



# Oral Cancer Drug Therapy Safe Use and Safe Handling Guidelines

## Introduction

The use and availability of oral cancer drug therapy<sup>a</sup> is a growth phenomenon internationally. Globally, 25-50% of the more than 400 new cancer drugs in development are for oral agents (1,2,3). In Canada, approximately 60% of the submissions to the pan-Canadian Oncology Drug Review are for oral agents, thereby increasing the likelihood of their availability in the Canadian market (4). Notwithstanding the numerous benefits that these drugs offer patients and their caregivers, concerns about safe patient use and safe handling of these hazardous drugs are being raised in many jurisdictions (5-9). Self-administration of oral cancer drug therapy transfers responsibility for administration and monitoring from a team of healthcare professionals to the patient, and may diminish opportunities to quickly identify and intervene when toxicity or side effects become apparent (10-12). From a systems perspective, processes that are in place to ensure the safe administration of intravenous cancer drug therapy are often lacking for self administration of oral cancer drug therapy. The absence of similar standards should raise serious concerns about the safe delivery of patient care given that oral cancer drug therapies are associated with potential for severe adverse events as well as dose limiting and fatal toxicities.

Many high-income countries and discipline-specific professional associations have reported similar concerns. Though there is little consolation in being among peers whose systems and processes may inadvertently and unintentionally place patients at risk, this knowledge provides the opportunity to learn from the global community to drive quality and safety at home. Our vision as leaders of Canada's cancer delivery system is to move beyond being amongst our peers to having the safest oral cancer drug therapy delivery system in the world.

The Canadian Association of Provincial Cancer Agencies (CAPCA) is a pan-Canadian association of provincial cancer agencies and programs who are responsible for setting standards for the delivery of cancer care in each province. In British Columbia, Alberta, Saskatchewan, Manitoba, and Newfoundland these agencies are also responsible for providing direct patient care. This position statement describes the shared opinions of the leaders of these organizations with respect to the safe use and safe handling of oral cancer drug therapy, and options to enhance prescribing, dispensing, administration, monitoring, and education. Most importantly, this position statement provides recommendations to close the gap that currently exists between the safe handling and safe use of intravenous and oral cancer drug therapy.

## Principles

Our vision to have the safest oral cancer drug delivery system in the world is a reflection of the following guiding principles:

- Patient focused: We are respectful and responsive to patient preferences, needs, values, and experiences, and have engaged patients in the development of this guideline and in articulating a path to move towards our vision.
- Evidence-informed: Our recommendations are based on the best evidence that exists. Where evidence is limited, consensus opinion and best practice have admittedly been influential.
- Performance driven: We are prepared to find, evaluate, test, and implement strategies that will enhance the safe use and handling of oral cancer drug therapy. Given the interconnectedness between provincial cancer agencies and programs, we are prepared to support and learn from pilot projects in other parts of country.

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<sup>a</sup> All antineoplastic agents used to treat cancer, given by mouth, excluding hormonal therapies.

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- Collaborative: We will work in partnership with those who have an ability to advance our vision. We cannot, and should not, do this alone.
- Respectful and inclusive: We believe that the only way to achieve our vision is to build on the expertise that exists in both the specialty and community setting. This work is not about transferring knowledge from the oncology community to community practitioners but rather to establish opportunities for them to learn from each other.
- Equal and measured: All of the safeguards that exist to ensure the safe use and safe handling of intravenous cancer drug therapy should also be in place to ensure the safe use and safe handling of oral cancer drug therapy, regardless of practice setting. Sadly, that is currently not the case. Where standards need to be modified to reflect local opportunity, service delivery models, and patient and community preferences and needs, they should remain as similar as reasonably practical and the decision to vary should be deliberate.
- Catalytic: the Canadian Association of Provincial Cancer Agencies' intention is to catalyze opportunity; to identify, learn from and find opportunities to replicate what is working well in Canada and in other parts of the world.

### Scope

Greater dialogue about the safe use and safe handling of oral cancer drug therapy in recent years has prompted several professional organizations to issue position statements regarding safe use and handling, including: Canadian Association of Nurses in Oncology, British Oncology Pharmacy Association, American Society of Clinical Oncology and Oncology Nursing Society, Irish Medication Safety Network, Canadian Association of Pharmacy in Oncology, and International Society of Oncology Pharmacy Practice. (12-17) The Medication Safety Self-Assessment in Oncology further compiles and clarifies various standard setting documents and best practice recommendations (18). This guideline is intended to complement, rather than replace or duplicate, professional standards, federal/provincial legislative or regulatory requirements and guidelines. It is intended, overall, to reflect a system, rather than a discipline-specific, approach.

