Submission No 64

INQUIRY INTO OFF-PROTOCOL PRESCRIBING OF CHEMOTHERAPY IN NSW

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Legislative Council

Select Committee on off-protocol prescribing of chemotherapy in NSW

Inquiry into off-protocol prescribing of chemotherapy in NSW

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Introduction

This inquiry concerns off-protocol prescribing of chemotherapy. Before making assumptions, it is first necessary to address whether this is inherently bad and should be avoided, which seems to be assumed in the nature of the inquiry.

The use of trial protocols has been extremely useful in advancing the treatment of cancer, but in practice there are many situations where patients do not fit into evidence based regimens. Although protocols are useful, their use still requires clinical judgement, just as a road map is only a guide to a journey and does not give you all the information you need to travel.

The development of clinical practice "guidelines" in NSW has been the result of a collaborative effort of many oncologists but none of us believe that they were intended to represent a rigid formula to which prescribing for individual patients requires 100% adherence. There can be catastrophic consequences of rigid prescribing by the application of guidelines advocating for strict dosing protocols. Limiting prescribing removes the expert from the equation and I would argue that this would be overwhelmingly detrimental.

Firstly “protocols” that are used in NSW Health EVIQ clearly state that they are only guidelines, and there are many factors that must be taken into account by the treating physician. I attach a copy of the dosing notes from the EVIQ website that set this out in more detail (Table 1). We aim for personalised medicine and know there is an inherent delay from protocol development to implementation.

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Table 1 – eviQ Guidelines from https://www.eviq.org.au/Copyright.aspx

Secondly, medicine and oncology in particular is very dynamic with new scientific discoveries all of the time. Bringing new discoveries from the bench to the bedside helps patients enormously. Sometimes there is limited evidence and it may take years for an idea to be proven. Without oncologists interpreting the data, there is no cutting edge treatment. For example, Carboplatin and Cisplatin in BRCA associated Breast Cancer. For years patients with BRCA associated ovarian cancer were thought to be more sensitive to platinum agents and extrapolation of this to BRCA patients who experience triple negative breast cancer has only been realised in recent years. As the numbers are low, the data is few and protocols are rare or non-existent. Does this mean we do not offer this treatment? I would argue it would be senseless to ignore.

Most oncologists in NSW operate in a peer review environment and at both formal and informal meetings oncologists discuss these issues at length. Most oncologists in Australia are members of the Medical Oncology Group of Australia (MOGA) and or the Clinical Oncological Society of Australia (COSA) and these associations provide forums for appropriate prescribing. The tumour stream interests allow for vigorous discussion and debate, and like anything there will always be controversy and disagreement.

It is also important for the Committee to appreciate that chemotherapy is given for two reasons; curative intent and palliation.

When giving chemotherapy for palliative reasons we seek to relieve pain and provide a better quality of life. Dose reduction may be relevant in these circumstances. Chemotherapy is inherently toxic, and the protocols are based on trials. Trials are usually conducted with suitable patients who are otherwise well and uncomplicated; there are strict criteria for inclusion and exclusion. We often have patients with other illnesses, and full dose chemotherapy may not be the best course of treatment in all cases. Indeed, Lyman has published data from patients being treated with curative intent in Breast Cancer. In a national practice pattern study, less than 50% of patients received 85% dose intensity. This is telling of the toxicity in the standard population that led clinicians to reduce the dose in normal day to day practices.

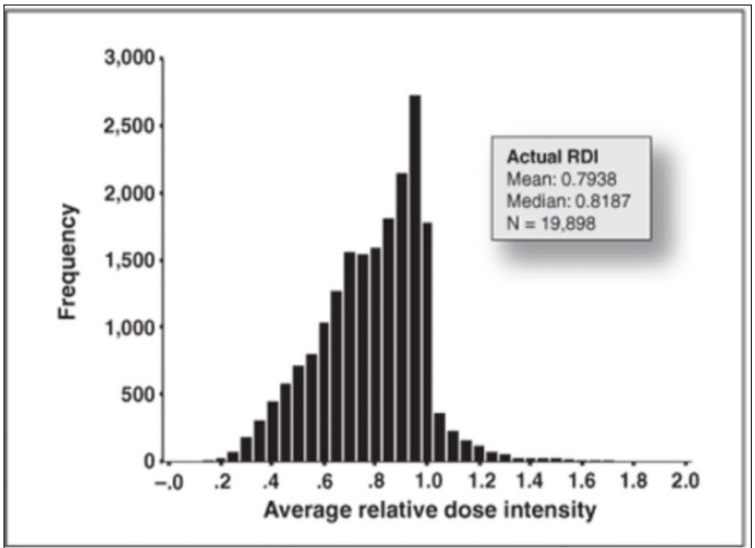

Figure 6: RDI Data From National Practice Pattern Study— Distribution of relative dose intensity observed among nearly 20,000 women receiving adjuvant chemotherapy for early-stage breast cancer in a US national practice pattern study. More than half of women received less that 85% of the standard dose intensity for their adjuvant regimen. RDI = relative dose intensity. Adapted, with permission, from Lyman.[4]

Table 2 – Lyman GH, Dale DC, Crawford J: incidents and predictors of low dose intensity in adjuvant breast cancer chemotherapy: a nationwide study of community practices. J Clin Oncol 21:4524-4531, 2003

There are often very sound reasons to use different starting doses. For example, Cabazitaxel was established in the 2nd line castrate-resistant prostate cancer setting in the TROPIC study using a dose of 25mg per metre square in a study where the majority of patients received GCSF (a colony stimulating factor that decreases risk of major infection). GCSF is not available on the PBS in the palliative setting in Australia. Without GCSF, the risk of neutropaenia is unacceptably high in some older patients. There were treatment-associated deaths reported in the pivotal study which used GCSF, so dose-modifcation at least initially is necessary in Australia with consideration to titrating the dose up as tolerated.

I will now address the specific terms of reference.

a) The efficacy of electronic prescribing systems, and their capacity to stop or limit off-protocol prescribing of chemotherapy.

St George and Sutherland Hospitals have an electronic medical record system called ARIA. While ARIA has a module for electronic prescribing, it is not available to clinicians at St George and Sutherland.

The system currently in place requires clinicians to clearly outline the treatment plan with the protocol and doses, discuss the dose schedule, and outline concurrent therapy. It also outlines the tests included in monitoring the patient and the plan for follow up. Chemotherapy is written on paper charts.

More recently it has been mandated to put the EVIQ protocol number on this treatment plan form. If there is no EVIQ protocol, then clinicians are encouraged to include an evidence based protocol such as a journal article, to support cytotoxic drugs being ordered. As far as I'm aware this is kept by the pharmacy and not included in the patient notes. More recently a chemotherapy write up meeting has been established which is supervised by senior clinicians and attended by registrars. This meeting is part of a peer-review process and an aid in teaching.

EVIQ is an online service of the Cancer Institute of NSW. It seeks to standardise treatment for patients so equitable care can be provided anywhere in the country. Before EVIQ, clinicians at each centre would have chemotherapy protocol books. Protocol would be included by the clinician if they thought they were best practice. These protocols were discussed at Journal Clubs or hospital meetings. Now, clinicians super-specialise and treat a specific tumour stream eg Breast, Gynaecological, Lung, Genitourinary, Brain etc. EVIQ annually hold protocol review committees for each tumour stream and the committee decides what stays on the protocol list and what is introduced. This has been enormously helpful as the rigorous debates by super-specialised oncologists lifts the standards and allow Australia to have one of the leading survival rates of cancer in the world.

Many members of staff at St George and Sutherland are members of the EVIQ protocols committee (I am a member of the Breast committee) and we encourage our registrars to attend these annual meetings where chemotherapy protocols are proposed and reviewed. The discussion at these

meetings is often around the evidence that is presented and discussed. Many of the experienced clinicians at this meeting discuss the toxicity they have seen with the standard doses that are recommended. Sometimes a protocol is left as is stated in the trial but full dosage is rarely used.

There is much data in the literature about appropriate prescribing, either under-dosing or over-dosing. The long term survival data is conflicting and controversial. The Clinical Oncological Society of Australia has produced a document for safe prescribing of chemotherapy in 2008 and I attach this document for your information (Appendix 1). Within this there is also a guideline about what suggested information is to be provided to the patients.

Recommendation: At St George and Sutherland Hospitals there is no electronic prescribing system and so this cannot be used to stop or limit off-protocol prescribing of chemotherapy. Electronic prescribing has many checks that may improve safety and should be a priority for NSW Health. Off EVIQ protocol prescribing of chemotherapy should be available but it needs to be justified and clearly documented. This allows new treatment into the clinic and prevents undue toxicity that may lead to excess costs to NSW health. Peer review is important and participation in these processes should be mandatory.

b) The value of a potential new patient information sheet on dose adjustment for patients and caregivers information.

