

Modifying oral cytotoxics: what are the considerations?

Dr Alison Haywood

Learning objectives

After reading this article you should be able to:

- Describe the problems associated with the use of oral cytotoxics not seen in traditional IV therapy.
- Describe the advice to be given to patients regarding the safe handling of oral cytotoxics.
- Describe the advice which should be given to patients and carers on the storage and disposal of oral cytotoxics.

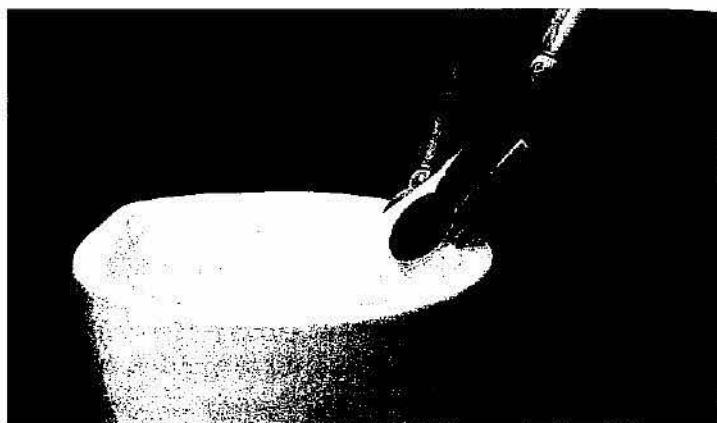
Competencies addressed: 4.2.2, 4.2.3, 4.3.3, 5.3.1.

Introduction

It is well known that Australia's population is ageing and that the incidence of cancer is highest in older age groups, so despite the fact that cancer incidence rates in Australia for both men and women are projected to remain stable to 2011,¹ the total number of new cases of cancer is projected to increase. To reduce the resulting burden on the health care system it is imperative that patients be treated at home. The introduction of several new oral cytotoxics, allowing the administration of chemotherapeutic agents outside of traditional clinic settings, is making this goal attainable.² While studies have shown that patients receiving chemotherapy prefer the oral route of administration over the parenteral route, there are many new challenges in administering these agents in non-traditional environments.^{2,3} Pharmacists, because of their accessibility, have an important role to play in counselling patients on the safe and effective use of these cytotoxics, thus playing a pivotal role in the achievement of favourable therapeutic outcomes for these patients.

Background and evidence

The changing paradigm in cancer treatment associated with the introduction of novel oral chemotherapeutic agents has shown many advantages, with greater convenience and flexibility in the location and scheduling of medication administration (i.e. ability to undergo treatment at home) being the primary advantage. Other advantages of oral chemotherapy include the potential to reduce the use of health care resources for inpatient services, since patients are able to self-administer treatment. Furthermore,



Advantages of oral chemotherapy include the potential to reduce the use of health care resources for inpatient services, since patients are able to self-administer treatment.

problems with IV access and patients' fear of needles are eliminated when using the oral route. Therapeutically, oral administration of chemotherapy can provide more prolonged drug exposure compared with intermittent IV infusion, which may be important for drugs with schedule-dependent efficacy.³

However, there are several potential problems associated with the use of oral chemotherapy not seen in traditional IV therapy. Patients and caregivers are required to assume greater responsibility for the patient taking the proper dose, in the correct manner, at the appropriate time. This administration of chemotherapy in a non-traditional environment may lead to an increased risk of dosing errors, side effects, drug interactions and non-adherence.²⁻⁴ Non-adherence may be as a result of confusion and misunderstanding about the treatment regimen, failure to remember dosages or inappropriately 'catching-up' doses. Further, difficulty or inability to swallow solid dosage forms and the subsequent safety issues which arise from this if patients or carers attempt to crush these tablets before administration (e.g. elderly patients, children, patients suffering from nausea and vomiting, and patients receiving medicines via enteral feeding tubes), and the high cost of the newer oral chemotherapeutic agents provide additional challenges in this area. Side effect profiles not associated with traditional chemotherapy have also been noted (e.g. rashes, hand-foot syndrome),^{3,5} highlighting the

Dr Alison Haywood is Senior Lecturer, Griffith University School of Pharmacy, Gold Coast Campus and Professor Beverley Glass is Chair of Pharmacy, School of Pharmacy and Molecular Sciences James Cook University, Townsville.

