The Oral Anticancer Medicines Handbook

A reference guide to oral chemotherapy and oral anticancer medicines, including advice on safe prescribing, handling and administration. As used in the North of England Cancer Network (NECN).

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Disclaimer

Whilst every care has been taken to ensure accuracy of the information, it is not intended to be a comprehensive guide to using these medicines. The authors and publishers cannot accept responsibility for any errors or omissions or for any consequences from application of information in this book and make no warranty, expressed or implicit with respect to the contents of this book. Readers are advised to exercise clinical judgement as it is acknowledged that drug protocols are being continually revised and new side effects recognised. For full information on the dosage, administration and possible adverse affects of the drugs and regimens listed we recommend that the manufacturer’s data sheets (SPC) and patient information leaflets (PILS) be consulted at www.medicine.org.uk. Please note: the regimens, combinations and indications described in this book are in many cases outside of the product licence.

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Version 3: Issued 25th July 2008: Readers are advised to check NECN website www.cancernorth.nhs.uk to ensure they are using most up to date version
Preface – How to use this Book

This document is primarily intended as a reference source for pharmacy and nursing staff to enable them to support patients receiving oral anticancer medicines. The document does not contain information on oral anticancer medicines that are not routinely in use in the NHS North East, i.e. medicines that do not have NICE and or North of England Cancer Drugs Group (NECDAG) approval.

The book is split into three main sections:

1. Section One, describes the principles behind the use of oral anticancer medicines and gives good practice advice on the set up and management of oral anticancer medicines services.
2. Section Two gives individual drug monographs for a quick reference source for pharmacy and nursing staff to enable them to support patients receiving oral anticancer medicines.
3. Section Three contains the full regimen protocol information.

Readers are also advised to consult the North of England Cancer Network Standards for the Safe Use of Oral Anticancer Medicines published in December 2007. This handbook is to be read in conjunction with these Standards and must be made available to all staff who prescribe, prepare, dispense or administer oral anticancer medicines. Trusts within the North of England Cancer Network are expected to comply with these standards. Section one of this book gives an outline on suggested best practice for working with oral anticancer medicines. Updates to the handbook including the latest drug monographs and can be found by visiting the North East Cancer Network website www.cancernorth.nhs.uk.

For the purposes of this document the term "Oral Anticancer Medicine" is used to refer to all drugs with direct anti-tumour activity, orally administered to cancer patients, including traditional cytotoxic chemotherapy such as capecitabine, hydroxycarbamide, chlorambucil and small molecule/ antibody treatments such as imatinib, erlotinib, sunitinib and other agents such as thalidomide or lenalidomide. It does not include hormonal or anti-hormonal agents such as tamoxifen and anastrazole.
Non-Cancer
It must be noted that some oral anticancer medicines are also used for non-cancer indications, e.g. methotrexate for rheumatoid arthritis, and pose similar risks to the patient. The use of the medicines in these scenarios is outside the scope of this handbook.

Drug Doses
All drug doses are given as a guide only, chemotherapy must always be prescribed by an oncology or haematology specialist. Oral chemotherapy for solid tumours should be given in accordance with an approved patient pathway. The dose modifications described in this handbook should be taken in the clinical context of the patient, while considering treatment intent and any toxicity experienced during previous cycles of chemotherapy.

Paediatrics
While there is clearly overlap between paediatric and adult oncology/haematology – the guidance in this book (especially with reference to dosage) should be considered to apply only to adults unless the book states otherwise.

Pregnancy and Breast feeding
While individual drug protocols may not specify that a combination is contra-indicated in pregnancy and breast feeding – all anti-cancer agents should as a principle be considered contra-indicated. There may be exceptional circumstances where use in pregnancy would be considered however that stretches far beyond the scope of this text.
Acknowledgements

This handbook would not have been possible without the co-operation and input of a number of people who contribute to the success of the North of England Cancer Network, in particular the members of the pharmacy and chemotherapy nursing group. Special mention goes to Penny Gamble, Pharmacist at Newcastle Hospitals NHS Foundation Trust for the work in preparing version one of the handbook.

The authors would like to thank Moira Davison, Director of the North of England Cancer Network for her inspired leadership and enthusiasm.

Steve Williamson would like to thank Prof. David Campbell, Chief Pharmacist/ Clinical Director for Medicines Management, Northumbria Healthcare NHS Foundation Trust for his vision and drive to develop pharmacy services and his wife Aly for her continuing support and sound advice.

Calum Polwart would like to thank the numerous clinicians who have reviewed and revised many of the protocols which are included in this handbook. In particular Diane Plews and Ann Lennard both deserve special mention.
CHAPTER 1  INTRODUCTION

Risks associated with oral agents

The majority of anticancer therapies for solid tumours have traditionally been given by the intravenous route. Historically, with the exception of haematological malignancies, very few of the available anticancer medicines were suitable for oral administration and most chemotherapy was supplied as ready to administer intravenous products prepared by specially trained pharmacy staff. The use of oral anticancer medicines offers advantages to patients and health care professionals; it can free nurse time and ease capacity pressures.

Whilst UK standards for dealing with intravenous chemotherapy are clearly defined in the NHS Manual of Cancer Standards there is increasing anecdotal evidence of oral anticancer medicines being handled differently to intravenous chemotherapy. Research in America has shown that few of the safeguards routinely in place for IV chemotherapy have been adopted in US cancer centres. The British Oncology Pharmacy Association (BOPA) recognised the risks with the medicines management of oral chemotherapy and issued a position statement on ‘The Safe Practice and Pharmaceutical Care of Patients Receiving Oral Anticancer Chemotherapy’. BOPA has traditionally set the standards for oncology pharmacists in the UK and provides a forum to develop practice and raise standards. BOPA has now been joined by the UK Cancer Network Pharmacist Forum (CNPF), a group which brings together all the pharmacists employed by Cancer Networks in the UK in looking at best practice in medicines management of oral anticancer medicines.

Oral anticancer medicines have the same potential for risk as IV medicines both in terms of managing treatment related toxicities and perhaps most importantly greater potential for medication errors if not handled to the same standard as intravenous medicines. In January 2008 the National Patient Safety Agency (NPSA) issued a Rapid Response Report entitled ‘Risks of Incorrect Dosing of Oral Anticancer Medicines’. This report highlights the potential for fatal outcomes if incorrect doses of oral anticancer therapy are prescribed, dispensed or administered. The NPSA indicate there were at least three deaths and over four hundred patient safety incidents concerning oral anticancer therapy between November 2003 and July 2007.
Benefits of oral treatments for patients

Patient preference has been a strong driver from the development of oral anticancer medicines. The use of oral anticancer medicines can empower patients and give them a feeling of control over their disease. Oral therapy is preferred by patients, in a scenario based questionnaire of 103 patients likely to receive palliative chemotherapy 89% of patients were shown to prefer oral treatment, provided it is as effective as intravenous therapy. Reasons stated by patients for preferring oral chemotherapy in this study were; convenience; avoiding problems with IV lines; reduced travel and it gave them more ‘control’. Much of the work looking at benefits of oral chemotherapy has been done in patients with colorectal cancer, in a cross-over patient preference trial with capecitabine vs. intravenous 5-fluorouracil 57% of patient’s preferred oral therapy. Again the main reason for preference was for home rather than hospital based treatment.

Patients prescribed oral chemotherapy, like intravenous (IV) chemotherapy, require high levels of specialised care in order to ensure their safety during the course of their treatment. Oral chemotherapy can be equally as toxic as IV chemotherapy and patients need counselling and education with regard to side-effect management, assessment of their tolerance to the treatment and performance status, and referral to other key members of the multi-disciplinary team; nurses are in a key position to provide this role. Unlike IV chemotherapy, oral chemotherapy requires the patient to have a more active role as the patient is often taking the tablets themselves at home. Patients need to understand the benefits of treatment and how to manage side-effects in order to ensure concordance with the prescription to gain optimal benefits. Patients need education about more serious toxicities, when to discontinue their medication and when to seek professional advice; if patients do not have a good understanding of the treatment they are taking their safety could be at risk.
Benefits of Switching To Oral Therapies –Service Capacity

Capacity for preparation and delivery of chemotherapy continues to be a challenge for NHS trusts in the UK. Chemotherapy activity has increased steadily over recent years evidence submitted to the House of Commons by the Cancer Capacity Coalition highlighted an increase in chemotherapy activity by around 200 percent in the three years prior to 2003 with some hospitals reporting increases as high as 500 percent. This was explained by a number of reasons

- The aging population increasing the number of people diagnosed with cancer
- Earlier diagnosis of patients
- New treatments are often in addition to existing treatments rather than replacements, with
- Treatments frequently being offered as second and third line
- Treatments often being offered at an earlier stage in the disease process
- Advances in treatments with new targeted biological therapies
- Increased complexity of some chemotherapy regimens.

