

## **1. Introduction and Who Guideline applies to**

There are an increasing number of licensed bispecific antibody therapies available for the treatment of haematological malignancies. Due to mechanism of action there are some similarities between the toxicity profiles of these bispecific antibodies including Cytokine Release Syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). These toxicities have defined mitigation and management strategies.

This document applies to all haematology consultants, SpR, junior medical staff, nursing, pharmacy and administrative staff responsible for the care of haematology patients within the University Hospitals of Leicester NHS Trust.

### **1.1 Glofitamab**

Glofitamab is a humanized anti-CD20 anti-CD3 bispecific monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology. It is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), after two or more lines of systemic therapy.

It has been recommended by NICE as an option for treating relapsed or refractory DLBCL in adults after 2 or more systemic treatments (Sept 2023). Trials have demonstrated that it can be an effective treatment for patients with relapsed or refractory lymphoma. In the first published trials patients with DLBCL had an overall response rate of 52% with a complete response rate of 39%.

CRS is mitigated by the use of pre-treatment with Obinutuzumab and the use of step-up dosing of Glofitamab and use of pre-mediation. In the clinical trial setting CRS of any grade occurred in 63% of patients with 12% having G2 & 4% G3 or 4 CRS. As CRS is most commonly seen with the step up Glofitamab dosing there is a requirement for monitoring for a least 24 hours after completion of the first dose infusion, this requires an in-patient admission.

### **1.2 Epcoritamab**

Epcoritamab is a humanised immunoglobulin G1 (IgG1)-bispecific antibody against CD3 and CD20 antigens, produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology. It is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), after two or more lines of systemic therapy.

It has been recommended by NICE as an option for treating relapsed or refractory DLBCL in adults after 2 or more systemic treatments if they have had polatuzumab vedotin or if polatuzumab vedotin is contra-indicated or not tolerated (March 2024). Trials have demonstrated that it can be an effective treatment for patients with

relapsed or refractory lymphoma. In the first published trials patients with DLBCL had an overall response rate of 63% with a complete response rate of 39%.

CRS is mitigated by step-up dosing and pre-medication. In the clinical trial setting any grade CRS occurred in 50% with 2.5% G3. CRS was most commonly seen with the first full dose on C1 D15 so there is a requirement for in-patient monitoring following this dose.

The majority of cases of ICANS occurred within the Cycle 1 of epcoritamab treatment, however some occurred with delayed onset.

### **1.3 Elranatamab**

Elranatamab is an IgG2 kappa bispecific antibody derived from two monoclonal antibodies (mAbs), produced using two recombinant Chinese hamster ovary (CHO) cell lines. It binds CD3 on T cells and B-cell maturation antigen (BCMA) on plasma cells, plasmablasts, and multiple myeloma cells. It is indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy

CRS occurred in 57.9% of patients who received ELREXFIO at the recommended dosing schedule, with Grade 1 CRS in 43.7%, Grade 2 in 13.7% and Grade 3 in 0.5% of patients. Most patients experienced CRS after the first step-up dose (43.2%) or the second step-up dose (19.1%), with 7.1% of patients having CRS after the first full treatment dose and 1.6% of patients after a subsequent dose. Recurrent CRS occurred in 13.1% of patients. The median time to onset of CRS was 2 (range: 1 to 9) days after the most recent dose, with a median duration of 2 (range: 1 to 19 days) days.

Due to the potential for ICANS, patients should be advised not to drive or operate heavy or potentially dangerous machinery during the step-up dosing schedule and for 48 hours after completing each of the 2 step-up doses and in the event of new onset of any neurological symptoms

### **1.4 Teclistamab**

Teclistamab is a full-size, IgG4-PAA bispecific antibody that targets the CD3 receptor expressed on the surface of T cells and B cell maturation antigen (BCMA), which is expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B cells and plasma cells.

It is indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

CRS was reported in 72% of patients following treatment with teclistamab. One-third (33%) of patients experienced more than one CRS event. Most patients experienced CRS following Step-up Dose 1 (44%), Step-up Dose 2 (35%), or the initial maintenance dose (24%). Less than 3% of patients developed first occurrence of CRS following subsequent doses of teclistamab. CRS events were Grade 1 (50%) and Grade 2 (21%) or Grade 3 (0.6%). The median time to onset of CRS was 2 (Range: 1 to 6) days after the most recent dose, with a median duration of 2 (Range: 1 to 9) days.

