

British Oncology Pharmacy Association

Guidance to Support BOPA Standards for Clinical Pharmacy Verification of Prescriptions for Cancer Medicines

	Section	Page Number
1	Scope of Document	3
2	BOPA standards	5
3	Limitations	6
4	Professional Responsibilities	7
5	Training Requirements	8
6	Check prescribers details	9
7	Checking Patient and Prescription Details	10
8	Check Chemotherapy Protocol	11
9	Pharmaceutical care plans	12
10	Check Body Surface area is correctly calculated	13
11	Check drug doses are calculated appropriately	13
12	Check drug administration details prescription	14
13	Check Laboratory Values: Full Blood counts	14
14	Check Laboratory Values: Renal and Hepatic function	15
15	Check Laboratory Values: Other clinical tests	16
16	Monitoring renal function for Carboplatin and Cisplatin	16
17	Medication Counselling/ Informational Care	18
18	Governance, Quality and Risk management	18
19	Emergency Planning	19
20	References	20
21	Document Control	21
Appendix 1	A suggested guide to responsibilities	22
Appendix 2	Examples of pharmaceutical care plans	23
Appendix 3	Appendix three: calculations	27

1 Scope of Document

- 1.1 BOPA has produced 'Standards for Clinical Pharmacy Verification of Prescriptions for Cancer Medicines'. Available at <http://www.bopawebsite.org>
- 1.2 The Department of Health cancer measures require that all chemotherapy prescriptions should be checked and authorised by a pharmacist (standard 3C-209.) The National Cancer Action Team report into the 'Quality and Safety of Chemotherapy Services' published in August 2009 states *'All chemotherapy prescriptions should be checked by an oncology pharmacist, who has undergone specialist training, demonstrated their appropriate competence and is locally authorised/ accredited for the task.'* The Scottish Government Health Department sets out its guidance in the Health Department Letter 2005 29 – Guidance for the safe use of chemotherapy. It states *"All prescriptions for chemotherapy must be verified by a suitably trained pharmacist in accordance with legislative requirements, national standards and guidelines".* In 2008 The National Confidential Enquiry into Patient outcome and Death (NCEPOD) report 'For better, for worse?' noted that there was only evidence of Systemic Anticancer Therapy (SACT) prescriptions being checked by a pharmacist in 53% of cases.
- 1.3 This document does not describe any novel clinical practice; it brings together established pharmacy practice and presents it in the form of standards. This will allow all Chemotherapy Services to assure themselves that their pharmacy policies, procedures and practices meet the required standard.
- 1.4 The document describes what key steps a pharmacist must take when checking prescriptions for anticancer medicines. For the purposes of this document this will be referred to as '**Verification**'. It is recognised that there are other terms in common use to describe this process e.g. 'clinical checking' or 'validation' etc.
- 1.5 This document is designed to give detailed guidance on applying the BOPA standards to assist pharmacists in undertaking each of the steps required for verification. This document is advisory, it support suggested good practice but is not mandatory.
- 1.6 It is recognised that capacity for pharmacists to clinically verify chemotherapy prescriptions and deliver pharmaceutical care to cancer patients must be assessed as part of the chemotherapy service capacity. Clinical capacity is distinct from pharmacy capacity to prepare anticancer medicines.
- 1.7 The BOPA standards are designed to be used alongside the performance criteria listed in 'PHARM56/ PHARM57: Verifying a prescription for chemotherapy against a protocol/ without using a protocol' listed on the Skills for Health website. Note Skills for Health is the Sector Skills Councils for Health. It is a UK-wide independent organisation, licensed by the Secretary of State for Education and Skills and funded through the four UK health departments. BOPA will seek to work with SFH on future standards.

- 1.8 This guidance applies to parenteral and oral administration of systemic anticancer therapies (SACT) including chemotherapy and non-cytotoxic medicines such as targeted therapies, antibody treatments and novel therapies, e.g. rituximab, sunitinib and lenalidomide. It does *not* include hormonal or anti-hormonal agents such as tamoxifen and anastrozole.
- 1.9 This document must be used in conjunction with local organisation/ Cancer Network/Health Board Policies on Medicines Management and safe use of SACT and the following national guidance documents:
 - Manual of Cancer Service Standards. Chemotherapy Measures DOH 2005 HSC 2008/001. Note this document will be replaced by new standards in mid 2010, Refer to new standards when available.
 - Updated National Guidance on the Safe Administration of Intrathecal Chemotherapy: DOH 2008
 - HSE Information Sheet MISC615- Safe Handling Of Cytotoxic Drugs,9/03
 - National Patient Safety Agency (NPSA) Rapid Response Report. 'Risks of Incorrect Dosing of Oral Anticancer Medicines.' 22Jan08.
 - Scottish Government Health Department HDL 2005(29) 'Guidance for The Safe Use Of Cytotoxic Chemotherapy'
 - Scottish Government Health Department CEL (2009) 21: Safe Administration of Intrathecal Cytotoxic Chemotherapy and CEL(2009)22: Safe Administration of Vinca Alkaloids.
 - Welsh and Northern Irish Cancer Standards.
 - COIN Chemotherapy Guidelines Clinical Oncology (2001)13:S211.The Royal College of Radiologists
 - The National Cancer Action Team report into the 'Quality and Safety of Chemotherapy Services' published in August 2009
 - PHARM56: Verify prescription for chemotherapy against a protocol available at <http://www.skillsforhealth.org.uk/against> a protocol available at <http://www.skillsforhealth.org.uk/>
- 1.10 Overall responsibility for the safe use of SACT and ensuring these standards are in place should sit with an appropriate senior clinical lead within each organisation, e.g. the Head of Pharmacy; Head of Service/ Lead Clinician for Chemotherapy or Trust Lead for Medicines Management.
- 1.11 Pharmacy staff verifying prescriptions for oral anticancer medicines should operate to the same safety standards used when verifying SACT prescriptions for all other routes of administration.
- 1.12 This document refers to pharmacists when describing verification, but it is recognised that suitably competent technicians may become involved in verification of chemotherapy. In this case governance leads must ensure these staff have documented competency and that clinical and corporate governance approval has been given for this professional role development.