These guidelines apply specifically to the use of oral cancer drug therapy in the treatment of adult cancer though we strongly believe they are broadly applicable and address important gaps and concerns regarding safe use and handling of these hazardous drugs in any practice setting. The information needs of patients who are prescribed oral cancer drug therapy and their caregivers, the occupational health and safety concerns of their care providers, and the overarching patient safety concerns remain constant even when settings change. Therefore, providers and administrators working in other care settings where oral cancer drug therapy is used, including community pharmacy, home care, pediatric and young adult cancer care, long-term care, penitentiaries, hospitals, respite and other day care facilities should, at minimum, review these guidelines to determine their relevance in each practice setting. Further, to ensure the full suite of recommendations regarding safe use and safe handling are considered, readers are strongly encouraged to use this document as a companion rather than stand alone reference. This is particularly true for occupational health and safety, where detailed, context specific provincial regulations, national and international standards exist (11,19-23). Standards that minimize exposure to hazardous drugs in hospital and ambulatory care settings are as relevant to those working in other settings. Enforcing the implementation of these standards across the full spectrum of settings where oral cancer drug therapy is dispensed, stored, administered, and disposed of would improve safe handling immeasurably. Employers who employ staff who are pregnant, planning to conceive, or who are breast feeding should consider policy options to limit exposure to hazardous drugs, including the possibility of protective reassignment.

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## Recommendations

There are opportunities to enhance the safe use and handling of oral cancer drug therapy in five broad clusters.

1. Prescribing
2. Dispensing
3. Monitoring
4. Training and Education
5. Research

The following defines each cluster and provides a brief description of current practice. Recommendations follow.

### *Prescribing*

Oral cancer drug therapy is prescribed by a variety of physician specialties with most, but not all, having focused and extensive specialty training and credentialing in the diagnosis and treatment of cancer. While the possibility of restricting prescribing of oral cancer drug therapy to a selected group of specifically credentialed healthcare professionals has been discussed, concern that it may unintentionally and inappropriately limit access to cancer care eliminates it as a feasible recommendation. However, it is reasonable to require that prescribers have formal training in oncology and experience treating the condition for which oral therapy is prescribed (6,14,24).

How oral cancer drug orders or prescriptions are written and what prescribers include on each order or prescription varies considerably across the country. Some jurisdictions are moving forward with province-wide implementation of computer-based systems that have been deliberately designed to automate the medication ordering process. These Computerized Prescriber Order Entry<sup>b</sup> (CPOE) systems have been demonstrated to reduce prescribing errors, thereby also reducing patient harm, and for this and other reasons are considered the gold standard in safe prescribing - if implemented fully. Other provinces, where the goal of electronic prescribing is unattainable in the short-term, are using a combination of pre-printed orders<sup>c</sup> (PPO) and hand written orders (25-30). Where CPOE is unavailable or until wide-spread use becomes a reality, the use of PPOs for oral cancer drug therapy is the minimum prescribing standard. Jurisdictions should move away from the use of hand written orders, and abandon the practice of allowing verbal or telephone orders for anything other than to hold or discontinue therapy. Approaches and incentives to move prescribers towards these goals should be expeditiously identified and implemented. Modified approaches may be required to engage prescribers working outside the cancer agency system, or those who prescribe oral hormonal therapy only.

In addition to prescribing documentation standards, there is a need to ensure that prescribers provide basic information on every oral cancer drug prescription. (31) The absence of this information limits the pharmacist's ability to verify the clinical appropriateness of the prescription, as well as the dispensing pharmacist's ability to complete the final product check. Ultimately, because these steps in the dispensing process ensure the safe delivery of patient care, prescriptions that do not include the necessary information will likely result in dispensing delays and increase otherwise avoidable workload for pharmacists. In extreme cases, when this basic information has not been provided and the prescriber

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<sup>b</sup> Computerized prescriber order entry systems, also referred to as computerized physician or provider order entry systems, denotes the direct entry of clinical orders into a healthcare system's electronic health record.

<sup>c</sup> Pre-printed orders are printed protocol specific order forms on which a standardized chemotherapy regimen is printed. They help simplify and standardize the ordering process because much of the basic information is already pre-filled such that the prescriber needs to only fill in patient specific information to complete the order.

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is difficult to reach, the onset of treatment may be briefly delayed. Failing to provide this information may result in prescriptions being dispensed without appropriate clinical review of necessary patient and treatment parameters which could lead to patient safety issues and possible patient harm.

At minimum, to avoid unnecessary delays and to ensure that all appropriate information is provided for the pharmacists conducting cognitive and dispensing checks, in addition to existing provincial regulation and professional practice standard requirements, it is recommended that the following information be included on every oral cancer drug therapy prescription<sup>d</sup>. In provinces with access to comprehensive electronic health records, data does not need to be transcribed onto the prescription if original source documentation is available and readily accessible.