Clinicians currently discuss with patients when a dose adjustment is being made and why. For example, in patients with abnormal liver function tests there is often a dose adjustment made, and this is often outlined in the original protocol. Dose adjustments are also made for myelosuppression, neurotoxicity, life threatening sepsis, and other grade 3-4 toxicities from previous cycles of treatment.

Recommendation: There is no value in providing a patient information sheet on dose adjustment as it would cause undue anxiety. Dose adjustments depend on the aim of treatment. If our aim of treatment is palliation, then dosing is adjusted for the quality of life of the patient. If our aim of treatment is cure, then clinicians favour standard dosing unless there are clear indices such as organ impairment, which necessitate dose reductions as mandated in the protocol.

c) The process and systems around informed consent for all medical interventions, including chemotherapy.

Informed consent is an essential component of prescribing chemotherapy. Information being discussed regarding side effects and toxicities is always discussed verbally and written information is provided at the same time. This has been standardised in recent years with the use of EVIQ protocols. If non-standard prescribing is used, then patients can be informed by using slides or protocols and papers presented at meetings, which have not yet been discussed at the EVIQ protocol meetings at the Cancer Institute.

Sometimes patient diaries are recommended and information on supportive medications, such as anti-nausea medication and anti-diarrheals are provided. Informed consent at St George and

Sutherland is very thorough. Major toxicities are always discussed and as cytotoxics are dangerous drugs, the possibility that the drugs could cause life threatening illness and death is discussed. This discussion also talks about the aim of treatment and personally I check to see that patients have understood what I have said, so that they don't ignore problems that may be quite serious. Their consent is documented in the notes.

Before administration of chemotherapy, the nursing staff repeats this process of educating the patients about potential toxicities. There is a rigorous 2 tier process at St George and Sutherland to ensure understanding, and this is often repeated and reinforced at subsequent consultations.

d) The capacity of the NSW Health system to have all notifiable cancer patients in New South Wales overseen by a Multidisciplinary Cancer Care Team and if this may prevent off-protocol prescribing.

I am the chair of the multidisciplinary team ("MDT") breast meeting at St George Public, Sutherland and St George Private Hospitals. We have a combined meeting every second Wednesday. All patients with newly diagnosed breast cancer are discussed and some patients who have progressed with advanced disease or who have unusual problems are also discussed. The purpose of an MDT is to decide overall management of each case to ensure each patient receives optimal care. Members of the team include surgeons, pathologists, radiation and medical oncologists, radiologists, nurses, geneticists, psychologists and trial coordinators.

Recommendations for treatment are a "pathway level" for example if radiation is thought to be necessary, then radiation is recommended or if chemotherapy is necessary, then chemotherapy is recommended and likewise with surgery. But we do not discuss which protocol of chemotherapy or what dose of radiation should be given or tell the surgeon which operative technique to use. These details are left to the clinician who will see the patient.

There is no way the multidisciplinary cancer care team can supervise or prevent off-protocol prescribing. As these meetings comprise of a diversity of professionals as well as medical oncologists, they are not an appropriate forum to discuss the particular type of chemotherapy or the doses used. Members other than medical oncologists have no expertise in dosing and drugs.

Recommendation: There is no capacity for the multidisciplinary team to oversee off-protocol prescribing.

e) St Vincent's Hospital capability to comply with relevant NSW Health Policy Directives and Guidelines, particularly Open Disclosure Policy (PD2014_028) and Incident Management Policy (PD2014_004).

I cannot comment on this, as I am not a clinician at St Vincent's Hospital.

f) The NSW Health Code of Conduct and specific programmes within NSW Health and St Vincent's Hospital, in relation to staff raising concerns about the practice of clinicians, and other breaches of the Code of Conduct.

The NSW core health values are collaboration, openness, respect and empowerment. Staff are recommended to promote a positive work environment, demonstrate honesty and integrity, act professionally and ethically, including maintaining and enhancing professional standard skills and keeping up to date with best practice, using official resources lawfully, efficiently and as authorised, and maintaining security and confidentiality, as well as maintaining professional relationships with patients.

Employees are encouraged to report any issues or incidents of clinical care that raises concern about standards of practice. Staff are encouraged to report to their manager. Additionally there are staff forums to discuss cases that are controversial including morbidity and mortality meetings; these are performed regularly within each department and generally within the divisions of medicine, surgery etc. to ensure that peer-review is an important part of practice.

All grievances are recommended to be discussed with the individual staff member with a manager proportionate to the issues raised, respecting the rights and perspective of the individual. This part of the code of ethics can be interpreted in many ways and with regards to the current inquiry to prescription of chemotherapy in NSW. At St George and Sutherland while the rights of the staff raising concern have been respected, the rights of the clinician have not sufficiently been taken into account. The dignity of a well-respected local clinician, Dr Kiran Phadke, has been removed. Subsequent vilification by the media of my colleague, Dr Phadke, could have been avoided and better processes could have been put in place.

Discussion of the cases at a department or Cancer Services level with scientific evidence presented is a far more effective way in providing guidance to clinicians which leads to best practice. Supervision and further education may remediate this situation and this is more respectful than suspension. It allows communication and reconciliation rather than persecution. When our junior colleagues underperform, they are performance managed. If a senior clinician's performance is thought to be unsatisfactory, the same methods should be applied.

Conclusion

Cancer treatment is complex and dynamic. For a clinician to avoid under-treating or over-treating a patient, scientific evidence and clinical judgment must be used. There is little level one evidence for a linear dose-cure relationship in many patients, such as those with early breast cancer. It is important that we don't simply rely on protocols that use a dose that will provide unacceptable toxicities. Protocols are often based on clinical trials on patients who are otherwise healthy with little comorbidities (ie other health issues). Many patients that are referred for clinical trials are rejected, as they do not fit the strict inclusion and exclusion criteria.

Patients that we see day to day are often sick and have multiple comorbidities, which must be taken into account. If we don't err on the side of caution, the implication to the health system may be worse with more admissions due to side effects that could have been prevented. Personalised care is ideal and it is important that oncologists are not mandated to follow outdated protocols or protocols that are flawed, rather than provide state of the art cancer treatment.

The oncologist's job is a balance between science and art. Protocols provide a solid foundation to practice that needs to be adapted from patient to patient according to the ethics of medicine; beneficence, non-maleficence, autonomy and justice. We must continue to advocate for "first do no harm".

The central conflict appears to be between the ability of other staff to question a medical oncologist with regards to choice of treatment and being able to collect information that can provide the checks and balances to ensure high quality care.

The key to ensuring better outcomes is collecting more data, in a well designed system that can give better feed back to clinicians on their choices of care. For example, so that comparisons could be made between different protocols for the same disease group. NSW Health has failed to provide clinicians with these tools. A more helpful inquiry would be one that investigates into the failure of implementing a unified patient record of treatment across hospitals. There are different systems in different hospitals, each implemented in a different manner, they do not talk to each other, and they are difficult (and different) to use.

The processes involving informed consent are rigorous and are documented. Multidisciplinary cancer care teams are not the appropriate vehicles to monitor chemotherapy prescribing as many members of the team are not trained in this regard.

Finally, the NSW Health Code of Conduct is a rigorous document and supports any staff member raising a concern about the practice of a clinician. However, the process to be followed whenever such a concern is raised is poorly outlined, subsequent dealings with the clinician concerned are haphazard, there is little proper process that is followed and the impact on the clinician can be devastating, regardless of the substance of the complaint.

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Clinical Oncological Society of Australia

Guidelines for the Safe Prescribing, Dispensing and Administration of Cancer Chemotherapy

November 2008

EXECUTIVE SUMMARY

The issue of medication safety is highly significant when anti-cancer therapy is used as a treatment modality due to the high potential for harm from these agents and the disease context in which they are being used. Medication errors can occur for a number of reasons, but the application of specific guidelines and procedures clearly reduces the incidence of errors along with a multidisciplinary approach. The purpose of this document is to provide guidance on the safe prescribing, dispensing and administration of chemotherapy and related agents used in the treatment of cancer. It is intended that this document be used as a guidance tool to inform local practice and that it will be adapted according to local service needs. The following recommendations are made:

- All staff involved in the management of cancer and its therapy must have the relevant knowledge and skills and be competent to perform the tasks.
- Appropriate staffing numbers and skill mix for all disciplines should be in place to ensure that safe practices can be followed effectively.
- Procedures and polices should be in place to provide direction and clear instruction on working practices to staff involved in providing chemotherapy and targeted therapy.
- All staff should have access to information applicable to the patient and the treatment including diagnosis, patient's history, pathology results and the treatment plan.
- All chemotherapy and targeted therapy should be prescribed on the basis of a documented, referenced protocol and a treatment plan documented for all patients. Protocols should outline all therapy, dosages and scheduling relevant to the treatment.
- The medication order for chemotherapy and targeted therapy should present the treatment information in a clear, consistent and unambiguous manner and include all supportive therapy associated with the protocol. Computer generated or pre-printed forms are preferable to handwritten orders.
- All treatment should be clinically verified by a pharmacist prior to dispensing. The pharmacist should have access to the patient information relevant to the treatment.
- All chemotherapy and associated therapy should be clinically verified by a nurse and the therapy checked against the order by 2 nurses prior to administration.
- Oral chemotherapy should be subject to the same procedures for prescribing and dispensing as parenteral therapy and labelled with clear instructions to minimise potential administration errors by the patient.
- Patients should be given both written and oral information about their treatment to include all medications, expected side effects, how to take supportive medication and who to contact in the event of an emergency or severe adverse events.
- A system should be in place for reporting adverse events, incidents and near misses with regular audits carried out to identify error prone areas or processes that require modification.

