

SOP for Thames Valley Cancer Network Pharmacy Standards for Verification of Prescriptions for Cancer Medicines

All chemotherapy for adult cancer patients in Thames Valley Cancer Network (Thames Valley) should be prescribed on the validated Thames Valley electronic chemotherapy prescribing (Aria) system (and paediatrics are in the process of implementing Chemocare). However this guidance includes information on all aspects of a prescription that should be checked if prescribed by another method, should the e-prescribing system be out of operation.

The validated electronic chemotherapy prescribing system calculates body surface area (BSA), doses, dose banding automatically. The regimens on the system have been validated by 2 pharmacists and 1 Clinician, prior to approval on the system, and include all the Thames Valley approved regimens and some exceptional use regimens. However Clinicians have the ability to modify doses, add and remove drugs and support medication and modify route and duration of administration.

Use in conjunction with Aria Quick reference guide for Pharmacist (Adult) and Thames Valley screening SOP.

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1 Check Prescribers Details

1.1 Check the prescriber is authorised to prescribe chemotherapy and for non electronic prescriptions their signature is recognised and check register. (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).

1.2 Prescribers other than consultants may see new patients following decision to initiate cycle 1 by the consultant in written documentation e.g. prescription referral form, notes or clinic letter.

1.3 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.

2 Checking Patient and Prescription Details

2.1 Check that it is on a prescription or proforma or clinical trial that is permitted within your Trust i.e. that it is an electronic prescription unless the electronic system is not operational.

2.2 Always ensure the prescription is checked against the regimen.

If Aria is not operational

2.3 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.

2.4 Unsecured pre-printed prescriptions could potentially be tampered with, always ensure the prescription is checked against the regimen.

2.5 There should be a locally agreed policy dealing with the occasional 'one-off' or 'off regimen' regimens where a handwritten prescription may be generated as an electronic version does not exist. This should be the exception. (See also 3.7 and 3.8)

2.6 Check the prescription is clearly legible. Some services accept faxed prescriptions; if any details are unclear **do not** accept the prescription.

3 Check chemotherapy regimen is Thames Valley regimen approved for indication. If not, ensure Clinician has completed exceptional use (IFR) or Cancer drug fund application form and followed the complete process. Check the regimen has NICE approval and meets criteria (template where applicable).

3.1 All anticancer medicines must be prescribed in context of a written regimen. These can be as individual regimens from the Thames Valley website (www.TVSCN.nhs.uk) or Clinical trial regimen or from within a validated electronic prescribing system. Paediatric regimens must be consistent with Children's Cancer and Leukaemia Group (CCLG) agreed regimens. Regimens *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)

3.2 Check the regimen / drugs prescribed comply with a recognised regimen which is appropriate for the patient's diagnosis. This must be done using locally approved chemotherapy regimens (www.TVSCN.nhs.uk) or clinical trial regimen or validated electronic prescribing system and by checking patient's medical notes or electronic record or treatment plan to ensure the regimen is appropriate for patient's diagnosis and the correct prescription form has been selected.

3.3 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.

3.4 Check the regimen has been through local approval processes e.g. clinical governance and financial approval or CDF funded and / or is included on a list of locally approved regimens, clinical trials or national algorithms. This could be the Thames Valley chemotherapy regimens.

3.5 Ideally check patient's diagnosis, medication history, chemotherapy history and allergy status to ensure the prescribed drugs are safe and appropriate for the patient.

3.6 Check there are no known drug interactions (including with food) or conflicts with patient allergies and other medication(s).

3.7 All new or non-approved chemotherapy regimens 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.

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3.8 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.

3.9 Check all the required patient details are present on the prescription. Check these details against patient referral form.

- Patient name
- Hospital (if appropriate) and Ward / Clinic
- NHS number (and Hospital number and Clinical trial number where appropriate) and / or date of birth and / or address
- Name of responsible consultant
- Name and Signature of the prescriber and date
- Private patient
- Clinical trial patient (microscope)

3.10 Check the prescription contains the following details:

- height, weight and body surface area (where used for dosing)
- check weight not > 30% IBW (if so do some reductions)
- check calculation (if not prescribed on e-prescribing system)
- frequency of administration
- regimen / 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
- 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)
- check blood results on flow sheet or hospital system.

If Aria is not operational

a) Check Body Surface Area is correctly calculated

i) 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.

ii) 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.

iii) 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.

- iv) In paediatrics a chart based on the Boyd formula and adopted by CCLG as standard should be used.
- v) If patients weight changes during course of treatment BSA drug doses may need to be recalculated and rechecked by pharmacy. (See 3.11)
- vi) 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 up to 2.4m² may be used in Thames Valley.

b) Check doses are calculated appropriately

- i) Check the drug dose calculations for the correct BSA, weight, AUC etc.
- ii) Check dose units are correct, e.g. milligrams, grams, international units.
- iii) 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.

If Aria is not operational

- i) 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.

- ii) 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 prefilled syringes or infusions can then be used to administer the standard dose.

c) Check drug administration details

- i) 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.
- ii) Check that hydration and supportive drugs have been prescribed as required per regimen. 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 regimen)
 - High dose methotrexate (at doses greater than 1000 mg/m²)
- iii) Check patients care plan or clinical notes for any record of administration problems in previous cycles of treatment, e.g. Infusion related reactions.

d) Check laboratory values: Full Blood Counts (FBC)

- i) 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 and ensure pharmacist responsibilities are clearly defined in local policy. Appendix 4 gives a suggested guide to responsibility.
- ii) 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.
- iii) 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.
- iv) 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 regimen agreed with the prescriber/the prescriber or the patient's clinical management plan see the Thames Valley regimen or Clinician trial regimen.
- v) 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 regimen.
- vi) A raised white cell count or absolute neutrophil count may indicate infection and may also be a reason not to treat.
- vii) 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.