- Name of prescriber, registration number, and contact information (i.e. pager or cell number) or designated point of contact within the prescriber's institution, such as the oncology pharmacy.
- Date of order; treatment start date and duration
- Two patient identifiers
- Name of prescribed drug – use full, generic drug name. No abbreviations. Drug names should be TALLman lettered according to Institute of Safe Medication Practices Canada recommendations.
- Diagnosis or disease specific indication for treatment (e.g. diagnosis = breast cancer, disease specific indication = HER2+)
- Drug dosage, including patient variables such as (recent) weight and height needed to calculate the dose
- When dose reduction is required, . When dose reduction is required, the start date, duration and reason for the reduction should be included on the prescription
- Protocol or regimen name, where relevant.
- Cycle number, including total number of cycles (e.g. 3 out of 6), when relevant.
- When required, relevant lab data to calculate dose, confirm drug eligibility or to determine appropriateness of the prescribed regimen (e.g. BRAF 600 mutation status prior to dispensing Vemurafenib).
- Quantity of drug to be dispensed.
- Route and frequency of administration, and any specific administration instructions, including any information regarding the effect of food on absorption of the prescribed drug. The prescribed schedule of administration must be unambiguously specified on every prescription (e.g., Drug A three weeks on and one week off).
- It is highly desirable that “no refills” be the default standard. If the intention is to allow for refills to accommodate those with limited local access to a pharmacy, for financial reasons, or to accommodate travel plans, for example, the prescriber should write the total quantity and specify the amount to be dispensed and any parameters that should be monitored.

In the event that these specific information requirements require CPOE software updates systemic therapy CPOE guidelines should be updated to reflect issues that are specific to oral cancer drug therapy, endorsed nationally, and used as a standardized starting point for discussions about change with CPOE system vendors. Not only will this begin to harmonize systems, but it may reduce any additional costs associated with the addition of new prescribing data entry fields or use of built in flags, warnings, or alerts.

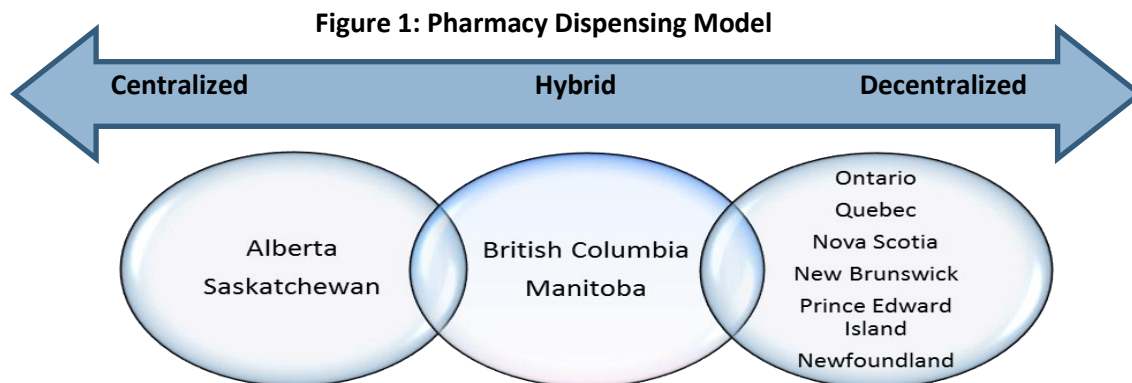
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<sup>d</sup> The only possible exception to this recommendation is for drugs that fall within Health Canada's Restricted Distribution Program, where specific prescribing requirements and training are mandated.

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### Dispensing

The need to close the gap between intravenous and oral cancer drug therapy processes is perhaps greatest in the dispensing area, largely as a result of the different dispensing models that exist in Canada. In Alberta and Saskatchewan, oral cancer drug therapy is dispensed by provincial cancer agency pharmacies by pharmacists with formal training in oncology and whose practices focus in oncology (see Figure 1). In the remaining provinces, oral cancer drug therapy is dispensed via a combination of hospital centres, community and specialty pharmacies (decentralized), or some combination of the two (hybrid).



It is common practice for intravenous cancer drug therapy prescriptions to be independently checked and for the prescription to be clinically verified by an oncology trained pharmacist. (14,32) With the exception of prescriptions dispensed directly from a provincial cancer agency pharmacy (i.e. in Alberta and Saskatchewan, and for most prescriptions in British Columbia and Manitoba) oral cancer drug therapy prescriptions are dispensed by pharmacists working in other settings where neither the process nor the requirements for clinical verification nor independent double checking are clear. To ensure patient safety, every oral cancer drug therapy prescription must undergo:

- Cognitive verification, whereby a licensed healthcare professional – ideally a pharmacist - with formal training in oncology or whose practice is focused on oncology verifies the clinical appropriateness of the prescription, including: body surface area calculation (where relevant), protocol or regimen name (including cycle number), drug name (s), drug dose (including dose modifications, if any), administration instructions, intended start date and exact duration of treatment, and relevant (ideally original) laboratory data, where available.
- Dispensing verification, whereby a licensed pharmacist verifies the minimum requirements in accordance with professional practice standards, and also verifies that every oral cancer drug therapy prescription has been cognitively verified.
- Independent double check involving separate verification by a minimum of two licensed health professionals to ensure that the following is present and correct on the prescription:
  - Two patient identifiers, drug name(s), drug dose, quantity to be dispensed, route and frequency of administration, and dose calculation (where relevant).

