Ontario Health
Cancer Care Ontario

Enrolment Form

CAR T-cell Therapy for Adults with Relapsed/Refractory B-cell ALL

Note: This form should be completed and **funding approved** before apheresis is performed.

Completed form and supporting documentation should be submitted through the online portal: https://mft.cancercare.on.ca.
Username: CARTSubmission
Password: Contact our program at **OH-CCO_CARTSubmissions@ontariohealth.ca**

Ontario Health collects and uses information on this form in order to determine if the patient meets the eligibility and funding criteria for the CAR T-cell Therapy Program, resulting in reimbursement to the treating facility. They also collect and use information on this form for purposes of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system, including the delivery of services, pursuant to Section 45 of the Personal Health Information Protection Act, 2004.

As part of the evaluation of the request, it may be necessary for Ontario Health to disclose the patient's personal health information (PHI) to other administrative programs for health services and insured benefits at the Ministry of Health.

*Required Fields

1. Patient Profile

*Surname: _____

*Given Name: _____

*Date of Birth: DD-MMM-YYYY *(DD-MMM-YYYY or click arrow down button to use calendar to enter the date)*

*Gender: ◯ Male ◯ Female ◯ Other Height (cm): _____ Weight (kg): _____

*Province/Territory of Patient Residence: ◯ AB ◯ BC ◯ MB ◯ NB ◯ NL ◯ NT ◯ NS ◯ NU ◯ ON ◯ PE ◯ QC ◯ SK ◯ YT

*Postal Code of Patient Residence: A1A 1A1

*Provincial/Territorial Health Card Number: _____

Note: If your patient is not a resident of Ontario, a funding approval letter from the patient's provincial/territorial Ministry of Health is required.

2. Enroling Site

*Enroling Site: _____

*Patient Chart Number (MRN) at Enroling Site: _____

*Enroling Physician: Given Name Surname

Enroling Physician CPSO Number (Ontario Only): _____

*Enroling Physician Specialty: _____

*Enroling Physician Email: _____

*Enroling Physician Cell Phone Number: XXX-XXX-XXXX

*Enroling Physician Fax Number: XXX-XXX-XXXX

Alternate Contact Email: _____

Note: If an alternate contact email is provided, the alternate contact will be copied on all email correspondence about this enrolment.

3. Treatment Centre and Product Information

Before submitting this form, confirm the CAR T-cell Therapy Centre has capacity and has agreed to treat your patient. Email or fax confirmation is required when submitting this enrolment package. CAR T-cell Therapy Centre contact details are available at https://www.cancercareontario.ca/en/find-cancer-services/car-t-cell-therapy-centres

*Will this patient receive CAR T-cell therapy in Ontario? ◯ Yes ◯ No

If patient will be treated **in Ontario**, select CAR T-cell therapy site:

◯ Juravinski Cancer Centre - Hamilton Health Sciences

◯ Kingston General Hospital - Kingston Health Sciences Centre

◯ Princess Margaret Cancer Centre - University Health Network

◯ The Ottawa Hospital

If patient will be treated **in another province** in Canada, please provide CAR T-cell therapy site name and city/province: _____

If patient will be treated **out of country**, please indicate the treating facility and **also complete section 8**:

◯ Roswell Park Comprehensive Cancer Center (Buffalo, New York)

◯ Cleveland Clinic (Cleveland, Ohio)

◯ Karmanos Cancer Institute (Detroit, Michigan)

*Treating Physician at CAR T-cell therapy site: Given Name Surname

*Requested CAR T-cell therapy product:

◯ Kymriah (tisagenlecleucel) - for patients between 18 and up to and including 25 years old only

◯ Tecartus (brexucabtagene autoleucel) - for patients 18 years old and above

Note: Switching CAR T-cell products will require replacement of the original funding letter that was issued. Contact the program immediately in case there is a need to use another product.

