

# Tisagenlecleucel (Kymriah®) (CAR-T) DLBCL and FL

## **INDICATIONS FOR USE:**

| INDICATION   | ICD10 | Regimen<br>Code | HSE approved<br>reimbursement<br>status* |
|--|-------|-----------------|--|
| Treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. | C83   | 00687a          | ODMS<br>01/07/2021                       |
| Treatment of adult patients with relapsed or refractory follicular lymphoma  | C82   | 00687b          | ODMS                                     |
| (FL) after two or more lines of systemic therapy.  |       |                 | 01/07/2025                               |

\* This is for post 2012 indications only.

#### TREATMENT:

Tisagenlecleucel (Kymriah®) must be administered in an NCCP designated CAR-T centre.

Tisagenlecleucel (Kymriah<sup>®</sup>) is intended for autologous use only.

Facilities to treat anaphylaxis MUST be present when lymphodepleting therapy and CAR-T cells are administered.

#### Pre-treatment conditioning:

- Lymphodepleting chemotherapy is recommended to be administered before tisagenlecleucel infusion unless the white blood cell (WBC) count within one week prior to infusion is ≤1x10<sup>9</sup>/L)
- Lymphodepleting chemotherapy may be omitted if a patient's white blood cell (WBC) count is  $\leq 1 \times 10^9$ /L within 1 week prior to tisagenlecleucel infusion
- Please refer to the relevant lymphodepletion regimen as decided by the treating clinician at the designated CAR-T centre

#### Tisagenlecleucel Administration:

- Please refer to the local CAR-T policy for tisagenlecleucel (Kymriah®) administration information
- DLBCL indication:
  - Tisagenlecleucel is recommended to be infused **2 to 14 days** after completion of the lymphodepleting chemotherapy as per table 1 below.
- FL indication:
  - Tisagenlecleucel is recommended to be infused **2 to 6 days** after completion of the lymphodepleting chemotherapy as per table 2 below.
- The total dose is contained in 1 or more infusion bags
- If there is a delay of more than 4 weeks between completing lymphodepleting chemotherapy and the tisagenlecleucel (Kymriah<sup>®</sup>) infusion and the WBC count is >1x10<sup>9</sup>/L, then the

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| Tumour Group: Lymphoma and Other Lymphoproliferative<br>DisordersIHS Contributor:<br>Dr Larry BaconPage 1 of 7NCCP Regimen Code: 00687Dr Larry BaconPage 1 of 7  |  |  |  |  |
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patient should be re-treated with lymphodepleting chemotherapy prior to receiving tisagenlecleucel

• Tocilizumab for use in the event of cytokine release syndrome and emergency equipment must be available for each patient prior to infusion. The treatment centre must have access to additional doses of tocilizumab within 8 hours

#### Table 1: Tisagenlecleucel Administration in DLBCL

| Day  | Treatment                     | Dose   | Route |  |  |
|--|-------------------------------|--|-------|--|--|
| Infuse 2 to 14 days after<br>completion of the<br>lymphodepleting<br>chemotherapyTisagenlecleucel<br>(Kymriah®)0.6 to 6 x 108 CAR-positive viable T cells<br>(non-weight based)IV infusion1  |                               |  |       |  |  |
| <sup>1</sup> Through latex-free intravenous t  | ubing without a leukocyte dep | leting filter, at approximately 10 to 20 mL per minute by gravity  | flow. |  |  |
| 51   | ,                             | solution for injection should be used to prime the tubing prior t<br>has been infused, the infusion bag should be rinsed with 10-30r |       |  |  |
| for injection by back priming to ensure as many cells as possible are infused into the patient.  |                               |  |       |  |  |
| The product should be administered immediately after thawing. After thawing, the product should be kept at room temperature (20°C-25°C) and infused within 30 minutes to maintain maximum product viability, including any interruption during the infusion. |                               |  |       |  |  |