Trusts face huge pressures on their chemotherapy services to meet the increasing demands. Switching from IV to oral therapies is one approach that has been promoted to manage these pressures. There are clear benefits to switching, work undertaken by the NHS Cancer Service Collaborative in preparing a capacity planning tool and more recently commissioning C-PORT a web based capacity tool which can be used to demonstrate the capacity savings by an IV to oral switch.

When considering the chemotherapy capacity challenge there are three key areas to focus on; the pharmacy staff time and availability of facilities to prepare anticancer therapies; the nursing time taken to administer the anticancer therapies and physical capacity on ward, know as ‘chair time’ i.e. the time the patient spends occupying a chair or bed on the ward whilst having the anticancer therapies. Switching to oral therapies releases staff time in both pharmacy and for nursing staff and in particular can free a significant amount of ‘chair time’ allowing more patients to be treated on the ward.
The shift to oral therapies for many cancer patients has implications for their care. It can bring service capacity benefits and free nurse and pharmacist time, but it must be remembered that these are still high risk medicines and patients need support. The responsibility for delivering the anticancer medicine to the patient has moved from the oncology nurse to the patient themselves with self-administration at home.
References
10 Taylor H (2005) Evaluation of the impact on nursing and pharmacy staff resources and patient waiting time of a switch from IV to oral chemotherapy: a time in motion audit. http://www.cancerimprovement.nhs.uk/%5Cdocuments%5Clung%5CImpact%20on%20Nursing%20and%20Pharmacy%20Staff%20Resources%20ver%201%20H%20Taylor%2020_10_05.ppt
CHAPTER 2  SAFE PRESCRIBING OF ORAL ANTICANCER MEDICINES

This chapter details the suggested good practice standards to be considered when prescribing oral anticancer medicines. The advice is based upon the standards developed for NHS Trusts in the North of England Cancer Network.

General Prescribing Standards

1. The prescribing of oral anticancer medicines should be carried out and monitored to the same standards as those in place parenteral (IV) chemotherapy.

2. Organisations should nominate a clinical lead for to take responsibility for ensuring the implementation of safe practice for oral anticancer medicines. This could be a pharmacist, nurse or doctor.

3. All organisations should have in place policies covering all aspects of prescribing oral anticancer medicines.

4. It is recommended that prescribing of the first cycle of oral anticancer medicines is undertaken by either a haematologist or oncology specialist at Consultant or SAS/SPR level who has been assessed as competent. Junior doctors (SHO/equivalent or lower) must **not** prescribe. It is suggested that non-medical prescribers may prescribe the second and subsequent course of oral anticancer medicines provided they have acquired approval from their organisation and are working within an agreed clinical management plan (supplementary NMPs) or following an treatment plan (independent NMPs).

5. Patients admitted to hospital wards on oral anticancer medicines are at risk from uncontrolled prescribing. The patient’s current medical condition must be assessed to ensure suitability for continued treatment with the medicine and a detailed medication history must be taken to ensure all information on the dosage of the oral anticancer medicine is known. If it is possible a copy of the original prescription for oral anticancer medicine should be obtained and the patient’s original prescriber contacted to prescribe the medicine on the inpatient drug Kardex.
All prescribers initiating treatment for oral anticancer medicines must:
- assess the patient’s suitability for oral treatment including ability to swallow tablets or capsules
- assess patient’s ability to comply with the proposed drug/regimen
- obtain consent from the patient following local Trust protocol
- provide verbal and written information about their oral anticancer therapy (this information should include contact details for specialist advice)
- ensure appropriate communication to patient’s GP and referring consultant about the medicines, ensuring the GP is clear on the role they play in managing patient.
- ensure patients are appropriately counselled on the use of their medicines, this information may be provided/reinforced by pharmacist/nurse according to local policy.
- record the planned course of treatment and arrangements for review/follow up in the patient’s notes and set a review date.

In patient prescribing must be done to same standards as prescribing for day case and out-patients.

Prescribing in the context of a written protocol or treatment plan

Prescribers must have access to agreed drug protocols for the regimens in use. The British national Formulæ BNF is **not** recommended as a primary source of anticancer drug prescribing information as it currently does not contain detailed regimen information.

Pharmacy departments dispensing and nursing staff administering oral anticancer medicines must have access to the agreed regimen protocols.

Written regimen protocols must be available for all oral anticancer medicines. These can be paper-based or within an electronic prescribing system. The protocols must be consistent with the Cancer Network and Children's Cancer and Leukaemia Group (CCLG) agreed regimens. Good practice would be for a copy of the specific protocol to be filed in the patient’s notes. Copies of protocols should be available on all wards where oral anticancer
medicines are routinely administered or where patients receiving oral anticancer medicines may be admitted (e.g. emergency admissions wards).

Written protocols must contain:
- definition of the clinical condition being treated
- names (approved) of all medicines to be given
- dosing schedule for each medicine
- maximum individual dose where applicable
- maximum cumulative doses where applicable
- supportive therapy
- tests needed before chemotherapy starts
- monitoring required during treatment
- special precautions, expected toxicities and contraindications
- potential interactions and medications to be avoided
- recommendations for dose modifications
- review period
- reference source

All intended deviations from protocol, such as dose modifications, should be clearly identified as such and recorded in patient’s notes / on the prescription form and communicated to the patient’s GP and pharmacy.

Oral anticancer medicines must not be prescribed by repeat prescriptions.

The NPSA advise that patients should be fully informed and receive verbal and up-to-date written information about their oral anticancer therapy from the initiating hospital. This information should include contact details for specialist advice, which can be shared with non-specialist practitioners. Written information, including details of the intended oral anticancer regimen, treatment plan and arrangements for monitoring, taken from the original protocol should be given to the patient.
Good Practice Standards for Prescription Forms

14 All prescriptions for oral anticancer medicines must be computer-generated using regimens from an agreed list of approved protocols. This can be via an electronic prescribing system or a regimen specific pre-printed prescription form. Prescriptions must contain:
• patient details including, height, weight and surface area
• protocol / regimen name
• drug names (generic), and doses (both as mg/m² or per kg and the final calculated dose)
• frequency of administration
• number of days or doses to be dispensed expressed in words
• avoid using abbreviations
• the intended start date
• for non-continuous treatment the exact duration of treatment and/or stop date
• for continuous treatment – the intended review date

15 Pre-printed prescriptions must be clear and unambiguous and available to all prescribers. Electronic documents must be ‘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.

Prescribing for External Healthcare Organisations

16 The majority of prescribing of oral anticancer medicines is likely to within in secondary care organisations. However the NPSA reported that during 2006-2007 nearly six million oral anticancer medicine doses were used in the community in England. The NPSA alert focuses on the need for all oral anti-cancer medicines to be prescribed only in the context of a written protocol and treatment plan, access to these protocols is particularly important for non-specialist practitioners in primary care. Prescribing oral anticancer medicines in primary care must only be undertaken within agreed shared care guidelines.
17 Good practice would be for any shared care guidelines to consider the following areas in addition to the usual clinical management issues of shared care:
- assessment of patient’s suitability to self administer
- assessment of patient’s home environment for suitability
- prescribing chemotherapy
- arrangements for pharmacist prescription verification
- dispensing chemotherapy
- checking clinical parameters including blood counts before administration
- assessing the patient is fit to receive chemotherapy
- administration of the chemotherapy
- delivery, storage and disposal arrangements,
- managing side effects and/or adverse events
- emergency contact(s)
- follow up arrangements

18 All prescribers who write prescriptions for oral anticancer medicines for patients who will have the medicines administered in organisations external to their Trust, e.g. nursing homes, prisons, children’s homes must ensure that the external organisation has access to the written protocols and treatment plan. In the case of organisations such as prisons where medications are re-prescribed by the prison’s medical officer in accordance with their own procedures it is recommended that the organisation ensures written protocols and treatment plans are always obtained before re-prescribing.
CHAPTER 3: DISPENSING AND SUPPLY OF ORAL ANTI CANCER MEDICINES

1 All prescriptions for oral anticancer medicines must be checked and authorised (validated) by an appropriately experienced pharmacist, ideally a trained oncology pharmacist.

