



Case-by-Case Review Policy for Cancer Drugs

Case-by-Case Review Program

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A. PURPOSE

The purpose of the *Case-by-Case Review Program (CBCRP) Policy for Cancer Drugs* is to:

- I. define the requirements for an eligible request to the CBCRP, a program operated by Cancer Care Ontario (CCO), and
- II. to outline the adjudication and reimbursement process.

B. SCOPE

- I. The CBCRP considers funding requests (**CBCRP request**) for take-home cancer drugs (THCDs) and hospital-administered injectable cancer drugs for patients who have rare clinical circumstances that are immediately life threatening, and who require treatment with an unfunded drug because there is no other satisfactory and/or funded treatment.
- II. The CBCRP is not intended to provide interim drug funding for indications (i.e., reason for use) that are currently being reviewed or expected to be reviewed for public funding in Ontario. Manufacturers are aware of the timeframe for funding decisions and it is at their discretion to provide a compassionate supply.
- III. In cases where CBCRP drug coverage is required to fund continued treatment for a drug that was previously funded by a clinical trial, or paid for by other means (such as a third party payor), the request must satisfy all policy criteria (*section E. and F.*) at the time therapy was initiated.
- IV. The CBCRP is intended for patients who require prompt drug funding for cancer therapy in the ambulatory setting. The CBCRP is not intended to fund drugs for acute or emergency use.

C. ELIGIBLE APPLICANTS

Patients cannot make a CBCRP application. The CBCRP applicant (**Applicant**) must be:

- I. a physician who specializes in the treatment of cancer (e.g., medical oncologist, hematologist); and
- II. a physician who is licensed to practice in Ontario (i.e., holds a valid license from the College of Physicians and Surgeons of Ontario); or
- III. a physician licensed in Quebec or Manitoba as per the current criteria of the Ministry of Health's Provincial Borders Drug Program (for THCDs only).



D. ELIGIBLE PATIENTS

To be eligible for drug coverage under the CBCRP, patients must be residents of Ontario and have a valid Ontario Health Insurance Number. If CBCRP coverage is requested for a THCD, the patient must also be eligible for benefits under the Ontario Drug Benefit Program (ODB).

E. APPLICATION CRITERIA

Application criteria will be used to determine whether the request is eligible for consideration under the CBCRP Policy. Requests that do not fulfill all the **application criteria** will not be considered for CBCRP funding.

1. DRUG ELIGIBILITY

- I. The drug must be intended to treat an existing cancer. Funding requests for drugs used in the supportive treatment of cancer (e.g., anti-emetics, colony-stimulating factors) are not eligible for funding.
- II. The drug must be intended for out-patient use (i.e., not for hospital in-patient use) in Ontario.
- III. The drug must be available on the Canadian market (i.e., has a Drug Identification Number) or the Applicant must provide evidence through the *CBCRP Request Form* that approval to import the drug has been obtained through Health Canada's [Special Access Programme](#) (SAP).
- IV. Where biosimilars are available on the Canadian market, CBCRP funding (if approved) will be for the least expensive available product (reference biologic or biosimilar).

2. OTHER FUNDING OPTIONS

Patients must have no other funding option available to them for the requested drug. For the requested indication, each of the following must be true for the request to be eligible:

- I. the patient cannot access the drug through a clinical trial;
- II. the patient cannot receive a compassionate supply or funding from the requested drug manufacturer;
- III. the requested drug is normally expected to be funded by the treating hospital or another public funding program (e.g., Systemic Treatment-Quality Based Procedure); and
- IV. the patient is not already receiving funding through another public drug funding program for the requested drug (e.g., ODB's Exceptional Access Program, New Drug Funding Program, etc.).



3. PUBLIC FUNDING STATUS

The drug for the requested indication cannot be currently funded or expected to be considered for a population-based funding program in Ontario. As such, requests that are ineligible for CBCRP funding consideration include the following:

- I. The drug for the requested indication is expected to be reviewed for public funding in Ontario (e.g., pending review by the pan-Canadian Oncology Drug Review or Common Drug Review, indications approved by Health Canada or the U.S., Food and Drug Administration, etc.).
- II. The drug for the requested indication is under review for public funding in Ontario.
- III. The drug for the requested indication has been reviewed and funding criteria has been established under another public drug funding program in Ontario (e.g., ODB's Exceptional Access Program, New Drug Funding Program, etc.).
- IV. The drug for the requested indication has been reviewed and rejected for public funding in Ontario.

Note: For the purpose of assessing **E.3**, an “indication” refers to the patient’s type of cancer, regardless of the line of therapy.

F. FUNDING CRITERIA

The request will be evaluated against the following **funding criteria** to determine whether it aligns with the intent of the program.

