Fludarabine & cycloPHOSphamide Lymphodepletion for Brexucabtagene Autoleucel (Tecartus®) B-cell ALL

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Lymphodepletion chemotherapy regimen pre-treatment for CAR-T therapy brexucabtagene autoleucel (Tecartus®) in adult patients 26 years of age and above with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (ALL)	C91	00899a	N/A

* This applies to post 2012 indications

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Brexucabtagene autoleucel (Tecartus®) must be administered in an NCCP designated CAR-T centre.

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

No steroids should be administered without approval of the treating Haematology Consultant.

Pre-treatment conditioning:

- Lymphodepleting chemotherapy is recommended to be administered before brexucabtagene autoleucel infusion.

Brexucabtagene autoleucel administration:

- Please refer to the local CAR-T policy for brexucabtagene autoleucel information.
- Brexucabtagene autoleucel is recommended to be infused **2 to 14** days after completion of the lymphodepleting chemotherapy.

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Day	Drug	Dose	Route	Diluent & Rate	Cycle
-4,-3,-2	**Fludarabine**[1]	25mg/m^2	IV	100mL NaCl 0.9% over 30 minutes	1
-2	**Mesna**	360mg/m^2	IV	Slow IV bolus (Into the side arm fast flowing NaCl 0.9% infusion immediately prior to cycloPHOSphamide)	1
-2	**cycloPHOSphamide**	900mg/m^2	IV	500mL NaCl 0.9% over 60 minutes	1
-2	**Mesna**	360mg/m^2	IV	At 2 and 6 hours after the start of cycloPHOSphamide infusion	1
0	**Brexucabtagene autoleucel (Tecartus®)**		IV	Please refer to the hospital's CAR-T policy for brexucabtagene autoleucel (Tecartus®)	

[1]All patients who have received fludarabine should receive irradiated blood products (lifetime recommendation)
Dose rounding:
Fludarabine doses ≤50mg to the nearest 2.5mg and doses ≥50mg to the nearest 5mg
cycloPHOSphamide to the nearest 20mg
Mesna to the nearest 100mg for IV route

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

Notes:

The availability of brexucabtagene autoleucel must be confirmed prior to starting the lymphodepleting regimen. If the infusion is delayed for more than 2 weeks after the patient has received the lymphodepleting chemotherapy, lymphodepleting chemotherapy regimen must be administered again.

ELIGIBILITY:

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

CAUTION IN USE:

- Due to the risks associated with brexucabtagene autoleucel 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 deterioration of patient following lymphodepleting chemotherapy

EXCLUSIONS:

- Known or suspected hypersensitivity to fludarabine, cycloPHOSphamide, brexucabtagene autoleucel or any of the excipients
- Pregnancy and lactation

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PRESCRIPTIVE AUTHORITY:

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

TESTS:

- Baseline and regular tests carried out in accordance with local 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:

- Any dose modifications of should be discussed with the treating Haematology Consultant.
- **Chemotherapy dosing in obese adult patients**: See local policy

Renal and Hepatic Impairment:

- Discuss with the treating consultant if hepatic impairment or if creatinine clearance is < 70mL/min for advice on fludarabine dosing
- Consult the following resources to inform any renal or hepatic dose modification discussions:
    - Summary of product characteristics (SPC) available at http://www.hpra.ie
    - Giraud EL, de Lijster B, Krens SD, Desar IME, Boerrigter E, van Erp NP. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Lancet Oncol 2023; 24: e229
    - Local hospital policy

MANAGEMENT OF ADVERSE EVENTS:

- Refer to local policy

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting - Available on the NCCP website

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Fludarabine: Minimal **(Refer to local policy)**

cycloPHOSphamide: Moderate **(Refer to local policy)**

For information:

Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Haemato-oncology) - Available on the NCCP website

Table 1: Suggested Regimen Specific Anti-emetics[a]

Prevention of acute emesis			Comments
Drug	**Dose**	**Admin day**	dexAMETHasone not used as part of anti-emetic regimen prior to brexucabtagene autoleucel infusion
Cyclizine	50mg PO TDS	-2, -1	
Ondansetron	8mg PO/IV TDS PRN	-2, -1	

[a]Based on local practice in St James Hospital

OTHER SUPPORTIVE CARE:

Table 2: Other Suggested Supportive Medication[a]