2 Where practical pharmaceutical care plans should be put in place to identify the key issues that need to be monitored with the oral anticancer medicine/ regimen.

3 It is recognised that it may not be possible to ensure that all prescriptions for oral anticancer medicines are checked by a trained oncology pharmacist. Trusts and PCTs must therefore ensure that appropriate training on the safety aspects of oral anticancer medicines is provided to pharmacy staff involved in dispensing and supply of these medicines.

4 Staff involved in the dispensing and supply of oral anticancer medicines should have access to an oncology pharmacist who is able to provide advice.

5 Pharmacists validating 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 and this should be doubled checked during dispensing.

6 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 short term or intermittent treatment.

Dispensing

7 The exact quantity of tablets/capsules required must be supplied unless a risk assessment of a particular drug pack size/type identifies it as not suitable to be split.

8 The quantity supplied must be physically checked by counting the number of number of tablets/capsules supplied.
All anticancer medicines must be dispensed and labelled to include the following information:
- patient name
- generic drug name
- strength of tablets or capsules, or concentration of oral liquid
- the number of tablets / capsules in the container, or volume of liquid
- administration instructions
- length of treatment, including stop date as appropriate
- storage conditions
- Caution: Cytotoxic Drug (as appropriate)
- name and address of pharmacy department

Ideally the dispensed prescription should be subject to a second independent check.

All patients must receive a manufacturer's Patient Information Leaflet, with their oral anticancer medicines.

Pharmacy staff must not break or crush tablets, capsules must not be opened. Queries about difficulties in taking the oral form should be directed to a specialist pharmacist. Use of a suspension or solution is preferred and a suitable preparation must be obtained from an NHS hospital pharmacy or commercial compounding/manufacturing facility with appropriate safe-handling facilities. It must be noted that in many cases there are no liquid alternatives, in these cases refer back to original prescriber.

Use of compliance aids is not routinely recommended. If there is thought to be a need a risk assessment must be undertaken and documented in the patient’s notes.

Where possible patient’s own medicines must be used when supplying to hospital inpatients. Patients should be advised to return any unused oral anticancer medication that they may have at home.
Medication Counselling and Informational Care

15 When pharmacy staff and other healthcare professionals supply the oral anticancer medicine to the patient (or relative or carer) they must ensure that the person receiving the medicines fully understands how and when to take their medicines.

16 The member of pharmacy staff handing the drugs 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 safely crushing of tablets or opening of capsules

17 It is recognised that, in practice, most of the information may be provided by the consultant/ specialist nurse in clinic or by the pharmacist on the oncology ward.

18 Oral anticancer patients must be able to access the same 24 hour telephone advice service provided for IV chemotherapy patients.

19 Patients must be provided with the same patient held record document used for IV chemotherapy patients.

20 Trusts must consider what action to be taken if after counselling the patient on their medication it becomes apparent that the patient does not understand how to take the medicines or will have difficulty in compliance.
Dispensing in Community Pharmacy

Oral anticancer medicines should not be dispensed by community pharmacies unless an appropriate framework has been developed to ensure the principles and safety standards outlined in this document are met, ideally this should include a service level agreement:

- suitability of drug/regimen, i.e. assessment of potential toxicity of the drug(s) and complexity of the regimen (more than one drug, pulsed schedule, variable dose)
- availability of drugs (wholesaler or direct)
- origin of prescription, primary or secondary care (the use of FP10 or FP10-HP prescriptions may be a barrier to the recommendation for regimen specific electronically generated prescriptions)
- requirement for specialist clinical oncology pharmacy advice
- requirement for Shared Care documentation
- training requirements for primary care pharmacists (It is suggested that this may be an area for the development of a Pharmacist with a Special Interest, PhwSI, in cancer)
- remuneration issues
- handling and disposal of cytotoxic drugs (COSHH)
- out of hours support
CHAPTER 4: ADMINISTRATION AND HANDLING OF ORAL ANTICANCER MEDICINES

1 Administration of oral anticancer medicines on Trust premises on oncology/haematology wards must be undertaken by appropriately qualified clinical staff who are competent to follow the same safeguards and checks as when administering IV anticancer medicines.

2 Clinical staff administering oral anticancer medicines on non-oncology/haematology wards to inpatients should contact members of the patient’s specialist team for information and advice about the oral anticancer medicine.

3 Two practitioners are required to check and administer oral anticancer medicines. Ideally Organisations should keep a register of which members of staff are able administer oral anticancer medicines.

4 When patients are self-administering their oral anticancer medicines, the responsibility for administration lies with the patient and their carer. The health care professional’s role is to support patients.

5 Before oral anticancer medicines are administered in a healthcare organisation premises, e.g. hospital Trust the patient must be clinically reviewed by an appropriately qualified and competent clinical staff member who will:
   - ensure that the patient’s medical condition and blood parameters support ongoing treatment
   - check results of all investigations, blood parameters and specific drug calculations specified within the treatment protocol/local guidelines
   - document the administration of the medicine(s) in the patient’s medical notes and patient held records (if used)

6 In the case of inpatients receiving their medications over a period of days the above checks must be done before the first dose is given in hospital and then regularly during treatment according to the parameters specified in the written protocol.

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7 Clinical staff administering oral anticancer medicines to patients in Trust premises must be familiar with their organisations procedures for safe handling of cytotoxic medicines and disposal of waste.

8 Patients must be given advice on how to safely store their oral anticancer medicines and told where and how to return unused medicines for disposal.
SECTION TWO
DRUG MONOGRAPHS
BUSULFAN (MYLERAN®)

Information for Nursing and Pharmacy Staff:

Available as: 2mg tablets (pack size 25)

Used for: CML (chronic myeloid leukaemia) and as conditioning regimen prior to bone marrow transplant

Common regimens:

- CML: usual dose 0.1 mg/kg/day for 5-10 days = 2 to 8mg once daily
- Bone marrow transplant: 0.8-1 mg/kg PO every 6 hours for 4 days for a total of 16 doses; may be used in combination with other drugs

Emetogenic potential: Low/non-emetogenic.

Safe handling/spillages: Tablets should not be divided, and, if outer coating on tablet intact, there is no risk in handling tablets.

Drug interactions: paracetamol, phenytoin, itraconazole, clozapine

Information for patients (counselling points):

Missed dose: Do not double next dose, inform doctor and keep to normal dosing schedule.

Post dose vomiting advice: Tell doctor as soon as possible; do not take an extra tablet without consulting doctor.

Side effects:

- Anaemia/tiredness from bone marrow suppression
- Hyperpigmentation
- Mucositis
- Diarrhoea
- High temperature/unexplained bruising/bleeding, contact doctor

Storage: Not above 25°C.

Disposal of medication/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines

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CAPECITABINE (XELODA®)

Information for Nursing and Pharmacy Staff:

Available as: 150mg tablets (pack size 60) & 500mg tablets (pack size 120)

Used for: Colorectal and Breast cancers

Common regimens:

• 1250mg/m² twice daily for 14 days every 21 days (table in SPC for dose banding) for eight cycles (adjuvant colorectal cancer) or until disease progression (advanced colorectal/breast cancer)

• Once a dose has been reduced from 1250mg/m² following toxicity it should not be increased again.

• 625mg/m² twice daily continuously as part of ECX regimen for upper GI cancers

• Can be given as 825mg/m² or 1000mg/m² twice daily during radiotherapy from the first day to the last day of radiotherapy.

• When in combination with radiotherapy, the maximum tolerated dose is decreased to 2000mg/m²/day (i.e. 1000mg/m² twice daily)

Emetogenic potential: Low/moderate.

Safe handling/spillages: See appendix 2 regarding spillages.

Pharmaceutical Care Issues:

• No liquid form available therefore unsuitable for those who can’t swallow. Note Royal Marsden recommend dissolving tablets in lukewarm water, stir for 15 minutes to dissolve then swallow with orange juice/other flavouring to mask the bitter taste.

• Pyridoxine 50mg three times daily has been traditionally prescribed for hand and foot syndrome, however there is no evidence of the effectiveness of this treatment so should not be routinely used.

Drug interactions: allopurinol, warfarin, phenytoin, itraconazole, sorivudine
Information for patients (counselling points):

Missed dose: Do not double-up doses or take extra doses at the end of the treatment cycle to make up for the missed doses. If remember 30 to 90 minutes after they should have taken their tablets, then take the missed dose, if it is near to the time when their next dose is due, do not take missed dose. Inform doctor/ chemotherapy unit and keep to normal dosing schedule.