#### **Table 2: Tisagenlecleucel Administration in FL**

| Day   | Treatment                      | Dose   | Route                    |
|---|--------------------------------|--|--------------------------|
| Infuse <b>2 to 6</b> days <u>after</u><br>completion of the<br>lymphodepleting<br>chemotherapy  | Tisagenlecleucel<br>(Kymriah®) | 0.6 to 6 x 10 <sup>8</sup> CAR-positive viable T cells<br>(non-weight based) | IV infusion <sup>1</sup> |
| <sup>1</sup> Through latex-free intravenous tubing without a leukocyte depleting filter, at approximately 10 to 20 mL per minute by gravity flow. |                                |  |                          |

All contents of the infusion bag(s) should be infused. NaCl 0.9% solution for injection should be used to prime the tubing prior to infusion and to rinse it after infusion. When the full volume of tisagenlecleucel has been infused, the infusion bag should be rinsed with 10-30mL NaCl 0.9% solution

for injection by back priming to ensure as many cells as possible are infused into the patient.

The product should be administered immediately after thawing. After thawing, the product should be kept at room temperature (20°C-25°C) and infused within 30 minutes to maintain maximum product viability, including any interruption during the infusion.

### **ELIGIBILITY:**

- Indications as above
- Medical assessment as per local CAR-T assessment

### EXCLUSIONS:

- Known or suspected hypersensitivity to tisagenlecleucel or the excipients
- Known or suspected hypersensitivity to fludarabine or cycloPHOSphamide or the excipients
- Contraindications of the lymphodepleting chemotherapy must be considered
- Pregnancy or lactation

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## **CAUTION IN USE:**

- Due to the risks associated with tisagenlecleucel treatment, infusion should be delayed if a patient has any of the following conditions:
  - Unresolved serious adverse reactions (especially pulmonary reactions, cardiac reactions or hypotension) from preceding chemotherapies
  - Active uncontrolled infection
  - Active graft-versus-host disease (GVHD)
  - Significant clinical worsening of leukaemia burden or lymphoma following lymphodepleting chemotherapy

### **PRESCRIPTIVE AUTHORITY:**

• Haematology Consultant working in the area of haematological malignancies who is trained in the administration and management of patients treated with tisagenlecleucel within a designated CAR-T treatment centre.

#### **TESTS**:

• Baseline and regular tests carried out in accordance with the hospital's CAR-T Protocol

#### **Disease monitoring:**

- Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant
- No steroids should be administered without approval of the treating Haematology Consultant

### **DOSE MODIFICATIONS:**

- No dose modifications are recommended for tisagenlecleucel
- Any dose modification consideration should be discussed with a Haematology Consultant

## **SUPPORTIVE CARE:**

#### **EMETOGENIC POTENTIAL:**

• Please refer to appropriate NCCP / local Lymphodepletion regimen for further information on anti-emetic regimen.

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#### **PREMEDICATIONS:**

- Please refer to hospital's CAR-T policy
- To minimise potential acute infusion reactions, it is recommended that patients be premedicated with paracetamol 1g PO once only 60 minutes prior to tisagenlecleucel infusion and chlorphenamine 10mg IV Injection once only 60 minutes prior to tisagenlecleucel infusion

#### **OTHER SUPPORTIVE CARE:**

• All patients should receive irradiated blood products (Refer to local policy)

| Table 3: Suggested Supportive Care <sup>a</sup>   |   |   |                             |
|---|---|---|-----------------------------|
| Table 3: Suggested Supportive Care <sup>a</sup> HSV prophylaxis   | <ul> <li>&gt;200/microlitre:</li> <li>Valaciclovi<br/>or</li> <li>Aciclovir 2:<br/>0.5X10<sup>9</sup>/L)</li> <li>Patients with an act</li> </ul> | receive the following until CD4 cou<br>r 500mg once daily PO<br>50mg TDS IV (if oral route not avai<br>tive herpes infection should receiv<br>r 1g TDS PO | lable or ANC <              |
|   | Aciclovir 10  | 0mg/kg TDS IV (if oral route not av   | ailable)                    |
| Antifungal prophylaxis  | lymphodepleting ch<br>≥1x10 <sup>9</sup> /L and comp<br>• Posaconaz   | axis is commenced on the first day<br>nemotherapy and continued until r<br>lete remission.<br>ole PO 300mg twice daily on first o<br>thereafter.          | neutrophil count            |
| PJP prophylaxis   | <u>T infusion or until</u>  | receive the following for three m<br>CD4 count >200/microlitre:<br>started on the first day of lymphoo<br>men.  |                             |
|   | <u>1st line therapy</u><br>● Co-trimoxa   | azole 960mg BD Mon/Wed/Fri PO   |                             |
|   | Pentamidir  | allergic to co-trimoxazole or cont<br>ne 300mg nebule and salbutamol 2<br>midine, every 4 weeks   |                             |
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## Table 3: Suggested Supportive Care<sup>a</sup>

