articles/s41409-020-01006-x#
23. Hodges PJ. and Kam PCA.. The peri-operative implications of herbal medicines. Anaesthesia. 2002; 57(9): 889-899. Available from: https://associationofanaesthetists-publications.onlinelibrary.wiley.com/doi/full/10.1046/j.1365-2044.2002.02781.x?
24. Tecartus (brexucabtagene autoleucel; KTE-X19) cessation of prior therapies in ZUMA-2 study 5. Oct 2022. Kite Pharma, Gilead Sciences Inc.

Medication Restrictions for Patients Having CAR-T Therapy

Please consider source of references provided & product/disease indication they are relevant to. They may be from a number of sources, including ongoing clinical trial protocols and occasionally may be contradictory. If the patient is in a clinical trial please follow the protocol rather than this document. Please consult the original references, the CAR-T manufacturer and the patient's medical consultant, the authors will take no liability for decisions taken. The information is for guidance only and the patient's condition and disease status need to be considered also. As lymphodepletion and CAR-T infusion are close in terms of timing please read guidance in both columns as information may be relevant to both time points.