2 The BOPA Standards

2.1 The key checks that an authorised pharmacist must undertake in order to verify any prescription for SACT prior to preparation and release are:

1. Check prescribers details and signature are present and confirm they are authorised to prescribe SACT
2. Ensure regimen has been through local approval processes e.g. clinical governance and financial approval and/ or is included on a list of locally approved regimens
3. On the first cycle check the regimen is the intended treatment as documented in a treatment plan, in the clinical notes or in the electronic record
4. Check regimen is appropriate for patient's diagnosis, medical history, performance status and chemotherapy history (using the treatment plan, clinical notes or electronic record)
5. Check there are no known drug interactions (including with food) or conflicts with patient allergies and other medication(s)
6. Check that the timing of administration is appropriate i.e. interval since last treatment
7. Check patient demographics (age, height and weight) have been correctly recorded on prescription
8. Check body surface area (BSA) is correctly calculated, taking into account recent weight. Note there should be local agreement for frequency of monitoring and checking patient's weight.
9. Check all dose calculations and dose units are correct and have been calculated correctly according to the protocol and any other relevant local guidance, e.g. dose rounding / banding
10. Check cumulative dose and maximum individual dose as appropriate
11. Check reason for and consistency of any dose adjustments, e.g. reduction(s) or escalations and ensure reason is documented.
12. Check method of administration is appropriate
13. Check laboratory values, FBC, U&Es and LFT's are within accepted limits if appropriate (see 2.4 below)
14. Check doses are appropriate with respect to renal and hepatic function and any experienced toxicities
15. Check other essential tests have been undertaken if appropriate
16. Check supportive care is prescribed and it is appropriate for the patient and regimen
17. Sign and date prescription as a record of verification. Note for electronic prescribing systems a digital signature/ record is sufficient.

- 2.2 BOPA believes that it is considered good practice to document identified pharmaceutical care issues that need to be monitored with SACT as part of the verification process. A structured care planning template supports effective practice, electronic patient records or pharmacy section in chemotherapy notes are another options. This document should be available to the multidisciplinary team. The best place to undertake verification is at ward/ clinic level to optimise access to treatment plan(s), clinical notes and the multi-professional team.
- 2.3 Verification provides assurance that the prescribed treatment is tailored and correct for the patients and their specific disease. It provides a check on treatment accuracy and is essential to avoid medication errors. Cancer medicines must not be administered to, or taken by patients until an appropriately trained pharmacist has verified the prescription. 'Appropriately trained' pharmacists should have undergone assessment of competency, see section 5.
- 2.4 In general chemotherapy doses must not be released from the control of a pharmacist until these checks are complete. However services operating pre-prescribing and pre-dispensing do allow dose checking of prescriptions in advance without access to laboratory values. This may not take into account patient's blood counts or toxicities and hence policies must be in place clearly defining who is responsible for checking full blood count results and monitoring toxicities for chemotherapy prepared in advance before administration is authorised.

3 Limitations

- 3.1 It is recognised that the clinical role of pharmacy encompasses more than verification of individual treatment episodes. Pharmacy staff improve the risk management of anticancer medicines by medication review; patient education, clinical monitoring of patients receiving anticancer medicines; direct clinical care to anticancer medicine patients, e.g. prescribing and managing the introduction of new medicines.
- 2.2 Anticancer medicines are also used for non-cancer indications, e.g. methotrexate for rheumatoid arthritis, and pose similar risks to the patient. Guidance for verification of prescriptions of these medicines is outside the scope of this document. Pharmacy departments should consider if any of the standards listed can be applied to the verification of these medicines and other high risk medications.
- 2.3 It has been acknowledged that in many centres prescriptions for oral SACT / outpatient prescriptions may be checked in an area where there is not access to patient notes/ treatment plans (see standards 4 to 6, section 2.1) however Trusts should review practices to work towards compliance.

4 Professional Responsibilities

- 4.1 Pharmacists verifying prescriptions are one part of the overall medicine management process for SACT and their supportive medicines. This document does not describe standards for the overall clinical monitoring of cancer patients. Pharmacists must define their responsibilities in areas where there is overlap to determine who has primary responsibility. Pharmacists must be aware of the clinical monitoring required for patients receiving chemotherapy and assure themselves a robust system for the monitoring of patients is in place within their organisation. This may vary between organisations.
- 4.2 Chemotherapy services are varied, it is recognised that there will be differences in pharmacists' responsibilities depending on the set up of their service. For example pharmacy may not prepare or not release anticancer medicines until the pharmacist has checked the full blood count. However as pre-prescribing and pre-preparation of chemotherapy becomes more widespread (to reduce waiting times and increase flexibility) there may be a requirement for drugs to be issued from pharmacy to a clinical area before full blood counts are known. In these circumstances pharmacists can still verify the prescription and allow the drugs to be released provided the organisation has a policy in place clearly defining the process and identifying who is responsible for checking full blood count results.
- 4.3 When a pharmacist non medical prescriber (NMP) initiates a prescription this does not eliminate the requirement for a (second) pharmacist's role in verifying the prescription. NMPs must not be directly involved in verifying, dispensing and checking of prescriptions they have written. The Royal Pharmaceutical Society of Great Britain (RPSGB) state that NMPs must 'ensure separation of prescribing and dispensing whenever possible. Where a pharmacist is both prescribing and dispensing a patient's medication, a second suitably competent person should normally be involved in the checking process.'
- 4.4 Pharmacists verifying prescriptions for SACT must be able to recognise situations where they need to seek advice / support from appropriate sources, e.g. senior colleague and respond appropriately; in particular, where the complexity required exceeds their own personal level of competence or where there is reason for concern about the individual's suitability for the prescribed treatment.