1. URGENCY

The patient presents with an immediately life-threatening condition (i.e., the patient’s condition is such that a loss of life is likely to occur within a matter of months).

2. RARITY

The patient must have a rare clinical circumstance (e.g., the cancer itself may not be rare, but the patient’s comorbidities, allergies, severity of symptoms, or other factors make the clinical situation rare) such that less than 25 similar requests are anticipated per year.

3. EVIDENCE

- I. The Applicant must submit published evidence supporting the use of the drug for the requested indication. The patient’s apparent response to treatment, in itself, is insufficient evidence of effectiveness.
- II. Based on the best available evidence and the totality of evidence, the therapy is expected to provide a clinically meaningful outcome in this patient. The following factors



will be evaluated:

- a. **Level of evidence:** The minimum level of evidence required is a case- series or multiple-case reports where $n \geq 25$ in total. Ideally, randomized controlled trial (RCT) data should be available; individual case reports and expert opinion provide the lowest level of evidence and may be considered insufficient data to support a CBCRP request.
- b. For requests where direct evidence is below the minimum level required due to the rarity of the cancer or the clinical presentation, the CBCRP may accept and consider data from comparable, and potentially more common, clinical circumstances as supporting evidence. The clinical justification for this extrapolation must be provided.
- c. **Clinical Benefits:** Under this clinical circumstance, evidence supports survival of a significant duration (e.g., prolong survival by months) with the requested drug. For requests where survival evidence is weak and survival is an unlikely treatment goal given the nature and stage of the disease, quality of life may be considered.
- d. **Safety:** Under this clinical circumstance, evidence supports that treatment-related toxicity is acceptable and manageable.
- e. **Overall Impact:** The expected clinical outcomes from the therapy must be meaningful and superior when compared to all other available treatment options.* The applicant must justify that the potential benefits of therapy outweigh the risks.

**Note:* Where palliative or best supportive care (BSC) is an alternative treatment option, the applicant must provide a rationale for the expected benefits to quality of life and survival for the requested drug compared to BSC.

4. ALTERNATE TREATMENT OPTIONS

The patient does not have other treatment options that are comparable or superior in effectiveness and/or toxicity to the requested drug for the requested indication. Specifically, each of the following options has been deemed a therapeutic failure or is clinically inappropriate:

- I. non-pharmacological alternatives;
- II. comparable alternatives available through another publicly funded drug program in Ontario (e.g., the New Drug Funding Program, the Ontario Drug Benefit Formulary, Exceptional Access Program, Systemic Treatment - Quality Based Procedure, etc.);
- III. any other comparable cancer regimens, including those that can be offered as part of a local clinical trial.



5. COST OF REQUESTED DRUG

- I. Where treatment options with comparable clinical benefits exist, the requested drug should be the least expensive treatment option. Should the requested drug be a more expensive option, the applicant must provide an objective rationale why a more expensive option is being requested (e.g., contraindications, unacceptable toxicity).
- II. Treatment with the requested drug is reasonably expected to avoid or defer other health care costs (e.g., hospitalization, physician visits, etc.).
- III. In cases where the cost impact of the requested drug is significant, a more detailed analysis of cost and benefit as it relates to the requested drug may be conducted before a funding decision is made.

G. REVIEW PROCESS

The review process for **new requests** is comprised of the following components:

- I. **Application Completeness:** CCO will screen each request for completeness. In the case of missing information, CCO will contact the Applicant as necessary. CCO may also contact the Applicant to further clarify some of the information provided on the Request Form. Applications which remain incomplete after 10 days from the date of submission will be closed. The application will be deemed incomplete if any of the following are missing:
 - Mandatory questions on the Request Form
 - Clinical documents
 - Supporting evidence
- II. **Evaluation of Application Criteria:** Upon receipt of a complete application, CCO will assess the request against the application criteria (*section E.*). If necessary, CCO may consult with external clinical experts to verify application criteria. Requests that **do not meet any one of the application criteria** are “CBCRP Ineligible” and will not be assessed further.
- III. **Evaluation of Funding Criteria:** CCO will assess the request against the funding criteria (*section F.*). In the evaluation, CCO will consider the clinical information and justification for therapy submitted by the applicant, the best available evidence and expert opinion. This evaluation will be omitted for requests that are “CBCRP Ineligible.”
- IV. **External Clinical Expert Opinion:**

CCO will forward requests for independent external review by clinical experts:

- Clinical experts may be either oncologists or hematologists as appropriate. At least one clinical expert must be a specialist with an understanding of the disease condition for which the request is being submitted.
- Clinical experts will provide an opinion on clinical appropriateness to CCO by considering the patient’s clinical situation, best available evidence, and intent of this policy.