ACKNOWLEDGEMENTS

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- Cancer Pharmacists Group (CPG)
- Cancer Nurses Society of Australia (CNSA)
- Medical Oncology Group Australia (MOGA)

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The input and comments from the many individuals and stakeholder groups that assisted in developing these guidelines is gratefully acknowledged.

CONTENT

LIST OF TABLES

GUIDELINES FOR THE SAFE PRESCRIBING, DISPENSING AND ADMINISTRATION OF CANCER CHEMOTHERAPY

Purpose

The purpose of this document is to provide guidance on the safe prescribing, dispensing and administration of chemotherapy and related agents used in the treatment of cancer. The aim is to assist in the prevention of medication errors and to improve patient safety with respect to the treatment of cancer.

These are consensus guidelines based on the best available evidence and expert opinion of professionals working in cancer care. It is intended that this document be used as a guidance tool to inform local practice and should be adapted locally according to service provision, applicability and availability of resources.

Whilst their purpose is to guide clinical practice these guidelines do not replace clinician judgment.

Scope

This guidance is intended for a multi-disciplinary audience and will have most relevance for medical, nursing and pharmacy staff concerned with the complex processes involved in delivering chemotherapy and associated treatment. Scope includes

- All patients receiving chemotherapy and targeted therapy for the treatment of cancer
- Administration by all routes
- All age groups
- Patients receiving therapy at hospital and at home

For the purposes of this document anti-cancer therapy includes chemotherapy and targeted therapy.

The guidelines DO NOT address

- Chemotherapy administered for non malignant conditions
- Workplace health and safety that arises from the preparation, administration and disposal of chemotherapy. Such issues are covered by individual State and Territory Occupational Health and Safety legislation
- Specific guidance related to the characteristics of electronic prescribing programs
- The roles or responsibilities of non medical staff in prescribing treatment (i.e. nurse practitioners, pharmacists)

Background

The issue of medication safety is highly significant when anti-cancer therapy is used as a treatment modality due to the high potential for harm from these agents and the disease context in which they are being used. The complexity of treatment regimens designed to achieve maximal anti-cancer effect balanced against acceptable toxicity leaves limited margin for error. Overdosage can result in death due to adverse effects of the treatment while underdosing can have significant implications for the management of the disease and patient outcome.

Prescribing, dispensing and administration errors relating to chemotherapy that result in patient harm are well documented in the literature. Medication errors can occur for a number of reasons including procedural, technical and behavioural reasons. Errors can occur when human and system factors interact with the complex process of prescribing, dispensing and administration to produce an unintended and potentially harmful outcome.

The complex scheduling and nomenclature associated with chemotherapy regimes has resulted in use of abbreviations and acronyms which can easily be misinterpreted. Dosages are not always expressed consistently leading to incorrect interpretation of individual and total doses for treatments. The complexity of calculations associated with surface area based dosing or area under the curve algorithms can lead to inappropriate dosing when not fully understood by the staff applying them.

Developments and changes in drug delivery mechanisms and the introduction of many newer targeted therapies increases the need for ongoing education and competence related to the specialised knowledge base.

Cancer treatments are not limited to specialised tertiary centres in metropolitan areas and may be delivered in smaller centres that provide services to rural and remote communities. The increasing use of oral agents for chemotherapy and targeted therapy puts additional responsibility on the patient to ensure appropriate self administration. Education and follow up of the patient is essential in this setting to avoid incorrect dosing.

Any safety initiative should target multiple stages of the treatment process and include all members of the team. Many potential errors are intercepted or prevented on a daily basis by medical, nursing and pharmacy staff involved in the process and by the application of local procedures. It is evident that success in reducing the incidence of errors is based on the multidisciplinary approach of the healthcare professionals involved in the prescribing, dispensing and administration of treatment.[1-8]

General Information

The following sections contain guidance relevant to all professional disciplines

Competency and Skills

All staff involved in the management of cancer and chemotherapy must be competent to perform the functions. Competency should be measurable as an indicator of actual ability to perform duties. Each health care facility should establish a process to ensure that designated personnel have been trained, accredited and are authorised to provide chemotherapy and targeted therapy as a treatment modality. Mechanisms should be in place to ensure appropriate training and supervision of inexperienced staff and trainees. All staff should maintain an appropriate knowledge and skill base with processes in place to ensure continuing professional education. **Table 1** is a suggested list of essential knowledge.

Staff involved in the patients care should be easily identifiable to the patient according to the discipline and speciality they represent (e.g. nursing, pharmacy, medical, pathology staff). This is to ensure patient can direct questions about their cancer treatment to the most appropriate person. Students and trainees must be identified to the patient.

Resources

Appropriate staffing numbers and skill mix should be in place to ensure that safe practices can be followed effectively.

All staff involved in the management of cancer and chemotherapy should have access to appropriate resources that include relevant support services

Table 1. *Suggested list of knowledge and skills applicable to health care professionals involved in the prescribing, dispensing and administration of cancer chemotherapy and targeted therapy. This list is not definitive*

The principles involved in treating patients with cancer
The basic principles of chemotherapy and targeted therapy including mechanism of action, dosage methods, scheduling and administration
Chemotherapy protocols commonly used within scope of clinical practice
Adverse effects and toxicities associated with chemotherapy and targeted therapy including, early identification, ongoing monitoring, principles of prevention and management
Principles of safe handling of chemotherapy and targeted therapy
Chemotherapy and targeted therapy medication preparation, storage and transportation
Information and support needs of patients and their families including psychological support for persons receiving treatment for cancer
Ethical and legal issues associated with the use of chemotherapy and targeted therapy as a treatment modality for cancer
Local policy and procedures as they relate to cancer treatment

and Information technology systems. The use of electronic programs to facilitate the prescribing, dispensing and administration of cancer therapy is recommended. [1, 5, 6, 9-13] Electronic prescribing programs should include safety alerts such as alerting prescribers to previous adverse drug events. Prescribing and dispensing programs should be linked to avoid possible duplication of therapy.

Policy and Procedures

Procedures and polices should be in place to provide direction and clear instruction on working practices to staff involved in providing chemotherapy. All staff should be familiar with the content of the policies and procedures and they must be approved, available and up to date to reflect current practice. Policies and procedures should be approved by an appropriate authoritative committee (e.g. Drug and Therapeutics). Mechanisms for regular review and updates should be in place and a review date included on the policy or procedure. Staff should be encouraged to use electronic sources for obtaining copies of policy and procedures and the number of paper copies in circulation minimised to avoid the possible use of superseded documents when a newer version is issued. Printed material should be clearly annotated with the date of printing.

Documentation

Access to all documentation pertaining to a patient's treatment is an important aspect of safety and includes patient's records and information sources. Information should be easily accessible and up to date. The primary patient medical record/chart and all documentation applicable to the process of providing chemotherapy treatment should be available to all staff.

Paper documentation must be legible, organised and up to date. Important and variable patient data should be made available to all staff in a timely, easy to read manner i.e. weight, laboratory results. Where electronic systems are used to obtain information, procedures should be in place for storage and access of information. Protocols, procedures and other documentation templates that are stored electronically should be in a read-only format to avoid unapproved or undetectable alterations that could lead to errors. Access to original templates should be restricted to named, authorised staff.

Dosage Calculations and Body Surface Area (BSA)

The majority of chemotherapy doses are individualised for each patient and most commonly calculated based on the Body Surface Area (BSA) or weight. The calculation for BSA should be standardised and the same method used by all clinicians at the institution. The Mosteller calculation method is the simplest and most widely used although others can be used e.g. the DuBois method. [14, 15] The use of printed tables and slide-rules for the calculation of BSA is an out dated practice and should be avoided.

The capping of the BSA should be avoided. Particular caution should be exercised for patients with extreme body weights or body mass index. For treatment of obese adult patients in the adjuvant setting the actual body weight should be used for the calculation of BSA. [16] It is important that other factors such as renal function, liver function and performance status also be taken into account for dose calculation.