ICANS, including Grade 3 and higher, were reported in clinical trials and with post marketing experience. The most frequent clinical manifestation of ICANS were confusional state, decreased level of consciousness, disorientation, dysgraphia, aphasia, apraxia, and somnolence. The onset of neurologic toxicity can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. The observed time to onset of ICANS ranged from 0 to 21 days after the most recent dose

## **2. Guidelines, Standards and Procedures**

### **Procedure for Initiation**

#### **Requesting and allocating treatment – at least 24 hours prior to initiation**

- 1) Patient discussed at MDT and considered suitable – clinical trial options considered
- 2) Complete Blueteq
- 3) Allocate treatment on chemocare & liaise with pharmacy to confirm
- 4) Paper drug chart for fluids / rasburicase if needed and rescue medication completed (or added to NerveCentre if possible)
- 5) Patient consented

### **Glofitamab Treatment Delivery**

- Obinutuzumab is administered as per standard of care. Further guidance can be found in the SPC.
- Patients should be well hydrated and unless contra-indicated maintenance iv fluids and regular paracetamol are recommended with cycle 1 day 8 & cycle 1 day 15 during the infusion.

*Table 1 Glofitamab Pre-medication:*

Treatment day		Pre-medication	Duration of infusion
C1 D8 & D15 C2 D1	All patients	20mg dexamethasone iv – <b>1 hour prior</b> 10mg <u>chloramphenamine</u> iv & 1g paracetamol – 30 mins prior	4 hours (up to 8 hours if previous CRS)
C3 D1	All patients	20mg dexamethasone iv – <b>1 hour prior</b> 10mg <u>chloramphenamine</u> iv & 1g paracetamol – 30 mins prior	2 hours if no prior CRS 4-8 hours if prior CRS
Subsequent	Prior CRS	20mg dexamethasone iv – <b>1 hour prior</b> 10mg <u>chloramphenamine</u> iv & 1g paracetamol – 30 mins prior	4-8 hours
	No CRS	10mg <u>chloramphenamine</u> iv & 1g paracetamol – 30 mins prior	2 hours

- Following initial ramp-up during cycle 1 glofitamab is administered 3-weekly for up to 12 cycles
- Patients receiving Glofitamab should have **hourly observations** performed during the infusion. Following cycle 1 day 8 hourly observations should continue for **4 hours** after completion of the infusion. The patient will then be admitted for a total of 24 hours of observation.

### **Epcoritamab Treatment Delivery**

Patients should be well hydrated if oral intake of 2-3L /day cannot be maintained they will require IV fluids.

*Table 2: Cycle 1 Epcoritamab Schedule and Pre-medication:*

Drug	Day(s)	Dose	Route	Details
<b>Paracetamol</b>	1, 8, 15, 22	1gram	PO	Pre-meds given 30 – 120 minutes prior to epcoritamab
<b>Cetirizine</b>	1, 8, 15, 22	10mg	PO	
<b>Prednisolone</b>	1 – 4 8 – 11 15 – 18 22 - 25	100mg OD	PO	
<b>Epcoritamab</b>	1	0.16mg	SC	Lower abdomen or thigh, with alternating sides is recommended
	8	0.8mg	SC	
	15 & 22	48mg	SC	

- Patients receiving epcoritamab should have observations recorded before and after the injection and at 4 hours following cycle 1 days 1, 8 & 15. If CRS has occurred previously observations 4 hours after the injection should continue until a dose is given with no CRS.
- Patients should also monitor their temperature at home. During cycle 1 patients should be advised to monitor their body temperature at least 3 times a day for the first 4 days following the epcoritamab dose.
- In-patient monitoring is required for 24 hours following cycle 1 day 15 for all patients. Further in-patient monitoring may be required if patients are high-risk or have had previous CRS on a case-by-case basis.
- In subsequent cycles steroid prophylaxis is only required if there was G2 or G3 CRS a previous epcoritamab dose. When needed 100mg prednisolone OD for 4 days is given until a dose of epcoritamab is given with no CRS.
- Epcoritamab is delivered in 28-day cycles until disease progression or unacceptable toxicity. In cycles 2 & 3 treatment is weekly. In cycles 4 – 9 treatment is fortnightly. Cycle 10 onwards treatment is 4-weekly. Some patients will be suitable for treatment at home.
- Further guidance can be found in the SPC.