In some community pharmacies and at certain times in hospital pharmacies it is likely that a single pharmacist may be on duty to manage all pharmacy related activity. Pharmacists working in community pharmacies typically dispense very few oral cancer drug therapies so their knowledge and comfort dispensing these hazardous drugs is low. It will be difficult and perhaps even unreasonable to expect pharmacists without a working knowledge of oncology pharmacy to complete a cognitive verification of the prescription. It may be similarly difficult to ensure that independent double checks are conducted. Innovative, possibly technologically based, solutions may offer a remedy: bar coding technology may

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enable automated independent double checking; and audio-visual computer equipment may enable remote access to a second healthcare professional with formal training and/or experience in oncology to enable cognitive verification to take place. The liability issues involved in remote verification will need to be discussed and systematically addressed.

Given limited interaction between providers and patients during treatment with oral cancer drug therapy, policies and approaches that limit the quantity of medication dispensed for the initial and all subsequent refills should be considered; and when limited quantities have been established, these should be documented on the PPO and embedded within the CPOE system. Exceptions to a limited fill policy should be explicitly described in an institution-wide policy and considered on an individualized basis, and for drugs that are associated with late onset toxicity. For example, larger initial fill quantities may be appropriate for those who live in remote communities for whom alternative arrangements can be made to monitor adherence, check applicable lab work, and assess regularly for the presence of toxicities and/or side effects or when other locally relevant issues need to be taken into account (i.e. asking an elderly patient living in a remote community to drive through heavy snow and ice conditions). When an exception to the limited initial and subsequent fill approach is warranted, a risk assessment must be performed by a member of the patient's cancer care delivery team to address any patient safety related risks. Institutions may wish to take into account the individual safety profiles of each oral cancer drug and develop policies that are specific to the anticipated appearance of side effects or toxicity. A drug-by-drug approach may help to reduce the likelihood that increasing the frequency of dispensing, even if only initially, will affect pharmacy workload and wait times while ensuring the overall goal of improving patient safety is upheld. There may be opportunities to learn from those who have already implemented limited the frequency of dispensing, such as the Non-Insured Health Benefit Program has done for opioid dispensing. (33) In addition to institution and system wide actions, manufacturers may play an important role in aligning drug packaging with common dosing.

The practice of dispensing more or less than the actual number of pills prescribed may reflect the challenge some pharmacies face in maintaining even a small residual stock of high cost drugs that are dispensed infrequently and where there is no reasonable assurance of continued therapy (Canadian Pharmacists Association and Canadian Association of Chain Drug Stores, personal communication, 2014). For some pharmacies, complying with this recommendation will be difficult and may necessitate that the pharmacy redirect the patient to another local retail store. If this proves to be problematic, remote and rural medication distribution options may need to be explored.

Finally, but importantly, pharmacy staff dispensing oral cancer drug therapy must follow all appropriate personal protective equipment (PPE) recommendations for each step of the medication circuit (Appendix B). Guidance regarding the exact type of PPE required should be sought from Cancer Care Ontario's Safe Handling of Cytotoxics or other evidence based reference. Employers must provide the necessary protective equipment and training on how to use the equipment. A quick reference guide, based on best available scientific evidence, would be helpful given the wide variety of pharmacy settings from which oral cancer drug therapies are dispensed.

### *Monitoring*

A high degree of adherence with prescribed cancer treatment is essential for optimal outcomes, and yet in spite of a very motivated population, data suggests that adherence with oral cancer drug therapy regimens can be quite low. (34-37) For intravenous treatment, lack of adherence is obvious and there are opportunities to intervene quickly when adherence is suboptimal or if toxicity or side effects appear. In contrast, opportunities to assess patient adherence, and understand reasons for non-adherence or

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the ability to tolerate oral cancer drug therapy when self-administered in the home can be significantly more limited.

As part of a comprehensive approach to monitoring adherence and establishing opportunities for regular assessment, individualized, proactive monitoring plans must be established before each new oral cancer drug therapy begins and reviewed with each dose modification, or as otherwise needed.

The difficulty addressing adherence is compounded by the lack of standardized assessment and reporting, unclear accountability for monitoring between patient visits to the oncologist, and lack of access to electronic health records outside the traditional cancer care delivery system. The absence of standardized assessment tools, data and reporting, and limited evidence base from which to select specific approaches, further accentuates the already difficult challenge of comprehensively monitoring patient's adherence and ability to tolerate treatment. The Multinational Association of Supportive Care in Cancer Oral Agent Teaching Tool (MOATT) is internationally recognized and recommended nationally, though there is still a need to determine its usefulness in specific populations. (38)

Development of a patient companion tool and an electronic format of the existing tool for healthcare providers may help to identify side effects, toxicity, or adherence-related issues that can be discussed with a healthcare provider. The availability and usefulness of other tools, including Edmonton Symptom Assessment Scale (ESAS-r) should also be systematically evaluated in a multitude of settings, including home and community, and with populations of varying demographics (e.g. elderly). Where necessary, new tools and mechanisms should be developed to ensure that appropriate patient assessments can take place and so that information can be relayed from the provider working outside the cancer system to the prescriber.