For adults

Although it is common practice that dose adjustments are made if the patient's weight varies by greater then 10% during treatment, there is no evidence that this should be undertaken. The re weighing of the patient during therapy to recalculate the BSA and subsequent doses will depend on local policy, treatment intent and the extent of weight change. Dose adjustment should be made according to the presence or absence of toxicity, as well as changes in other factors that

may affect drug elimination such as renal and hepatic function and concomitant medication.[17, 18]

For children

The patient's height and weight should be measured prior to each treatment and the new BSA and subsequent doses calculated. Many paediatric protocols require dosing on a dose (mg or gram) per weight basis and in these circumstances the weight must be measured prior to each treatment and the dose adjusted accordingly.

The Protocol

All chemotherapy should be provided on the basis of a documented and referenced protocol. The use of pre-documented protocols has been shown to reduce errors in prescribing. [1-5, 19] The protocol should come from an evidence-based, published source wherever possible and there should be a process of initial review by a multi disciplinary team before a protocol is implemented in clinical practice. The use of an abstract or journal paper as a direct source for writing a chemotherapy order should be discouraged unless an exceptional case arises. Misinterpretations of articles and errors in original papers have led to fatal outcomes.[20] Requirements associated with the delivery of the protocol at a local level should be considered including availability of supportive services e.g. pathology and the ability to manage expected adverse effects. Protocols should be reviewed on a regular basis for currency and changes in practice.

The format of the protocol should be

- Standardised and easily recognisable
- Clear and unambiguous.
- Typed or computer generated, not handwritten. Protocol templates stored electronically should be in read-only format to avoid unapproved alterations on the original. Access to the original protocol document should be restricted to authorised persons.
- Clearly referenced.
- Authored, signed and dated with a review date.
- Easily available to all staff. Local intranet sites or the internet are useful in ensuring access to protocols for all staff including those outside the speciality or institution i.e. emergency staff, G.P's or patients. It must be ensured that the content is maintained regularly.

Table 2 indicates details to be included in a protocol.

Clinical Trials

Treatment given as part of a clinical trial may utilise drugs, doses and scheduling outside those that staff are familiar with. Whilst guidance for clinical trials is beyond scope of this document the principles described in this document to reduce medication errors apply. Clinical trial protocols should clearly outline the treatment protocol however the format may differ according to the originating investigator and local ethics requirements. Steps should be taken to ensure that information is presented in a clear manner in the clinical trial protocol through a multi disciplinary review process. Fatal errors have occurred where trial protocols have been misinterpreted by staff. [21] All clinical trial protocols will require ethics approval. The management of the treatment should be limited to those familiar with the trial protocol. All staff involved in the prescribing, dispensing and administration of the treatment as part of the trial must be appropriately trained and educated according to the trial requirements.

Table 2. *Suggested content of the chemotherapy protocol*

Name of the protocol Care should be taken to distinguish protocols with similar names e.g. *CHOP/CHOP14, FOLFOX4/ FOLFOX6* [27]
Tumour group and stage for which it is intended to be used Multi-use protocols should not be used i.e. weekly paclitaxel for lung/breast.
Usual number of cycles to be given for a course of treatment and total length of the course
Other treatment modalities that may accompany the protocol e.g. for concurrent or sequential chemo radiation, surgery following chemotherapy debulking.
References sources that support the use of the protocol in clinical practice Where the protocol details vary from the detail in the original reference then the reasons should be stated clearly on the protocol e.g. *'This institute uses dose A and not dose B as stated in the original reference due to excessive toxicity reported with the original regimen'.*
All chemotherapy and targeted therapy relevant to the protocol including those to be administered by the oral route and other routes Generic names (not trade names) must be used as the primary drug name. Names must not be abbreviated to the chemical or trial names however it may be useful to include names the drug may also be known by as a reference source. Information should be present on the order of administration for each drug.
Route of administration of all drugs
All drug doses in appropriate measurement/units and the method of calculation (Body Surface Area (BSA), Area under the curve (AUC), weight, flat dose) Multiday regimens should specify the dose per m^2 for **EACH** day. Dose units should be written in full to avoid misinterpretation. Mathematical equations for dose calculations should be included for AUC dosing. Dose limits for individual and cumulative doses per dose, cycle and lifetime
Drug vehicle and volume (where appropriate) *e.g. cyclophosphamide in sodium chloride 0.9%, 500mL.*
Rate and duration of administration This should specify whether an infusion is intermittent or continuous. Infusions that run over several days should clearly state the daily dose and total dose. e.g. *100mg/m2 per day for days 1-7, total dose 700mg/m2 over 7 days.*
Frequency of dosing and time intervals
Scheduling A dash mark should NEVER be used when communicating dosing schedules on specified days to avoid misinterpretation e.g. day **1 AND 8** should be used NOT days 1 – 8. [5, 28] Diagrams should be used for complex scheduling.
Laboratory tests required to monitor toxicities Parameters for initiating the next cycle of chemotherapy should be defined. e.g. *neutrophil count > 1 for cycle to proceed*
Dose modifications for each agent in the protocol This should be stated according to laboratory results and side effects
Expected side effects and their management
Supportive therapy that is required to be given with the protocol To include doses and scheduling e.g. *hydration, anti emetics, growth factors, mesna*

Oral anti-cancer therapy

Oral chemotherapy and many targeted therapy agents may carry the same risks in terms of potential for error and toxicities as chemotherapy administered by other routes. The prescribing and dispensing should be undertaken by staff with the appropriate competency and skills. [22-26]

The use of oral therapy frequently requires the patient to self administer treatment at home where drug, dose or scheduling errors are unlikely to be detected. Patients may misinterpret instructions and inadvertently take an incorrect dose or continue therapy beyond that prescribed.

Oral chemotherapy and targeted therapy may continue for weeks at a time without direct professional supervision. The intermittent treatment that is characteristic of cancer chemotherapy may be difficult for some patients to understand. Fatal outcomes have been associated with patient misinterpretation of dosage instructions.[29, 30] Specific instructions are given in the prescribing, dispensing and patient education sections.

Patient Information

All health care professionals have a role in the provision of patient information with respect to treatment. The role of the doctor, nurse and pharmacist in providing this information may vary across institutions however the legal and professional requirements of each discipline must be considered and information provision must be carried out by appropriately trained staff. It is essential that provision of information is coordinated across the disciplines to ensure the patient and/or carer receives information appropriate and relevant to their treatment.

Information provision should be recorded in the patient's medical record as being carried out.

Each patient should be provided with verbal and written information which should enable the patient to comprehend the aims, the effects and likely outcomes of the proposed treatment. Outpatients, day admitted patients and inpatients should all receive the same education and information about their treatment. Written information leaflets should be verified by all 3 disciplines and approved by the hospital drug and therapeutics committee or similar. The information must be readable and take into account the literacy competence of the general public. Many patient support groups and other organisations produce leaflets on the treatment of cancer (e.g. Leukaemia Foundation, The Cancer Council, The NSW Cancer Institute website; CiSCAT) in an easy to understand format and in different languages.

With the wealth of information available through the internet it is useful to provide patients with a list of websites appropriate for them to obtain further evidence based information on their disease and treatment. Information should be given on the first visit and reinforced on subsequent visits. Questions regarding compliance, treatment tolerance, and adverse events must always be addressed at each appointment. **Table 3** outlines suggested information that should be provided to patients.

Patients receiving oral chemotherapy and targeted therapy should be provided with additional information stated in **Table 4** in accordance with the Society of Hospital Pharmacists of Australia (SHPA) Standards of Practice for the Pharmaceutical Care of Patients Receiving Oral Chemotherapy.[25]

Medication guides and the use of patient diaries can assist patients to remember when to take medications and to record any adverse effects. Institutions should consider using these, particularly for complex self administration schedules.

Table 3. *Suggested information to be provided to patients*

The treatment process Expected location of treatment (e.g. day-care, ward). Expected duration of appointments, laboratory tests and other procedures. The method of delivery of treatment (e.g. intravenous, oral) and associated delivery devices e.g. portacath. Other therapeutic modalities involved (e.g. radiation). Overall treatment length and expected follow up.
The name and indication of each anti-cancer medication and related supportive medication that the patient will receive The generic name of the drug should be given however other common names (trade names) the drug is known by should also be provided where appropriate. The phonetics of each drug can be useful for patients to aid pronunciation. Where the medicine forms part of a protocol, then the protocol name should also be provided.
General and specific side effects expected from the treatment to include Immediate effects (e.g. hypersensitivity reactions, extravasation). Short term effects (e.g. nausea and vomiting, neutropenia, alopecia). Long term effects (e.g. infertility, carcinogenesis, cardiotoxicity). Where appropriate, information about potential teratogenic effect of cytotoxic agents and pregnancy precautions should be given.
The management of expected side effects e.g. mucositis and mouth care, neutropenia and taking regular temperatures, diarrhoea and the use of loperamide.
How and when to take each medicine on discharge It is particularly important to differentiate between those medicines which are used as treatment or to prevent side effects and those which only need to be used if symptoms develop. This information should include ○ What to do if the patient misses one or more doses. ○ What to do if the patient vomits after taking a dose. ○ The maximum daily dose for 'when required' medications.
The need for, and how to obtain, further supplies of supportive therapy and other medication It is essential that patients are aware of medication that can be obtained through the GP and those that need to be obtained through the treating doctor.
Details of appropriate and readily accessible 24-hour contact Medical, nursing and pharmacy staff to which patients can contact regarding their treatment and its effects.
All information should be provided as verbal and written information