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## NCCP National SACT Regimen



| Sodium chloride 0.9% 10ml QDS mouthwash     Nystatin 1ml QDS PO (use 15 minutes after sodium chloride     0.9% mouthwash)     Mucositis WHO grade ≥ 2: <ul> <li>Chlorhexidine digluconate 0.12% (Kin*) 10mls QDS PO</li> <li>Nystatin 1ml QDS PO (use 15 minutes after Kin* mouthwash)</li> </ul> <li>Sastro protection         <ul> <li>Lansoprazole 30mg / omeprazole 40mg once daily PO</li> <li>Or</li> <li>Esomeprazole 40mg once daily IV (if oral route not available)</li> </ul> </li> <li>Prevention of vaginal bleeding         <ul> <li>If required for menstruating female patients until platelets &gt; 50 x10°/L</li> <li>Norethisterone 5mg TDS PO if &gt;55Kg</li> <li>Norethisterone 5mg BD PO if &lt;55kg</li> <li>Consider allopurinol in active disease pre CAR-T infusion</li> <li>Allopurinol 300mg once daily PO for 5-7 days and review</li> <li>A virology screen is completed as part of CAR-T workup. Hepatitis B prophylaxis/treatment</li> <li>A virology consultant or Hepatology Consultant if required.</li> <li>Options may include:                 <ul> <li>Lamivudine 100mg once daily PO</li> <li>Entecavir 750microgram once daily PO</li> <li>Senna two tablets (15mg) nocte PO while on ondansetron</li></ul></li></ul></li>   | Mouthcare Gastro protection Prevention of vaginal bleeding Tumour Lysis syndrome Hepatitis B prophylaxis/treatment Prevention of constipation Antibiotic standing order | <ul> <li>Sodium chloride 0.9% 10ml QDS mouthwash</li> <li>Nystatin 1ml QDS PO (use 15 minutes after sodium chloride 0.9% mouthwash)</li> <li>Mucositis WHO grade ≥ 2:         <ul> <li>Chlorhexidine digluconate 0.12% (Kin®) 10mls QDS PO</li> <li>Nystatin 1ml QDS PO (use 15 minutes after Kin® mouthwash)</li> <li>Lansoprazole 30mg / omeprazole 40mg once daily PO Or</li> <li>Esomeprazole 40mg once daily IV (if oral route not available)</li> <li>If required for menstruating female patients until platelets &gt; 50 x10<sup>9</sup>/L</li> <li>Norethisterone 5mg TDS PO if &gt;55Kg</li> <li>Norethisterone 5mg BD PO if &lt;55kg</li> </ul> </li> <li>Consider allopurinol in active disease pre CAR-T infusion         <ul> <li>Allopurinol 300mg once daily PO for 5-7 days and review</li> <li>A virology screen is completed as part of CAR-T workup. Hepatitis B prophylaxis or treatment may be initiated in consultation with a Virology Consultant or Hepatology Consultant if required.</li> </ul> </li> <li>Options may include:         <ul> <li>Lamivudine 100mg once daily PO</li> <li>Entecavir 750microgram once daily PO</li> <li>Consider laxatives if appropriate e.g.</li> </ul> </li> </ul> |
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| Sastro protection <ul> <li>Lansoprazole 30mg / omeprazole 40mg once daily PO<br/>Or</li> <li>Esomeprazole 40mg once daily IV (if oral route not available)</li> </ul> Prevention of vaginal bleeding <ul> <li>If required for menstruating female patients until platelets &gt; 50 x10°/L</li> <li>Norethisterone 5mg TDS PO if &gt;55Kg</li> <li>Norethisterone 5mg BD PO if &lt;55kg</li> </ul> Fumour Lysis syndrome <ul> <li>Consider allopurinol in active disease pre CAR-T infusion</li> <li>Allopurinol 300mg once daily PO for 5-7 days and review</li> </ul> Hepatitis B prophylaxis/treatment       A virology screen is completed as part of CAR-T workup. Hepatitis B prophylaxis or treatment may be initiated in consultation with a Virology Consultant or Hepatology Consultant if required.         Options may include: <ul> <li>Lamivudine 100mg once daily PO</li> <li>Entecavir 750microgram once daily PO</li> <li>Consider laxatives if appropriate e.g.