Anticipated date of apheresis: DD-MMM-YYYY *(DD-MMM-YYYY or click arrow down button to use calendar to enter the date)*

4. Funding Criteria

***A. The patient must meet the following criteria:** ☐ I confirm that my patient meets the funding criteria outlined below:

- Patient has CD19+ relapsed[1] or refractory[2] B-cell lymphoblastic leukemia (B-cell ALL)[3] and:
  - Philadelphia (Ph) chromosome negative and has:
    - Primary refractory disease[2a] or
    - First relapse if remission is ≤ 12 months[4] or
    - Relapsed or refractory disease after two or more lines of systemic therapy[5], or
    - Relapsed or refractory disease after allogeneic stem cell transplant[6]

  or
  - Philadelphia (Ph) chromosome positive and is/has:
    - Intolerant to tyrosine kinase inhibitors (TKI) or
    - Relapsed or refractory disease despite treatment with at least two different TKIs
- Patient has morphological disease in the bone marrow or evidence of peripheral blood or extramedullary disease
- Patient is sufficiently stable to facilitate planned CAR T-cell therapy (e.g., not rapidly progressing on temporizing therapy, no significant compromise of vital organ functions, no need for intubation or dialysis, does not require ICU/pressors and does not have active or uncontrolled infection) and has good performance status[7]
- Patient has not previously received a CAR T-cell therapy

***B. Patient has CD19+ B-cell ALL and is one of the following:** Click arrow down to select (Do not write on this field)

Notes: As evidence and clinical practice evolve, eligibility criteria is subject to change. Additional notes are provided on page 4.

1. Relapse disease occurs in patients who have previously obtained remission and includes:

a. Bone marrow relapse:

· A single bone marrow sample with M3 morphology (>25% lymphoblasts) OR

· A single bone marrow sample with M2 morphology (5-25% lymphoblasts) and confirmatory testing showing ≥5% leukemia blasts by flow cytometry, FISH testing or other molecular method OR

· A single bone marrow sample with M1 morphology (<5% lymphoblasts) and at least two tests showing ≥1% leukemic blasts by flow cytometry, karyotypic abnormality (must display at least 1 metaphase similar/identical to diagnosis), FISH abnormality identical to one present at diagnosis, PCR or NGS-based demonstration of Ig or TCR rearrangement that matches diagnosis and is quantifiable as ≥1% or PCR or NGS-based demonstration of validated leukemogenic lesion (e.g., fusion, mutation) that matches diagnosis and is quantifiable as ≥1%

b. CNS relapse:

· A single CSF sample with CNS-3 status OR

· Clinical signs of CNS leukemia such as facial nerve palsy, brain/eye involvement, or hypothalamic syndrome OR

Notes (continued): Additional notes are provided on page 4.

· A first CSF sample with CNS-2 status and second consecutive CSF sample with CNS-2 status with lymphoblasts confirmed by flow cytometry and/or FISH

c. Extramedullary Relapse, including testicular (biopsy-proven)

2. Refractory disease is defined as patients with detectable leukemia after appropriate therapeutic attempts. This includes:
   a. Primary refractory disease in patients with de novo leukemia who have > 1% disease after two cycles of chemotherapy (commonly considered "end consolidation")
   b. Refractory disease in patients after a relapse who have > 1% disease after one cycle of re-induction chemotherapy
3. Diagnosis of Burkitt's leukemia (mature B-cell ALL)/lymphoma according to the World Health Organization (WHO) classification, or chronic myelogenous leukemia lymphoid blast crisis is not eligible for funding.
4. First relapse with first remission ≤ 12 months: Achieved complete remission (CR) after receiving initial induction standard therapy (minimum residual disease (MRD) negative) but relapsed within 12 months. If bone marrow study shows MRD negative by morphological assessment, submit also results of MRD testing by flow cytometry..
5. Relapse/refractory (r/r) to 2nd- or greater-line therapy: Failure to achieve CR or relapsed after the 2nd- or greater-line therapy.
6. Patients must be at least 100 days from stem cell transplant and off of immunosuppressive medications for at least 4 weeks.
7. The patient does not have active central nervous system involvement or CNS-3 disease (as defined by NCCN Guidelines for acute lymphoblastic leukemia version 4.2023).

5. Treatment History

Date Initiated	Date Completed	Name of Therapy/Regimen	No. of Cycles (if applicable)	Best Response to Therapy
MMMM, YYYY	MMMM, YYYY			Click arrow down to select
MMMM, YYYY	MMMM, YYYY			Click arrow down to select
MMMM, YYYY	MMMM, YYYY			Click arrow down to select
MMMM, YYYY	MMMM, YYYY			Click arrow down to select
MMMM, YYYY	MMMM, YYYY			Click arrow down to select
MMMM, YYYY	MMMM , YYYY			Click arrow down to select