Table 4. *Additional information to be provided to patients receiving oral chemotherapy and targeted therapy*

The need to swallow tablets/capsules whole and not to chew them The risks of crushing tablets and mixing with food or emptying the contents of capsules into food or drink must be highlighted.
Instructions on what side effects may require an immediate suspension of therapy or urgent medical attention e.g. severe diarrhoea with capecitabine
Details of appropriate and readily accessible 24-hour contact Medical, nursing and pharmacy staff to which patients can direct queries
Principles of safe handling, storage and disposal Patients must be advised ○ To store all medications including any requiring refrigeration, in a secure manner away from children ○ To store empty containers and unused medicine in a strong designated container or bag and return these to the hospital or pharmacy for appropriate disposal ○ To avoid or minimise the handling of tablets/capsules by family members/carers ○ To wash hands after handling tablets/capsules

Consumer medication information leaflets (CMI's) must be provided if available and appropriate. The nature and the context in which anti-cancer therapies are used often limits the availability or suitability of CMI's. Therapy may be used outside Therapeutic Goods Administration (TGA) indications and doses or as part of a protocol which may induce possible effects not listed in a CMI. Guidance on how to use CMI's may be found in the SHPA Standards of Practice for the Provision of Consumer Medicines Information by Pharmacists in Hospitals. [31]

Patients that understand their treatment regimen and therapy can be valuable in enhancing the medication safety process. Patients who know the name of the drug they are receiving and what it looks like may be valuable in identifying discrepancies prior to administration. [32] Patients may request information about complementary therapies. Steps must be taken to ensure the patient is given adequate and unbiased information about complementary therapies and the impact that using complementary therapy may have on the treatment they are receiving and their disease.

Risk Assessment and Quality Assurance

A system should be in place for reporting adverse events, incidents and near misses.[1-3, 33] The 'Root, Cause, Analysis' process should be undertaken for sentinel events and where a near miss could have resulted in a serous adverse outcome it is recommended the staff undertake a 'Failure Mode Effectiveness Analysis'. The review of process measures (such as rate and type of incidents and near misses) and outcome measures (such as chemotherapy related adverse events and readmission rates) should be undertaken regularly to identify 'error prone' areas that require modification. The NSW Therapeutic Advisory Group (TAG) manual of *'Indicators for Quality Use of Medicines in Australian Hospitals'* is a useful resource for monitoring of practice related to safe medication use and includes specific indicators relating to cancer therapy.[34] A management

committee consisting of all disciplines involved in the treatment process should be established to oversee these activities.

Vinca alkaloids

Whilst any agents can potentially be administered by the incorrect route if appropriate safety steps are not followed, vinca alkaloids have been implicated in the majority of errors involving administration of incorrect therapeutic agents by the intrathecal route. Virtually all cases have resulted in death or permanent disability. [35, 36] Separate requirements for these agents have been specified by the Australian Safety and Quality Council. [37]

All vinca alkaloids for administration to **adult patients** must be supplied in an infusion bag. The minimum recommended volume is 50mL to be administered over 5-15 minutes.

All vinca alkaloids for administration to **paediatric patients** over 10 years of age must be supplied in an infusion bag in a volume of 20mL-50mL to be administered intravenously over 5-10 minutes. For patients younger than 10 years a risk assessment must be carried out to support any decision to use syringes instead of infusion bags.

Distinctive warning labels must be placed on all Vinca alkaloids preparations, *"FOR INTRAVENOUS USE ONLY. FATAL IF ADMINISTERED BY ANY OTHER ROUTE"*

Intrathecal Therapy

All staff responsible for prescribing, dispensing and administering intrathecal chemotherapy should be made aware of the catastrophic outcomes associated with the errors in administering incorrect chemotherapy drugs via the intrathecal route. A register of staff designated as competent to prescribe, prepare, dispense, supply, receive or administer intrathecal therapy for cancer should be in operation and accessible across the institution. Only staff listed on the register may undertake the specified tasks.

Occupational Health and Safety Precautions

Chemotherapy is known to be mutagenic, carcinogenic and teratogenic. It is beyond the scope of this document to address the issues of safe handling and prevention of occupational exposure. Health care professionals should refer to individual state guidance on health and safety related to safe handing of chemotherapy and targeted therapy.

PRESCRIBING CHEMOTHERAPY, TARGETED THERAPY AND RELATED TREATMENT. THE ROLE OF THE PRESCRIBER

Responsibilities

The prescriber is responsible for

- Making treatment decisions and ensuring that each treatment is appropriate for the patient according to diagnosis, laboratory parameters, performance status and organ function.
- Monitoring the effects of the treatment and ensuring appropriate medical review of patients during and after treatment.
- Ensuring that all professional and legal responsibilities are met with respect to prescribing.

Competency and Skills

Chemotherapy and targeted therapy must only be prescribed by clinicians with appropriate skills, training and qualifications in the management of cancer. Local accreditation processes should be considered for clinicians prescribing chemotherapy and targeted therapy. General Practitioners should only prescribe chemotherapy under the direction of the medical oncologist or haematologist.

The Treatment Plan

A treatment plan should be completed by the doctor initiating treatment. It is preferable that a patient's overall treatment plan is discussed in a multidisciplinary meeting. The plan should reflect other decisions made such as surgery and radiation therapy and requirements in relation to nursing and allied health. The plan should ideally be in a computer generated format and should be kept with the patient record at all times. Where the plan changes during treatment, i.e. the patient is commenced on a new protocol or the dose changes then this should be clearly documented on the treatment plan. **Table 5** indicates content that should be included in a treatment plan.

The Order

The order (i.e. the medication chart) should present the treatment information in a clear, consistent and unambiguous manner. The following guidance is in addition to legislative requirements of State/ Territory Health regulations (Drugs and Poisons).

- The medication chart should be designed specifically for the purpose of prescribing chemotherapy and targeted therapy.
- The chemotherapy chart should be used for all parenteral and oral drugs used in the treatment of cancer and should be approved by the institution's therapeutics committee or medical records committee.
- Sufficient space should be available to allow clear description of the medication, date and time of administration, the dose, route and frequency and the signatures of the prescriber, pharmacist and nurse
- Prescribers should avoid the use of handwritten prescriptions (drugs AND doses) and the use of pre-printed or computer generated orders is preferable. Where handwritten orders are unavoidable the order should be PRINTED using permanent black ink.
- Verbal orders for the initiation of chemotherapy should not be permitted under any circumstance.
- Where a copy of a chemotherapy order is to be sent to an offsite location it should be scanned not faxed. Faxing produces a poor copy of the original and can result in errors where lines obscure decimal points or where dosage details appear incomplete. Carbon copies should not be used.
- A PBS script alone should not be used to prescribe chemotherapy by any route as it has insufficient space to provide the information required to ensure safe dispensing. An order written on an appropriate chemotherapy order chart should accompany a PBS script.

Table 5. *Suggested content of treatment plan*

Patient name and TWO other unique identifiers (e.g. hospital number, date of birth)
Diagnosis
Name of the chemotherapy protocol to be given
The date the it is intended that the treatment commences
Intended duration of treatment and the no of cycles for treatment
Tests to be performed after specified number of cycles
Therapeutic goal of treatment (e.g. curative, palliative)
Details of other therapeutic modalities i.e. surgery, radiation
Any treatment variations such as dose reductions If dose reduction occurs then the reduction factor should be clearly documented along with the reason for the reduction. e.g. Dose reduced to 75% of scheduled dose due to diarrhoea.
The name and contact details of the physician completing the treatment plan

Physical and staffing resources should enable the prescriber to complete an order away from distractions and interruptions to maximise safety. Table 6 details information that should be included on a chemotherapy order. [26]

Prescribing oral anti-cancer treatment (chemotherapy and targeted therapy)

Oral therapy carries the same risks in terms of potential for error and toxicities as therapy administered by other routes and must be written to the same standards as parenteral therapy.[23-25] **Table 7** outlines additional details that should be included. Oral chemotherapy and targeted therapy must only be prescribed by clinicians with appropriate skills and qualifications in the management and treatment of cancer. GP's should not prescribe oral therapy unless directed by the patient's oncologist or haematologist.

Prescribing Intrathecal therapy [37]

Medical staff who prescribe and administer intrathecal therapy must be deemed competent to do so and must receive education, training and assessment with respect to the prescribing and administration of intrathecal therapy. Prescriptions for intrathecal therapy must specify the route of administration as **"INTRATHECAL"** written in full, in capitals and in bold for computer generated proformas. The abbreviation 'IT' is unacceptable. Methotrexate, cytarabine, hydrocortisone and dexamethasone are commonly given by the intrathecal route. Occasionally rituximab and thiotepa may be given by this route. Where practical, intrathecal injections should be scheduled to be administered on a day that no other intravenous chemotherapy is being administered to the patient.