5 Training Requirements

- 5.1 All prescriptions for anticancer medicines must be verified by *an oncology pharmacist, who has undergone specialist training, demonstrated their appropriate competence and is locally authorised/ accredited for the task.* This is a required of the DH 'Quality and Safety of Chemotherapy Services'
- 5.2 A single pharmacist must be identifiable as having validated the prescription. It is recognised that there may be some delegation/ sharing of verification to suit service models, i.e. technician checking.
- 5.3 All members of staff undertaking the role must have demonstrated suitable competence and be locally accredited for the task. It is recommended that local competency training programmes for verification of oncology pharmacy staff include as a minimum:
- A documented training programme listing the areas of competency and knowledge required
 - A list of specific competencies that must be obtained, note BOPA competencies provide a template of suitable competencies as does the Skills for Health PHARM56 standard. The Specialist Curriculum Group are also developing competencies for clinical pharmacy that include oncology (<http://www.specialistcurriculumgroup.org/>)
 - A period of supervised verification of chemotherapy prescriptions. During this period all prescriptions should be double checked by trained and competent pharmacist(s) and log sheet recording each prescription/ item maintained. Note a suitable minimum number of items for the log sheet should be agreed locally. It is suggested that 50 items should be the minimum and must include a variety of different prescriptions that reflect local case mix.
 - Signature of pharmacist clinical lead responsible for cancer services confirming that the individual is competent and entry into Trust list of 'designated pharmacists' who are competent to verify cancer medicine prescriptions.
- 5.4 It is recognised that in some organisations it may not be possible to always ensure that all oral prescriptions are verified by a trained oncology pharmacist e.g. when oral prescriptions are presented to dispensary staff. Trusts **must** therefore ensure that appropriate training and accreditation on the safety aspects of oral anticancer medicines is provided to any pharmacy staff involved in dispensing and supply of these medicines. Oral SACT poses the same as risks as IV SACT. Trusts should work towards only having trained oncology pharmacists checking **all** prescriptions for SACT.
- 5.5 In order to support dispensary staff involved in the dispensing and supply of oral anticancer medicines, there must always be available in the organisation a trained oncology pharmacist who is able to provide oncology pharmacy advice to dispensary staff.

- 5.6 Further work is ongoing in defining specific educational competencies outlining the knowledge and understanding that an appropriately trained pharmacist verifying a prescription must have. The BOPA committee's work plan for 2010 includes a commitment to develop e-based learning to support oncology pharmacists. In future BOPA will seek to work with the new Professional Leadership Body (PLB) in setting standards for cancer pharmacy.
- 5.7 The Centre for Pharmacy Postgraduate Education (CPPE) has produced a distance learning package 'Cancer: in relation to pharmacy practice' which provides 10 hours of training. It is suggested completion of this package could be used as part of the background knowledge that underpins the competency training. The programme is available to download from <http://www.cppe.manchester.ac.uk/Bookings/FullNewProgs.asp>

6 Check Prescribers Details

- 6.1 Check the prescriber is authorised to prescribe chemotherapy and their signature is recognised. In accordance with the NHS Cancer Measures only Consultant Specialists in Oncology/ Haematology and Staff and Associate Specialists (SAS) in Oncology/Haematology are allowed to initiate a course of chemotherapy. Staff Grades and Non-Medical Prescribers (NMPs) with adequate training & experience in Oncology/Haematology are allowed to prescribe chemotherapy on subsequent courses.
- 6.2 Some services may allow prescribers other than consultants to see new patients following decision to initiate treatment by the consultant and prescribe chemotherapy from the first cycle onwards. For example NMPs working to a clinical management plan. However, at present BOPA has to recommend that the cancer quality measures are applied and that the first cycle of chemotherapy is prescribed by a Consultant Oncologist or Haematologist.
- 6.3 Non-medical prescribers may prescribe the second and subsequent course of anticancer medicines provided they are working within an agreed clinical management plan for supplementary prescribers (SP) and/or treatment record plan for independent prescribers (IP). If the NMP is a pharmacist a different pharmacist must verify the prescription.

7 Checking Patient and Prescription Details

- 7.1 Check the prescription form has been computer-generated. This can be via an electronic prescribing system or a regimen specific pre-printed prescription form that complies with current legal requirements and local prescribing policy.
- 7.2 Chemotherapy services must only use pre-printed prescription forms that are 'secured' to prevent accidental changes to the pre-printed information and subject to appropriate levels of documentation control, e.g. a master copy approved by a different person to that who prepared the document.

- 7.3 Unsecured pre-printed prescriptions could potentially be tampered with. Always ensure the prescription is checked against the regimen protocol.
- 7.4 There should be a locally agreed policy dealing with the occasional 'one-off' or 'off protocol' regimens where a handwritten prescription may be generated as an electronic version does not exist. This should be the exception. See also 8.7 and 8.8
- 7.5 Check the prescription is clearly legible. Some services accept faxed prescriptions; if any details are unclear **do not** accept the prescription.
- 7.6 Check all the required patient details are present on the prescription
- Patient name
 - Hospital (if appropriate) and Ward/ Clinic
 - Hospital number and /or date of birth and/ or address
 - Name of responsible consultant
 - Name and Signature of the prescriber and date
- Note** Check these details against patient addressograph if hand written
- 7.7 Check the prescriptions contain the following details:
- height, weight and body surface area (where used for dosing)
 - protocol / regimen name
 - drug name(s) (generic)
 - intended drug doses as mg/m² or per kg or flat dose or by AUC (for carboplatin)
 - the final calculated dose to be administered
 - frequency of administration
 - indication of any dose modifications made
 - the intended start date and exact duration of treatment
 - relevant haematology and biochemistry results (these may not be completed at the time the prescription is presented to pharmacy)
- 7.8 Check patient's notes or electronic records for record of height and weight, if there is any doubt over the accuracy of the patient's weight (i.e. has patient gained or lost weight) then the patient may need to be reweighed. The patient should always be reweighed at the start of any new course of chemotherapy. The need for checking weight and potentially adjusting doses should be discussed locally and agreement for frequency of monitoring and checking patient's weight decided in advance.
- 7.9 Pharmacists verifying oral anticancer medicine prescriptions should calculate the exact amount (number of tablets/capsules) to be supplied when validating the prescription. The prescription must then be endorsed with the correct quantity to be supplied.
- 7.10 The pharmacist must ensure the directions on the prescription are clear and unambiguous and include, where relevant, the intended period of treatment, including start and stop dates for oral treatments.