HSV prophylaxis	All patients should receive the following until CD4 count >200/microlitre, and for 1 year post CAR-T infusion. • Valaciclovir 500mg once daily PO or • Aciclovir 250mg TDS IV (if oral route not available or ANC < $0.5X10^9$/L) Patients with an active herpes infection should receive the following: • Valaciclovir 1g TDS PO or • Aciclovir 10mg/kg TDS IV (if oral route not available)
Antifungal prophylaxis	Anti-fungal prophylaxis is commenced on the first day of lymphodepleting chemotherapy (D-5) and continued until neutrophil count ≥$1x10^9$/L without GCSF support • Posaconazole PO 300mg twice daily on D-5, then 300mg once daily thereafter

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PJP prophylaxis	**<u>All patients should receive the following for one year post CAR-T infusion or until CD4 count >200/microlitre:</u>** **<u>PJP prophylaxis is started on the first day of lymphodepleting chemotherapy (D-5)</u>** **<u>1st line therapy</u>** • Co-trimoxazole 960mg BD Mon/Wed/Fri PO **<u>2nd line therapy (if allergic to co-trimoxazole or contraindicated):</u>** • Pentamidine 300mg nebule and salbutamol 2.5mg nebule pre-pentamidine, every 4 weeks
Mouthcare	Mucositis WHO grade < 2: • NaCl 0.9% 10mL QDS mouthwash • Nystatin 1mL QDS PO (use 15 minutes after NaCl 0.9% mouthwash) Mucositis WHO grade ≥ 2: • Chlorhexidine digluconate 0.12% (Kin®) 10mL QDS PO • Nystatin 1mL QDS PO (use 15 minutes after Kin® mouthwash)
Gastro protection	• Lansoprazole 30mg / omeprazole 40mg once daily PO Or • Esomeprazole 40mg once daily IV (if oral route not available)
Prevention of vaginal bleeding	If required for menstruating female patients until platelets > 50 x10^9/L • Norethisterone 5mg TDS PO if >55Kg • Norethisterone 5mg BD PO if <55kg
Tumour Lysis syndrome	Consider allopurinol in active disease pre transplant • Allopurinol 300mg once daily PO for 5-7 days and review
Hepatitis B prophylaxis/treatment	A virology screen is completed as part of transplant workup. Hepatitis B prophylaxis or treatment may be initiated in consultation with a Virology Consultant or Hepatology Consultant if required. • Entecavir 500 microgram 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 *Ciprofloxacin 400mg BD IV may be considered instead of amikacin in cases of renal impairment Refer to local hospital antimicrobial guidelines for antibiotic choice where a patient is allergic to any of the above

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Magnesium and potassium standing order	Magnesium and potassium standing orders should be prescribed for all transplant patients in accordance with stem cell unit practice
VTE prophylaxis	Consider VTE prophylaxis in accordance with local policy
Bone Health	Consider calcium and vitamin D supplementation prior to discharge for patients who are on high dose steroids. Other medications for maintenance of bone health may need to be considered as appropriate. • Calcium carbonate and colecalciferol (Caltrate® 600mg/400units) one tablet BD

[a]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 Stem Cell Transplant Programme PPPGs 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

Educational materials for healthcare professionals and for patients available on the HPRA website:

- https://www.hpra.ie/find-a-medicine/for-human-use/authorised-medicines/details/36725#edumaterials

REFERENCES:

1. Shah BD, et al. KTE-X19 for relapsed/refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results from the single-arm, multi centre ZUMA-3 study. Lancet. 2021 Jun 4;398(10299):491–502
2. Giraud EL, de Lijster B, Krens SD, Desar IME, Boerrigter E, van Erp NP. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Lancet Oncol 2023; 24: e229.
3. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
4. NCCP BACKGROUND DOCUMENT EXTRAVASATION CLASSIFICATION OF SYSTEMIC ANTI-CANCER THERAPY V2 2019. Available at:

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https://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/sactguidance/classification.pdf

5. Brexucabtagene autoleucel (Tecartus®) Summary of Product Characteristics. Last updated 20/08/2025. Accessed August 2025. Available at: https://ec.europa.eu/health/documents/community-register/2023/20231207160997/anx_160997_en.pdf
6. Fludarabine Summary of Product Characteristics HPRA. Last updated: 02/06/2023. Accessed August 2025. Available at: https://assets.hpra.ie/products/Human/30862/Licence_PA2315-035-001_02062023143321.pdf
7. cycloPHOSphamide (Endoxana®) Summary of Product Characteristics HPRA. Last updated: 21/12/2018. Accessed August 2025. Available at: https://assets.hpra.ie/products/Human/15729/Licence_PA2299-027-002_21122018112109.pdf

Version	Date	Amendment	Approved By
1	07/10/2025		Dr Larry Bacon

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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