- Requests that **definitively do not meet any of the application criteria or the funding criteria** will not be forwarded for external review.

V. **Funding Recommendation:** CCO will summarize how the request aligns with the policy and provide a funding recommendation to the Executive Officer. For a **positive funding** recommendation, each of the following must be met:

- a. The request satisfies all of the Application Criteria.
- b. Upon evaluation against the Funding Criteria, the request meets the intent of the policy.
- c. At least two clinical experts support the use of the drug for the requested indication in this patient. In cases of divergent clinical opinions, a third opinion by a clinical expert will be obtained.*

**Note:* If necessary and where appropriate, CCO may make a positive funding recommendation to the Executive Officer where only one clinical expert has reviewed the request. This will not be permitted for drugs and indications that have not been previously reviewed by the CBCRP following the typical external review process.

H. FINAL FUNDING DECISION

- I. The Executive Officer will review each CBCRP request and will make the final funding decision with respect to the drug. Requests that definitively do not meet the application criteria (*section E.*) or the funding criteria (*section F.*) will be reviewed by the Executive Officer, as necessary.
- II. CCO will inform the Applicant, in writing, of the Executive Officer's final decision.
- III. When a decision is made not to approve a CBCRP request, CCO will inform the Applicant, in writing, of the rationale for rejection and the options available to the Applicant for a negative funding decision.

I. CONDITIONS OF REIMBURSEMENT

For approved requests, the cost of the drug will be reimbursed and is subject to the conditions outlined below:

- I. The dose, frequency, duration, and route of administration that will be approved for the drug will be determined on a case-by-case basis, and based on the information provided in the application. The decision will be based on the Applicant's proposed treatment plan, the best available evidence, and clinical expert opinion provided to the CBCRP during its evaluation of the request. In the event of treatment plan changes, the Applicant should contact the CBCRP to confirm continued eligibility and reimbursement.



- II. Hospital-administered injectable cancer drugs (e.g., *intravenous cancer drugs*), will be funded by the CBCRP as follows:
 - a. The CBCRP will directly reimburse CCO-affiliated hospitals, for doses administered, where the patient is receiving treatment.
 - b. For any of the following situations, doses will not be reimbursed by the CBCRP :
 - i. Doses administered in a private clinic.
 - ii. Doses administered while the patient is admitted to the hospital (i.e., occupying a bed in any hospital ward).
 - iii. Doses administered in the setting of known disease progression.
 - c. The reimbursement rate will be as follows:
 - i. If the drug is currently funded by the New Drug Funding Program (NDFP), the reimbursement rate will be based on the current Provincial Drug Reimbursement Programs (PDRP) price list at the time the dose is administered.
 - ii. If there is an NDFP-funded biosimilar to the reference biologic requested, the CBCRP will only reimburse hospitals at the best available price for the listed biosimilar (if available) or reference biologic.
 - iii. The CBCRP will follow the NDFP reimbursement policies (e.g., price adjustments, biosimilar policies) as required.
 - iv. If the approved drug is not on this list, the reimbursement rate will be based on the hospital acquisition cost.
 - d. To be reimbursed, the hospital must submit treatment data for each patient on a monthly basis and invoices, as requested, by the CBCRP.
- III. THCDs (e.g., oral chemotherapy) will be funded by ODB. Patients must qualify for benefits under ODB to be reimbursed.
- IV. The Systemic Treatment – Quality Based Procedure will reimburse eligible hospitals for delivery costs associated with CBCRP approved hospital-injectable cancer drugs or THCDs.
- V. Date of coverage begins on the “effective date” and extends to the “expiry date” stated on the approval letter issued to the applicant by the CBCRP. Doses administered **prior to the effective date will not be reimbursed.**
- VI. If there is a significant change in patient circumstances, treatment plan, a lengthy delay (e.g., > 30 days) to initiating treatment or a lengthy treatment interruption (e.g., > 30 days), the CBCRP may request additional documentation and/or reassess eligibility prior to providing reimbursement. Failure to provide the required documentation will result in the termination of coverage.



J. RENEWALS

- I. Once the duration of drug coverage is near expiration, the CBCRP will accept requests for renewals (**Renewal**).
- II. To allow for adequate review time, a request for Renewal should be initiated at least 3 weeks prior to the patient finishing his/her current supply of the requested drug. Doses dispensed or administered in the absence of approved funding may not be reimbursed.
- III. A renewal will be evaluated on the following criteria:
 - a. **Treatment response:** There must be evidence of an objective measure(s) of response.
 - b. **Toxicity:** Treatment-related toxicity is acceptable and manageable.
 - c. **Expected Outcome:** At the time of renewal, there have been no significant changes in the patient's clinical condition, treatment plan, or other factors to suggest that the outcome of therapy for which the drug was initially approved is no longer expected.
- IV. CCO reviews each Renewal, in consultation with clinical experts, and makes a funding recommendation to the Executive Officer. **For a positive funding recommendation**, the criteria stated in *section J(III.)* must be satisfied and the opinion of at least one clinical expert supports continued therapy.
- V. The Executive Officer makes the final funding decision for each Renewal.
- VI. CCO may close applications for missing information as per *section G(I.)*.