8 Check Chemotherapy Protocol

- 8.1 All anticancer medicines must be prescribed in context of a written protocol. These can be as individual protocols from the local Cancer Network Handbook/ Website or from within a validated electronic prescribing system. Paediatric protocols must be consistent with Children's Cancer and Leukaemia Group (CCLG) agreed regimens. Protocols *should* contain:
- definition of the clinical condition being treated
 - names (approved) of all medicines to be given
 - dosing schedule for each medicine
 - maximum individual doses and cumulative dose where applicable
 - supportive therapy
 - laboratory tests that need to be performed before and during treatment
 - special precautions, expected toxicities and contraindications
 - potential interactions and medications to be avoided
 - recommendations for dose modifications and review of patient
 - reference source(s)
- 8.2 Check the regimen/ drugs prescribed comply with a recognised regimen protocol which is appropriate for the patient's diagnosis. This must be done using locally approved chemotherapy protocol files and by checking patient's medical notes or electronic record or treatment plan to ensure the protocol is appropriate for patient's diagnosis and the correct prescription form has been selected.
- 8.3 Check the regimen has been through local approval processes e.g. clinical governance and financial approval and/ or is included on a list of locally approved regimens. This could be the Cancer Network Approved list.
- 8.4 On the first cycle check the regimen is the intended treatment as documented in a treatment plan, in the clinical notes or in the electronic record
- 8.5 Ideally check patient's diagnosis, medication history, chemotherapy history and allergy status to ensure the prescribed drugs are safe and appropriate for the patient.
- 8.6 Check there are no known drug interactions (including with food) or conflicts with patient allergies and other medication(s)
- 8.7 All new or non-approved chemotherapy protocols must be queried with the prescriber. Trusts must have an agreed policy for monitoring and preventing use of regimens not on the accepted list of regimens.
- 8.8 Pharmacists must satisfy themselves that the prescriber of any new /non-approved regimen is following appropriate guidance for regimens not on the approved network list, has valid clinical reason and peer approval, e.g. MDT and local clinical governance and funding approval.

9 Pharmaceutical Care Plans

- 9.1 It is recommended that pharmaceutical care plans are put in place to identify the key issues that need to be monitored for each patient with SACT. The best place to undertake verification is at ward/ clinic level to allow access to clinical notes. (This may not always be the case depending on organisation of local services.) Appendix 2 gives example pharmaceutical care plans.
- 9.2 The pharmaceutical care plan should act as a chemotherapy patient record and be maintained for all chemotherapy patients. This should be checked and updated with treatment details every time a prescription is received.
- 9.3 The pharmaceutical care plan should contain space to record
 - summary of patient details
 - baseline monitoring (i.e. lab values, clinical tests etc)
 - record of any allergies
 - medication history checked
 - previous anticancer medicine treatment(s)
 - relevant medical history
 - identification of ongoing monitoring issues and lab values
 - record of treatments given and lab values checked
 - check for chemotherapy appropriateness
- 9.4 The care plan could exist as a stand alone pharmacy paper document, be electronic or be incorporated into the patient's chemotherapy/ medical notes.
- 9.5 Using the care plan check that all drugs and doses are scheduled correctly with regard to time and date of administration. Has the correct time interval passed since the regimen was last administered?
- 9.6 Check care plan / patients notes for any record of dose modifications or delays in previous cycles of treatment.
- 9.7 Check that any additional prescriptions for supportive treatments, e.g. anti- emetics have been ordered.
- 9.8 Whilst not essential, the care plan can be used to assist clinical verification allowing pharmacist to;
 - Check the patients' previous medical history, noting in particular any medical problems which may have a bearing on current management e.g. factors affecting metabolism and excretion of drugs, drug sensitivities
 - Note any previous treatment that the patient may have received for their cancer: chemotherapy and any relevant cumulative doses of cytotoxic drugs; radiotherapy and where known the sites irradiated; surgery and any other treatments such as hormones, bisphosphonates etc.
 - Check the patients concurrent medication including over the counter medicines and complementary therapies to ensure there are no potential interactions with planned anticancer medicine

10 Check Body Surface Area is Correctly Calculated

- 10.1 Check the patient's body surface area BSA using a nomogram/ formulae or other suitable method and the height and weight on the prescription. This may have been done by an electronic system, in which case the system should be suitably validated to ensure it calculates correctly.
- 10.2 Check with prescriber if BSA on prescription differs by your calculation check by more than 0.05. Note in some areas prescribers may round BSA values to the nearest 0.1, this is often done to facilitate dose banding.
- 10.3 The DuBois or Mosteller formulae are accepted as the standard BSA nomogram for adults. The overriding principle is one of consistency; prescribers must be consistent in their choice of BSA calculation method and Trusts must agree which formulae should be used. (see appendix three)
- 10.4 In paediatrics a chart based on the Boyd formula and adopted by CCLG as standard should be used.
- 10.5 If patients weight changes during course of treatment BSA drug doses may need to be recalculated and rechecked by pharmacy. See 7.8.
- 10.6 The COIN guidelines for clinical oncology recommend 'In the absence of specific information, BSA should usually be "capped" at 2.0–2.2 m² in obese patients'. Depending on patient, regimen and treatment intent e.g. curative intent or palliative, heavy (but not obese) patients, BSA area values greater than 2m² may be used. In the absence of specific local guidelines on this issue it is suggested pharmacists double check with prescriber if a BSA of greater than 2m² is given (it may be prudent to observe the patient to see if they are obese or not).

11 Check Doses Are Calculated Appropriately

- 11.1 Check the drug dose calculations for the correct BSA, weight, AUC etc.
- 11.2 Check dose units are correct, e.g. milligrams, grams, international units.
- 11.3 Check the prescribed dose can be accurately measured. The prescribed dose may be rounded up or down within 5% to ensure the dose can be accurately measured or to allow dose banding to be applied.

Note Do not round prescription if banding is already applied, i.e. within an e-prescribing system.

- 11.4 Check the calculation of any dose modifications or dose reductions. Unless there is a documented reason for a dose increase any decision to reverse a previous dose reduction should always be queried with the prescriber.
- 11.5 Check calculation of banded doses complies with dose banding guidelines.

Note Dose banding is a system whereby, through agreement by pharmacy and prescribers, calculated doses of intravenous cytotoxic drugs are rounded up or down to pre-determined standard doses. It is generally accepted that the maximum variation of the adjustment between the prescribed dose and the banded dose issued to the patient will not be more than 5%. A range of pre-filled syringes or infusions can then be used to administer the standard dose.

12 Check Drug Administration Details

- 12.1 Check the administration details are appropriate for the drug, i.e. route and rate of administration and that the drug is compatible with diluent or infusion solutions.
- 12.2 Check that hydration and supportive drugs have been prescribed as required per protocol. Hydration is essential for the following drugs:
 - Cyclophosphamide (at doses greater than 1000- 2000 mg/m²)
 - Ifosfamide
 - Melphalan
 - Cisplatin (double check hydration regimen agrees with agreed protocol)
 - High dose methotrexate (at doses greater than 1000 mg/m²)
- 12.3 Check patients care plan or clinical notes for any record of administration problems in previous cycles of treatment, e.g. Infusion related reactions.