*A. Did the patient have a previous allogeneic stem cell transplant? ◯ Yes ◯ No

i. If yes, provide the date of the patient's allogeneic stem cell transplant? MMMM, YYYY *(Click arrow down button to use calendar to enter the date)*

ii. Did the patient experience graft versus host disease (GvHD)? ◯ Yes ◯ No

If yes, a. Does the patient have active GvHD? ◯ Yes ◯ No

b. Is the patient still undergoing treatment for GvHD? ◯ Yes ◯ No

*B. Did the patient receive any prior non-cellular anti-CD19 therapy? ◯ Yes ◯ No

If yes, i. Provide the date when the patient received the therapy: MMMM, YYYY *(Click arrow down button to use calendar to enter the date)*

ii. Specify the non-cellular anti-CD19 therapy: ◯ Blinatumomab ◯ Tafasitamab ◯ Other: _____

6. Confirmation of Patient Suitability for Therapy

*A. CNS disease status:

◯ No CNS involvement
◯ CNS-1 disease
◯ CNS-2 disease
◯ CNS-3 disease (not eligible for CAR T-cell therapy)
◯ Treated CNS disease

*B. Patient has acute life threatening bacterial, viral (HIV, active hepatitis B or C) or fungal infection:

◯ No infection
◯ Controlled infection
◯ Uncontrolled infection

*C. Karnofsky Performance Status (KPS): ◯ ≤70% ◯ 80% ◯ ≥90%

Date of KPS assessment: DD-MMM-YYYY *(DD-MMM-YYYY or click arrow down button to use calendar to enter the date)*

Renal Function:

*D. Creatinine ≥141.44 µmol/L (1.6 mg/dL): ◯ Yes ◯ No

*E. Estimated glomerular filtration rate (eGFR) ≤45 ml/min/1.73m^2: ◯ Yes ◯ No

Liver Function:

*F. ALT or AST ≥3x upper limit of normal value: ◯ Yes ◯ No

*G. Bilirubin ≥2x upper limit of normal value: ◯ Yes ◯ No

Pulmonary Function:

*H. Pulse oxygenation ≤91% on room air: ◯ Yes ◯ No

Cardiac Function:

*I. Left ventricular ejection fraction (LVEF) ≤40% confirmed by echocardiogram or multiple-gated acquisition (MUGA) scan or radionuclide angiography: ◯ Yes ◯ No

Bone Marrow Function:

*J. Absolute lymphocyte count (ALC) <0.1x10^9/L ◯ Yes ◯ No

Note: If ALC is below 0.1x10^9/L, application can be considered; but for apheresis to proceed, ALC must be at least 0.1x10^9/L.

7. Additional Notes

a. Tisagenlecleucel or brexucabtagene autoleucel is funded only as a one-time therapy.
b. Tisagenlecleucel or brexucabtagene autoleucel is not funded when combined with other treatments for relapsed/refractory B-cell ALL.
c. CAR T-cell therapy infusion must not be within 6 weeks from donor lymphocyte infusion.
d. Patient who have had an allogeneic stem cell transplant and have no active graft versus host disease (GvHD) and are not on immunosuppressive therapy may be eligible for CAR T-cell therapy.
e. A patient with another malignancy may be considered for CAR T-cell therapy if they meet the funding criteria, are suitable for therapy, and are either in complete remission or not undergoing any active drug therapy that could cause serious toxicity and preclude them from receiving CAR T-cell therapy.
f. Patients with history of CNS disease that have been effectively treated are eligible for CAR T-cell therapy.
Active CNS involvement or CNS-3 disease is defined per NCCN guidelines for acute lymphoblastic leukemia (version 4.2023):
CNS-1: No lymphoblasts in cerebrospinal fluid (CSF) regardless of white blood cell (WBC) count.
CNS-2: WBC <5/mcL in CSF with presence of lymphoblasts.
CNS-3: WBC ≥5/mcL in CSF with presence of lymphoblasts.
If the patient has leukemic cells in the peripheral blood and the LP is traumatic and WBC ≥5/mcL in CSF with blasts then compare the CSF WBC/red blood cell (RBC) ratio to the blood WBC/RBC ratio. If the CSF ratio is at least-two fold greater than the blood ratio, then the classification is CNS-3; if not, then it is CNS-2.
g. Patient has no concomitant genetic syndrome such as Fanconi anemia, Kostmann syndrome, Shwachman-Diamond syndrome or any other known bone marrow failure syndrome.
h. At least 3 half-lives must have elapsed from any prior systemic inhibitory/stimulatory immune checkpoint molecule therapy prior to enrolment
i. Patients with an active, uncontrolled infection should not start treatment with CAR T-cell therapy until the infection has resolved or has been appropriately treated. This includes both the lymphodepleting chemotherapy and the CAR T-cell infusion.
j. Patients must meet the funding criteria at the time of enrolment and must continue to be eligible and suitable for therapy at the time of product infusion.