Table 6. *Information to be included on a chemotherapy order*

Patient name and TWO other unique identifiers (e.g. hospital number, date of birth)
Patient height, weight and BSA
Drug allergies and relevant laboratory results
Name of the protocol being used and the diagnosis
Date the treatment is to be given and the cycle number (i.e. cycle 1 of 4)
All drugs to be given as part of the protocol This includes targeted therapy, oral chemotherapy and supportive therapy that accompany the protocol. e.g. Hydration, anti emetics, supportive medication for home use. Drugs should be prescribed using the generic name.[3, 13, 38] Trade names, abbreviations and chemical names should not be used. Care should be taken where a number precedes a drug name e.g. 6-mercaptopurine, 5-fluorouracil as this can be misinterpreted as a dosing instruction. The preceding number can be omitted in most cases.
Dose per specific patient factor (i.e. X mg/m2) and the actual calculated dose to be administered The rounding of doses to whole numbers or one decimal point should be considered for larger doses in adults. e.g. Cisplatin 186 mg is preferable to 185.62 mg and reduces the likelihood of overdose where the decimal point is missed. Doses must be in arabic numbers (i.e.1, 2, 3, 4 etc), metric units and should represent the recognised measurement of the drug. e.g. Bleomycin is expressed as international units NOT mg. **Table 8** is a list of dangerous unit measure abbreviations whose use is NOT recommended.[39]
Directions where applicable Abbreviated directions must be avoided. [39-42] **Table 9** is a list of dangerous dosing instruction abbreviations whose use is NOT recommended.
Days, dates and times when each drug is to be given Multiday regimens should be written in a format that specifies the dose per m^2 for each day. Where doses are to be given on specified days e.g. day 1 AND 8 this must be clear to avoid misinterpretation as days 1 through to 8.[28]
Diluents, volume and rate of administration where applicable for each drug Rates of administration should be unambiguous. e.g. q24 hrly can be misinterpreted as every 2-4 hours and should be written as 'to be administered over 24 hours'.
Dosage form and administration route for each drug **Table 10** is a list of dangerous route of administration abbreviations whose use is NOT recommended.[39-41]
Dose modifications for the patient according to laboratory result and side effects
The prescriber's name, signature and the date the order was written The date should be clearly differentiable from intended date of administration if the two differ.

Table 7. *Prescribing oral chemotherapy and targeted therapy* [23, 24]

Oral chemotherapy and targeted therapy should be prescribed on the basis of an approved protocol
Oral therapy should be written on a designated chart where possible A PBS script alone should not be used to prescribe oral chemotherapy as it has insufficient space to provide the information required to ensure safe dispensing. An order written on an appropriate chart should accompany a PBS script.
The quantity prescribed should be the quantity of tablets/capsules the patient requires for that cycle of treatment The use of PBS quantities as whole patient packs may pose a risk to patients if they contain more tablets than are needed for the cycle.
Repeat prescriptions preferably should not be issued for oral chemotherapy due to the risk of misdosing Chemotherapy doses may change according to blood results, side effects and therapeutic response. If this option is utilised within the PBS regulation then the patient should be directed to destroy any repeats or return them to the doctor or pharmacy if treatment is changed or stopped to avoid any inadvertent dispensing.
Steps must be taken to round doses according to the strengths available when calculating dose requirements according to BSA The strengths of oral formulations are often limited and chemotherapy and targeted therapy tables/capsules cannot generally be broken. Where rounding is inappropriate it may be necessary to alter dosing scheduling e.g. where a patient requires a daily dose of 175mg of cyclophosphamide the dose could be given as a 150mg one day and 200mg the next to make up the total dose.
Do not advise a patient to crush or dissolve tablets at home Where a patient has difficulty in swallowing advice should be sought from a pharmacist. Crushing of tablets carries both exposure risks and changes to drug bioavailability. Pharmacists will have information on what formulations can be dissolved or made into a mixture.

Table 8. *Dangerous abbreviations to be avoided for units of measurement* [39-42]

Abbreviation to AVOID	Intended meaning	Reason for avoiding	Acceptable alternative
ug or μg	microgram	Mistaken for milligram	Write microgram in full
U or U/s	unit	Mistaken for 0	Write units in full
IU	International units	Mistaken for IV or the number 10	Write international units in full
No zero before decimal point. e.g. .5mg	0.5mg	Misread as 5mg	Write 0.5mg or write 500 microgram
Zero after decimal point e.g. 5.0mg	5mg	Misread as 50mg	Do not use decimal points after whole numbers

Table 9. *Dangerous abbreviations to be avoided for dosing instructions* [39-42]

Abbreviation to AVOID	Intended meaning	Reason for avoiding	Acceptable alternative
OD, od or d	ONCE a day	Mistaken for twice a day	Write mane or morning, nocte or night or specific time
QD or qd	EVERY day	Mistaken as qid (four times a day)	Write mane or morning, nocte or night or specific time
QOD	Every other day	Mistaken as qid (four times a day)	Write on alternate days or every second day
m	Morning	Mistaken for n (night)	Write mane or morning
n	Night	Mistaken for m (morning)	Write nocte or night
6/24	Every 6 hours	Mistaken for 6 times a day	Write 6 hourly
1/7	For ONE day	Mistaken for 1 week	Write for ONE day ONLY in full
X 3d	For 3 days	Mistaken for 3 doses	Write for THREE days ONLY in full

Table 10. *Dangerous abbreviations to be avoided for route of administration* [39-42]

Abbreviation to AVOID	Intended meaning	Reason for avoiding	Acceptable alternative
SC	subcutaneous	Mistaken for sublingual	Write subcutaneous or subcut
S/L	sublingual	Mistaken for S/C and interpreted as subcutaneous	Write sublingual or under the tongue
IT	Intrathecal	Can be confused with IV	Write INTRATHECAL in full
IP	Intraperitoneal	Can be confused with IV	Write INTRA PERITONEAL in full

DISPENSING OF CHEMOTHERAPY AND RELATED TREATMENT. THE ROLE OF THE PHARMACIST

Responsibilities

The pharmacist is responsible for

- The clinical verification of the drug order including chemotherapy, targeted therapy and supportive medications, according to the protocol, the patient's treatment plan and patient parameters, [26, 43]
- The clarification and resolution of any identified discrepancies with the prescriber.
- The accurate dispensing of chemotherapy, targeted therapy and related treatment including supportive care therapies.
- Ensuring the appropriate preparation of treatment.
- Ensuring that all components of the prescription are supplied in a timely and safe manner.
- Ensuring that all professional and legal responsibilities with respect to dispensing are met.

Competency and skills

The pharmacist carrying out the verification of order should have the appropriate training, knowledge and skills in cancer chemotherapy as defined by the SHPA Standards of Practice for Clinical Oncology Pharmacy Services. [43] Pharmacists with insufficient knowledge or experience in cancer treatment should not be delegated to manage patients receiving chemotherapy and related treatment. The application of competency testing for the verification and dispensing of chemotherapy should be considered for all staff involved in these tasks.

Clinical Verification

A written, up to date procedure for verification of the order should be available that includes an individual systematic check of all the components of the prescription. **Table 11** indicates parameters that should be checked by the pharmacist.

Physical and staffing resources should enable the pharmacist to verify an order away from distractions and interruptions to maximise safety. An independent check by a second person should be performed when possible. This should be a pharmacist with appropriate knowledge and skills in cancer therapy. Calculations performed manually should be independently checked. Where computerised systems are in place a validation process must be implemented to ensure accuracy of automated calculations. In verifying the prescription the pharmacist must have access to the following information.

- An original or legible copy of the drug order. Scans are preferable to faxes for clarity and legibility. The prescription must be completed with the detail specified in the prescribing section of this document.
- An order written on an appropriate chart must be made available to clinically verify the treatment for administration by ALL routes. A PBS script alone will contain insufficient information to enable safe dispensing of chemotherapy treatment and should not be supplied against a PBS script in isolation of other information.
- Current diagnosis and relevant medical history.
- Patient parameters (height, weight, BSA) and relevant laboratory values including blood counts, urea and electrolytes, liver function tests. A patient treatment plan which includes details of the protocol being used.
- Treatment history and patients medication profile/records including over-the-counter medications herbal medications, drug allergies and drug related adverse events.