Post dose vomiting advice: Tell doctor as soon as possible.

Side effects:

- Altered taste
- Gastrointestinal disturbances (diarrhoea, constipation, abdominal pain, nausea)
- Stomatitis (mouth ulcers)
- Hand-foot syndrome (pain, swelling or redness in hands and/or feet)
- Fatigue

Advise patients of the risk of Hand-and-foot skin-reaction (Palmar/Plantar Erythrodysesthesia) and that they should stop taking capecitabine and contact their Chemotherapy Unit if they have pain, swelling, and redness of hands and/or feet.

Diarrhoea is common, and may require intervention with fluids and electrolytes if severe. If diarrhoea is a problem give loperamide 2 to 4 mg four times daily when required (maximum 8 in 24 hours) or codeine phosphate 30mg four times daily and stop taking Capecitabine if diarrhoea moderate or severe.

If palmar-plantar erythrodysesthesia is a problem could consider pyridoxine 50 mg TDS, though the clinical evidence for efficacy of this intervention is lacking.

Storage: Do not store above 30°C

Disposal of medication/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.
**Advice for patients:**

Take tablets 12 hours apart within 30 minutes after a meal/with food, not to be crushed.

Swallow whole with a full glass of water.

Caution with driving/operating machinery.

Advise patients about the strong possibility of developing hand-foot syndrome and discuss options for managing this.

Contact chemotherapy day unit if:

- **Diarrhoea:** More than four bowel movements/ in 24 hours day or have diarrhoea at night
- **Vomiting:** More than once in 24 hours
- **Nausea:** loss of appetite/eating less food than normal
- **Stomatitis:** pain/redness/swelling/sores in mouth
- **Hand-and-foot skin-reaction:** pain/swelling/redness on hands and feet
- **Fever or infection:** temp >38°C or other signs
CHLORAMBUCIL (LEUKERAN®)

Information for Nursing and Pharmacy Staff:

Available as: 2mg tablets (pack size 25)

Used for: chronic leukaemia’s and lymphomas.

Common regimens:

- 20mg/m² once daily for 3 days (with dexamethasone 4mg twice daily for 5 days)
- 30mg once daily for 4 days weeks 1 to 4, 6, 8, 10 and 12 (prophylactic phenytoin 300mg nocte for 5 days with each cycle in patients > 60 years old starting night before first chlorambucil dose). This is a high dose regimen – always double check.
- PECC: 20mg/m² days 1 to 4 (with etoposide, lomustine and prednisolone)
- CLL4 trial: 10mg/m² for 7 days every 28 days (can divide dose into 3 to reduce sickness)
- CLVPP & PVACE-BOP for Hodgkin’s disease: 6mg/m² once daily (max 10mg) for 14 days with oral procarbazine, prednisolone (oral etoposide in PVACE-BOP)
- LOPP: 10mg daily for 1 to 10 days (with procarbazine 100mg/m² – max 200mg – and prednisolone 25mg/m² daily – max 60mg – for 14 days)

Emetogenic potential: Low

Safe handling/spillages: Provided the outer coating of chlorambucil is intact, there is no risk in handling. Urine produced for up to 48 hours after a dose should be handled wearing protective clothing.

Pharmaceutical Care Issues:

- Only available in tablet form therefore patients who cannot swallow should not use.
- Cross sensitivity with melphalan can manifest as a rash.

Drug interactions: None significant
Information for patients (counselling points):

Missed dose: Do not take double next dose, inform doctor and keep to normal dosing schedule.

Post dose vomiting: Tell doctor as soon as possible; do not take another tablet without consulting doctor.

Side effects:
- Bone marrow suppression
- Mouth ulcers/loss of appetite
- Gastrointestinal disturbances (nausea/vomiting/diarrhoea)

Storage: Refrigerate (between 2 to 8°C)

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines

Advice for patients:
- Not to be broken/crushed/chewed.
- Swallow with water.
- Tell doctor if more tired than usual, unexplained bruising/bleeding, persistent cough, weakness in muscles.
CYCLOPHOSPHAMIDE (ENDOXANA®)

Information for Nursing and Pharmacy Staff:

Available as: 50mg tablets (pack size 100)

Used for: Myeloma, chronic leukaemia’s, breast cancer

Common regimens:

- CMF: 100 mg/m²/day for 14 days (days 1 to 14 of 3 weekly CMF))
- Myeloma: 500mg weekly (with dexamethasone 40mg/day on days 1 to 4)
- 400mg/m² weekly (with prednisolone 40mg/m² alternate days for 6 weeks with tail off weeks 7 to 8). Reduce dose in renal impairment to 200mg/m² weekly.
- LYOS trial (with fludarabine): 250mg/m² from days 1 to 3
- CLL4 trial (with fludarabine): 150mg/m² daily for 5 days
- Note also used for non-cancer indications, e.g. vasculitis, rheumatology

Emetogenic potential: High. Onset 4 to 12 hrs, duration 4 to 10+ hrs

Safe handling/spillages: Pregnant or breast-feeding women should not handle tablets. Urine and faeces produced for up to 72 hours and 5 days respectively after a dose should be handled wearing protective clothing. Also present in sweat and saliva; advise caution for 72 hours after a dose when bathing the patient or carrying out oral procedures

Pharmaceutical Care Issues:

- Report any signs of cystitis; cyclophosphamide should be avoided until treated.
- Tablets are coated and should not be divided.
- Antiemetics should be given before and during therapy to reduce nausea and vomiting.

Drug interactions: clozapine, warfarin, phenytoin, digoxin, chloramphenicol
Information for patients (counselling points):

Missed dose: Take as soon as remember if it is the same day. If a day’s worth of tablets is missed, contact the doctor. Never take more tablets in one day than you were meant to. Do not take double next dose, inform doctor and keep to normal dosing schedule.

Post dose vomiting: Tell doctor as soon as possible; do not take another tablet without consulting doctor. Anti-emetics should be given before and during therapy to reduce nausea and vomiting.

Side effects:

- Nausea, vomiting
- Hair loss/thinning (20%) within 3 weeks regrowth after 3 months of treatment
- Headaches
- Nail/skin colour changes

Storage: In original container less than 25°C protected from light.

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines

Advice for patients:

- Pregnant or breast-feeding women should not handle tablets.
- Swallow whole preferably on an empty stomach but if gastrointestinal irritation is severe, can be taken with food.
- Taken early in the day and plenty water through day to avoid cystitis.
- Any sign of cystitis should be reported to doctor.
- When in combination with fludarabine – take cyclophosphamide at breakfast and fludarabine at lunchtime.

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ERLOTINIB (TARCEVA®)

Available as: Presented as 25mg, 100mg and 150mg Tablets (pack size 30)

Used for: Alternative 2nd line treatment to Docetaxel (Taxotere) for Patients with locally advanced or metastatic non-small cell lung cancer.

Common regimens:

- One 150mg dose orally, taken once daily until disease progression.

Emetogenic potential: Low/Moderate. Antiemetic not usually required but can be controlled with metoclopramide if needed.

Safe handling/spillages: No special precautions.

Pharmaceutical Care Issues:

- Standard dose is 150mg daily; patients may be dose reduced to either 100mg or 50mg daily depending on severity of side effects.

- Patients taking erlotinib must be supplied with loperamide 2mg and advised to take for diarrhoea as required (max 16mg in 24 hours)

- Provide emollients e.g. Diprobase, Epaderm, E45 or Neutrogena and encourage patients to use regularly to prevent skin dryness.

Drug interactions

Systemic anti-fungals e.g. ketoconazole, itraconazole, voriconazole; ciprofloxacin, protease inhibitors, erythromycin and SSRI’s e.g. fluoxetine, fluvoxamine, rifampicin, phenytoin, carbamazepine, phenobarbital or Hypericum perforatum (St John’s Wort)

Proton Pump Inhibitors such as omeprazole (and probably other drugs affecting Gastric pH) will reduce absorption by around 50%. Dose escalation does not compensate.

Information for patients (counselling points):

Missed dose If the scheduled days dosing is missed, advise patient to not take dose and contact their named chemotherapy contact.

Post dose vomiting: If the patient vomits after taking an erlotinib tablet, the patient should NOT take another tablet, until the next dose is due.
Side effects:
- Skin rash (may be severe)
- Nausea and vomiting
- Diarrhoea
- Mild nausea and vomiting
- Fatigue

Storage: Between 10 to 25°C.