### *Training and Education*

Patients, their caregivers, and specialty and community healthcare professionals have distinct training and education needs. Patients and their caregivers should be offered culturally sensitive information about the oral cancer drug therapy they have been prescribed, ideally from a member of the patient's cancer healthcare team before the medication is initially dispensed, and then subsequently reviewed by the dispensing pharmacist. Verbal instructions should be supplemented with take-home written material. Topics should include safe handling, storage, administration, monitoring and adherence, disposal, the effect of food on absorption, expected side effects and management. If at all feasible, information about safe handling of oral cancer drug therapy among pregnant and breastfeeding mothers should be included.

If it is not already clear, a process should be in place to address who provides which piece of information and how comprehension will be evaluated. (39) The teach-back method is the preferred approach, but given the time and training required may only be an appropriate expectation of specialized oncology healthcare providers. Written information, such as the Consumer Information Part III of the Product Monograph or locally developed information, should be provided to supplement any verbal instruction that has been provided. Continued efforts to provide information in languages other than English and French should be sustained given Canada's multicultural, multilingual population.

Patients on oral cancer drug therapy receive care in a variety of practice settings, including ambulatory clinics, hospitals, long-term care facilities, and at home. Members of the healthcare team who are involved in prescribing, handling, dispensing, administering, and monitoring patients who are receiving oral cancer drug therapy regardless of the type of setting must undergo a standardized competency evaluation of knowledge and skills related to safe medication practices that are specific to oral cancer

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drug therapy and practice setting, and address both safe medication use and safe handling practices. Further, a process should be in place for regular re-evaluation. (10) This may be particularly important and relevant for healthcare professionals in non-oncology settings as formal training may be more limited. In these situations, the value of in depth education about oncology may prove to have little lasting impact when the opportunity to dispense oral medications is relatively low. Access to drug-specific information about the indication, dosing, and safety precautions, at a minimum, must be available as close to the point of dispensing as possible. The only exception to the requirement for ongoing training and competency assessment is for drugs that are part of a Restricted Distribution Program, where mandatory training and certification is required for prescribers, pharmacists and patients prior to dispensing.

### *Future Directions*

The use and availability of oral cancer drug therapy is expected to continue to grow as a treatment modality. As use of these drugs move from clinical trials to the eligible Canadian population, the importance of monitoring for adverse drug reactions, close calls and actual medication incidents becomes increasingly important. While there is no mandatory requirement to report medication incidents occurring in a patient's home or in the community, there are a number of options for both healthcare professionals, patients and families to voluntarily share information: safemedicationuse.ca, local and provincial reporting systems, or through one of three national reporting systems: ISMP Canada Individual Practitioner Reporting System, CIHI National System for Incident Reporting, or Health Canada's Vigilance Program. At a pan-Canadian level, resources are required to integrate or at least share data across these systems to inform quality improvement and patient safety efforts.

Relative to the delivery of intravenous cancer drug therapy there is little research to guide practice in community settings. Dedicated research funding to address gaps in knowledge across the full spectrum of activities from prescribing to administration, use of risk mitigation strategies including TALLman lettering for name differentiation and Look-Alike, Sound-Alike names and solutions, would significantly advance the safe use and handling of oral cancer drug therapy. A process to identify and prioritize research priorities in this emerging area would provide a framework for the cost-effective and rationale allocation of limited research dollars.

Another important area of focus lies within the domain of information technology (IT) and information management (IM) within healthcare. IT solutions have a potential to facilitate best practice, patient safety and quality of care in each aspect of oral chemotherapy from prescribing to administration. CPOE systems are in evolution from stand-alone solutions, possibly oncology specific, towards becoming one component of larger medication management systems (MMS). MMS provide enhanced features of a medication profiling, drug-drug interactions, better inter-professional communication and importantly, one system for the whole medication process. Careful evaluation of features and functionalities within these systems that will facilitate and enhance the oral chemotherapy processes need evaluation i.e. features to allow for the decision support and documentation of the cognitive clearance of the oral chemotherapy prescription. Electronic prescribing (e-Prescribing) is having increased adoption and requires development of oral chemotherapy standards (based on the clinical parameters described previously) as well as the transmission standards. E-Prescribing is not just about transmitting a prescription but also about facilitating bidirectional communication between prescribers and pharmacists. The needs for oral chemotherapy will be unique for e-prescribing. Mobile applications are the next phase of the IT boom in healthcare and provide applications that are both provider and patient facing. These types of applications can be used for clinical decision support at any phase of the medication process from a provider perspective. For patients, such applications can be used for



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diaries/calendars to help with adherence, for clinical decision support as it relates to symptom management and more recently, as a tool for communication between the patient and their health care team. Lastly, the back end of the IT systems provides significant data collection which can be used for quality measurement and research evaluation.