13 Check Laboratory Values: Full Blood Counts (FBC)

- 13.1 **It is recognised that pharmacists take responsibility for checking and monitoring laboratory values, but that this is a shared responsibility with medical and nursing staff. Trusts should agree which staff are ultimately responsible for monitoring described in sections 13 to 16 below and ensure pharmacist responsibilities are clearly defined in local policy. Appendix one gives a suggested guide to responsibility.**
- 13.2 It is essential to perform a FBC before administering chemotherapy. A low neutrophil count is often the limiting factor with regard to patients being able to receive their chemotherapy on time.
- 13.3 Depending on local circumstances chemotherapy may be prepared and delivered to the ward before FBC results are received. Pharmacy departments releasing chemotherapy before FBC results are known must ensure a robust system is in place to ensure the FBC is checked and is acceptable before administration. A local policy should clearly define who is responsible for checking full blood count results, including how these will be documented.

- 13.4 The levels at which treatments are delayed may vary from regimen to regimen and even from prescriber to prescriber. In general pharmacists should not authorise the prescription without consulting the protocol agreed with the prescriber/the prescriber or the patient's clinical management plan if the values are less than shown below:

Example of commonly used limits

Platelets	100 x 10 ⁹ cells/L
White Cell Count	3 x 10 ⁹ cells/L
Absolute Neutrophil Count*	1.5 x 10 ⁹ cells/L

- 13.5 Absolute neutrophil count is most important parameter and should be used in preference to white cell count. If patient is in clinical trial, follow limits specified in trial protocol.
- 13.6 A raised white cell count or absolute neutrophil count may indicate infection and may also be a reason not to treat.
- 13.6 Check with prescriber /nursing staff if patient has low haemoglobin Hb, e.g. less than 10g/dl. For chemoradiation patients check if less than 12g/dl. Whilst low Hb does not normally result in chemotherapy being deferred it is common practice to give blood transfusions prior to or after chemotherapy to restore Hb levels.

14 Check Laboratory Values: Renal and Hepatic Function

- 14.1 It is important to monitor renal and hepatic function with anticancer medicines as they can be toxic to the liver and kidneys; they may often have a narrow therapeutic index and the excretion of the drug can depend on normal renal and hepatic function.
- 14.2 Monitoring of renal and hepatic function may be required prior to each cycle of chemotherapy dependant on the drugs being given. If renal function or hepatic function is abnormal, consult the protocol for advice on dosage adjustments or drug Summary of Product Characteristics (SPC). If no information is provided a good resource to check is the 'Hepatic/Renal impairment dose adjustment for cytotoxics' documents produced by the North London Cancer Network, <http://www.nlcn.nhs.uk/BChemoGui>. Note an older version of these is included in the appendix of 'Practical Chemotherapy a Multidisciplinary Guide' textbook. The 2001 COIN Chemotherapy standards also give advice on this subject.
- 14.3 Any patient with impaired renal function, GFR < 60ml/min, should be carefully evaluated for the need for dose adjustments. Note the limit for fludarabine is higher at GFR < 70ml/min. See also 16.1.
- 14.4 Check regimen protocols and drug information for detailed information. Renal function is critical for the checking of cisplatin, carboplatin and high dose methotrexate doses. (Section 16 below gives specific information on monitoring of platinum drugs.)

15 Check Laboratory Values: Other Clinical Tests

- 15.1 Other biochemical markers may be monitored by the prescriber depending on the specific chemotherapy, for example tumour markers indicating response to treatment such as CA125 in ovarian cancer. The responsibility for this monitoring lies with the prescriber. Pharmacists can refer to regimen protocols and drug information for detailed information on other clinical tests. For example a pharmacist may spot a rapidly rising tumour marker which could indicate the treatment is not working, when checking other results.
- 15.2 Certain drugs are potentially cardiotoxic and require monitoring of cardiac function, e.g. anthracyclines, trastuzumab and potentially 5-fluorouracil. Consult the protocol for advice on monitoring requirements and check that the prescriber has ensured the required tests are undertaken, e.g. 3 monthly ECHO cardiogram / MUGA with trastuzumab.
- 15.3 If pharmacy is not undertaking checks of biochemistry or haematology results there must be a clear audit trail of which staff are undertaking those checks and their competence to do so – including understanding of the implications of biochemistry on pharmacokinetics of drug clearance. These checks should be independent from the process of prescribing. However pharmacists are best placed to recommend dose adjustments on the basis of biochemical values.

16 Monitoring Renal Function for Carboplatin And Cisplatin

- 16.1 Renal function, measurement of GFR, can be assessed by two methods.
- The most accurate method is determination of non- corrected radio-isotopic clearance. An accurate determination of GFR obtained by measuring the clearance of either chromium 51 EDTA (⁵¹Cr-EDTA), or Technetium DTPA (Tc99m DTPA) usually undertaken by medical physics.
 - GFR can be corrected for body mass (normalised to a body surface area of 1.73 m²) or uncorrected. The uncorrected version should always be used for carboplatin, the corrected version *may* be used for cisplatin.
 - Estimation of GFR (eGFR) can be done by directly using the Wright formula or indirectly using Cockcroft and Gault formula to measure creatinine clearance. Note the Wright formula is preferable to the Cockcroft formulae for dosing Carboplatin. (see appendix three)
 - A common method for calculating eGFR, as reported by laboratories in the UK, is the abbreviated Modification of Diet in Renal Disease (MDRD) formula. This should not be routinely used for chemotherapy.
- 16.2 When using GFR measurements for calculating drug doses pharmacy staff must have access to the original result, either paper or electronic version, which must be double checked to avoid drug dosing errors resulting from transcription errors of GFR results. If not available pharmacy must contact the medical physics department performing the tests for the patients to ensure the results can be accessed by pharmacy.