Table 1: Counselling notes for the provision of cytotoxic substances

Indication of use	A patient's knowledge and understanding of their disease is an important factor affecting adherence to any drug therapy.
Complexity and duration of the regimen	Many oral cytotoxics have complex dosing regimens. Patients need to know how and when to take their medication, for how long and what to do in case of missed doses or vomiting after a dose. Patients should also be made aware of any expected tests during treatment (e.g. blood tests).
Adverse effects	Oral cytotoxics may each have unique adverse effect profiles; patients need to be aware of expected adverse effects, strategies for managing them (e.g. when to take antiemetics) and when to seek professional help, especially since patient monitoring is less frequent with oral therapy.
Drug, food and nutritional supplement/herbal medicine interactions	It is important that patients are aware of potential interactions and inform health professionals about all their current treatments, including those not prescribed by their doctor.
Storage and disposal of unused oral cytotoxics	Medicines should be stored in an appropriate place according to the manufacturer's requirements, away from undue exposure to light, heat and humidity and away from children and pets. To avoid contaminating landfills and the water supply, patients/carers should not discard of unused oral cytotoxics in the household trash or flush them down the toilet, but bring them back to the pharmacy for proper disposal. ⁴

importance of appropriate counselling that addresses the unique adverse effect profile associated with the individual agents. This puts the pharmacist in an important position since they have the knowledge to provide guidance on the safe storage, dispensing, administration and disposal of oral cytotoxics as well as counsel patients to ensure the safe and effective use of their oral chemotherapy.

Safe and effective use of oral cytotoxics

There are established policies and procedures in traditional chemotherapy for the safe handling of cytotoxics and other hazardous substances, e.g. *Preparation of cytotoxic drug products* in the *PSA Professional Practice Standards*⁶ and the *SHPA Standards of practice for the provision of oral chemotherapy for the treatment of cancer*,⁷ and for the *safe handling of cytotoxic drugs in pharmacy departments*.⁸ These are for the protection of health care personnel and

patients from harmful exposure to hazardous substances and also for the protection of the workplace and environment from contamination. However, there are limited guidelines specific to safe handling of oral cytotoxics in the home or other non-traditional settings.⁹ Further, little information is available to pharmacists on effective means of managing non-adherence to ensure positive therapeutic outcomes. The following information will provide valuable insight into the safe and effective use of oral cytotoxics.

Patient/carer education

Patient and/or carer counselling is the most critical step in ensuring effective therapeutic outcomes, since patients will be self administering treatment and will therefore not have ready access to traditional sources of specialised information provided at the inpatient setting by health care professionals.³⁻⁵ Self administration at home or other non-traditional settings may increase the risk of medication errors, compromise therapeutic efficacy and patient safety, and lead to inadvertent exposure of family members to hazardous substances and contamination of landfills and the water supply.⁹ Further, many oral cytotoxics have a narrow therapeutic index and complex dosing regimens, and patients may perceive oral drug therapies as being less dangerous than parenteral therapies.⁹ Important patient counselling notes are listed in Table 1.^{3,5-7}

Special administration requirements and safe handling

Patients should handle their medication themselves, if at all possible. If a family member/carer needs to assist the patient they should wash their hands before and after they handle the medication and should wear nitrile gloves.⁴ The following guidelines are given for modifying solid dosage forms for patients unable to swallow a tablet or capsule:¹⁰

Making a tablet dose into a mixture

- 1 You will need: (i) A pair of gloves; (ii) an oral syringe and (iii) a plastic measuring cup or glass.
- 2 Put on the gloves.
- 3 Place the required number of tablets or part of a tablet into the measuring cup or glass.
- 4 Pour a little water on the tablets and allow to disperse. This may take a few minutes. Do not try to make the tablet disperse faster by stirring or shaking the container.
Alternative method: Place the required number of tablets or part of tablet into a tablet crusher; gently add some water making sure the powder is washed off the crusher.
- 5 Draw up the dose into an oral syringe and give the dose to your patient.
- 6 Wash the gloves, oral syringe and measuring cup/glass in warm, soapy water. These can be used again for further doses but do not use them for any other purpose.

solutions through compounding

The articles in this series are independently researched and compiled by PSA commissioned authors and peer reviewed.

