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| **National CAR T Clinical Panel for lymphoma Application Form:** **SECOND LINE THERAPY** **Axicabtagene ciloleucel for treating relapsed/refractory diffuse large B-cell lymphoma (DLBCL) or high grade B-cell lymphoma and either in patients who relapse within 12 months of completion of 1st line chemoimmunotherapy AND who would otherwise be intended for potential stem cell transplantation or who are refractory to 1st line chemoimmunotherapy AND who would otherwise be intended for potential stem cell transplantation** Forms must be submitted to england.nccp@nhs.net by 5pm each Friday for consideration at the NCCP lymphoma on the following Tuesday |
| **SECTION A - to completed by current treating Clinician and updated as appropriate by CAR T Cell Clinician****Patient Details** |
| Name |  |
| NHS No |  |
| Age |  |
| **Clinical background** |
| Referral details | Consultant name:Hospital:Date of referral for consideration of CAR T: |
| 1. Confirmed histological diagnosis
 | *Delete as appropriate.** Diffuse large B-cell lymphoma (DLBCL) NOS (including ABC and GCB types) **or**
* High grade B-cell lymphoma (HGBCL) with or without MYC and BCL2 (double hit) and BCL6 (triple hit) re-arrangements **or**
* Transformed follicular lymphoma (TFL) to DLBCL **or**
* T cell/histiocyte-rich large B-cell lymphoma **or**
* Primary cutaneous DLBCL of leg type **or**
* HHV8 positive DLBCL
* DLBCL associated with chronic inflammation **or**
* EB virus positive DLBCL

Note: Patients with Burkitt lymphoma or primary mediastinal B cell lymphoma or primary CNS lymphoma or Richter’s transformation to DLBCL are not eligible for treatment with axicabtagene ciloleucel in this indication. |
| 1. Overview of the patient’s treatment
 | *Please include :** *The exact start date of First line therapy (DDMMMYYYY)*
* *The number of cycles given*
* *Specify any dose modifications applied*
* *The exact date of the START of the last cycle of first line therapy given. (DDMMMYYYY )*

*Note:** *To be eligible Patients must be assessed as fit for an Autologous Stem cell Transplant and have received an approved FULL DOSE Front line regimen*
* *Radiotherapy is not counted as a line of treatment*

*HOLDING therapy is permitted but for a maximum of 2 cycles, if this is exceeded then a disease re assessment should be made and a third line application considered****Please provide a narrative of the patient’s treatment to date:***

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| Treatment regimen  | Start date | Stop date | Number of cycles | Response to treatment |
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*If current treatment is ongoing write ‘ongoing’ under ‘response to treatment’* |
| 1. The histological diagnosis has been either made by or reviewed and confirmed by a designated lymphoma stem cell transplant centre.
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| Biopsy number | Date performed | Conclusion from report |
| 1st |  |  |
| 2nd |  |  |
| 3rd |  |  |
| Most recent (if not one of above) |  |  |