### Elranatamab Treatment Delivery

*Table 3: Cycle 1 Elranatamab Schedule and Pre-medication:*

Drug	Day(s)	Dose	Route	Details
<b>Paracetamol</b>	1,4, 8, 15, 22	1000mg	PO	Pre-meds given 60 minutes prior to elranatamab
<b>Chlorphenamine</b>	1,4, 8, 15, 22	4mg	PO	
<b>Dexamethasone</b>	1,4, 8, 15, 22	20mg OD	PO	
<b>Elranatamab</b>	1 (1 <sup>st</sup> step up dose)	12mg	SC	Abdomen (preferred injection site) but may be injected into the subcutaneous tissue of the thigh. It should not be injected into areas where the skin is red, bruised, tender, hard, or areas where there
	4 (2 <sup>nd</sup> step up dose)	32mg	SC	
	8, 15 & 22	76mg	SC	

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- Due to the risk of CRS and ICANS, patients should be monitored for signs and symptoms for 48 hours after administration of each of the 2 step-up doses. Initially, patients will be admitted for the first 5 days.
- Complete Obs every 4 hours for the first 48 hours following day 1 & day 4 treatment on cycle 1.
- A minimum of 6 days should be maintained between weekly doses

### Teclistamab Treatment Delivery

*Table 3: Cycle 1 Teclistamab Schedule and Pre-medication:*

Drug	Day(s)	Dose	Route	Details
<b>Paracetamol</b>	1,3,5, 12, 19	1000mg	PO	Pre-meds given 1- 3 hours prior to teclistamab
<b>Chlorphenamine</b>	1,3,5, 12, 19	4mg	PO	
<b>Dexamethasone</b>	1,3,5, 12, 19	16mg OD	PO	
<b>Teclistamab</b>	1 (1 <sup>st</sup> step up dose)	0.06mg/kg	SC	Inject the required volume into the subcutaneous tissue of the abdomen (preferred injection site). Alternatively, may be injected subcutaneously at other sites (e.g., thigh). If multiple injections are required, injections should be at least 2 cm apart. Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard or not intact.
	3 (2 <sup>nd</sup> step up dose)	0.3mg/kg	SC	
	5 (First maintenance dose)	1.5mg/kg	SC	
	12 and weekly thereafter	1.5mg/kg	SC	

- Due to the risk of CRS, patients should be monitored for signs and symptoms daily for 48 hours after administration of all doses within the step-up dosing schedule

### Management of toxicity for bispecific antibodies - CRS

- CRS is a potentially serious but expected side effect of bispecific antibodies. It is an acute inflammatory process characterised by pyrexia, hypotension, hypoxia and elevated serum cytokines (predominately IL-6, IL-1, IL-2, TNF $\alpha$  and IFN $\gamma$ ) with increased C- reactive protein (CRP) and hyper-ferritinaemia that usually occurs during step-up or initial doses.
- Severity is graded as per the ASTCT Consensus Grading System (Table 2). The signs and symptoms of CRS can mimic neutropenic sepsis and should be treated as per UHL guideline. Specific licensed medicines used to treat CRS are tocilizumab and corticosteroids. Alternative, unlicensed, treatments include Anakinra and Siltuximab. A maximum of 3 doses of Tocilizumab are permitted in a 6-week period,

## Management of toxicity for bispecific antibodies - CRS

for glofitamab. For Epcoritamab only 2 doses are allowed in a 24-hour period. For teclistamab a maximum of 3 doses in a 24-hour period and maximum total of 4 doses are permitted. Refer to SPC for further information

- Patients admitted for observation after bispecific antibody therapy with glofitamab or epcoritamab should have observations carried out **4-hourly until 24 hours** post completion of treatment or if the patient appears unwell. In the case of elranatamab and teclistamab patients should have observations recorded **every 4 hours for the first 48 hours** following step up doses (Day 1 & 4 of cycle 1). If there are any concerns about CRS a medical review is required.
- Immediately contact the haematology registrar or escalate to consultant if CRS grade 2 or higher or for persistent grade 1 CRS. A full assessment of cause of fever should be carried out. Further details of specific management of CRS are shown in Table 2.
- Symptoms of CRS should have resolved at least 72 hours prior to the next treatment. If the patient experiences any CRS a slower infusion rate should be considered (where applicable) and in-patient monitoring following subsequent doses. Bispecific therapy should be permanent discontinued if a patient experiences G4 CRS or recurrent G3 CRS.

