Ontario Health
Cancer Care Ontario

Enrolment Form

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

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

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 - Click arrow down button to use calendar to enter the date)*

*Gender: ◯ Male ◯ Female ◯ Other

*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: ◯ SickKids ◯ Other

If Other, specify: _____

*Enroling Physician: Given Name Surname

Enroling Physician Email: _____

*Enroling Physician Phone Number: XXX-XXX-XXXX

*Enroling Physician Fax Number: XXX-XXX-XXXX

Alternate Contact Email: _____

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

3. Treatment Centre

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

If your patient will be treated out-of-country, please also complete Section 6.

*If patient will be treated **in Ontario**, select CAR T-cell therapy site:
- ◯ SickKids
- ◯ Juravinski Cancer Centre - Hamilton Health Sciences
- ◯ 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 and location: _____

If patient will be treated **out of country**, please indicate the treating facility:
- ◯ Roswell Park Comprehensive Cancer Center (Buffalo, New York)
- ◯ Cleveland Clinic (Cleveland, Ohio)

*CAR T-cell therapy treating Physician: ◯ Same as enroling physician ◯ Other

If Other, specify: _____

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

4. Eligibility Criteria

Standard eligibility criteria are as follows:

- Patient has CD19+ B-cell acute lymphoblastic leukemia (ALL) and: is refractory, has relapsed after allogeneic stem cell transplant (SCT), is ineligible for SCT, or has experienced second or later relapse.
- Patient is younger than 18 years of age.
- Patient has not received prior CAR T-cell therapy.
- Patient is clinically stable, and expected to remain so through to the planned CAR T-cell infusion date. Patient is expected to tolerate the therapy.

All applications that do not satisfy all eligibility criteria are subject to additional review. This may extend the turnaround time to a funding decision.

Patient has CD19+ B-cell acute lymphoblastic leukemia (ALL) and is one of the following:

- ◯ is refractory
- ◯ has relapsed after allogeneic stem cell transplant (SCT)
- ◯ is ineligible for SCT
- ◯ has experienced second or later relapse
- ◯ has Down Syndrome and first relapse of CD19-positive B precursor acute lymphoblastic leukemia (B-ALL)
- ◯ is 4-years or younger with early relapse (within 18 months from diagnosis) of B-ALL involving the CNS (isolated CNS relapse or combined CNS and bone marrow relapse)
- ◯ other[1]

If other, specify: _____

Patient is younger than 18 years of age: ◯ Yes ◯ No

Patient has not recieved prior CAR T-cell therapy: ◯ Yes

Patient is clinically stable, and expected to remain so through to the planned CAR T-cell infusion date. Patient is expected to tolerate the therapy: ◯ Yes

Notes:
1. May require clinical epert review. All supporting documents listed on Section 8 below must be submitted.

For consideration of commercial supply, definitions of relapsed and refractory disease, based on the Children's Oncology Group standards, are outlined below.

Relapse occurs in patients who have previously obtained a remission and includes:

1. Bone marrow relapse:
    - A single bone marrow sample with M3 morphology OR
    - A single bone marrow sample with M2 morphology 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 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%

2. CNS relapse:
    - A single CSF sample with CNS3 status OR
    - Clinical signs of CNS leukemia such as facial nerve palsy, brain/eye involvement, or hypothalamic syndrome OR
    - A first CSF sample with CNS2 status and second consecutive CSF sample with CNS2 status with lymphoblasts confirmed by flow cytometry and/or FISH

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

Refractory disease is defined as patients with detectable leukemia after appropriate therapeutic attempts. This includes:

1. primary refractory disease in patients with de novo leukemia who have > 1% disease after two cycles of chemotherapy (commonly considered "end consolidation")

2. refractory disease in patients after a relapse who have > 1% disease after one cycle of re-induction chemotherapy

5. Notes

1. CAR T-cell therapy infusion must be at least 4 months from date of stem cell transplant.
2. CAR T-cell therapy infusion must be at least 6 weeks from donor lymphocyte infusion.
3. Patient should have no evidence of grade 2-4 graft-versus-host disease (GVHD).
4. Patient should not currently be receiving or require immunosuppression.
5. Patient must not have Burkitt's lymphoma/leukemia (i.e. patients with mature B-cell ALL, leukemia with B-cell [surface Immunoglobulin (sIg) positive and kappa or lambda restricted positivity] ALL, with French-American-British [FAB] L3 morphology and/or a MYC translocation).
6. Patient should not have had a prior malignancy, except carcinoma in situ of the skin or cervix treated with curative intent and with no evidence of active disease.
7. Patients being considered for CAR T-cell therapy who have CNS disease at time of eligibility assessment must have no evidence of active CNS disease at the time of CAR T-cell infusion.
8. Patients with history of CNS disease that have been effectively treated are eligible for CAR T-cell therapy.
    - Active CNS involvement is defined as CNS-3 per National Comprehensive Cancer Network (NCCN) guidelines: white blood cell (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.
9. Patient has no concomitant genetic syndrome (i.e., Fanconi anemia, Kostmann syndrome, Shwachman or other known bone marrow failure).
10. Patient has not received prior treatment with CAR T-cell therapy or any other autologous or allogeneic T-cell immunotherapy.

6. 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" below in Section 8.
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: http://www.forms.ssb.gov.on.ca/mbs/ssb/forms/ssbforms.nsf/FormDetail?OpenForm&ACT=RDR&TAB=PROFILE&SRCH=&ENV=WWE&TIT=4520&NO=014-4520-84

- Complete as indicated below:
  - Section 1: patient name, mailing address and phone number only
  - Section 2: physician name and office address only
  - Section 3: all fields
  - Section 5: all fields up to but not including anything after “If treatment is not available in Ontario”
  - Sections not required: Section 4, 6, and Patient/physician signatures

7. 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 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.

8. Supporting Documents

If the enrolment is for an Out-of-Country treatment for an Ontario patient, the following documentation **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 following documentation **may be requested**. The following should be available upon request to document eligibility.

- 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
- Relevant laboratory results showing adequate organ function (e.g., kidney and liver function tests, viral serology, cardiac ECHO/MUGA if applicable)
- Bone marrow studies
- Cerebrospinal fluid (CSF) studies
- Documentation of CD19 tumour expression in bone marrow or peripheral blood by flow cytometry (within 3 months)
- Cytogenetic testing/molecular marker testing results
- Multidisciplinary case conference (MCC)/tumour board notes confirming that the patient is fit for the treatment and fulfills all eligibility criteria.

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.

*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 - 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