Ontario Health
Cancer Care Ontario

Policy: Public Funding of Cancer Drugs within the Context of Clinical Trials

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Introduction

The Ministry of Health (ministry) and Ontario Health are strongly supportive of clinical trial research and believe it is an important component of high quality care that strives to improve the outcomes of cancer patients in Ontario.

Clinical trials help to advance the scientific understanding of cancer and its treatment. Patients may be given the option to enter into clinical trials at some point in their cancer treatment journey. Increasingly, public payers are being asked to reimburse publicly funded cancer drugs when they are used as a component of clinical trials research, or after the patient has participated in a clinical trial.

In the past, drug reimbursement programs were faced with difficult adjudication decisions when it was identified that patients participating in clinical trials had become ineligible for publicly funded cancer drugs. Patients and clinicians may not have been aware of cancer drug funding implications when patients were enrolled into a clinical trial.

These challenges have led to the development of this policy, which introduces an application and assessment process to provide guidance as to how participation in a particular clinical trial may impact eligibility for public cancer drug funding. The intent of this policy is to clarify how access to public cancer drug funding may be affected by participation in a clinical trial, both during or subsequent to a trial.

Background on public funding of cancer drugs

Ontario has an established process for evaluating cancer drugs for public funding. The drug funding policies under the New Drug Funding Program (NDFP), High Cost Therapy Funding Program (HCTFP), the Ontario Drug Benefit (ODB) Program (Exceptional Access Program (EAP) and Formulary listing either as General Benefit (GB), GB with Therapeutic notes, or Limited Use (LU)), or the Systemic Treatment-Quality Based Procedure (ST-QBP) are aligned with the evidence from the trials that established their clinical benefit.

The ministry funds cancer drugs for eligible patients when the drugs are used in accordance with the reimbursement criteria that have been approved through an established process for publicly funded drugs within the province. If the eligible patient happens to be a participant in a clinical trial involving the cancer drug for which the patient meets usual public funding criteria, then the drug administered to the patient in the trial would be publicly funded. The ministry also provides funding for the administration costs when the drugs or regimens are listed as evidence-informed for funding through the Systemic Treatment-Quality Based Procedure. However, it is important to note that the ministry does not directly fund clinical trials.

Definitions

Aligned for the purpose of drug funding: A publicly funded cancer drug used within or subsequent to a clinical trial is used in accordance with the existing drug funding policy.

Aligned to Systemic Treatment-Quality Based Procedure (ST-QBP): For the purpose of funding through the Systemic Treatment-Quality Based Procedure, a clinical trial is an intervention to evaluate a drug or biologic agent for its anti-cancer activity, which has undergone institutional (peer) review and received ethics approval at the institutional or provincial level. Clinical trials meeting this definition will receive funding for the cost of evidence-informed drugs (and their administration) if the drugs are not funded through Provincial Drug Reimbursement Programs or Ontario Public Drug Programs (i.e., older and inexpensive drugs). Clinical trials that do not evaluate the anti-cancer impact of a new drug or regimen

but are designed to assess only a diagnostic, symptom management or resource utilization question, for example, would be considered to be "not aligned". However, if patients are receiving an evidence-informed standard of care within the context of a "non-aligned" trial, the hospital will still receive funding for the evidence-informed treatment and its administration.

Applicant: A practising physician affiliated with an Ontario hospital who is involved in the clinical trial that is recruiting patients at his/her hospital.

Application: A completed Clinical Trial Request Intake form.

Biologic drug (or biologic): A medicine derived from living organisms or from their cells, often made using biotechnology. Biologics are used to treat diseases and medical conditions including anemia, diabetes, inflammatory bowel disease, psoriasis, rheumatoid arthritis, hormone deficiency, and some forms of cancer. These medicines are generally larger and more complex than chemically produced pharmaceuticals.

Biosimilars: A drug demonstrated to be highly similar to a biologic drug that was already authorized for sale (known as the reference biologic drug). There are no expected clinically meaningful differences in efficacy and safety between a biosimilar and the biologic drug that was already authorized for sale. Biosimilars are approved based on a thorough comparison to a reference drug and may enter the market after the expiry of reference drug patents and data protection.