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e) Check laboratory values: Renal and hepatic function

i) 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.

ii) 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 regimen 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.

iii) Any patient with impaired renal function as per Thames Valley or clinical trial regimen.

iv) Check regimens and drug information for detailed information. Renal function is critical for the checking of cisplatin, carboplatin and high dose methotrexate doses. (See below for specific information on monitoring of platinum drugs.)

f) Check laboratory values: Other clinical tests

i) 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 regimens 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.

ii) Certain drugs are potentially cardiotoxic and require monitoring of cardiac function, e.g. anthracyclines, trastuzumab and potentially fluorouracil. Consult the regimen 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.

iii) 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.

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g) Monitoring renal function for carboplatin and cisplatin

- i) Renal function, measurement of GFR, can be assessed by two methods.
 - The most accurate method is determination of non- corrected radioisotopic clearance. An accurate determination of GFR obtained by measuring the clearance of either chromium 51 EDTA (^{51}Cr -EDTA), or Technetium DTPA ($\text{Tc}99\text{m}$ DTPA) usually undertaken by medical physics.
 - GFR can be corrected for body mass (normalised to a body surface area of 1.73 m^2) 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. 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. The Thames Valley agreed method on Aria is Wright. For obese and anorexic patients the formulae may not give accurate results and measured GFR is recommended.
 - 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.
- ii) 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.
- iii) The dose of cisplatin in most regimens is modified by the prescriber as per Thames Valley regimen or Clinical trial regimen. The total dose may be reduced or split over two days to allow time for the drug to be cleared from the body.
- iv) 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.
- v) On the first course of carboplatin look at and check 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.
- vi) 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%. If the chemotherapy has been prescribed and the creatinine is 20% worse contact the prescriber about the dose.

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vii) Alternatively calculate the GFR using either Wright or Cockcroft & Gault 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.

If Aria is not operational

i) Carboplatin doses are calculated from renal function (GFR) using the Calvert formulae, (see appendix 6). 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 per regimen

ii) Check if this GFR is measured and check the original result (see g ii) above). Double check the calculation using the Wright formula or Cockcroft & Gault. Check that the correct AUC had been used.

3.11 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.

3.12 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 in the administration notes.

3.13 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.

3.14 Clinical trial prescriptions require additional checks

- i) Trial regimen version number
- ii) Patient trial number
- iii) Bottle or vial numbers

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Appendix 1

Medication Counselling / Informational Care

1.1 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.

1.2 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

1.3 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.

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Appendix 2

Governance, Quality and Risk management

2.1 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.

2.2 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.

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Appendix 3 Emergency Planning

3.1 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.

3.2 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.

3.3 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.

3.4 This guidance is referring to clinical check only. It is presumed that Trust aseptic departments will have separate contingency plans for production.

3.5 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

BSA
Regimen
Doses
Route
Fluids
Infusion times
Start and stop dates for oral
Supportive meds
Liver & renal function (if applicable)

Subsequent cycles

Correct patient
Interval
No dose change
Confirm any prescribed change
Start and stop dates for oral

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Appendix 4

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: Regimen/ Proforma	P
N,P,D	↓	
	FBC U + E and LFTs	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	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 5

Pharmaceutical care plans

5.1 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.

5.2 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.

5.3 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

5.4 The care plan could exist as a stand alone pharmacy paper document, be electronic or be incorporated into the patient's chemotherapy/ medical notes.

5.5 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?

5.6 Check care plan / patients notes for any record of dose modifications or delays in previous cycles of treatment.

5.7 Check that any additional prescriptions for supportive treatments, e.g. anti- emetics have been ordered.

5.8 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.

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Appendix 6 Calculations

6.1 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.

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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.

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6.2 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)

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6.3 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.

6.4 Maximum Cumulative Anthracycline Life Time Dosage

Higher cumulative anthracycline doses are associated with cardiomyopathy and therefore it is usual to limit cumulative doses to prevent symptomatic and potentially fatal heart failure is common above these doses.

Bleomycin –

300000 units can cause pulmonary fibrosis

100000 units may be at risk of developing respiratory failure with high oxygen concentrations

Daunorubicin –

550mg/m² (normal cardiac function)

400-450mg/m² (in combination with thoracic radiation or prior anthracycline therapy)

Liposomal daunorubicin -

LVEF must be determined when a cumulative dose of 320mg/m² has been reached, then every 160mg/m² thereafter, in order to identify at an early stage any changes in LVEF that may be a precursor to cardiomyopathy if liposomal daunorubicin (DaunoXome) therapy is continued

Doxorubicin –

450-550 mg/m² (normal cardiac function)

400 mg/m² (patients with cardiac dysfunction or exposed to mediastinal irradiation)

Liposomal doxorubicin -

450-550 mg/m² (normal cardiac function)

400 mg/m²(patients with cardiac dysfunction or exposed to mediastinal irradiation)

Epirubicin –

1000mg/m² (normal cardiac function)

650mg/m² (patients with cardiac dysfunction or exposed to mediastinal irradiation)

Idarubicin (IV) –

The cumulative dose associated with cardiotoxicity is not known, but it is believed that a total dose of 150 mg/m² but is lower for high risk patients eg pre-existing cardiac disease or prior chest irradiation.

Idarubicin (oral) –

400 mg/m² but consider previous anthracycline usage.

Mitoxantrone -

140-160mg/m² cardiac examinations recommended

110mg/m² (patients with prior anthracycline treatment)