- 16.3 It must be noted the Cockcroft & Gault formula gives less accurate results than measured GFR and should therefore not be exclusively used, the Wright formula is preferred. For obese and anorexic patients the formulae may not give accurate results and measured GFR is recommended.
- 16.4 The dose of cisplatin in most protocols is modified by the prescriber if the GFR is less than 60 mL/min. The total dose may be reduced or split over two days to allow time for the drug to be cleared from the body.
- 16.5 Carboplatin doses are calculated from renal function (GFR) using the Calvert formulae, see appendix A3.2. A pharmacist must check the calculation of the carboplatin dose using the formulae;

$$\text{Carboplatin dosage (mg)} = \text{AUC (mg/ml x min)} \times [\text{GFR* (ml/min)} + 25]$$

Where AUC = target AUC (area under the curve) is usually given as;

AUC = 4 to 6 for previously treated patients and as part of
combination chemotherapy regimens

AUC = 6 to 8 for previously untreated patients or as single agent

- 16.6 Check that uncorrected GFR has been used in the calculation.
Note: Pathology labs use different techniques for measuring GFR; the uncorrected value is not adjusted for patient's weight.
- 16.7 Check if this GFR is measured and check the original result (see 16.2 above). Double check the calculation using the Cockcroft & Gault or Wright formula. Check that the correct AUC had been used.
- 16.8 On the first course of carboplatin record the patient's current serum creatinine value in the care plan /chemotherapy record. Ideally this should be reported at the same time as the GFR to give a baseline level.
- 16.9 On each subsequent cycle record the patient's latest serum creatinine value in the patient record/profiles and check the serum creatinine level has not deviated from the baseline level by 20%* or more. If the serum creatinine level has deviated from the baseline level by 20%* or more, then the chemotherapy should not be authorised until a new GFR has been obtained. Contact the prescriber if this is the case. *It is recognised that a locally agreed alternative value may be used instead of 20%.
- 16.10 Alternatively calculate the GFR using either Cockcroft & Gault or Wright formula. If the GFR has deviated from the baseline level by more than 10% then the chemotherapy should not be authorised until the prescriber has been contacted and the changes discussed. It may be the case that the dose needs to be recalculated.
- 16.11 According to the SPC, carboplatin is contra-indicated if the creatinine clearance is less than 20mL/min. Contact the prescriber if creatinine clearance falls below this level.

17 Medication Counselling/ Informational Care

- 17.1 Pharmacists verifying prescriptions for oral anticancer medicine must ensure that there is a system in place to ensure the person receiving the medicines fully understands how and when to take their medicines.
- 17.2 Verifying pharmacists must check that staff who will give the oral anticancer medicines to the patient must also ensure the patient understands:
- What to do in the event of missing one or more doses
 - What to do in case of vomiting after taking a dose
 - Likely adverse effects and what to do about them
 - Any need for and how to obtain further supplies
 - The role their GP is expected to play in their treatment
 - The need to inform their health care team if they are taking any over the counter medications/ supplements.
 - Principles of safe handling, storage and disposal
 - That if used, medicine spoons or measures should be used once only and then disposed of safely
 - Any drug specific advice regarding safe crushing of tablets or opening of capsules
- 17.3 It is recognised that, in practice, most of the information above may be provided by the consultant/ specialist nurse in clinic or by the pharmacist on the cancer ward. If the patient is not provided with this advice in clinic or on the ward pharmacy staff responsible for cancer services must ensure that systems are in place to provide the advice at the point of dispensing.

18 Governance, Quality and Risk management

- 18.1 It is recommended that Trusts audit their adherence and application of these standards on an annual basis to ensure the policy is still relevant to the service provided.
- 18.2 Organisations must ensure they have robust system for recording clinical incidents and near misses with pharmacists who verify chemotherapy. It is recommended that learning from these incidents be shared by using existing clinical governance frameworks to report to the relevant Trust / Network clinical groups.

19 Emergency Planning

- 19.1 In 2009/10 the NHS had to plan for provision of services under emergency conditions with severely reduced members of staff, e.g. pandemic flu. It is acknowledged that in emergency conditions that normal service will not be able to be provided since there may be higher than average hospital admissions coupled with staff shortages. One consequence of this may be that patients who would normally be cared for on specialist wards by staff with specialist knowledge may end up on general wards and specialist staff and covering staff may be off sick.
- 19.2 There is therefore a need to consider the minimum checks that must be performed on a SACT prescription during such a crises as it is recognised that untrained pharmacy staff may have to undertake this duty.
- 19.3 In all cases where a Standard Operating Procedure for verifying a chemotherapy prescription exists then this should be used by the checker. If no SOP exists then Trusts should consider producing one or using this document.
- 19.4 This guidance is referring to clinical check only. It is presumed that Trust aseptic departments will have separate contingency plans for production.
- 19.5 For outpatient/ day case prescriptions the following should be checked either by the pharmacist or the pharmacist should be satisfied that the parameter will be checked before the chemotherapy is administered.

First Cycle 1	Subsequent cycles
BSA regimen doses route fluids infusion times start and stop dates for oral supportive meds liver & renal function (if applicable)	correct patient interval no dose change confirm any prescribed change start and stop dates for oral

20 References

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21 Document Control

Title		Guidance to support BOPA Clinical Verification Standards v1.5	
Editor/ Author		Steve Williamson	
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Draft	Date	Author/Editor	Summary of Change
1.1	21.09.09	Steve Williamson	Initial draft
1.2	07.10.09	David Thomson, Ewan Morrison Mary McClean	Split document into 2 separate documents. General updates and Editorial comments
1.3	30.11.09	Steve Williamson	Updated in line with standards
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Contributor			Section/Contribution
Calum Polwart & NECN Pharmacy Group			Sections 6-16
Julie Mycroft / Denise Blake			Appendix 1 adapted with permission from Royal Marsden
Scottish Oncology Pharmacy Practice (SOPPG)			Original check list for standards general comments
Libby Hardy, Bruce Burnett, June So, Ian Costello			General Comments
Helen Flint, Susanna Daniels, Gemma Hills			General Comments

Information Reader Box

Proposed Target Audience	Oncology and Haematology Pharmacists, Provider Trust Chief Pharmacists, NHS Scotland Boards Directors of Pharmacy, Oncologists and Haematologists, PCT Prescribing Advisors, Cancer Networks, SHA, Welsh and NI Health board(s).
Proposed Circulation List	BOPA Members, FCP Members, Chief Pharmaceutical Officers for each home country, CAT, UKONS, Provider Trust Chief Pharmacists, NHS Scotland Boards Directors of Pharmacy, RCP, PCT Prescribing Advisors, Heads of Schools Pharmacy , RSPGB/PLB, NES Scotland, Paediatric Oncology Pharmacists
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APPENDIX ONE A SUGGESTED GUIDE TO RESPONSIBILITIES