Table 11. *Chemotherapy order details to be verified by the pharmacist*

Patient Body Surface Area (BSA) The patients BSA must be recorded on the chemotherapy order and an independent check carried out.
The drugs Ensure that all drugs have been prescribed according to protocol and that there are no omissions with respect to the requirements of the protocols including chemotherapy, targeted therapy, pre medication and supportive therapy. Check that additional medication has been prescribed. e.g. anti emetics, mesna. Verify they are appropriate for the protocol and the length of the course. Verify that the administration route for each drug is correct and is specified. Verify that the duration of infusion and diluent requirements are specified where needed. Verify that the frequency and sequencing (i.e. day 1, day 2 etc.) is correct. Ensure that the patient has no documented allergies / hypersensitivity reactions to any of the medication prescribed.
The doses Verify that all doses are correct according to protocol, patient weight, BSA, creatinine clearance. Verify maximum and cumulative doses are not exceeded for the dose or the course. Verify dose reductions are correct according to the protocol, patient parameters.
Scheduling Verify that the length of course and time interval between each cycle is appropriate for the protocol and tumour type. Verify that the appropriate time period has passed between last cycle and current cycle. It is important to maintain an up to date treatment history relating to all chemotherapy drugs, doses and treatment dates.
The patient blood counts and other results Verify that the absolute neutrophil count is appropriate for administration of the chemotherapy. Verify that the renal and liver function is appropriate for the dose of the drug to be administered. Where appropriate obtain results of other tests specific to certain drug toxicities, e.g. lung function prior to bleomycin, methotrexate levels, urine pH level for methotrexate, and ejection fraction for anthracyclines.
Protocol variations Verify that variations from the original protocol are valid for the patient and protocol. Ensure they are authorised by the prescriber and documented.
Drug-drug, drug-disease interactions A medication history should be taken by the pharmacist at the initial and subsequent cycles to include prescribed medication, over the counter and herbal medication and must take into account any changes in medication during treatment. The pharmacist must investigate and advise on any potential drug or disease interactions.
Adverse Drug reactions Details of previous and current adverse drug reactions should be verified with the patient and documented. Adverse drug reactions may occur with chemotherapy agents, targeted therapies and supportive therapy during treatment and appropriate recording and reporting must be ensured. Documentation of rechallenges and subsequent reactions is also essential.

Oral anti cancer therapy

Staff dispensing oral anti-cancer medicines in the community setting must have access to the above information to ensure they can confirm that the prescribed dose is appropriate for the patient. Access to a pharmacist with experience in cancer treatment at the hospital where treatment is initiated should be available.

Labelling

A uniform labelling method must be applied to ensure easy identification of the drug, route, dose and patient. In addition to the legal requirements for labelling **Table 12** indicates information that should be included. **Table 13** indicates additional detail required for dispensing of oral anti-cancer therapy.[25]

Preparation and Delivery

The process of clinical validation of the order and the actual preparation of the chemotherapy and targeted therapy should be considered as two separate functions. Preparation processes must be performed according to Australian standards and the SHPA Preparation of cytotoxic drugs and the transportation of cytotoxic drugs. [44, 45] The preparation process must ensure that the therapy is stable in the required diluent for the required length of time.

- There must be a reconciliation check with the product and the prescription before issue. Where preparation is carried out off-site by a 3rd party there must be a process in place to ensure the final prepared product is checked by the pharmacist responsible for the clinical

Table 12. *Details required for labelling chemotherapy and targeted therapy*

Patient's name and unique patient identifier
The name of the drug This should appear in the generic form. If the trade name is required this should not form the main part of the drug name Abbreviations and chemical names are not acceptable Clinical trial names must only be used in the context of approved clinical trials.
The strength of the drug Where the drug is in parenteral form the total dose should be expressed as a total concentration e.g. 25mg in 52 mL.
The form of drug and the drug diluent Where appropriate for infusional chemotherapy.
Intended route of administration for parenteral therapy Distinctive warning labels are to be placed on vinca alkaloids, "FOR INTRAVENOUS USE ONLY. FATAL IF ADMINISTERED BY ANY OTHER ROUTE". With the increasing use of chemotherapy given by the Intraperitoneal route steps should be taken to ensure drugs intended for administration by this route are clearly annotated.
The expiry date and storage conditions Where appropriate for infusional chemotherapy.
Cytotoxic warning label Chemotherapy must be labelled with a cytotoxic warning sticker in accordance with local Health and Safety requirements. Suggested labelling is a permanent, adhesive purple cytotoxic warning label with the distinctive warning; "Cytotoxic, Handle with Care". Cautionary and advisory labels must be added to the container as required.

verification of the order. The product should be checked against the original order before being handed over to nursing staff for administration.

- The therapy must be delivered to *'the right place at the right time for the right person'* to enable treatment to commence.
- All chemotherapy must be delivered separately from other drugs in a plastic hard walled container dedicated to the purpose.
- Intrathecal chemotherapy has special requirements for preparation, transportation and delivery (see section on intrathecal chemotherapy).

Dispensing Intrathecal chemotherapy[37]

- All intrathecal doses for cancer therapy must be dispensed and packaged separately from other chemotherapy.
- All intrathecal chemotherapy should be stored in a designated and clearly labelled storage container in the pharmacy until the patient is ready for the Intrathecal administration. This container must only be used for Intrathecal doses.
- On receipt of the intrathecal dose a signature should be requested by either the authorised nurse or doctor attending to the patient receiving the intrathecal therapy.

Table 13. *Additional requirements when labelling oral anti-cancer therapy*[25]

Clear and unambiguous dosing instructions 'As directed' should never be used regardless of the doctor's instruction or of the patient's knowledge of the dosing regimen. The intended period of treatment including start and stop dates for short term or intermittent treatment e.g. if chemotherapy is to be taken on days 1 to 4 inclusively then the label must specify the actual calendar dates to start and stop.
The total dose of required If the patient is required to take 2 different strengths of tablets to make up the dose (e.g. Capecitabine 150mg and 500mg) then the dose instructions must include the number of tablets to take of each strength dose and the total dose. Steps must be taken to highlight different strengths of the same tablets/capsules to aid patient understanding.
All boxes /bottles must be clearly labelled Boxes must NEVER be taped together with a label on one box. Where more than one container of the same medicine is given then the following label (or similar) must be used *'This is x of y number of containers containing the same medicine. Please use the contents of one container before starting another'.*

THE ADMINISTRATION OF CHEMOTHERAPY AND RELATED TREATMENT – THE ROLE OF THE NURSE

Responsibilities

The nurse is responsible for

- Ensuring that the medication is stored appropriately prior to administration
- Verifying the medication order. including chemotherapy, targeted therapy and supportive medications, according to the protocol, the patient's treatment plan and patient laboratory parameters.
- Administering the therapy and associated treatments to the patients in a safe and timely manner.
- Ensuring that any immediate and longer term effects are managed appropriately.
- Ensuring that all professional and legal responsibilities with respect to administration of medications are met.

Competency and Skills

All nursing staff required to administer chemotherapy and related therapy should receive training in cancer chemotherapy and related agents. Nursing staff should have satisfactorily completed education and achieved competency in chemotherapy administration prior to administering any chemotherapy medication according to the Cancer Nurses Society of Australia (CNSA) guidelines and local policy. [46]

Nursing staff administering parenteral therapy must be supported by staff who have cannulation skills and should be trained and deemed competent to use infusion devices to administer parenteral therapy according to the devices used at their institution. Nursing staff required to administer parenteral therapy through a central line device should have successfully completed central venous access device competencies.

Policies for educational requirements for the administration of oral anti-cancer agents may vary within local institutions. Procedures to be followed should be placed clearly in patient care plans and notes

Pre-administration

The following should be available prior to commencing administration of therapy

- Current diagnosis, medical and medication history of relevance including treatment history. Details of any drug allergies
- A patient treatment plan and an original or legible copy of the order. These should be completed with the detail specified in the prescribing section of this document
- Patient parameters (height, weight, BSA) and relevant laboratory values including blood counts, urea and electrolytes, liver function tests. Nursing staff should confirm the performance of required tests and results and contact the medical officer where results fall outside acceptable parameters
- Policies, procedures and equipment required for safe administration and handling of cytotoxic drugs and related waste including emergency procedure protocols, medications and the management of extravasation.
- An appropriately qualified registered nurse, nurse practitioner, medical officer or pharmacist who has training and experience in the management of adverse events should be present.

An assessment of the patient should be carried out by the nurse prior to administration according to **Table 14.** Questions regarding compliance, treatment tolerance, and adverse events must always be addressed at each appointment. The

order should be verified and any discrepancies identified discussed with the prescribing medical doctor and /or the pharmacist prior to administering the medication(s). Documentation of any discrepancy and the resolution must be completed by the nurse in the patient's medical record. **Table 15** defines areas that should be verified. Physical and staffing resources should enable the nurse to check an order away from distractions and interruptions to maximise safety.

Pre treatment medications

It is essential that administration of pre medications allows an appropriate time span to elapse before the chemotherapy is administered. For some anti emetics 30 minutes is the minimum time period required before chemotherapy is administered following administration of the pre medication, however this time period may vary according to route of administration and time of onset of action of the drug.