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:
- Erlotinib should be taken with water 1 hour prior to or 2 hours after food
- Avoid strong sunlight or use a good sunscreen SPF 15 or higher
- Patients should be counselled on how to manage most common side effects of skin rash and diarrhoea.
ETOPOSIDE (VEPESID®)

Information for Nursing and Pharmacy Staff:

Available as: 50mg caps (pack size 20) & 100mg caps (pack size 10)

Used for: Ovarian cancer, Lung cancer, Lymphomas

Common regimens:

- Relapsed ovarian cancer: 50mg twice daily days 1 to 14
- CE for SCLC: 240mg/m² as divided dose (twice daily) rounded to the nearest 50mg on days 2 and 3
- PVACE-BOP for Hodgkins 200mg/m² days 2 and 3 (with procarbazine, chlorambucil and prednisolone 40mg/day for 14 days)
- PECC for Hodgkin’s; 200mg/m² days 1, 2 and 3 (with lomustine CCNU, chlorambucil days 1 to 4 and prednisolone 40mg once daily on days 1 to 7)
- VEPEMB for Hodgkin’s 60mg/m² for 5 days (days 15 to 19) every 28 days (with procarbazine and prednisolone 30mg/m² days 1 to 5)
- AML (with idarubicin): 80mg/m² daily for 3 days every 21 days

Emetogenic potential: Low. Onset 3 to 8hrs, duration 12hrs

Safe handling/spillages: Do not open blister if there is evidence of capsule leakage. Urine and faeces produced for up to 4 and 7 days, respectively after a dose should be handled wearing protective clothing.

Pharmaceutical Care Issues:

- As a last resort if unable to swallow capsules, the injection, can be given orally as an alternative. This should be packed into oral syringes in pharmacy. The injection is unpleasant to take, the taste can be masked by advising patient to swallow with cola.

- There is an interaction with grapefruit juice which should be avoided.

Drug interactions ciclosporin, aprepitant, St Johns Wart
Information for patients (counselling points):

Missed dose: Do not take double next dose, inform doctor and keep to normal dosing schedule.

Post dose vomiting: Tell doctor as soon as possible; do not take another tablet without consulting doctor.

Side effects:

- Nausea and vomiting
- Alopecia (reversible)
- Altered taste / loss of appetite
- Hand and food syndrome

Storage: Between 10-25°C.

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines (appendix 3).

Advice for patients:

- To be taken on an empty stomach.
- Grapefruit juice should be avoided.
- Do not open blister if there is evidence of capsule leakage.
FLUDARABINE (FLUDARA®)

Information for Nursing and Pharmacy Staff:
Available as: 10mg tabs (pack size 20)
Used for: Chronic Lymphocytic Leukaemia CLL / lymphomas

Common regimens:
- Single agent: 40mg/m² once daily for 5 days every 28 days
- LYOS trial (with cyclophosphamide): 40mg/m² once daily, days 1 to 3
- CLL4 trial (with cyclophosphamide): 24mg/m² daily for 5 days

Emetogenic potential: Low/ transient (30% patients).
Safe handling/spillages: Should not be handled by pregnant women.

Pharmaceutical Care Issues:
- Combinations with cyclophosphamide – take cyclophosphamide at breakfast and fludarabine at lunchtime.
- Unless contra-indicated, co-trimoxazole (960mg three times/week) may be required for PCP prophylaxis. Should be prescribed during and for 6-12 months after taking fludarabine.
- Patients who require blood transfusion and who are undergoing, or who have received, treatment with fludarabine should receive irradiated blood only.
- Monitor renal function, dose reduction needed with mild renal failure (CrCl <70 mL/min)

Drug interactions, pentostatin, and dipyridamole

Information for patients (counselling points):
Missed dose: Should be taken at the same time every treatment day. Missed tablets should be taken at the earliest opportunity and a compromise reached for subsequent doses. No other dose should be taken within 12 hours of taking the drug. A gap of 18 to 24 hours should ideally be left between doses.
Post dose vomiting: Do not double the dose for that day. Continue with the next dose on the next day. If vomiting is proving an issue for patients, it is advised they speak to their doctor or nurse regarding anti-emetics.

Side effects:

- Infection
- Fever/chills
- Fatigue
- Peripheral neuropathy
- Visual disturbances
- Gastrointestinal disturbances (nausea, vomiting, anorexia)
- Stomatitis

Storage: No special storage precautions.

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:

- Take on empty stomach or together with food, swallowed whole with water.
- Do not chew or break tablets.
- Should not be handled by pregnant women.
HYDROXYCARBAMIDE (HYDREA®)
(Formerly known as Hydroxyurea)

Information for Nursing and Pharmacy Staff:
Available as: 500mg caps (pack size 100)
Used for: Chronic Myeloid Leukaemia CML

Common regimens:
- CML initially: 1000 to 2000mg/m² continuous until remission then;
- CML maintenance: 500 to 1000mg/m² continuous (dose is titrated to response)
- Capsules only available as 500mg therefore the total weekly dose should be calculated and divided into manageable daily doses i.e.: if dose works out 800mg/day (5600mg/week) a dosing regimen may be 500mg on Monday, Wednesday and Friday, 1000mg on other days.
- Note also used for non-cancer indications, e.g. Primary thrombocythaemia (PT dose titrated according to response.)

Emetogenic potential: Low (drug rapidly absorbed)

Safe handling/spillages: The contents of capsules should not be inhaled or allowed to come into contact with the skin or mucous membranes. Spillages must be wiped immediately. Urine produced for up to 48 hours after a dose should be handled wearing protective clothing.

Pharmaceutical Care Issues:
- Not to be used in combination with antiretroviral treatments for HIV. May cause treatment failure and toxicities in HIV patients.

Drug Interactions: None significant

Information for patients (counselling points):
Missed dose: Do not take double next dose, inform doctor and keep to normal dosing schedule.
Post dose vomiting: Tell doctor as soon as possible; do not take another capsule without consulting doctor. Due to low emetogenic potential it is unlikely to be a problem.

Side effects:
- Anaemia
- Bone marrow suppression

Storage: Not greater than 25°C

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:
The contents of the capsules may be emptied into a glass of water, stirred and taken immediately. Particles floating on the top of water are the inactive bulking agent.
**IDARUBICIN (ZAVEDOS®)**

**Information for Nursing and Pharmacy Staff:**

**Available as:** 5mg capsule (pack size 1) and 10mg capsule (pack size 1) and 25mg capsule (pack size 1)

**Used for:** chronic leukaemia’s and lymphomas

**Common regimens:**

- AML: 20mg/m² daily for 3 days in combination with etoposide 8mg/m² daily every 21 days
- Myeloma: 10mg/m²/day on days 1 to 4 in combination with dexamethasone 40mg/day.

**Emetogenic potential:** High (80%)

**Safe handling/spillages:** If accidental contact with powder from capsule into the eye, skin or mucosa, immediately rinse with water and seek medical attention.

**Pharmaceutical Care Issues:**

- Cardiac toxicity is cumulative across members of the anthracycline (doxorubicin, epirubicin, daunorubicin, idarubicin) class of drugs. Patients who have received these agents are at increased risk of toxicity, and should be carefully monitored

**Drug Interactions:** None significant

**Information for patients (counselling points):**

**Missed dose:** Do not take double next dose, inform doctor and keep to normal dosing schedule.

**Post dose vomiting:** Tell doctor as soon as possible; do not take another tablet without consulting doctor.

**Side effects:**

- Alopecia (reversible)
- Gastrointestinal disturbances (nausea, vomiting, diarrhoea)
- Cardiac toxicity
- Rash
- Fever/chills
- Sore mouth (can appear 3-10 days post treatment)

**Storage:** In a dry place

**Disposal of medicine/spoons:** Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

**Advice for patient:**
- Intact capsules should be swallowed whole with water, not sucked, bitten or chewed.
- Take with a light meal.
- Powder in capsules is red and urine may appear red for 1 to 2 days after treatment.
**IMATINIB (GLIVEC®)**

**Information for Nursing and Pharmacy Staff:**

**Available as:** 100mg tablets (packs size 60) & 400mg tablets (pack size 30)

**Used for:** Chronic Myeloid Leukaemia CML, GIST gastro intestinal stromal tumour

**Common regimens:**

- CML: 400 to 600mg/day (chronic phase) titrated according to response
- 600 to 800mg/day in accelerated phase/blast crisis
- GIST: 400mg daily

**Emetogenic potential:** Low/moderate (10%)

**Safe handling/spillages:** No special precautions.

**Drug interactions:** Warfarin, simvastatin, phenytoin, rifampacin & other enzyme inducers, erythromycin and enzyme inhibitors.