</li> <li>Senna two tablets (15mg) nocte PO while on ondansetron</li> </ul> Antibiotic standing order <ul> <li>Piptazobactam 4.5g QDS IV</li> <li>Pilus</li> <li>Amikacin* 15mg/kg once daily IV</li> </ul>  | Prevention of vaginal bleeding Tumour Lysis syndrome Hepatitis B prophylaxis/treatment Prevention of constipation   | <ul> <li>Lansoprazole 30mg / omeprazole 40mg once daily PO<br/>Or</li> <li>Esomeprazole 40mg once daily IV (if oral route not available)</li> <li>If required for menstruating female patients until platelets &gt; 50 x10<sup>9</sup>/L</li> <li>Norethisterone 5mg TDS PO if &gt;55Kg</li> <li>Norethisterone 5mg BD PO if &lt;55kg</li> <li>Consider allopurinol in active disease pre CAR-T infusion</li> <li>Allopurinol 300mg once daily PO for 5-7 days and review</li> <li>A virology screen is completed as part of CAR-T workup. Hepatitis B<br/>prophylaxis or treatment may be initiated in consultation with a<br/>Virology Consultant or Hepatology Consultant if required.</li> <li>Options may include:         <ul> <li>Lamivudine 100mg once daily PO<br/>Or</li> <li>Entecavir 750microgram once daily PO</li> </ul> </li> </ul>  |
| Or       Esomeprazole 40mg once daily IV (if oral route not available)         Prevention of vaginal bleeding       If required for menstruating female patients until platelets > 50 x10°/L         • Norethisterone 5mg TDS P0 if >55Kg       • Norethisterone 5mg BD P0 if <55kg         Fumour Lysis syndrome       Consider allopurinol in active disease pre CAR-T infusion         • Allopurinol 300mg once daily P0 for 5-7 days and review         Hepatitis B prophylaxis/treatment       A virology screen is completed as part of CAR-T workup. Hepatitis B prophylaxis or treatment may be initiated in consultation with a Virology Consultant or Hepatology Consultant if required.         Options may include:       • Lamivudine 100mg once daily PO or         • Entecavir 750microgram once daily PO or       • Entecavir 750microgram once daily PO         Or       • Senna two tablets (15mg) nocte PO while on ondansetron         Antibiotic standing order       Antibiotic standing order should be prescribed for neutropenic sepsis/neutropenic fever based on previous microbiology and renal function         • Piptazobactam 4.5g QDS IV       Plus         • Amikacin* 15mg/kg once daily IV       *Ciprofloxacin 400mg BD IV may be considered instead of amikacin in  | Prevention of vaginal bleeding Tumour Lysis syndrome Hepatitis B prophylaxis/treatment Prevention of constipation   | Or<br>Esomeprazole 40mg once daily IV (if oral route not available)<br>If required for menstruating female patients until platelets > 50 x10 <sup>9</sup> /L<br>Norethisterone 5mg TDS PO if >55Kg<br>Norethisterone 5mg BD PO if <55kg<br>Consider allopurinol in active disease pre CAR-T infusion<br>Allopurinol 300mg once daily PO for 5-7 days and review<br>A virology screen is completed as part of CAR-T workup. Hepatitis B<br>prophylaxis or treatment may be initiated in consultation with a<br>Virology Consultant or Hepatology Consultant if required.<br>Options may include:<br>Lamivudine 100mg once daily PO<br>Or<br>Entecavir 750microgram once daily PO<br>Consider laxatives if appropriate e.g.  |
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| Prevention of vaginal bleeding       If required for menstruating female patients until platelets > 50 x10 <sup>9</sup> /L         • Norethisterone 5mg TDS PO if >55Kg       • Norethisterone 5mg BD PO if <55kg         Fumour Lysis syndrome       Consider allopurinol in active disease pre CAR-T infusion         • Allopurinol 300mg once daily PO for 5-7 days and review         Hepatitis B prophylaxis/treatment       A virology screen is completed as part of CAR-T workup. Hepatitis B prophylaxis or treatment may be initiated in consultation with a Virology Consultant or Hepatology Consultant if required.         Options may include:       • Lamivudine 100mg once daily PO Or         • Entecavir 750microgram once daily PO         Or       • Senna two tablets (15mg) nocte PO while on ondansetron         Antibiotic standing order       Antibiotic standing order should be prescribed for neutropenic sepsis/neutropenic fever based on previous microbiology and renal function         • Piptazobactam 4.5g QDS IV       Plus         • Amikacin* 15mg/kg once daily IV  | Tumour Lysis syndrome<br>Hepatitis B prophylaxis/treatment<br>Prevention of constipation  | If required for menstruating female patients until platelets > 50 x10 <sup>9</sup> /L <ul> <li>Norethisterone 5mg TDS PO if &gt;55Kg</li> <li>Norethisterone 5mg BD PO if &lt;55kg</li> </ul> <li>Consider allopurinol in active disease pre CAR-T infusion <ul> <li>Allopurinol 300mg once daily PO for 5-7 days and review</li> </ul> </li> <li>A virology screen is completed as part of CAR-T workup. Hepatitis B prophylaxis or treatment may be initiated in consultation with a Virology Consultant or Hepatology Consultant if required.