Primary Responsibility		Ultimate Responsibility
D,P	Prescription for Chemotherapy - Standard Regimen	D
D,P	Unknown Regimen (care with acronyms/ abbreviations) countersigned by consultant or SpR	D
N	Height and weight patient	N
N,P,D	Check and record patient allergies	D
N,P,D	Calculate Body Surface Area	P
N,P,D	Check doses with respect to: Protocol/ Proforma	P
N,P,D	FBC U + E and LFT's	D
N,P,D	EDTA/Creatinine Clearance & additional tests if specified	D
N,P,D	Drug induced dosage reduction	D
N,P,D	Are all drugs prescribed (including supportive meds)	P
D,P	Check drug interactions with existing medicines	P
D,P	Prescription signed and dated (Prescriber and Verifier)	D & P
N,D	Has the patient suitable venous access	N
N,P,D	Course number & lifetime cumulative dose (if applicable)	D
N,P,D	Check sequence & timing of regimen (** see note)	P
N,P,D	Check appropriate day/week of regimen	N
N,P,D	Check appropriate pharmaceutical stability	P
N,P,D	Check appropriate dilution & rate of administration	N
N,P,D	Check - hydration - antiemetics - adjuvant treatments - other supplementary medicines	P
** i) give in order: - prehydration (if any) bolus injection mannitol (if any) - infusions ii) Peripheral administration - Give vesicant drugs first iii) Oral drugs to have start and stop date indicated as appropriate		

N = Nurses, P = Pharmacist, D = Doctors

APPENDIX 2.1 EXAMPLES OF PHARMACEUTICAL CARE PLANS

Northumbria Healthcare NHS Foundation Trust
Chemotherapy Monitoring Sheet / Pharmaceutical Care Plan

[illegible]

Please record any dose changes, any reasons for delay, any modifications to the protocol and relevant blood results or toxicity.

APPENDIX 2.2 EXAMPLES OF PHARMACEUTICAL CARE PLANS

Diagnosis:		Date:				Patient Name:			
		Height:							
Regime: MINI-PECC		Weight:							
Regime Source: www.canceralliance.nhs.uk If Not CCA Approved Attach Copy of 'Non Approved' Form		BSA:				DoB: Age:			
						CRN No:			

Treatment / Regime Details					Cycle Number / Dose Given							
Day	Drug	Route	Diluent	Date:	1	2	3	4	5	6	7	8
1 - 2	Chlorambucil 20mg/m ² od	Oral										
1 - 2	Etoposide 200mg/m ² once daily	Oral										
1	Lomustine 100mg/m ² once	Oral										
1 - 7	Prednisolone 40mg once daily	Oral	To nearest 5mg									
1 - 7	Ranitidine	Oral	150mg BD									
1 - 5	Ondansetron	Oral	8mg BD									
1 - 7	Metoprolol	Oral	10mg TDS									
1 - 7	Allopurinol	Oral	300mg OD									

Pharmaceutical Care Plan				1	2	3	4	5	6	7	8
Day	Action	Rationale	Date:								
1	Check Renal Function	Dose reduce Etoposide if CrCl < 40ml/min. Dose reduce Lomustine if CrCl < 40ml/min. Dose reduce allopurinol?									
1	Check Liver Function	Dose reduce Etoposide if Bilirubin > 26 or AST > 40 Lomustine if may also need reduced If LFTs grossly abnormal - chemotherapy also may need reduced									
1	Ensure dose is 'measurable'	Use of 5 tablets/capsules is not appropriate Crushing or suspension is not appropriate									
1	Ensure appropriate antiemetic Rx	Need cover for highly emetogenic regimen									
1	Ensure treatment will be labelled for 1 day, 2 days 2days and 7days only	Treatment is given on day 1, through to 7 according to schedule above and repeated every 28 days (14days later).									
1	Ensure treatment GI Prophylaxis with Prednisolone	Risk of GI bleeding with low platelets and high dose steroids.									
1	Ensure adequate gap between treatments	Minimum 28 day cycle (sometimes given 6 weeks)									
1	Notify Blood Bank of need for irradiated Blood	Patient requires irradiated blood if having a transfusion.									
Pharmacist Initials:											

General Comments, Additional Monitoring etc. Nursing staff will check FBC is within range before handing treatment to patient. If pharmacy handing to patient ensure FBC OK (Neutrophils > 1.5x10⁹ cells/l, Platelets > 100x10⁹ cells/l). Ensure patient understands dosage instructions, and has instructions about what to do if toxicity (as detailed in Northern Cancer Network oral chemotherapy handbook) occurs. If not discuss with chemo clinic/ seek specialist advice. Note: there is also a regimen called PECC	
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APPENDIX 2.3 EXAMPLES OF PHARMACEUTICAL CARE PLANS

GENERIC PHARMACEUTICAL CARE PLAN : CANCER CARE

Surname	Date of birth / age	Sex	Consultant	Ward
Forename	Patient number		General practitioner	
Diagnosis:	Chemotherapy Regimen:		Community Pharmacist	

RELEVANT MEDICAL HISTORY				
Approx date	Problem description	Approx Date	Problem description	
1		4		
2		5		
3		6		
Known drug sensitivities:				

PREVIOUS TREATMENT FOR CANCER			
Chemotherapy:	Date	No of cycles	Response / toxicities / cumulative doses
1.			
2			
3			
Radiotherapy:	Date	No Fractions	Response / toxicities
Other treatments (including surgery):			

CONCURRENT MEDICATION: update on each cycle of treatment							
		DATES				DATES	
		start	stop			start	stop
1				8			
2				9			
3				10			
4				11			
5				12			
6				13			
7				14			
ADR's / OTC medications:							

Initials / Dates of cycles							
Height:	Weight						
Surface Area (m ²)							

Generic Care Issue	Action	Output (initial)
1	Chemotherapy Eligibility (only complete on first cycle) Refer to local protocol to verify treatment plan from diagnosis, tumour type and performance status ☐ LP ☐ OLP ☐ CT	☐ Verified ☐ Modified
2	Chemotherapy Appropriateness A: Drugs / doses ☐ ☐ ☐ ☐ ☐ ☐ (Cross if verified) B: Administration ☐ ☐ ☐ ☐ ☐ ☐ tick if adjusted) (see monitoring plan for FBC/ CrCl/ LFT's)	
3	Immunosuppressive therapy Patients taking concurrent immunosuppressive therapy in addition to chemo ☐ ☐ ☐ ☐ ☐ ☐ (cross if verified, tick if adjusted)	
Comments/dose reductions:		