*Table 2 AT SCT CRS grading and Management:*

Grade	Features	Management
1	Fever 38 °C or higher	Withhold treatment or pause infusion if running. In the case of glofitamab restart at lower rate on resolution Treat symptoms Consider steroids +/- tocilizumab if CRS lasts more than 48 hours or patient is high risk Assess and consider treatment for neutropenic infections
2	Fever 38 °C with hypotension (not requiring vasopressors) and/or hypoxia requiring low-flow oxygen	Withhold treatment or discontinue infusion (if running) Treat symptoms Administer corticosteroids Consider tocilizumab Discuss with ITU if not responding
3	Fever 38 °C with hypotension requiring vasopressors and/or hypoxia requiring high-flow oxygen	Withhold treatment or discontinue infusion (if running) Treat symptoms & discuss with ITU Administer corticosteroids Administer tocilizumab  In the case of recurrent Grade 3 CRS, permanently discontinue elranatamab and teclistamab therapy.
4	Fever 38 °C with hypotension requiring	Permanently discontinue treatment and treat symptoms

### Management of toxicity for bispecific antibodies - CRS

	multiple vasopressors and/or hypoxia requiring oxygen with positive pressure	Discuss with ITU Administer corticosteroids Administer tocilizumab
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- Once CRS established, ongoing fever is not required for grading (as this may have resolved with subsequent treatment). Other causes of fever, hypotension, hypoxia should be considered.
- Recommended corticosteroid is 10mg dexamethasone iv (1mg/kg methylprednisolone od-bd is an alternative).
- Tocilizumab is given at a dose of 8mg/kg (max dose 800mg) iv in 100ml 0.9% Saline over 1 hour. There should be 4 vials kept on Ward 41 which will be replaced after use. Instructions for preparation can be found on Medusa. Further guidance for management of CRS can be found in the Cellular therapy SOPs (HPC-IS-23, HPC-P-74 and HPC-F-96) available on QPulse . If Tocilizumab is required a Blueteq should be completed (one per patient episode).
- In the case of Glofitamab and Epcoritamab, ensure symptoms are resolved for at least 72 hours prior to the next dose. For elranantamab and teclistamab, doses should be held until resolution of symptoms.

### Management of toxicity for bispecific antibodies - ICANS

- Assessment and grading of ICANS using the Immune Effector Cell-Associated Encephalopathy (ICE) & ICANS Score should be done at least every 8 h at the following time points:
- Glofitamab: ICE score should be performed if there is concern about neurological toxicity
- Epcoritamab: For 24 hours after administration of the Cycle 1 Day 15 dose of 48 mg
- Elranatamab: For 48 hours after administration of each of the 2 step-up doses
- Teclistamab: Patients who experience Grade 2 or higher ICANS or first occurrence of Grade 3 ICANS with the previous dose of teclistamab should be instructed to remain within proximity of a healthcare facility and monitored for signs and symptoms daily for 48 hours.
- The HPC-F-94: Neurotoxicity assessment for CAR-T cell therapy form (available on QPulse) should be used to record ICE Score.
- If ICANS is suspected, contact the Haematology registrar immediately and take aspiration precautions

Grade	Features	Management
1	ICE score 7-9. Awake spontaneously.	Withhold treatment until ICANS resolves Supportive measures Exclude alternate causes Consider non-sedating anti-epileptics eg Levetiracetam 500mg - 750mg bd as seizure prophylaxis