</li> <li>Options may include: <ul> <li>Lamivudine 100mg once daily PO or</li> <li>Entecavir 750microgram once daily PO</li> </ul> </li>   |
| Norethisterone Smg TDS PO if >55Kg     Norethisterone Smg BD PO if <55kg     Norethisterone Smg BD PO if <55kg     Consider allopurinol in active disease pre CAR-T infusion     Allopurinol 300mg once daily PO for 5-7 days and review     A virology screen is completed as part of CAR-T workup. Hepatitis B     prophylaxis/treatment     A virology consultant or Hepatology Consultant if required.     Options may include:         Lamivudine 100mg once daily PO         Or         Entecavir 750microgram once daily PO         Or         Entecavir 750microgram once daily PO         Consider laxatives if appropriate e.g.         Senna two tablets (15mg) nocte PO while on ondansetron     Antibiotic standing order     Antibiotic standing order Antibiotic fever based on previous microbiology and renal     function         Piptazobactam 4.5g QDS IV         Plus         Amikacin* 15mg/kg once daily IV     *Ciprofloxacin 400mg BD IV may be considered instead of amikacin in   | Tumour Lysis syndrome<br>Hepatitis B prophylaxis/treatment<br>Prevention of constipation  | <ul> <li>Norethisterone 5mg TDS PO if &gt;55Kg</li> <li>Norethisterone 5mg BD PO if &lt;55kg</li> <li>Consider allopurinol in active disease pre CAR-T infusion</li> <li>Allopurinol 300mg once daily PO for 5-7 days and review</li> <li>A virology screen is completed as part of CAR-T workup. Hepatitis B prophylaxis or treatment may be initiated in consultation with a Virology Consultant or Hepatology Consultant if required.</li> <li>Options may include:         <ul> <li>Lamivudine 100mg once daily PO or</li> <li>Entecavir 750microgram once daily PO</li> <li>Consider laxatives if appropriate e.g.</li> </ul> </li> </ul>   |
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| • Entecavir 750microgram once daily PO         Prevention of constipation       Consider laxatives if appropriate e.g.         • Senna two tablets (15mg) nocte PO while on ondansetron         Antibiotic standing order       Antibiotic standing order should be prescribed for neutropenic sepsis/neutropenic fever based on previous microbiology and renal function         • Piptazobactam 4.5g QDS IV       Plus         • Amikacin* 15mg/kg once daily IV   |   | Entecavir 750microgram once daily PO Consider laxatives if appropriate e.g.  |
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| function <ul> <li>Piptazobactam 4.5g QDS IV</li> <li>Plus</li> <li>Amikacin* 15mg/kg once daily IV</li> </ul> *Ciprofloxacin 400mg BD IV may be considered instead of amikacin in  |   |  |
| Plus<br>• Amikacin* 15mg/kg once daily IV<br>*Ciprofloxacin 400mg BD IV may be considered instead of amikacin in   |   |  |
| Amikacin* 15mg/kg once daily IV     *Ciprofloxacin 400mg BD IV may be considered instead of amikacin in  |   | Piptazobactam 4.5g QDS IV  |
| *Ciprofloxacin 400mg BD IV may be considered instead of amikacin in  |   |  |
| L cases of renal impairment  |   |  |
|  |   | cases of renal impairment  |
| Refer to local hospital antimicrobial guidelines for antibiotic choice<br>where a patient is allergic to any of the above  |   |  |
| Magnesium and potassium standing         Magnesium and potassium standing orders should be prescribed for  | Magnesium and potassium standing  |  |
|  | order   | Magnesium and potassium standing orders should be prescribed for   |
| VTE prophylaxis Consider VTE prophylaxis in accordance with local policy   | VTE prophylaxis   |  |