There is an ongoing momentum within the various provinces in the enhancement of IM/IT solutions and processes to facilitate health care which may range from standards development to one provincial system. It is important to leverage the provincial assets to facilitate the oral chemotherapy agenda. Importantly, cancer patients are a complex patient population often with multiple co-morbidities and on many medications, hence, unifying solutions that facilitate complex care under one system are required. As we move towards better clinical interoperability between various IT systems, solutions such as Health Information Exchanges are emerging to provide a single sign on view of the patient for all providers. Our starting point of pan-Canadian oral chemotherapy guidelines will provide the corner stone for any IM/IT solution.

### *Limitations*

These guidelines were informed by the results of a pan-Canadian survey of provincial cancer agencies and programs completed during the summer of 2013. Information from the Territories was not obtained from the survey. With the exception of two provinces, respondents submitted a single centralized response. It is possible that there may be greater variation than we have been able to identify. It is also possible that innovative practices at the local level have not been captured.

A systematic literature review was not conducted, but every attempt to gather relevant literature was made by reviewing reference lists from existing position statements and guidelines, and by speaking with experts in this field in Canada, the US, and France.

Surveys about community pharmacy knowledge and education provide considerable insight. However, community pharmacists were not directly surveyed as part of this initiative. Greater collaboration between the oncology and community settings, and conducting specific surveys of community pharmacists and the organizations that employ them, will lead to a deeper understanding of the issues and opportunities that may still need to be addressed.

Concerns regarding environmental contamination and safe handling appear legitimate given: the hazardous nature of many oral chemotherapeutic drugs; limited dispensing volumes by most community pharmacies; and infrequent opportunity for oncology-specific undergraduate or continuing education. (40) However, few studies have been conducted in the community setting. Those that have been done have shown some degree of environmental contamination in community pharmacies but the ability to draw conclusions is limited by the small number of studies, limited number of practice settings, and small number of drugs.(41) While concern has also been raised about the potential risks associated with caregiver exposure to cytotoxic drugs stored and self-administered in the home, there is little evidence to confirm or rule out any potential risk. In stark contrast, the possibility of accidental ingestion and poisoning of both humans and pets remains a much more significant concern. Better consolidation of existing information with regards to environmental contamination and accidental poisoning in community and home settings is required, and more research in both areas would be beneficial.

### *Summary*

The cancer system was designed to optimize the care of patients receiving intravenous therapy. Processes that are in place to ensure the safe administration of intravenous cancer drug therapy are lacking for self-administration of oral cancer drug therapy, and the need for such processes is

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substantial. The growth in availability and use of oral cancer drug therapy demonstrates substantial gaps and opportunities for change. Intravenous cancer treatment administered within a hospital or ambulatory setting provides the opportunity for healthcare providers (who typically have additional training in oncology) to assess a patient's response to treatment, side effects, and toxicity. In addition, centralized prescribing and dispensing functions foster communication between physician, pharmacy, and nursing care providers. In contrast, the use of oral cancer drug therapy may diminish healthcare provider interaction; limit adherence monitoring; and reduce communication between providers, particularly with respect to prescribing and dispensing functions where dispensing is not completely centralized. Institutions that provide care to this patient population should carefully review and strive to implement the 12 recommendations outlined in these guidelines. It is not only our expectation that implementation of these recommendations will be variable, but our hope as it will allow us to become progressively more effective as we learn from our peers in real time. Ultimately, deliberate and focused attention on the safe use and safe handling of oral cancer drug therapy and coordinated action across provider organizations locally, provincially, and at a pan-Canadian level will accelerate the potential for Canada to have the safest oral cancer drug therapy delivery system in the world.

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### APPENDIX A: SUMMARY OF RECOMMENDATIONS