K. OPTIONS IN THE EVENT OF A NEGATIVE FUNDING DECISION

Where a negative funding decision has been rendered by the Executive Officer, the Applicant has the following options:

- I. Within thirty days of the funding decision being communicated to the Applicant by the CBCRP, the Applicant may:
 - a. Resubmit additional evidence in response to the reason for the rejection **(Resubmission)**. A Resubmission will be assessed as per *sections E. through G.* of this Policy. The clinical experts who assessed the initial CBCRP request may also assess the Resubmission;

or

 - b. Appeal the funding decision; where there is no new additional evidence, but the Applicant feels that the CBCRP policy has been improperly applied to his/her request **(Appeal)**. Appeals will be assessed in accordance with the *CBCRP Appeals Policy*.
- II. After thirty days of a negative funding decision being communicated to the Applicant by the CBCRP, the Applicant must submit a new application for the request to be re-considered by the CBCRP.

L. TIMELINES FOR REVIEW

Upon receipt of a complete application, the CBCRP will aim to provide a funding decision from the Executive Officer within two weeks.

M. POST-TREATMENT DOCUMENTATION REQUIREMENTS

Upon completion of therapy or if treatment is discontinued for any reason, the CBCRP may, in its sole discretion, request that the Applicant provide certain follow-up information regarding patient response and program measures. This information will be used by CCO for planning and program management purposes.



N. GLOSSARY

ABBREVIATIONS

BSC	Best Supportive Care
CCO	Cancer Care Ontario
EAP	Exceptional Access Program, Ministry of Health
EO	Executive Officer, Ontario Public Drug Programs, Drugs and Devices Division, Ministry of Health
NDFP	New Drug Funding Program
ODB	Ontario Drug Benefit Program, Ministry of Health
PDRP	Provincial Drug Reimbursement Programs
RCT	Randomized Control Trial
SAP	Health Canada’s Special Access Programme
THCD	Take-Home Cancer Drug

TERMS

I. Drug Classifications:

Biologic: Refers to the Health Canada definition of a biologic drug:¹ *A drug listed in Schedule D to the Food and Drugs Act.*

Biosimilar: Refers to the Health Canada definition of a biosimilar biologic drug:¹ *A biologic drug that obtains market authorization subsequent to a version previously authorized in Canada, and with demonstrated similarity to a reference biologic.*

Reference biologic: Refers to the Health Canada definition of a reference biologic drug:¹ *A biologic drug authorized on the basis of a complete quality, non-clinical, and clinical data package, to which a biosimilar is compared to demonstrate similarity.*

Hospital-administered injectable cancer drug:

Refers to any injectable cancer medication which is administered in an outpatient hospital setting (e.g., chemotherapy suite, infusion or day clinic).

¹ Health Canada. Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs. <https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/information-submission-requirements-biosimilar-biologic-drugs-1.html#def>



Take-home cancer drug (THCD):

Typically refers to oral medications, but also include drugs for self-injection (e.g., drugs injected into the skin or muscle). These medications may be used in the active treatment of cancer or as supportive therapies. These medications are may be dispensed from retail/community pharmacies or cancer centre pharmacies.

II.Request Types

- New:** The first request to the CBCRP for a given drug and indication for a specific patient.
- Renewal:** A request that was previously approved for CBCRP funding has been re-submitted for continued funding.
- Appeal:** The initial request has been declined for funding and the applicant feels that the CBCRP policy has been improperly applied. An “appeal” is filed within 30 days of the negative funding decision and assessed against the *CBCRP Appeals Policy*.
- Resubmission:** The initial request has been declined for funding but the applicant submits new additional evidence within 30 days of being notified of the negative funding decision. The “resubmission” is re-assessed against the *Case-by-Case Review Policy for Cancer Drugs*.

III.Request Outcomes

- Approved:** Request meets both application and funding criteria and is approved by the Executive Officer, Ontario Public Drug Programs for funding.
- Declined:** Request meets the application criteria but does not meet one or more of the funding criteria.
- Ineligible** Request does not meet one or more application criteria.
- Closed** Request closed by the CBCRP for missing information or other reasons. For missing information, the file is closed 30 days from date of application or if the applicant fails to respond to a request for missing information with 10 days.
- Withdrawn** Applicant withdraws request prior to the funding decision being rendered.