## Management of toxicity for bispecific antibodies - CRS

		Consider dexamethasone 10mg every 12 hours. Refer to HPC-IS-28 FLOWSHEET – ICANS MANAGEMENT Review medication and consider stopping other sedatives
2	ICE score 3-6. Awakes to voice.	Withhold treatment until ICANS resolves Supportive measures Critical care outreach referral Urgent CT brain and MRI brain Request EEG Administer dexamethasone 10 mg intravenously every 6-12 hours. Consider anakinra if no improvement Consider non-sedating anti-epileptics eg Levetiracetam 500mg - 750mg bd as seizure prophylaxis Refer to HPC-IS-28 FLOWSHEET – ICANS MANAGEMENT Review medication and consider stopping other sedatives
3	ICE score 0-2.  Awakens only to tactile stimulus.	Withhold treatment until ICANS resolves and permanently discontinue treatment if recurrence Supportive measures Consider non-sedating anti-epileptics eg Levetiracetam 500mg - 750mg bd as seizure prophylaxis or anti-epileptics to control seizures if present Critical care outreach referral Urgent CT brain and MRI brain Request EEG Administer dexamethasone 10 mg intravenously every 6 hours. Consider anakinra if no improvement Refer to HPC-IS-28 FLOWSHEET – ICANS MANAGEMENT Review medication and consider stopping other sedatives
4	ICE score 0.  Patient is unarousable or stupor or coma.  Life-threatening prolonged seizure (>5 min); or Repetitive clinical or electrical seizures without	Permanently discontinue treatment Supportive measures Consider non-sedating anti-epileptics eg Levetiracetam 500mg - 750mg bd as seizure prophylaxis or anti-epileptics to control seizures if present Critical care outreach referral Urgent CT brain and MRI brain Request EEG Mechanical ventilation may be required

## Management of toxicity for bispecific antibodies - CRS

	return to baseline in between.	Consider hyperosmolar therapy if diffuse brain oedema on scans Administer Methylprednisolone Sodium Succinate Consider anakinra if no improvement Consider Siltuximab (Needs CMA approval) Refer to HPC-IS-28 FLOWSHEET – ICANS MANAGEMENT
	Deep focal motor weakness	Review medication and consider stopping other sedatives
	Diffuse cerebral edema on neuroimaging;	

- For ICE Score refer to HPC-IS-26 ICE Score and ICANs grading
- In the case of Glofitamab and Epcoritamab, ensure symptoms are resolved for at least 72 hours prior to the next dose. For elranantamab and teclistamab, doses should be held until resolution of symptoms

## Management of Other Complications

**Tumour flare** can occur, leading to increased pain. Consideration of a management strategy is required if there is a critical site tumour which could cause airway compromise or vascular or ureteric compression.

**Tumour lysis syndrome** can occur, and patients should be individually risk assessed. Patients may require rasburicase prophylaxis and TLS blood monitoring.

**Cytopenias** may require GCSF support or transfusion support but there is no requirement for routine use of GCSF.

**Infections** are common and antibiotic / antiviral prophylaxis may be required. The individual treatment and infection history will determine this. Bispecific antibodies must not be administered to patients with an active infection

## Ward Procedures

Patient is admitted from OTC after receiving bi-specific antibody infusion. The on-call SpR should be made aware of the patient by the OTC SpR or lymphoma consultant. The patient should be reviewed by the SpR prior to them leaving the hospital site.

The patient will require observations every 4 -hours (even if normal) including overnight.

In the event of a temperature >38°C the on-call SpR should be contacted.

The discharge letter should document if CRS occurred, the grade and any treatment given. A note should be added to Chemocare by the ward SpR / a consultant if CRS occurred. The patient is likely to already have their next appointment booked but if there is any doubt please clarify with their named consultant, relevant buddy or a CNS.

## Key Points for Nursing staff – step up dosing of bispecifics

### OTC

## Management of toxicity for bispecific antibodies - CRS

- Pre-medication should be administered as per ChemoCare
- Observations should be recorded **hourly** during the infusion
- Patients should be well hydrated & have regular paracetamol
- Fever – could represent IRR or CRS.
  - Stop infusion if running & give paracetamol +/- chlorphenamine
  - If does not improve alert Haem SpR
  - In the case of glofitamab, if does improve infusion can be restarted at a slower rate
- Pain is likely to represent tumour flare and may require morphine sulphate liquid or subcutaneous morphine
- Patient should have obs every **4hours** for 24 – 48 hours post-infusion as detailed above

### Ward

- Patient remains at risk of CRS
- **Obs must be done 4-hourly (even if normal) including overnight**
- If the patient develops a fever (temp 38°C+) please alert Haem SpR directly