**Information for patients (counselling points):**

**Missed dose:** Do not take double next dose, inform doctor and keep to normal dosing schedule.

**Post dose vomiting advice:** Do not take an extra tablet without consulting doctor.

**Side effects:**

- Headache
- Gastrointestinal disturbances (nausea, vomiting, diarrhoea, dyspepsia, abdominal pain)
- Muscle cramps
- Oedema (if water retention severe, tell doctor immediately)
- Rash
- Blurred vision
Storage: Original packaging, below 30°C.

Disposal of medication/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:

- With food and large glass of water.
- Caution with driving/operating machinery (possibility of blurred vision/dizziness).
- For patients unable to swallow the film-coated tablets, they may be dispersed in a glass of mineral water or apple juice. The required number of tablets should be placed in the appropriate volume of beverage (approximately 50 ml for a 100 mg tablet, and 200 ml for a 400 mg tablet) and stirred with a spoon. The suspension should be administered immediately after complete disintegration of the tablet(s).
LOMUSTINE (CCNU)

Information for Nursing and Pharmacy Staff:

Available as: 40mg capsules (pack size 20)

Used for: Hodgkin’s disease, Brain tumours

Common regimens:

- PECC: 100mg/m² for ONE DAY ONLY (with chlorambucil, etoposide, and prednisolone given every 4 to 6 weeks).
- 30mg/m² days 1 to 3 on alternate courses (with prednisolone 10mg FOUR TIMES DAILY days 1 to 14)

Emetogenic potential: High (54%) 45mins to 6hrs post dose. Duration approximately 24 hours.

Safe handling/spillages: If a capsule becomes damaged, avoid contact of the powder contents with skin or mucous membrane. If contact does occur, wash the affected area.

Drug interactions: Cimetidine

Information for patients (counselling points):

Missed dose: Do not take double next dose, inform doctor and keep to normal dosing schedule.

Post dose vomiting: Nausea and vomiting usually followed by anorexia for 2-3 days. If vomiting persists for 30-45 minutes do not repeat the dose and report to doctor as soon as possible.

Side effects:

- Nausea/vomiting
- Myelosupression

Storage: In original container not more than 25°C.

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.
Advice for patients:

- Can impair ability to drive/use machinery if nauseous.
- Given at night on an empty stomach can help reduce nausea.
MELPHALAN (ALKERAN®)

Information for Nursing and Pharmacy Staff:

Available as: 2mg tabs (pack size 25)
Used for: Multiple Myeloma

Common regimens:

- MP: 7mg/m² per day for days 1 to 4 (with prednisolone 20mg TWICE DAILY or 40mg once daily days 1 to 4)

Emetogenic potential: Low. Onset 6-12hrs

Safe handling/spillages: Urine and faeces produced for up to 48 hours and 7 days, respectively after a dose should be handled wearing protective clothing.

Pharmaceutical Care Issues:

- Cross sensitivity with chlorambucil manifests as a rash

Drug interactions: nalidixic acid, ciclosporin, Phenytoin, clozapine

Information for patients (counselling points):

Missed dose: Do not take double next dose, inform doctor and keep to normal dosing schedule.

Post dose vomiting: Do not take another tablet without consulting doctor.

Side effects:

- Sickness
- Diarrhoea
- Sore mouth (dose related)
- Cross sensitivity with chlorambucil manifests as a rash

Storage: Refrigerate between 2-8°C.

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.
Advice for patients:

- Swallow tablets before food with water.
- Do not crush/break tablets.
MERCAPTOPURINE, 6-MP (PURI-NETHOL®)

Information for Nursing and Pharmacy Staff:

Available as: 50mg tabs (pack size 25)

Used for: Acute leukaemia’s, Chronic Granulocytic leukaemia

Common regimens:

- ALL protocol (adults 15 to 20yrs) 100mg/m² (max 150mg/day) as per schedule (given under supervision of RVI)
- Standard ALL 60mg/m² daily as maintenance
- T-ALL – 60mg/m² weeks 4 to 7 and 9 to 16 then 75mg/m² weeks 25 to 31 and weeks 40 to 51
- APML -90mg/m²/day (with tretinoin 45mg/m²/day) for 15 days every 3 months

Emetogenic potential: Low

Safe handling/spillages: Wash hands immediately after handling/halving tablets, avoid contact with eyes, and avoid inhalation of particle. Urine and faeces produced for up to 24 hours and 5 days, respectively after a dose should be handled wearing protective clothing.

Pharmaceutical Care Issues:

- Caution in renal impairment
- Caution in patients with inherited deficiency of the enzyme thiopurine methyltransferase (TPMT) who may be unusually sensitive to the myelosuppressive effect of 6-mercaptopurine and at risk of developing rapid bone marrow depression

Drug interactions: allopurinol (mercaptopurine dose must be reduced to 25%), warfarin, olsalazine, mesalazine or sulphasalazine

Information for patients (counselling points):

Missed dose: Do not take double next dose, inform doctor and keep to normal dosing schedule.

Post dose vomiting: Do not take another tablet without consulting doctor.
Side effects:

- Bone marrow suppression
- Rarely nausea and vomiting

Storage: Below 25°C.

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines

Advice for patients:

- Swallow with water.
METHOTREXATE, MTX (MAXTREX®)

Information for Nursing and Pharmacy Staff:

Available as: 2.5mg tablets (pack size 100)

Used for: Acute leukaemia’s, rheumatoid arthritis and psoriasis.

Common regimens:

Used for the regression of a wide range of neoplastic conditions.

- Adult ALL – methotrexate as maintenance 15mg/m² (max 20mg) weekly for weeks 30 to 120 (combination with mercaptopurine 100mg/m² to max 150mg)
- Standard ALL – methotrexate 10mg/m² weekly for weeks 1 to 12 (combination with mercaptopurine 60mg/m² and prednisolone 40mg/m²)
- T-ALL – methotrexate 20mg/m² weekly for weeks 11 to 16, 26 to 31 and 41-51 (combination with prednisolone 40mg/m² and mercaptopurine 60mg/m²)
- Note also used for a wide range of non-cancer indications, e.g. dermatology, rheumatology etc.

Emetogenic potential: Low to moderate

Safe handling/spillages: See appendix 2 regarding spillages.

Pharmaceutical Care Issues:

- Once weekly dosing for non cancer patients.
- Most hospital pharmacies now only stock 2.5mg tabs for safety reasons.
- Patients should be warned of risks of NSAID usage (especially as some are available OTC) as concomitant use of NSAID’s has been associated with fatal methotrexate toxicity.
- Concomitant administration of folate antagonists such as trimethoprim and co-trimoxazole should be avoided.
- Caution with renal and hepatic impairment. Drugs toxic to these organs should be avoided.
Renal function should be closely monitored before, during and after treatment.

Methotrexate has some immunosuppressive activity and therefore the immunological response to concurrent vaccination may be decreased.

Concomitant use of a live vaccine could cause severe antigenic reaction.

If acute methotrexate toxicity occurs, patients may require treatment with folinic acid.

Patients should have a full blood count and renal and liver function tests before starting treatment. These should be repeated weekly until therapy is stabilised, thereafter patients should be monitored every 2-3 months throughout treatment.

**Drug Interactions:** alcohol, NSAIDS, phenytoin, pyrimethamine, corticosteroids, cisplatin, theophylline, trimethoprim, ciprofloxacin, tetracyclines

**Information for patients (counselling points):**

**Missed dose:** Take dose as soon as remember if this is within two days. However, if dose has been missed by more than two days, contact doctor for advice.

**Post dose vomiting:** If you are sick just after taking the tablet tell your doctor, as you may need to take another dose. Do not take another tablet without first telling your doctor.

**Side effects:**

- Nausea and vomiting
- Skin changes – pigmentation changes, rash
- Bone marrow suppression
- Mucositis
- Gastrointestinal problems (i.e.: diarrhoea, bleeding)
- Hepatic toxicity
- Pulmonary toxicity – interstitial pneumonitis
- Renal failure
Storage: Room temperature

Disposal of medicine/spoons: If your doctor decides to stop the treatment, return any remaining tablets to the pharmacist to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:

- Following administration to a man or woman conception should be avoided by using an effective contraceptive method for at least 3 months after using methotrexate.