Making a capsule dose into a mixture

- 1 You will need: (i) A pair of gloves; (ii) a mask; (iii) an oral syringe and (iv) a plastic measuring cup or glass.
- 2 Put on the gloves and mask.
- 3 Put a little water into the glass.
- 4 Empty the contents of the capsule onto the water.
- 5 Draw up the dose into an oral syringe and give the dose to your patient.
- 6 Wash the gloves, oral syringe and measuring cup/glass in warm, soapy water. These can be used again for further doses but do not use them for any other purpose.
- 7 Wrap the empty plastic capsule shell in paper and throw it away with the mask as described below. A new mask should be used for each dose.

What to do in case of a spill

- If contact occurs with your skin, you must wash the area immediately, using plenty of water. If the skin is sore you should contact your GP for advice.
- If contact occurs with your eyes, wash immediately with plenty of water for at least 10 minutes. If after this your eyes are sore you should go to your nearest emergency department.
- If you spill any cytotoxic medicines on the work surface or floor, wearing gloves, cover the spillage with kitchen paper. Wipe the area with water then clean with household cleaner and water. Used kitchen paper and other items used to clean up the spillage should be double bagged and disposed of with the household waste. If any cytotoxic medicine is spilt on clothing, the spill should be blotted dry with kitchen paper. Clothing should be removed immediately and washed separately from other items.
- Waste products, such as used paper towels, vomit and dirty disposable nappies, should be placed in a double-lined plastic rubbish bag. The double bag should be disposed of as for normal household waste.

Oral cytotoxics and enteral feeding tubes

Crushing tablets to administer them via an enteral feeding tube not only increases the incidence of tube occlusion but also increases the risk of adverse effects. Wherever possible, health care professionals should consider an alternative formulation of the same drug or a different drug that has the same therapeutic effect. Occupational exposure would also need to be considered – contact with the skin and inhalation of dust should be avoided and protective equipment/devices should be used, such as closed-system crushing syringes.¹¹ Detailed guidelines, including drug monographs, are given in texts such as the *Handbook of Drug Administration via Enteral Feeding Tubes*.¹¹

Adherence and memory aids

Patient non-adherence is an issue that oncology clinicians struggle with in various practice settings. Suggestions for improving patient adherence include:^{4,5}

- There is strong advocacy for the use of diaries to monitor patient adherence, since this method has been shown to be fairly effective, i.e. asking patients to maintain a diary of doses taken and then present the diary at the time of drug renewal to verify that doses were taken as prescribed. The times of administration and whether the dose was taken with food can also be recorded.
- Patients can also be asked to bring their medication containers with them so that pill counts can be performed to ascertain whether the correct number of doses was taken as prescribed.
- Patients with complex medication schedules can be provided with a customised calendar listing each prescribed dose. Patients can then be asked to place a checkmark on the calendar after taking each dose, and to bring the calendar to every visit.

Advice for safe dispensing to prevent medication errors and inadvertent exposure of health care providers, patients, and caregivers to hazardous drugs has been incorporated into the prescribing information for many oral cytotoxics.⁹

- New electronic methods allowing health care providers to monitor patient adherence are being explored, where the prescriber, patient and laboratory are wirelessly linked enabling the prescriber to communicate patient instructions for dosage modification based on laboratory test results.

Generally, cytotoxic preparations or other medicines posing occupational health and safety risks are generally unsuitable for packaging into Dose Administration Aids, however the risk-benefit of packing must be considered; for example, packing may be appropriate where non-compliance is considered to be a greater risk.¹²

Pharmacist education

Advice for safe dispensing to prevent medication errors and inadvertent exposure of health care providers, patients, and caregivers to hazardous drugs has been incorporated into the prescribing information for many oral cytotoxics.⁹ Information about the proper use of the medication is often



Patients can also be asked to bring their medication containers with them so that pill counts can be performed to ascertain whether the correct number of doses was taken as prescribed.

available from many manufacturers for use as handouts and in the CMIs. Pharmacy owners may consider developing a counselling program for their community practice or delegating specialised patient education to a specific healthcare team member within their practice.⁴ Pharmacists should be encouraged to engage in relevant CPE activities to remain abreast of new chemotherapeutic treatments.