Version 4.2
September 2002

Monitoring Issues:			
Cross if no problem, tick if a problem and document in care issues section or annotate N/A if not assessed			
Nausea and vomiting ☐ ☐ ☐ ☐ ☐	Mucositis/Mouthcare ☐ ☐ ☐ ☐ ☐	Neurology ☐ ☐ ☐ ☐ ☐	Bowel habit ☐ ☐ ☐ ☐ ☐
Neutropenic Sepsis ☐ ☐ ☐ ☐ ☐	Skin Toxicity ☐ ☐ ☐ ☐ ☐	Pain control ☐ ☐ ☐ ☐ ☐	Insomnia ☐ ☐ ☐ ☐ ☐
Depression ☐ ☐ ☐ ☐ ☐	Absorption / distribution ☐ ☐ ☐ ☐ ☐	Counselling/Education ☐ ☐ ☐ ☐ ☐	Discharge/ self med issues ☐ ☐ ☐ ☐ ☐
FBC ☐ ☐ ☐ ☐ ☐	LFT's / bilirubin ☐ ☐ ☐ ☐ ☐	Renal function ☐ ☐ ☐ ☐ ☐	Other: ☐ ☐ ☐ ☐ ☐

[illegible]

Recurring care issues:

APPENDIX THREE: CALCULATIONS

A3.1 Body Surface Area

Body Surface Area (BSA), commonly use for the calculation of chemotherapy drug doses, can be calculated from one of four formula, the DuBois, Mostellar, Gehan and George and Haycock. **DuBois or Mostellar are preferred.** BSA is not accurate for obese patients, BSA cannot account for inter-patient variation. The formulas all give slightly different results .e.g. for a patient of height 1.7m and weight 75kg

- BSA = 1.86 m² when calculated using formula of DuBois and DuBois
- BSA = 1.88 m² when calculated using formula of Mostellar / Gehan and George
- BSA = 1.82 m² when calculated using formula of Haycock, et al

Formula of DuBois and DuBois:

$$\text{BSA (m}^2\text{)} = \text{Wt (kg)}^{0.425} \times \text{Ht (cm)}^{0.725} \times 0.007184$$

This is the classic formula, published in 1916, on which most nomograms are based. It was based on measurements of 9 individuals, one of whom was a child.

Ref.: DuBois D, DuBois DF. A formula to estimate the approximate surface area if height and weight be known. Arch Int Med 1916;17:863-71.

Mostellar formula

$$\text{BSA (m}^2\text{)} = ([\text{Height(cm)} \times \text{Weight(kg)}] / 3600)^{1/2}$$

The Mostellar formula is popular because it is the simplest and can and easily calculated with a hand-held calculator

Ref: Mostellar RD. Simplified calculation of body-surface area. New Eng J M 1987; 317:1098

Formula of Gehan and George:

$$\text{BSA (m}^2\text{)} = \text{Wt (kg)}^{0.51456} \times \text{Ht (cm)}^{0.42246} \times 0.02350$$

This formula is based on direct measurements of 401 individuals.

Ref.: Gehan EA, George SL. Estimation of human body surface area from height and weight. Cancer Chemotherapy Rep 1970; 54:225-35.

Formula of Haycock, et al:

$$\text{BSA (m}^2\text{)} = \text{Wt (kg)}^{0.5378} \times \text{Ht (cm)}^{0.3964} \times 0.024265$$

Haycock et al reported that the DuBois formula increasingly underestimated BSA as values fell below 0.7 m². Their formula was based on measurements of 81 individuals ranging from premature infants to adults.

Ref.: Haycock GB, Schwartz GJ, Wisotsky DH. Geometric method for measuring body surface area: A height-weight formula verified in infants, children and adults. J Pediatr 1978; 93:62-6.

A3.2 Glomerular Filtration Rate / Creatinine Clearance

Glomerular Filtration Rate (GFR) gives an estimate of renal function. Creatinine Clearance (CrCl) can be used to give an estimate of GFR in adult patients with stable renal function.

Measured Glomerular Filtration Rate / Creatinine Clearance

The preferred method for estimating GFR is a measured non-corrected CR⁵¹-EDTA clearance, undertaken by medical physics departments.

CrCl can be estimated from a 24 hour collection of urine and the serum creatinine (SCr). This method should **not** be used for calculating carboplatin dosage.

Calculated Creatinine Clearances

If a measured CR⁵¹-EDTA is not available an estimated CrCl can be calculated from one of the formulae below which use SCr.

Wright Formula

There are two versions of the formula depending on how serum creatinine values are obtained, by the kinetic Jaffe method or the enzymatic method. The formula can be further adapted if covariant creatine kinase (CK) values are available (not shown).

1 *SCr measured using enzymatic assay.*

$$\text{GFR (ml/min)} = \frac{(6230 - 32.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.23 \times \text{Sex})}{\text{SCr } (\mu\text{mol/min})}$$

2 *SCr measured using Jaffe assay (commonly used by most biochemistry labs).*

$$\text{GFR (ml/min)} = \frac{(6580 - 38.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.168 \times \text{Sex})}{\text{SCr } (\mu\text{mol/min})}$$

Key: Sex = 1 if female, 0 if male; Age in years; BSA= DuBois BSA

Ref. Estimation of glomerular filtration rate in cancer patients; JG Wright, AV Boddy, M Highley, J Fenwick, A McGill and AH Calvert; British Journal of Cancer(2001) 84(4) 452-459.

Cockcroft & Gault formula

Variations of this formula are used depending on the units used to report SCr.

$$\text{ClCr (ml/min)} = \frac{(140 - \text{Age}) \times \text{Wt (kg)}}{72 \times \text{SCr (mg/dl)}}$$

Multiply above by 0.85 for women

Ref. Prediction of creatinine clearance from serum creatinine; Cockcroft D.W., Gault M.H. Nephron; 16:31-41 (1976)

A3.3 Calvert Formula for Carboplatin Dosage

Carboplatin dosage is calculated from GFR and target AUC (area under the curve) of carboplatin.

$$\text{Carboplatin dosage (mg)} = \text{AUC (mg/ml x min)} \times [\text{GFR (ml/min)} + 25]$$

For Lung AUC = 5 if a measured CR⁵¹-EDTA or the Wright formula is used
 AUC = 6 if the Cockcroft & Gault formula is used

In general AUC = 4 to 6 for previously treated patients and for combination chemo
 AUC = 6 to 8 for previously untreated patients

Ref. Carboplatin dosage: prospective evaluation of a simple formula based on renal function A.H. Calvert & Col. Journal of Clinical Oncology. Vol. 7, N°11, Nov, 1989: 1748-1756

Note:

Advice from Professor Hilary Calvert at University of Newcastle Cancer Research Centre is that the Wright formulae should be used in preference to Cockcroft and Gault when calculating carboplatin doses. Personal Communication 2009.