- Vitamin preparations containing folic acid or its derivatives may alter response to methotrexate. Some patients (typically non-cancer patients) may be prescribed folic acid – this should not be taken on the day of the methotrexate.

- Contact doctor immediately if develop a cough or dyspnoea.

- Patients should report all symptoms and signs suggestive of infection, especially sore throat.

- Patients should not breast feed whilst taking methotrexate.

- Tablets should be swallowed whole with plenty of water.
NILOTINIB

Information for Nursing and Pharmacy Staff:

Available as: 200mg capsules (pack size 112)

Used for: Chronic Myeloid Leukaemia CML

Common regimens:
- CML: 400mg TWICE a day (chronic phase)

Emetogenic potential: Low/moderate (10%)

Safe handling/spillages: No special precautions.

Drug interactions: Warfarin, simvastatin, phenytoin, rifampacin & other enzyme inducers, erythromycin and enzyme inhibitors.

Pharmaceutical Care Issues:
Must be used with caution in patients with uncontrolled or significant cardiac disease (e.g. recent myocardial infarction, congestive heart failure, unstable angina). Double check with prescriber if patient is taking concurrent cardiovascular medicines in particular anti-arrhythmics.

Information for patients (counselling points):

Missed dose: Do not take double next dose, inform doctor and keep to normal dosing schedule.

Post dose vomiting advice: Do not take an extra tablet without consulting doctor.

Side effects:
- Headache
- Fatigue
- Gastrointestinal disturbances (nausea, constipation, diarrhoea, abdominal pain)
- Muscle cramps
- Rash, pruritus
Storage: Original packaging, below 30°C.

Disposal of medication/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:

• Take at least 2 hours after any food and then wait at least 1 hour before eating again.

• Do not drink grapefruit juice or eat grapefruit
PROCARBAZINE

Information for Nursing and Pharmacy Staff:

Available as: 50mg caps (pack size 50)

Used for: Hodgkin’s disease

Common regimens:

- for 14 days (with chlorambucil and prednisolone 40mg once daily for 14 days

Emetogenic potential: Moderate (>50%) decrease in potential by taking at bedtime or in divided doses.

Safe handling/spillages: Handling of urine produced for up to 48 hrs after taking a dose of procarbazine should be handled wearing protective clothing.

Pharmaceutical Care Issues:

- Procarbazine is a weak monoamine oxidise inhibitor (MAOI) therefore can possibly potentiate the pressor effect of tyramine.

Drug interactions: alcohol (disulfiram like reaction), phenytoin, clozapine

Information for patients (counselling points):

Missed dose: Take as soon as remember unless next dose is due within a couple of hours (2-3 hours) in which case skip the missed dose and carry on as normal. Do not take double doses.

Post dose vomiting: Usually nausea/vomiting occur within the first few days of treatment and then wears off. Antiemetics should prevent symptoms but if they persist longer than a few days, contact doctor as possible the dose may need adjustment.

Side effects:

- Nausea and vomiting
- Loss of appetite for first few days
- Insomnia/nightmares

Version 3: Issued 25th July 2008: Readers are advised to check NECN website www.cancernorth.nhs.uk to ensure they are using most up to date version
Storage: Below 25°C.

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:

- Counselling regarding the possible interaction with tyramine containing foods/drink.
SUNITINIB

Information for Nursing and Pharmacy Staff:

Available as: Presented as 12.5mg, 125mg and 50mg hard capsules (pack size 30)

Used for: First line treatment of metastatic renal cell carcinoma (MRCC) and 2nd line treatment of GIST, gastro intestinal stromal tumour.

Common Regimens

50mg once daily for four weeks followed by a two week rest period to comprise a complete cycle of six weeks. Dose modifications by oncologist, may decrease dose to 37.5mg.

Emetogenic potential: Low/Moderate

Safe handling/spillages: No special precautions.

Pharmaceutical Care Issues:

- Patients taking sunitinib must be supplied with loperamide 2mg and advised to take for diarrhoea as required. (max 16mg in 24 hours)

- Pfizer will provide the first cycle of sunitinib free of charge (via a refund scheme)

Drug interactions

- Drugs that are CYP3A4 inhibitors such as ketoconazole, and to a lesser extent itraconazole, erythromycin, clarithromycin and grapefruit juice may decrease metabolism and increase sunitinib plasma concentrations. Drugs that are CYP3A4 inducers such as rifampicin and to a lesser extent dexamethasone, phenytoin, carbamazepine, phenobarbital or Hypericum perforatum (St. John’s Wort) may increase metabolism and decrease sunitinib plasma concentrations.

Information for patients (counselling points):

Missed dose If the scheduled days dosing is missed, advise patient to not to take dose and contact their named chemotherapy contact.
Post dose vomiting: if the patient vomits after taking a sunitinib capsule, the patient should NOT take another tablet, until the next dose is due.

Side effects:

- Diarrhoea
- Nausea and vomiting
- Fatigue
- Rash
- Hypertension
- Mucosal Inflammation
- Hand-foot syndrome (pain, swelling or redness in hands and/or feet)

Storage: Between 10 to 25°C.

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:

- Can be taken with or without food; however must not be taken with grapefruit juice
- Patients should be counselled on how to manage most common side effects of skin rash and diarrhoea.
TEGAFUR/URACIL (UFTORAL®), UFT

Information for Nursing and Pharmacy Staff:

Available as: Tegafur/uracil is presented as capsules containing tegafur (100 mg) and uracil (224 mg). There are 2 pack sizes available: 35 capsules or 42 capsules.

Used for: Metastatic colorectal cancer

Regimen: Given for 28 days of a 35 day cycle at a Daily Dose of 300 (tegafur) and 672 (uracil) mg/m²/day in three divided doses. Given with calcium folinate 30mg three times daily

Emetogenic potential: Low/Moderate

Safe handling/spillages: Refer to local guidelines.

Pharmaceutical Care Issues: No liquid form available therefore unsuitable for those who can’t swallow.

Drug interactions:
Inhibitors of dihydropyrimidine dehydrogenase including sorivudine should not be co-administered with Uftoral. Other drug interactions include warfarin, phenytoin, substrates or inhibitors of CYP2A6.

Information for patients (counselling points):

Missed dose: Do not double-up doses or take extra doses at the end of the treatment cycle to make up for the missed doses. If patients miss a dose, they should carry on taking the normal dose when the next dose is due. Inform doctor/ chemotherapy unit and keep to normal dosing schedule.

Post dose vomiting advice: if the patient vomits after taking a UFToral capsule, the patient should NOT take another tablet, until the next dose is due.

Side effects:

- Diarrhoea and/or Abdominal Pain
- Nausea And Vomiting
- Soreness Of The Mouth And Tongue
• Decrease Or Loss Of Appetite,
• Fatigue and Bone Marrow Suppression.

Storage: Do not store above 25°C

Disposal of medication/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:
• Take capsules 3 times a day (preferably every 8 hours) at least 1 hour before or 1 hour after meals.
• Capsules should not be opened.
• Swallow whole with a glass of water.
• As confusion has occasionally been reported patients should be advised to exercise caution when driving/operating machinery.
• Contact chemotherapy day unit if suffer diarrhoea:
  Diarrhoea: More than four bowel movements/ in 24 hours day or have diarrhoea at night
  Vomiting: More than once in 24 hours
TEMOZOLAMIDE

Information for Nursing and Pharmacy Staff:

Available as: 5 mg, 20 mg, 100 mg, 140 mg, 180 mg or 250 mg hard capsules. A liquid preparation is available as a special from Newcastle Hospitals NHS Trust.

Used for: Brain tumours (adjuvant use for newly diagnosed glioblastoma multiforme concomitantly with radiotherapy (RT) or 2nd line treatment of recurrent/ progressive malignant glioma)

Regimen:

- Temozolomide is administered (for adults and children) orally at a dose of 75 mg/m² daily for 42 days concomitant with radiotherapy. Four weeks after completing the Temozolomide + Radiotherapy phase, it is administered for up to 6 cycles of monotherapy treatment. Dose in Cycle 1 (monotherapy) is 150 mg/m² once daily for 5 days followed by 23 days without treatment. At the start of Cycle 2, the dose is escalated to 200 mg/m² dependant on tolerance.

- 200 mg/m² for five days every 28 days for 2nd line use (may start at 150 mg/m² once daily for 5 days for first cycle)

Emetogenic potential: Moderate

Safe handling/spillages: If a capsule becomes damaged, avoid contact of the powder contents with skin or mucous membrane. If contact does occur, wash the affected area.