| No.  | Recommendation   | Keyword                              |
|--|--|--------------------------------------|
| <b>Cluster 1: Prescribing oral cancer drug therapy</b> |  |                                      |
| R1   | While computerized prescriber order entry (CPOE) is recognized as the gold standard, the minimum prescribing standard for all oral cancer drug therapy orders is pre-printed orders (PPO).   | <i>Standard Order Format</i>         |
| R1.1   | Verbal and telephone orders for anything other than holding or discontinuing therapy are not accepted.   | <i>No Verbal or Telephone Orders</i> |
| R1.2   | Existing Systemic Therapy Computerized Prescriber Order Entry (ST CPOE) Guidelines should be revised to incorporate oral cancer drug therapy prescribing requirements and should be adopted and followed nationally.   | <i>ST CPOE Guidelines</i>            |
| R1.3   | National pre-printed order (PPO) guidelines that address oral cancer drug therapy prescribing requirements should be developed, adopted, and followed nationally.  | <i>PPO Guidelines</i>                |
| R1.4   | Existing pre-printed orders (PPO) should be readily accessible.  | <i>PPO Registry</i>                  |
| R2   | <p>In addition to existing provincial laws, regulations, and professional practice standards, and with the exception of drugs that fall under Health Canada’s Restricted Distribution Program, prescribers must include the following minimum content on every oral cancer drug therapy prescription regardless of whether prescriptions are documented on a pre-printed order or via computerized prescriber order entry. In provinces with access to comprehensive electronic health records, data does not need to be transcribed onto the prescription if original source documentation is available and readily accessible.</p> <ul style="list-style-type: none"> <li>• Name of prescriber, registration number, and contact information (i.e. pager or cell number) or designated point of contact within the prescribers institution, such as the oncology pharmacy (i.e. telephone number, email address).</li> <li>• Date of order; start date and duration of treatment.</li> <li>• Two patient identifiers.</li> <li>• Name of prescribed drug – full, generic name. No abbreviations. Drug names should be TALLman lettered according to ISMP Canada recommendations</li> <li>• Diagnosis or disease specific indication for treatment (e.g. diagnosis=breast cancer, disease specific indication = HER2+)</li> <li>• Drug dosage, including patient variables such as (recent) weight and height needed to calculate the dose.</li> <li>• When dose reduction is required, the start date, duration and reason for the reduction should be included on the prescription</li> <li>• Protocol or regimen name, where relevant</li> <li>• Cycle number, including total number of cycles (e.g. 3 out of 6), when relevant</li> <li>• When required, relevant lab data to calculate dose, confirm drug eligibility or to determine appropriateness of prescribed regimen (e.g. BRAF 600 mutation status prior to dispensing Vemurafenib)</li> <li>• Quantity of drug to be dispensed</li> <li>• Route and frequency of administration, including specific administration instructions, including any information regarding the effect of food on absorption of the prescribed drug. The prescribed schedule of administration must be unambiguously specified on every prescription (e.g. Drug A three weeks on and one week off)</li> <li>• It is highly desirable that “no refills” be the default standard. If the intention is to</li> </ul> | <i>Order Content</i>                 |

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### APPENDIX A: SUMMARY OF RECOMMENDATIONS

| No.   | Recommendation  | Keyword                          |
|---|---|----------------------------------|
|   | allow for refills, the prescriber should write the total quantity and specify the amount to be dispensed, as well as parameters for monitoring.   |                                  |
| R3  | All initial and subsequent cycles of oral cancer drug therapy must be ordered by a prescriber with formal training in oncology and experience treating the specific condition for which therapy is required.  | <i>Competency</i>                |
| <b>Cluster 2: Dispensing oral cancer drug therapy</b> |   |                                  |
| R4  | Before every oral cancer drug therapy prescription is dispensed, it must undergo clinical verification, dispensing verification, and an independent double check by licensed healthcare professionals with the competencies and knowledge that are required to complete each task.  | <i>Prescription Verification</i> |
| R4.1  | Before every oral cancer drug therapy prescription is dispensed, the following items must be clinically verified by a licensed healthcare professional with formal training in oncology or whose practice is focused in oncology: <ul style="list-style-type: none"> <li>• Body surface area calculation (where used for dosing).</li> <li>• Protocol or regimen name (including cycle number, where relevant).</li> <li>• Drug name(s).</li> <li>• Drug dose, including dose modifications made if any.</li> <li>• Administration instructions.</li> <li>• Intended start date and exact duration of treatment.</li> <li>• Relevant, ideally original laboratory data including most recent results and trends over time, when available.</li> </ul> | <i>Cognitive Verification</i>    |
| R4.2  | The dispensing pharmacist must ensure that every oral cancer drug therapy prescription has been clinically verified. If there is no evidence that clinical verification has been done, s/he will take all reasonable steps to clinically verify the prescription before dispensing.   | <i>Dispensing Verification</i>   |
| R4.3  | Before every prescription for oral cancer drug therapy is dispensed, a minimum of two licensed healthcare professionals with formal training in oncology or whose practice is focused in oncology must independently verify that the following are documented on the prescription: two patient identifiers, drug name(s), drug dose, quantity to be dispensed, route and frequency of administration, and dose calculation (where relevant). An independent double check will have been deemed to occur if the clinical verification and dispensing or final product check are completed by two licensed healthcare professionals separate from each other.   | <i>Independent Double Check</i>  |
| R5  | Policies and approaches that limit the number of initial and subsequent refill quantities must be developed and followed. The intention of these policies and approaches is to maximize the safe use and handling of oral cancer drug therapy, and to enable regular assessment of patient adherence and monitoring for side effects and toxicity.  | <i>Dispensing Limits</i>         |
| R5.1  | The quantity of oral cancer drug therapy dispensed must be the exact quantity required by the patient.  | <i>Patient Specific Quantity</i> |