| NCCP Regimen: Tisagenlecleucel Therapy (CAR-T) for DLBCL and FL  | Published: 02/11/2021<br>Review: 04/03/2029 | Version number: 3a |  |
|--|---|--------------------|--|
| Tumour Group: Lymphoma and Other Lymphoproliferative<br>Disorders<br>NCCP Regimen Code: 00687  | IHS Contributor:<br>Dr Larry Bacon          | Page 5 of 7        |  |
| The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of |   |                    |  |

individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at <a href="http://www.hse.ie/eng/Disclaimer">http://www.hse.ie/eng/Disclaimer</a>

This information is valid only on the day of printing, for any updates please check <u>www.hse.ie/NCCPSACTregimens</u>



| Bone Health | Consider calcium and vitamin D supplementation prior to discharge<br>for patients who are on high dose steroids. Other medications for<br>maintenance of bone health may need to be considered as<br>appropriate. |
|-------------|---|
|             | <ul> <li>Calcium carbonate and colecalciferol (Caltrate<sup>®</sup></li> <li>600mg/400units) 1 tablet BD</li> </ul>   |

<sup>a</sup>Based on local practice in St James Hospital when V1 of regimen developed

## **ADVERSE EFFECTS**

• Please refer to the relevant Summary of Product Characteristics and local CAR-T/Stem Cell Transplant Programme PPGs for full details.

#### **DRUG INTERACTIONS:**

• The relevant Summary of Product Characteristics and current drug interaction databases should be consulted.

### COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP

• <u>https://www.hcp.novartis.com/products/kymriah/diffuse-large-b-cell-lymphoma-adults/</u>

### **REFERENCES:**

- 1. Schuster, SJ et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. NEJM 2019; 380:45-56 DOI:<u>10.1056/NEJMoa1804980</u> (Including supplementary material)
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| Tumour Group: Lymphoma and Other Lymphoproliferative<br>DisordersIHS Contributor:<br>Dr Larry BaconPage 6 of 7NCCP Regimen Code: 00687Dr Larry BaconPage 6 of 7  |  |  |  |  |
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| Version | Date       | Amendment   | Approved By    |
|---------|------------|---|----------------|
| 1       | 02/11/2021 |   | Dr Larry Bacon |
| 2       | 04/03/2024 | Reviewed.   | Dr Larry Bacon |
| 2a      | 19/07/2024 | Typographical errors removed                        | NCCP           |
| 3       | 14/03/2025 | New indication added for follicular lymphoma        | Dr Larry Bacon |
| 3a      | 25/06/2025 | Reimbursement status updated for indication 00687b. | NCCP           |

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

| NCCP Regimen: Tisagenlecleucel Therapy (CAR-T) for DLBCL and FL  | Published: 02/11/2021<br>Review: 04/03/2029 | Version number: 3a |
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