Clinical trial: A type of clinical study in which participants are assigned to groups that receive one or more intervention/treatment (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study's protocol. Participants may receive diagnostic, therapeutic, or other types of interventions. [1]

Drug funding policy: Lists the eligibility criteria for a specific cancer drug or combination of cancer drugs for a given indication (i.e., reason for use) that are publicly funded under the New Drug Funding Program (NDFP), High Cost Therapy Funding Program (HCTFP), the Ontario Drug Benefit (ODB) Program (Exceptional Access Program (EAP) and Formulary listing either as General Benefit (GB), GB with Therapeutic notes, or Limited Use (LU)). The criteria in each drug funding policy is approved by the Executive Officer of the Ontario Public Drug Programs (OPDP), Ministry of Health.

Exceptional Access Program (EAP): Facilitates patient access to drugs not funded on the Ontario Drug Benefit (ODB) Formulary, or where no listed alternative is available. In order to receive coverage, the patient must be eligible to receive benefits under the ODB program. EAP requests are reviewed on a case-by-case basis according to reimbursement criteria developed through an established evidence-based drug review process.

Indication: The purpose or use of a treatment or intervention.

Limited Use (LU): Drugs that are listed in the Ontario Drug Benefit (ODB) Formulary with specific clinical criteria/conditions for use and will be reimbursed under the ODB program only when those criteria/conditions have been met.

[1] Clinicaltrials.gov. (2020). Clinical trial. Glossary of common site terms. Retrieved April 5, 2021, from https://clinicaltrials.gov/ct2/about-studies/glossary

Line of therapy: For many cancers, a sequence of standard treatment options is used. A line of therapy refers to a place in this sequence. Historically, clinical trials and health technology assessments of cancer drugs have been established on lines of therapy and consequently, lines of therapy have been included in the eligibility criteria of publicly funded cancer drugs. As a general principle, a cancer drug used within a clinical trial is considered a line of therapy. In certain circumstances, it may be reasonable to consider the cancer drug or regimen used within a clinical trial as an investigational line (i.e., not a line of therapy) if any of the following applies:

- Sufficient evidence does not exist for that cancer drug in that type of cancer and treatment setting (e.g., metastatic or adjuvant).
- The cancer drug does not have a Health Canada Notice of Compliance (NOC) for the requested indication.
- The cancer drug is used in a dose, route or schedule substantially different from the publicly funded dose, route or schedule.
- The cancer drug is used in combination with other drugs for an indication for which the combination is not publicly funded even if each of the individual agents is publicly funded for the clinical indication.

New Drug Funding Program (NDFP): A publicly funded drug program within the Ontario Public Drug Programs (OPDP). NDFP directly covers the cost of many newer, and often very expensive, injectable cancer drugs administered in hospitals and cancer centres.

Not aligned for the purpose of drug funding: A publicly funded cancer drug used within or subsequent to a clinical trial that is not in accordance with the existing drug funding policy.

Ontario Drug Benefit Program (ODB): The ODB Program provides coverage for over 4,400 drug products. With funding provided by the Ministry of Health and the Ministry of Community and Social Services, the ODB Program covers most of the cost of prescription drug products listed in the Formulary. As well, drugs that are not listed in the Formulary are considered for coverage, on a case-by-case basis, through the Ministry of Health's Exceptional Access Program (EAP).

Ontario residents: Residents of Ontario who have a valid Ontario Health Card.

Reconsideration: The applicant may request a reconsideration of an initial application or a resubmission request with a negative assessment (i.e., not aligned), if the applicant believes the assessment criteria were wrongfully applied to the application in the absence of new pertinent information that may change the assessment.

Regimen: A drug or combination of drugs that is given according to a specific dose, schedule, and duration.

Resubmission: The applicant may request a resubmission of an initial application with a negative assessment (i.e., not aligned), if the applicant has new evidence or pertinent information that may change the assessment.

Systemic Treatment-Quality Based Procedure (ST-QBP): Funds hospitals for the cost of administering cancer chemotherapy. Funding from ST-QBP may also cover the cost of some older and inexpensive generic drugs not otherwise funded through other drug funding programs.

Scope

This policy will

- Provide clarity and transparency as to how participation in a clinical trial may potentially impact the patient's eligibility for public funding of cancer drugs
- Describe the framework, criteria and process by which clinical trial applications will be assessed
- Clarify when older or inexpensive drugs, the preparation and delivery of treatment, and related clinical care for patients on clinical trials is provided through the ST-QBP.

This policy will not

- Promote funding of a cancer drug or regimen beyond the original evidence-informed intent for which it is publicly funded either through NDFP, HCTFP, ODB (EAP, LU), or ST-QBP
- Provide interim drug funding for indications that are under review or expected to be reviewed for public funding in Ontario
- Approve or fund clinical trials.