8. Out-of-Country Applications - Additional Requirements

Only complete this section if you are an Ontario physician applying for an Ontario patient to be treated out-of-country:

1. Submit all the documents listed under "Supporting Documents" in section 10.
2. Download, complete and submit the Ministry form “Request for Prior Approval for Full Payment of Insured Out-of-Country (OOC) Health Services." The form can be found in the Central Forms Repository at: https://forms.mgcs.gov.on.ca/en/dataset/on00314

Complete as indicated below:

- Part 1: Patient name, OHIN number, date of birth, mailing address and telephone number
- Part 2: Physician name, office address, telephone number, email address, and OHIP billing number
- Part 3: All required fields, check box confirming completion of CCO Questionnaire; in lieu of the questionnaire form, a completed copy of this enrolment form will be submitted
- Part 4: Auto-completed
- Part 5: All required fields
- Part 6: Submit a completed copy of this enrolment form

9. Acknowledgement

☐ *Yes, I confirm that the patient named above, or relevant substitute decision-maker where applicable, consents that Ontario Health collects and uses information on this form to make funding decisions pursuant to section 38(1)(b) of the Personal Health Information Protection Act, 2004; and for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system, including the delivery of services, pursuant to section 45 of the Personal Health Information Protection Act, 2004. As part of the evaluation and reimbursement process for the CAR T-cell Therapy Program, it may be necessary for Ontario Health to disclose or share the patient's personal health information to other administrative programs for health services and insured benefits at the Ministry of Health or at Ontario Health.

10. Supporting Documents

If the enrolment is for an Out-of-Country treatment for an Ontario patient, the following documentation (from **Lists A and B**) **must be** submitted with the enrolment form. The Ministry form "Request for Prior Approval for Full Payment of Insured Out-of-Country (OOC) Health Services" must also be included in the enrolment package.

If the enrolment is for in-Ontario treatment, the documents under **List A must be** submitted and documents under **List B** should be available upon request (including for the purpose of audit) to confirm eligibility.

***List A: Required upon enrolment**

☐ If any of the answers to section 6 are "Yes", submit relevant and recent laboratory results showing adequate organ function (e.g., kidney and liver function tests, viral serology, cardiac ECHO/MUGA)

☐ Pathology report including the result of BCR-ABL1 (Philadelphia chromosome) genetic test

☐ Documentation of CD19 tumour expression in BM or peripheral blood by flow cytometry. For patients who previously received non-cellular anti-CD19 therapy, submit test result that was performed after completion of therapy. If bone marrow study shows MRD negative by morphological assessment, submit also results of MRD testing with CD19 testing by flow cytometry..

☐ Recent clinic notes that describe the patient's current clinical status and rationale for CAR T-cell therapy over other treatment options. Include any specialist notes (e.g., BMT, neurology, nephrology, cardiology) that informed the treatment plan

☐ If the request is from a treating physician outside an Ontario CAR T-cell treating facility, email or fax from the treating facility/physician confirming that they have capacity and are willing to accept this patient

☐ If the request is for treatment out of country, email or fax from the Ontario CAR T-cell treating facilities confirming no capacity and email or fax from the out-of-country treating facility confirming their capacity and willingness to accept this patient

☐ If the request is for a non-Ontario resident, a funding approval letter from the patient's provincial/territorial Ministry of Health is required, specifying CAR T-cell product(s) that is/are funded by the patient's provincial/territorial Ministry of Health

List B: Available upon request

☐ Bone Marrow (BM) studies including most recent studies

☐ Cerebrospinal Fluid (CSF) studies documenting CNS disease status (within the last 30 days)

☐ Pre- and post-treatment imaging reports e.g., CT scan (post-treatment imaging reports must be within the last 30 days)

☐ Multidisciplinary cancer conference (MCC)/tumour board notes (if available)

*By checking this box, I certify that the information set out in this questionnaire is true and accurate, to the best of my knowledge: ☐ Yes

*Enroling Physician: Given Name Surname *Date: DD-MMM-YYYY *(DD-MMM-YYYY or click arrow down button to use calendar to enter the date)*

Need this information in an accessible format? 1-877-280-8538, TTY 1-800-855-0511, info@ontariohealth.ca