I confirm that prior to consideration of CAR-T cell therapy the patient’s disease has been re-biopsied unless **either** the patient had outright progressive disease on standard 1st line chemo-immunotherapy **or** a biopsy is unsafe in which case the patient must have progressive disease at previously known sites of active disease. In such situations the original diagnostic biopsy review is acceptable. All patients with transformed follicular lymphoma to DLBCL who fulfil criteria 6 below must have a re-biopsy and have confirmation of DLBCL histology prior to consideration of CAR-T cell therapy.Please delete as appropriate:* no biopsy necessary as the patient had outright progressive disease during 1st line chemo-immunotherapy **or**
* re-biopsy has confirmed DLBCL or HGBCL **or**
* re-biopsy has confirmed transformed follicular lymphoma to DLBCL **or**
* re-biopsy is unsafe for the patient and the patient has progressive disease at previously known sites of active disease and the previous histology was DLBCL or HGBCL
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| 1. I confirm that the patient fulfils one of the following clinical scenarios relating to the definition of relapsed or refractory lymphoma
 | Refractory disease is definedas progressive disease as the best response to 1st line standard chemo-immunotherapy after at least 2 cycles of chemo-immunotherapy **or** stable disease as the best response after at least 4 cycles of 1st line standard chemo-immunotherapy **o**r a partial response as the best response after at least 6 cycles of 1st line standard chemo-immunotherapy with biopsy-proven residual disease **or** a partial response with biopsy-proven progressive disease within 12 months or less from completion of treatment.Relapsed disease is defined as disease that was in complete remission following 1st line standard chemo-immunotherapy and has been followed by a biopsy-proven disease relapse within 12 months or less from completion of treatment.Progressive disease should be defined radiologically as per RECIST version 1.1 and be based on CT or MR scans and aided if necessary, after discussion at the National CAR T Clinical Panel, with the use of Lugano lymphoma response criteria.Delete as appropriate: * progressive disease after at least 2 cycles of chemo-immunotherapy as the best response to 1st line standard chemo-immunotherapy OR
* stable disease as the best response after at least 4 cycles of 1st line standard chemo-immunotherapy with biopsy-proven residual disease OR
* a partial response as the best response after at least 6 cycles of 1st line standard chemo-immunotherapy with biopsy-proven residual disease OR
* a partial response to 1st line standard chemo-immunotherapy with biopsy-proven progressive disease within 12 months or less from completion of treatment OR
* a complete response to 1st line standard chemo-immunotherapy with biopsy-proven disease relapse within 12 months or less from completion of treatment.
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| 1. I confirm that that the patient has been previously treated with a full dose anthracycline-containing regimen for his/her lymphoma
 | I confirm that the patient has been previously treated with a full dose 1st line anthracycline-containing standard regimen for his/her lymphoma or with the Marietta protocol if presenting with CNS involvement.Note: acceptable anthracycline-containing regimens include R-CHOP, Pola-R-CHP, R-CODOX-M/R-IVAC, DA-EPOC-R and the Marietta protocol |
| 1. I confirm that the patient has been previously treated with at least one anti-CD20 monoclonal antibody unless there is clear documentation of the determination of CD20 negative disease
 | I confirm that on the date that the patient was confirmed as having refractory or relapsed disease according to the above definitions, the patient had only received 1st line of therapy for the DLBCL or HGBCL or TFL to DLBCL.*Note: it is recognised that some patients at the time of the demonstration of refractory or relapsed disease have very rapidly progressive disease and thus have to commence urgent 2nd line treatment. It is therefore acceptable for patients to have received a maximum of 2 cycles of standard 2nd line chemotherapy regimens with one of the following regimens as holding therapy: R-GDP, R-GemCarbo, R-ESHAP, R-ICE, R-IVE, R-BendaPola and the Marietta protocol.*Please enter below whether the rate of disease progression as outlined above required urgent 2nd line salvage chemotherapy (Holding therapy) in this patient:* no urgent chemotherapy required prior to this application **or**
* a maximum of 2 cycles of one of the above standard salvage chemotherapy regimens have been given prior to this application on grounds of urgent need and all other treatment criteria on this form are fulfilled
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| 1. Eligible for Second Line CAR T cell therapy as per ZUMA 7 Trial criteria – both by prior treatment received and eligibility for ASCT.
 | I confirm that in the absence of the availability of axicabtagene ciloeucel for this 2nd line indication the patient would have been fit and intended for **both** standard 2nd line salvage chemotherapy (see note below) **and potential stem cell transplantation**.Note: Second line treatment regimens which are appropriate include: R-GDP, R-GemCarbo, R-ESHAP, R-ICE, R-IVE, R-BendaPola and the Marietta protocol. |
| 1. I confirm that the patient has either had no previous therapy with any genetically modified autologous or allogeneic T cell immunotherapy or the patient has been treated with doses of genetically modified autologous or allogeneic T cell immunotherapy within an abandoned dosing cohort in a first in human dose-escalation phase I clinical trial.
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| 1. I confirm that the patient has not previously been treated with an anti-CD19 antibody-drug conjugate or if previously treated with an anti-CD19 antibody-drug conjugate (that a biopsy of the relapsed/refractory disease has been done and has been shown to be CD19 positive
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| 1. I confirm that the patient does not have primary CNS lymphoma
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| 1. I confirm that the patient does not have known active CNS involvement by the lymphoma
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| 1. I confirm that the patient has an ECOG performance score of 0 or 1
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| **Grade** | **ECOG performance status** |  |
| 0 | Fully active, able to carry on all pre-disease performance without restriction |  |
| 1 | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work |  |
| 2 | Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours |  |
| 3 | Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours |  |
| 4 | Completely disabled; cannot carry on any selfcare; totally confined to bed or chair |  |

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| 1. Please provide details of any active co-morbidities
 | Please list all active co-morbidities

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| *Active co-morbidity* | *Severity score (see score under table)* |
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*1: Current mild problem or past significant problem. 2: Moderate disability or morbidity and/or requires therapy. 3: Severe problem and/or constant and significant disability and/or hard to control chronic problems. 4: Extremely severe problem and/or immediate treatment required and/or organ failure and/or severe functional impairment.* |
| **Allogeneic centre review (if applicable)** |
| 1. I confirm that the patient would have been eligible for ASCT and has sufficient end organ function to tolerate treatment with CAR T cell therapy
 | *Please specify** Patient is clearly eligible and has been forwarded to a CAR T centre for consideration without review.
* Patient reviewed and deemed eligible by autograft centre clinician. Eligibility required confirmation by CAR T centre
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| 1. I confirm that this patient should be referred to a CAR T centre for consideration for CAR T Therapy
 | Name:Signature:Hospital:Date: |
| **SECTION B****Details of consultation at CAR T Centre** |
| Referral Details | Consultant name:CAR T Centre:Date: |
| 1. The histological diagnosis, as stated in FIELD 1 has been either made by or reviewed and confirmed by a designated lymphoma stem cell transplant centre.
 | I confirm that prior to consideration of CAR-T cell therapy the patient’s disease has been re-biopsied unless **either** the patient had outright progressive disease on standard 1st line chemo-immunotherapy **or** a biopsy is unsafe in which case the patient must have progressive disease at previously known sites of active disease. In such situations the original diagnostic biopsy review is acceptable. All patients with transformed follicular lymphoma to DLBCL must have a re-biopsy and have confirmation of DLBCL histology prior to consideration of CAR-T cell therapy.Please enter appropriately below as to which scenario applies to this patient:* no biopsy necessary as the patient had outright progressive disease during 1st line chemo-immunotherapy **or**
* re-biopsy has confirmed DLBCL or HGBCL **or**
* re-biopsy has confirmed transformed follicular lymphoma to DLBCL **or**
* re-biopsy is unsafe for the patient and the patient has progressive disease at previously known sites of active disease and the previous histology was DLBCL or HGBCL
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| 1. I confirm that the patient has an ECOG performance score of 0 or 1
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| **Grade** | **ECOG performance status** |  |
| 0 | Fully active, able to carry on all pre-disease performance without restriction |  |
| 1 | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work |  |
| 2 | Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours |  |
| 3 | Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours |  |
| 4 | Completely disabled; cannot carry on any selfcare; totally confined to bed or chair |  |

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| 1. Prior to infusion 4 doses of tocilizumab are available for use in this patient in the event of the development of cytokine release syndrome
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| **Available clinical trials** |
| 1. List the clinical trials available to this patient
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| **CAR T Centre endorsement** |
| I confirm that I endorse this application for treatment | Name:Position: |