Application and assessment overview

The clinical trials application and assessment process will enable Ontario Health to provide guidance as to how clinical trial participation may impact eligibility for public cancer drug funding. An application for assessment of a clinical trial will not necessarily ensure that there will be funding available for the drugs used in the trial or used subsequent to the trial in the management of the patient. A patient-specific NDFP or HCTFP enrolment, EAP application or LU prescription by a referring clinician would still be required to confirm patient eligibility. A patient's eligibility for public cancer drug funding is determined by the existing NDFP, HCTFP, EAP, LU or other drug funding program processes and criteria, which are initiated by a referring clinician on behalf of an individual patient.

Clinicians must apply directly to EAP if requesting EAP drugs within or subsequent to clinical trial participation. Clinicians must document the trial identifier and the use of the investigational agent(s) in the EAP application. Further, patients must be eligible to receive ODB benefits. All copays and deductibles associated with the program must continue to be satisfied.

After receiving a Clinical Trial Request Intake form, Ontario Health will provide an assessment of the clinical trial to the applicant in accordance with this policy. The assessment will be made publicly available on the Ontario Health (Cancer Care Ontario) website, and will clarify whether participation in the clinical trial is likely to render the patient ineligible for publicly funded cancer drugs (and if so, which drugs and under what circumstances), based on the drug funding policies in effect at the time of the assessment. However, funding decisions are made on a patient-specific basis through existing drug funding programs. A clinical trial assessment does not constitute a funding decision, but provides general guidance based on current drug funding policies.

Since drug funding policies could change over time, patients must meet criteria at the time funding is sought. The clinical trial assessment does not replace patient-specific NDFP, HCTFP, EAP, LU or other drug funding program approvals required at the time of the funding request.

Application process

- An application must be completed by a practising physician in Ontario. A single applicant may apply on behalf of multiple participating hospitals in Ontario.
- An application must be completed in full for each trial and submitted to OH-CCO_ClinicalTrials@ontariohealth.ca.
- It is recommended that a completed application be submitted for review as soon as the information is available. This can be submitted prior to or simultaneously with a submission to a Research Ethics Board for review.
- Upon receipt of a completed application, Ontario Health will aim to provide a full assessment to the applicant within 30 days. Turnaround time may be extended if additional information is required or if the assessment is complex and requires further consultation with disease site experts and the ministry.

Application screening criteria

- Ontario Health will screen each application for completeness. Applicants will be contacted as necessary if there is missing information. Requests will not be assessed until the application is deemed complete. The onus is on the applicant to provide complete and accurate information.
- For an application to be complete, the following must be included
    - The clinical trial schema
    - The cancer drug(s) and indication(s) for which cancer drug funding is being requested
    - The cancer drug(s) and indication(s) funded by the clinical trial sponsor
    - The dosing schedule
    - The standard of care the patient would receive if not on a clinical trial
- The application must clearly identify the treatment algorithm for all study arms subsequent to trial participation. This includes an explanation of patient management if
    - The patient is withdrawn from study due to excessive toxicity
    - There is disease progression
    - The patient refuses further participation on the trial
    - There is disease recurrence after the trial is completed
- Potential cancer drug funding implications associated with clinical trial participation, particularly those related to the use of publicly funded cancer drugs subsequent to participating in a clinical trial, should be identified in the application (e.g., when eligibility criteria for the requested cancer drug funding policy may not be met if the patient participates in a clinical trial). Ontario Health may identify additional potential policy implications in the context of its evaluation and will communicate to the applicant via the assessment.

Assessment criteria

The following assessment criteria and considerations will be used to provide guidance as to whether a publicly funded cancer drug used within a trial, or subsequent to a trial may be eligible for public funding in Ontario, based on current drug funding policy.

Drug Eligibility

- The use of the publicly funded cancer drug within a clinical trial must meet the current eligibility criteria and cancer drug funding policy in Ontario.
- If there is a publicly funded biologic cancer drug used within trial that meets the publicly funded criteria and indication for the biosimilar, only the biosimilar will be eligible for public funding.