### Cluster 3: Monitoring patients receiving oral cancer drug therapy

## Oral Cancer Drug Therapy Safe Use and Safe Handling Guidelines

### APPENDIX A: SUMMARY OF RECOMMENDATIONS

| No.  | Recommendation   | Keyword                   |
|------|--|---------------------------|
| R6   | When a new prescription for oral cancer drug therapy is started, an individualized, proactive monitoring plan must be put in place to enable regular assessment of patient adherence and monitoring for side effects and toxicity. At each dose modification or as otherwise needed, this plan will be reassessed and modified. These recommendations should complement information provided in the product monograph. | <i>Monitoring Plan</i>    |
| R6.1 | The Multinational Association of Supportive Care in Cancer Oral Agent Teaching Tool (MOATT) should be adopted nationally and used routinely.   | <i>Preferred Tool</i>     |
| R7   | All medication incidents and close calls should be reported through safemedicationuse.ca (patients), hospital or provincial reporting system, ISMP Canada's Individual Practitioner Reporting Program, CIHI's National System for Incident Reporting; Community Pharmacy incident Reporting (Cipher) system, or Health Canada's Vigilance program.   | <i>Incident Reporting</i> |

### Cluster 4: Training and education of patients, caregivers, and healthcare professionals

| Patient and Caregiver |   |   |
|-----------------------|---|---|
| R8                    | Before an oral cancer drug therapy prescription is filled for the first time, prescribers and other licensed healthcare professionals must provide information on safe handling, storage, administration, monitoring and adherence, disposal, expected side effects and their management. If feasible and appropriate, before each refill the same information should be reviewed with the patient. | <i>Patient Education Content and Format</i>                 |
| R8.1                  | A clear process should be in place to address who in the health care team provides which piece of information.  | <i>Accountability for Patient Education</i>                 |
| R8.2                  | Supplemental written information must also be provided to the patient before the initial prescription is filled and if necessary, after each subsequent refill.   | <i>Written Information</i>                                  |
| R9                    | A structured counselling strategy is used to assess patient and/or caregiver comprehension of the information that has been provided. The teach-back method is a preferred approach for confirming a patient's understanding of the information they have been given.   | <i>Comprehension Assessment</i>                             |
| Healthcare Provider   |   |   |
| R10                   | All members of the healthcare team involved in handling, prescribing, dispensing, administering, and monitoring patients receiving oral cancer drug therapy must undergo a standardized competency evaluation of knowledge and skills related to safe administration and safe handling practices with regular re-evaluation.  | <i>Provider Training and Competence</i>                     |
| R11                   | Undergraduate and graduate level discipline specific as well as multi-disciplinary educational and training programs should be expanded to include oral cancer drug therapy.  | <i>Discipline Specific &amp; Multidisciplinary Training</i> |

### Cluster 5: Research

|     |  |                        |
|-----|--|------------------------|
| R12 | Dedicated research funding to address areas that would improve safe use and handling of oral cancer drug therapy is needed. The following topics are examples of gaps in knowledge that need to be addressed: effective interventions to measure and improve adherence; use of technology including development and pilot testing of a patient and healthcare provider electronic of the Multinational Association of Supportive Care in Cancer Oral Agent Teaching Tool (MASCC MOATT) and evaluation of its use in specific populations (e.g. elderly); drug utilization; medication reconciliation in the ambulatory versus inpatient settings;; prescriber education gaps and needs assessment; Failure Mode and Effects Analysis (FMEA); and | <i>Research Agenda</i> |
|-----|--|------------------------|

## Oral Cancer Drug Therapy Safe Use and Safe Handling Guidelines

### APPENDIX A: SUMMARY OF RECOMMENDATIONS

| No. | Recommendation | Keyword |
|-----|----------------|---------|
|-----|----------------|---------|

measurement of exposure to oral cancer drug therapy in community pharmacy (occupational), home and other non-traditional settings. A robust, multidisciplinary process to prioritize and complete a research agenda should be undertaken.

### APPENDIX B: PERSONAL PROTECTIVE EQUIPMENT DURING STEPS OF THE ORAL CHEMOTHERAPY MEDICATION CIRCUIT

| Personal Protective Equipment  | Steps in the medication circuit  |
|--|--|
| 1 pair of gloves   | Waste management (collection and transport)  |
| 1 pair of gloves, 1 gown   | Non-sterile preparations: Counting solid oral forms  |
|  | Cleaning of other oncology pharmacy rooms  |
| 1 pair of gloves, 1 gown, cap and shoe cover   | Cleaning of sterile preparation room   |
| 2 pairs of gloves, 1 gown  | Unpacking and cleaning   |
|  | Crushing tablets   |
|  | Preparing oral solutions (* face protection should also be used if there is a risk of splashing when preparing liquid oral preparations) |
| 2 pairs of gloves, 1 gown, face protection, cap, shoe covers                                     | Sterile preparations   |
| 2 pairs of gloves, 1 gown, 1 respiratory protection apparatus, face protection, shoe covers      | Spill or damaged or broken container   |
| 2 pairs of gloves, 1 gown, 1 respiratory protection apparatus, face protection, cap, shoe covers | Cleaning of preparation cabinets (biological safety cabinets)  |

1. Adapted with permission, Easty A, Coakley N, Cheng R, Cividino M, et al. Safe handling of cytotoxics. Toronto (ON): Cancer Care Ontario; 2013 December 4. Program in Evidence-Based Care Evidence Based Series No. 16-3

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