Pre medications should not be given too early (usually > 60 minutes prior to the dose) unless specified as this may lead to insufficient therapeutic levels of the drug when therapy is given. Where information is not contained in a protocol advice from a pharmacist should be sought.

Administration

Anti-cancer therapy and associated treatment can be administered by several routes including: oral, intravenous infusion, intravenous bolus, intrathecal, intraventricular, subcutaneous , intradermal and intraperitoneal. Many of these routes would require administration by an appropriately credentialed medical practitioner, The patient should receive their treatment in an area that is equipped to manage any reasonably foreseeable adverse events that may be associated with the medication or route of administration. Nursing staff involved in the administration of therapy in the home nursing staff should ensure that appropriate procedures are in place to manage any complications and are able to access medical assistance and medications for the management of an adverse event. Local occupational health and safety workplace guidelines must be followed when handling and administering chemotherapy and associated waste.

Verification of the medication

The chemotherapy, targeted therapy and related treatment must be checked at the point of administration by two registered nurses with the appropriate training and skills. [3, 6, 26] Where a second nurse is not available then a pharmacist or a medical practitioner with appropriate knowledge and skills should perform the function. The following information stated on the medication chart must be checked with a second competent person.

- The patient name (first name and surname), date of birth and unique identifying number.
- The name of the medication.
- The dose of the medication.
- The route of administration.
- The date and time of administration.
- The expiration date of the medication.
- Patient drug allergies.

The performance of these checks must be verified by signing and dating on the chemotherapy medication chart by both persons Preparations for parenteral administration must be checked for leaks, cloudiness or signs of precipitation. Some preparations will require gentle agitation prior to administration to ensure an even dispersion of drug in the diluent as medication can settle on storage e.g. paclitaxel. Qualified advice should be sought where this information is not present.

Post administration

Many protocols require the administration of medication post therapy including fluids, folinic acid rescue or anti emetics. Nursing staff must ensure that these medications are prescribed and administered according to the protocol.

Where the patient is to be discharged home the nurse should check that the patient has the following:

- Arrangements in place for laboratory tests and other tests relevant to the disease and treatment.
- An appointment for medical review and the next cycle of treatment.
- All prescribed post chemotherapy medication e.g. anti emetics, anti diarrhoeals is available for the patient to take at home.
- Written information or access to information on the treatment administered including expected side effects, precautions to be taken and what to do in the event of an adverse effects e.g. uncontrolled nausea and vomiting, a febrile episode or severe diarrhoea.
- The name and phone number of a health care professional who is available as a 24 hour contact for advice and emergencies.

All actions must be documented in patient records including side effects and care of patient during and after administration.

Table 14. *Assessments to be performed by the nurse prior to administration*

The patient's history and treatment plan The diagnosis, treatment plan and protocol should be confirmed.
The patients weight and body surface area Changes in weight and weight (for paediatrics) should be assessed and the subsequent impact on BSA and dose.
Pathology results Blood counts should be documented and confirmation given by the prescriber that they are appropriate for treatment to proceed.
Response to previous treatment and previous toxicities that may impact on treatment. e.g. nausea and vomiting, mucositis, neuropathy Ensure that existing conditions or toxicities do not preclude tratement from proceeding.
The patient's coping mechanisms, anxiety level, and any cultural issues that may have an impact on the administration process Where concerns are identified, referral to another health care professional should be considered according to local procedure. Ensure that identified issues do not preclude tratement from proceeding.
The patients physical and performance status that may impact on the treatment process Using a physical assessment and subjective performance status assessment e.g. Eastern Cooperative Oncology Group (ECOG). [47]
Pre-medication required to be taken at home has been taken by the patient as instructed e.g. Steroids required to be commenced 24 hours prior to docetaxel.
Baseline observations specific to the protocol e.g. Patients taking nephrotoxic medications must be assessed for urine output and urinalysis.
Access devices required for administration are in place and patent e.g. peripheral inserted central line, venous catheter.

After administration ensure that cytotoxic chemotherapy precautions are observed when handling patient waste. The period of time can vary depending on the route of administration, dose and half life.

Generally precautions should be observed for 48 hours following parental administration or up to 7 days following oral therapy. These times may be longer according to the protocol or local policy.

Table 15. *Checks to be performed against the order by the nurse prior to administration*

The protocol Verify that all medications are prescribed according to documented protocol including all pre and post supportive medication and oral chemotherapy.
Doses Verify that all doses are correct according to protocol and patient parameters e.g. weight, BSA, creatinine clearance and that maximum and cumulative doses are not exceeded for the dose or the course according to the protocol. Check any dose reductions are correct according to the protocol, patient parameters and doctor's instructions.
Scheduling Verify the appropriate time period has passed between last cycle and current cycle.
Administration route Verify that this is present and correct for each medication.
Administration rate Verify that the rate is specified and is correct for each medication.
Adverse drug reactions Verify that the patient has no reported or documented allergies or history of hypersensitivity to any of the medications to be administered.

Administration by specified routes

The following provide additional detail specific to the stated administration routes

Administration via the Intravenous route

Intravenous therapy may be administered through a central or peripheral vein via a bolus, intermittent infusion or continuous infusion. For all prolonged infusions and vesicant medications a Central Venous Access Device (CVAD) is the preferred route of administration.[48]

- Intravenous chemotherapy and targeted therapy should be administered during operational hours where possible to ensure appropriately trained doctors are available to assist in an emergency. For protocols with complex scheduling times this may not always be possible.
- All therapy must be given according to the sequencing of the protocol where stated or according to local administration policy including line flushing.
- Programming for infusion pumps should be independently checked by a second competent nurse to include calculation of infusion rates. Care must be taken to ensure the rate is correctly set according to the time span i.e. mLs/hour

or mLs/24 hours.[49] The use of error reduction software or smart pumps should be considered.

- Intravenous lines must not be primed with chemotherapy unless specific instructions are given
- The nurse should be aware of the risk of extravasation and be able to identify which medications are vesicants or irritants. Staff must be able to manage an extravasation according to local procedure.(50)
- The nurse should be aware of the risk of hypersensitivity reactions, be able to identify which medications have potential for these reactions and be able to manage them according to local procedure as well as other side effects associated with the therapy during and after administration (e.g. extravasation, nausea, vomiting, pruritus, rashes).
- The infusion must be stopped immediately and medical doctor notified if the patient shows any sign of an anaphylactic reaction or a drug extravasation .
- After administration the intravenous line must be flushed with a sufficient volume of compatible fluid to ensure the medication is cleared from the line.
- All observations and actions must be documented in the patient records including education provided, side effects and care of patient during and after administration.

Administration via the Intramuscular and Subcutaneous route

Checking and cautionary points that apply to intravenous administration apply to the Intramuscular and Subcutaneous route

- Intramuscular injections may be administered into the deltoid, dorsogluteal, rectus femoris, vastus lateralis and ventrogluteal muscle groups.
- Subcutaneous injections are administered through the epidermal and dermal layers into the subcutaneous tissue.

Administration via the Oral route

Oral therapy carries the same risks in terms of toxicity and risk of medication errors as therapy administered by other routes.[23, 25]

- Ensure that the patient can swallow the medication and that there are no risk factors for aspiration.
- If an anti emetic is required then this should be administered not less than 30 minutes prior to and not more then 90 minutes before the administration of oral therapy unless instructed otherwise in the protocol.
- Oral chemotherapy and targeted therapy should be administered using the “no touch technique’ when placing medication in a disposable pill container.
- If the patient experiences emesis immediately after ingestion a further dose must not be administered. Inform the treating physician of the episode for further guidance.
- Many patients will receive their oral therapy at home. Where the therapy is to be administered outside the hospital setting by the patient or their carer it must be ensured that appropriate education has been provided on how to take the medicine and the precautions required to prevent carer exposure.

Chemotherapy tablets and capsules must not be crushed. Crushing tablets carries both exposure risks and change to bioavailability. If a patient is unable to swallow or medication is being administering via a PEG tube or a nasogastric tube, then the pharmacist must be contacted for advice on alternative dose formulations.

Administration via the Topical route

Topical chemotherapy is usually applied for treating non melanoma skin cancer and other skin conditions. The medication may be in the form of an ointment, solution or suspension.

- The formulation should be applied in a thin layer to the affected area with an applicator at the frequency ordered by the prescriber (usually once or twice a day). Care should be taken to avoid contact with the unaffected skin, the mucous membranes of eyes, nose and mouth.
- The skin should be observed for hypersensitivity reactions. The patient should be advised that the skin may be temporarily unsightly in appearance and local discomfort may be experienced during the application of the product but they need to report any “burning” pain.

Administration via the Intrathecal route

Formal training and regular competency assessment for all staff involved in the administration of Intrathecal medicines should be implemented.

- Staff administering intrathecal medicines must use checking procedures that includes a ‘time out’ involving at least two health professionals. ‘Time Out’ is a final patient safety check undertaken immediately before commencing the treatment. It should be carried out in a quiet place without interruption.

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