Considerations

- Additional treatments, cycles, or duration of therapy for the publicly funded cancer drug that is significantly different from the approved cancer drug funding policy will not be funded.
- Additional cumulative dose or duration of administration for the publicly funded cancer drug that is significantly different from the approved cancer drug funding policy will not be funded.
- A cancer drug within a clinical trial will only be publicly funded if the patient meets the usual public funding criteria for that drug which considers the indication and specific clinical criteria.
- Assessment of line of therapy
    - As a general principle, a cancer drug used within a clinical trial is considered a line of therapy. In certain circumstances, it may be reasonable to consider the cancer drug or regimen used within a clinical trial as an investigational line (i.e., not a line of therapy) if any of the following applies:
        - Sufficient evidence does not exist for that cancer drug in that type of cancer and treatment setting (e.g., metastatic or adjuvant).
        - The cancer drug does not have a Health Canada Notice of Compliance (NOC) for the requested indication.
        - The cancer drug is used in a dose, route or schedule substantially different from the publicly funded dose, route or schedule.
        - The cancer drug is used in combination with other drugs for an indication for which the combination is not publicly funded even if each of the individual agents is publicly funded for the clinical indication.
    - When a cancer drug funding policy stipulates a line of therapy, the following will be assessed for each requested drug
        - The current cancer drug funding algorithm or expected sequence.
        - The current cancer drug funding policy criteria.
        - A comparison of the mechanism of action of the cancer drug(s) used within the clinical trial to cancer drug(s) used subsequent to the clinical trial.
- A clinical trial that evaluates an investigational agent in a single arm study may receive funding through the ST-QBP for the administration of the investigational agent.
- Clinical trials evaluating new drug treatments against a standard of care intervention in a phase II or III trial may receive funding support for the administration of the standard of care regimen. The participating hospitals may also receive reimbursement for the drugs used within the clinical trial either through ST-QBP (for older and inexpensive generic drugs), HCTFP, NDFP and/or ODB, upon meeting the public funding criteria.

Review process

The review process consists of the following:

- Upon receipt of a complete application, Ontario Health program staff will assess the request against the current drug funding policy.
- Ontario Health program staff will consult with ministry program staff as appropriate (i.e., when requests involve cancer drugs funded through ODB (EAP or LU) or where interpretation of this policy is required).
- Ontario Health program staff will consult with disease site specific experts as appropriate (i.e., if clinical input is required).
- Ontario Health program staff will prepare the assessment and notify the applicant via email. The use of identified publicly funded cancer drugs during or subsequent to the trial will be deemed "aligned" or "not aligned" with current drug funding policy. The administration costs of treatment will be deemed "aligned" or "not aligned" with ST-QBP's definition of a clinical trial. Where applicable, Ontario Health will provide the applicant with information on potential funding implications. The applicant is responsible for communicating the outcome of the assessment and relevant information to other Ontario investigators, as appropriate.
- Assessment results, and a list of all assessed and under review applications will be published weekly on the clinical trials assessment table posted on Ontario Health (Cancer Care Ontario)'s Systemic Treatment Clinical Trials webpage.

Re-evaluation, reconsideration and resubmission

Re-evaluation

Over time, new information may emerge that may change the assessment of an application (e.g., a new cancer drug becomes publicly funded or a revision is made to an existing drug funding policy). Patients must meet funding criteria at the time funding is sought. In the event that Ontario Health becomes aware that new information may impact the assessment of a clinical trial, the application(s) will be re-evaluated, the original applicant will be informed if there is a change in the assessment, and the clinical trials assessment table will be updated and posted on Ontario Health (Cancer Care Ontario)'s Systemic Treatment Clinical Trials webpage.

There are two options available to an applicant who has received a negative assessment (i.e., "not aligned"):

Resubmission

The applicant may file another submission following an initial application with an assessment of "not aligned" if the applicant has new evidence or pertinent information that may change the assessment. To resubmit, the applicant must highlight the new information on the initially submitted application form and email it to OH-CCO_ClinicalTrials@ontariohealth.ca. Ontario Health will review resubmissions filed at any point after a negative assessment.

Ontario Health will aim to provide a re-assessment to the applicant within 30 days. Turnaround times may be extended if additional information is required or for complex requests that require further consultation with disease site experts and/or the ministry.

Reconsideration

Within 30 days of the date specified on the final assessment, the applicant may request a reconsideration of an initial application or a resubmission request with a negative assessment (i.e., not aligned), if the applicant believes the assessment criteria were wrongfully applied to the application but does not have new evidence or pertinent information that may change the assessment. The applicant must file for reconsideration to OH-CCO_ClinicalTrials@ontariohealth.ca with the following information:

- Identify and explain which criteria were wrongfully applied.
- Describe how the drug funding policy was incorrectly applied or interpreted.

The reconsideration will be reviewed by a panel, which may include disease site specific experts, Ontario Health program staff and clinical leads, and ministry program staff who may or may not have previously assessed the application.

No new information will be allowed in the case of a reconsideration. Applicants with new information should file a resubmission, as described above.