### Key Points for Medical Staff

- OTC SpR or lymphoma consultant should handover to the ward SpR/on-call SpR
- Rescue steroids should be prescribed on NerveCentre (10mg dexamethasone) along with regular paracetamol and iv fluids unless contra-indicated.
- On-call SpR should review patient prior to leaving the hospital and ensure regular observations are planned
- If CRS progresses to G2 the patient will need an SpR review:
  - Review if alternative cause for fever eg infection
  - Give rescue dexamethasone + paracetamol (if not recently given)
  - If hypotensive give iv fluids
  - If no response to steroid +/- fluids low threshold for tocilizumab
  - If no response to tocilizumab will need discussion with ITU
  - Discuss with on-call consultant

If CRS occurs: Request FBC, U&Es, LFTs, Ca<sup>2+</sup>, Mg<sup>2+</sup>, Phosphate, uric acid, LDH, CRP, procalcitonin, lactate, ferritin, PT/APTT, fibrinogen, urinalysis, urine culture, blood cultures, sputum culture if present, COVID19 PCR. Consider empiric iv wide spectrum antibiotics especially if the patient is neutropenic

## 3. Education and Training

- Approved guideline will be disseminated.
- Medical staff and CNS team have received education at a lunchtime meeting. An introduction to CRS will also be added to the junior doctor induction programme.

- Pharma companies have provided training to OTC staff and ward 41 manager. Further training will be provided as needed.

#### **4. Monitoring and Audit Criteria**

Key Performance Indicator	Method of Assessment	Frequency	Lead
Compliance with admission protocols	Audit	Annually	CNS /Clinical Lead
Management of CRS	Audit	Annually	CNS /Clinical Lead

#### **5. Equality Analysis Assessment**

5.1 The Trust recognises the diversity of the staff and local community it serves. Our aim therefore is to provide a safe environment free from discrimination, harassment and victimisation and treat all individuals fairly with dignity and respect and, as far as is reasonably possible, according to their needs.

5.2 As part of its development, an Equality Analysis on this policy have been undertaken and its impact on equality have been reviewed and no detriment was identified.

##### **EDI Statement**

We are fully committed to being an inclusive employer and oppose all forms of unlawful or unfair discrimination, bullying, harassment and victimisation.

It is our legal and moral duty to provide equity in employment and service delivery to all and to prevent and act upon any forms of discrimination to all people of protected characteristic: Age, Disability (physical, mental and long-term health conditions), Sex, Gender reassignment, Marriage and Civil Partnership, Sexual orientation, Pregnancy and Maternity, Race (including nationality, ethnicity and colour), Religion or Belief, and beyond.

We are also committed to the principles in respect of social deprivation and health inequalities.

Our aim is to create an environment where all staff are able to contribute, develop and progress based on their ability, competence and performance. We recognise that some staff may require specific initiatives and/or assistance to progress and develop within the organisation.

We are also committed to delivering services that ensure our patients are cared for, comfortable and as far as possible meet their individual needs.

#### **6. Supporting Documents and Key References**

1. Dickinson MJ, et al. Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2022 Dec 15;387(24):2220-2231. doi: 10.1056/NEJMoa2206913. Epub 2022 Dec 11. PMID: 36507690.
2. Thieblemont C et al. Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell-Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial. JCO 41, 2238-2247 (2023).
3. Consensus Framework for the Safe Delivery of Bispecific Antibodies in Multiple Myeloma Consensus Framework for the Optimal Delivery of Bispecific Antibodies for patients with Multiple Myeloma A pathway document produced by the Equity in Multiple Myeloma Bispecific Research and Access (EMMBRAce) Bispecific Antibody Implementation Group. (2024). Available at: [https://www.ucl.ac.uk/lifesciences-faculty/sites/lifesciences\\_faculty/files/consensus\\_framework\\_for\\_the\\_optimal\\_delivery\\_of\\_bispecific\\_antibodies\\_for\\_patients\\_with\\_multiple\\_myeloma\\_v1\\_oct\\_2024.pdf](https://www.ucl.ac.uk/lifesciences-faculty/sites/lifesciences_faculty/files/consensus_framework_for_the_optimal_delivery_of_bispecific_antibodies_for_patients_with_multiple_myeloma_v1_oct_2024.pdf) [Accessed 19 Nov. 2024].

## 7. Key Words

Bispecific, Glofitamab, Epcoritamab, Elranatamab, Teclistamab, Cytokine Release Syndrome, CRS, ICANS

CONTACT AND REVIEW DETAILS	
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<b>Details of Changes made during review:</b> New Document	