Questions

1. Problems associated with the use of oral cytotoxics in patients **not** seen in the traditional IV regimens include:
 - a) Patients and caregivers assuming less responsibility in the administration of a correct dose.
 - b) A decreased risk of side effects, drug interactions and lack of patient compliance.
 - c) Inability of elderly populations to swallow tablets and safety concerns regarding crushing of cytotoxics.
 - d) Low cost of oral chemotherapeutic agents.
 - e) c and d.
2. The following represents advice given by the pharmacist, which patients **should** adhere to in respect of the administration of their oral cytotoxics:
 - a) If at all possible do not handle the medication yourself.
 - b) If a family member assists in administering your medication, they should wash their hands prior to and after handling the medication.
 - c) It is not necessary for the person assisting in the administration of the oral cytotoxics to wear gloves.
 - d) a, b and c.
 - e) b and c.

By understanding the mechanism of action and metabolic pathways of the newer oral agents, pharmacists will be able to predict and take steps to avoid unwanted drug interactions and toxicity¹³ and are thus fulfilling an important role in ensuring the provision of optimal pharmaceutical care and drug therapy for people with cancer.

References

1. McDermid I. Cancer series 30. Cancer incidence projections Australia 2002 to 2011. Canberra: Australian Institute of Health and Welfare 2005.
2. Goodin S. Advancing the safe and appropriate use of oral chemotherapy agents: Introduction. *Am J Health Syst Pharm* 2007;64(9 Suppl 5):S35-40.
3. Aisner J. Overview of the changing paradigm in cancer treatment: oral chemotherapy. *Am J Health Syst Pharm* 2007 May 1;64(9 Suppl 5):S4-7.
4. Goodin S, Aisner J, Bartel SB, Wiele CS. Current issues associated with oral chemotherapy: a roundtable discussion. *Am J Health Syst Pharm* 2007 May 1;64(9 Suppl 5): S33-5.
5. Wiele CS. Managing oral chemotherapy: the healthcare practitioner's role. *Am J Health Syst Pharm* 2007 May 1;64(9 Suppl 5):S25-32.
6. Professional Practice Standards - Version 3. Preparation of Cytotoxic Drug Products. Curtin: Pharmaceutical Society of Australia 2006.
7. SHPA Committee of Speciality Practice in Cancer Services. SHPA Standards of practice for the provision of oral chemotherapy for the treatment of cancer. *JPPR* 2007;37(2):149-52.
8. SHPA Committee of Speciality Practice in Oncology. SHPA Standards of practice for the safe handling of cytotoxic drugs in pharmacy departments. *JPPR* 2005;35(1):44-52.
9. Bartel SB. Safe practices and financial considerations in using oral chemotherapeutic agents. *Am J Health Syst Pharm* 2007 May 1;64(9 Suppl 5):S8-S14.
10. Great Ormond Street Hospital for Children NHS Trust. Special handling requirements for oral cytotoxics and cytotoxic immunosuppressant medicines. 2nd Edition, Mar 2006 [cited 2 Jun 2009]; At: www.ich.ucl.ac.uk/gosh_families/information_sheets/medicines_chemotherapy_handling/medicines_chemotherapy_handling_families.pdf
11. White R, Bradnam V. Handbook of Drug Administration via Enteral Feeding Tubes. London: Pharmaceutical Press 2007.
12. Professional Practice Standards - Version 3. Dose Administration Aids Service. 3rd ed. Pharmaceutical Society of Australia, 2005.
13. Goodin S. Oral chemotherapeutic agents: Understanding mechanisms of action and drug interactions. *Am J Health Syst Pharm* 2007;64(9 Suppl 5):S15-24.

(A score of 3 out of 4 attracts three quarters of a credit point.)

3. If during the manipulation of an oral cytotoxic (e.g. crushing of tablets or emptying of capsule contents) an accidental spillage occurs, the following practices **should** be followed:
 - a) There is no need to wash any area of skin that has come into direct contact with the cytotoxic, but contact your GP.
 - b) If contact occurs with the eye, wash immediately with water.
 - c) If any spillage occurs on clothing, there is no need to wash these items separately.
 - d) Any waste products such as paper towels used in the spillage should be placed in a double-lined plastic rubbish bag.
 - e) b and d.
4. Pharmacist advice on correct storage and disposal of oral cytotoxics should include the following:
 - a) Oral cytotoxic medicines should be stored away from heat and humidity.
 - b) Unused oral cytotoxics may be disposed of in the household trash, but not flushed down the toilet.
 - c) Patients should always return unused cytotoxics to the pharmacy for appropriate disposal.
 - d) a, b and c.
 - e) a and c.