Pharmaceutical Care Issues: None noted

Drug interactions: No significant interactions, co-administration with valproic acid was associated with a small but statistically significant decrease in clearance of temozolomide.

Information for patients (counselling points):

Missed dose: Do not double-up doses or take extra doses at the end of the treatment cycle to make up for the missed doses. If patients miss a dose, they should carry on taking the normal dose when the next dose is
due. Inform doctor/ chemotherapy unit and keep to normal dosing schedule.

**Post dose vomiting advice:** if the patient vomits after taking a temozolomide capsule, the patient should NOT take another tablet, until the next dose is due.

**Side effects:**
- Nausea
- Alopecia
- Constipation
- Bone Marrow Depression; anaemia, Neutropenia, thrombocytopenia
- Lethargy
- Anorexia
- Headaches

**Storage:** Do not store above 25°C

**Disposal of medication/spoons:** Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

**Advice for patients:**
- Temozolamide should be administered on an empty stomach.
- The capsules must be swallowed whole with a glass of water and must not be opened or chewed.
THALIDOMIDE (Thalidomide Pharmion™)

Information for Nursing and Pharmacy Staff:

Available as: 50mg capsule (pack size 28) from Celgene

Used for: Myeloma

Common regimens:

- Single agent; Start at 50 to 100mg then titrated according to blood counts/response
- CTD: Thalidomide 100mg once daily for 3 weeks then increasing to 200mg once daily. Taken continuously. (Combination with weekly cyclophosphamide 500mg and dexamethasone 40mg once daily days 1 to 4 and 12 to 15) repeated 3 weekly maximum 6 cycles.
- CTDa: Thalidomide 50mg once daily for 4 weeks increasing every 4 weeks by 50mg increments to 200mg once daily (combination with cyclophosphamide 500mg weekly and dexamethasone 20mg once daily days 1 to 4 and 15 to 18). Repeated every 4 weeks maximum 9 courses (9 months)
- MP-T Thalidomide 200mg once daily for 28 days combined with Melphalan 4 mg/m²and Prednisolone 40 mg/m²once daily days 1 to 7.

Emetogenic potential: low – moderate

Safe handling/spillages: See appendix 2 regarding spillages.

Pharmaceutical Care Issues:

- Prescribing must only be performed via Thalidomide Pharmion Pregnancy Prevention Programme. (see protocols)
- Capsule may be opened for those with problems swallowing
- Confirm no medications are being taken which may interact with oral contraceptives to reduce their effectiveness (see BNF for details) in women taking thalidomide.
- If these drugs must be used concurrently with thalidomide, use two other reliable methods of contraception (other than oral contraceptives).
Drug interactions: None known

Information for patients (counselling points):
Missed dose: Contact prescriber as soon as possible who will advise on next step to take. Do not double dose.
Post dose vomiting: Contact prescriber as soon as possible who will advise on next step to take.

Side effects:
- Anaemia
- Weakness and fatigue
- Thrombosis
- Rash (tell doctor immediately)
- Constipation
- Teratogenicity
- Peripheral neuropathy (if have tingling/pain/numbness in hands or feet, stop taking thalidomide and tell doctor immediately)
- Drowsiness

Storage: Store at room temperature

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines

Advice for patients:
- Take medication preferably one hour after meals.
- Alcohol may enhance drowsiness caused by thalidomide. It is advised to not drink alcohol whilst taking thalidomide.
- Drowsiness may affect driving ability. If affected do not drive or operate any tools or machinery.
- To reduce effect of drowsiness during the day, can be taken in the evening
• If necessary dose can be divided into two daily doses (morning and evening) – both doses should be taken at least one hour after food.

• Do not donate blood or sperm during treatment or within 8 weeks of stopping thalidomide.

• Breastfeeding is not recommended due to the potential secretion into breast milk.

• Do breast feed during treatment or start breast feeding for 4 weeks after stopping thalidomide

Information regarding pregnancy/sexual intercourse:

• Prior to treatment initiation, women of childbearing potential must have a pregnancy test immediately (e.g. within 3 days) prior to beginning therapy and regularly (e.g. monthly) during therapy. A pregnancy test is required for all women are under the age of 50 years old and who have:
  i. not undergone a hysterectomy,
  ii. not been naturally postmenopausal for 24 consecutive months,
  iii. experienced artificial menopause (e.g. chemotherapy or radiation induced menopause) or
  iv. tubal ligation.

• Women of child bearing potential must have a negative blood pregnancy test (performed by a healthcare professional):
  i. Within 72hrs before starting thalidomide
  ii. Every 3-4 weeks in women with regular menstrual cycles or every 2 weeks in women with irregular menstrual cycles while on thalidomide
  iii. 4 weeks after the last dose of thalidomide

• Contraception (or abstinence) must be used for the first 4 weeks before start taking thalidomide and continue birth control methods for the duration of treatment and for one month after stopping treatment.
• Women must use effective contraception for at least one month before, during, and one month after thalidomide therapy.

• Reliable contraception is indicated even where there has been a history of infertility, unless due to hysterectomy or because patient has been naturally postmenopausal for at least 24 months.

• To reduce the pregnancy risks on initiation of thalidomide try to start treatment within 3 days following the onset of menstrual bleeding.

• If patient has engaged in sexual contact without using birth control thalidomide should be stopped and the doctor contacted.

• A pregnancy test should be performed if a patient misses her period or if there is any abnormality in menstrual bleeding.

• If a woman taking thalidomide misses a period, treatment should be stopped and the doctor informed immediately.

• If pregnancy does occur during thalidomide therapy, thalidomide must be discontinued immediately.

• If the female partner of a male being treated with thalidomide misses a period or has abnormal menstrual bleeding during treatment the doctor should be informed immediately.

• Male patients should use a condom with every sexual intercourse with a female partner.

• If a male patient has an allergy to condoms, their female partner should use at least one very effective method of birth control. This should be started one month prior to the start of a sexual relationship and continue throughout the thalidomide treatment and for an additional month following cessation of treatment.
TIOGUANINE (LANVIS®)

Information for Nursing and Pharmacy Staff:

Available as: 40mg tablets (pack size 25)

Used for: Acute leukaemia’s

Common regimens:

- S-DAT and H-DAT: 100mg/m² 12 hourly on days 1 to 10 (20 doses course 1) and days 1 to 8 (16 doses course 2) in combination with cytarabine and daunorubicin

Emetogenic potential: Low (if affected will occur within hours)

Safe handling/spillages: Wash hands immediately after handling/halving tablets, avoid contact with eyes, and avoid inhalation of particle. Urine and faeces produced for up to 24 hours and 5 days, respectively after a dose should be handled wearing protective clothing.

Pharmaceutical Care Issues:

- Cross resistance occurs with mercaptopurine
- Caution in patients with inherited deficiency of the enzyme thiopurine methyltransferase (TPMT) who may be unusually sensitive to the myelosuppressive effect of 6-mercaptopurine and at risk of developing rapid bone marrow depression
- Contra indication in pregnancy – women of childbearing age must be counselled

Drug interactions: olsalazine, mesalazine or sulphasalazine

Information for patients (counselling points):

Missed dose: Do not take double next dose, inform doctor and keep to normal dosing schedule.

Post dose vomiting: Do not take another tablet without consulting doctor.
Side effects:

- Bone marrow suppression (reversible)
- Gastrointestinal intolerance
- Stomatitis
- Anaemia
- Hepatic toxicity

Storage: Room temperature

Disposal of medicine/spoons: Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

Advice for patients:

- Swallow whole with plenty of water on an empty stomach
TRETINOIN or ATRA (VESANOID®) – not cytotoxic

Information for Nursing and Pharmacy Staff:

Available as: 10mg caps (pack size 100)

Used for: AML (acute myeloid leukaemia)

Common regimens:

- AML at 45mg/m² in 2 divided doses until remission (max 90 days)
- AML Maintenance (with methotrexate and mercaptopurine): 45mg/m²/day for 15 days every 3 months.

Emetogenic potential: Rare.

Safe handling/spillages: No special precautions.

Pharmaceutical Care Issues:

- Retinoic acid syndrome has been reported in up to 25% of APML patients treated with tretinoin. Retinoic acid syndrome is characterised by fever, dyspnoea, acute respiratory distress, pulmonary infiltrates, pleural and pericardial effusions, hypotension, oedema, weight gain, hepatic, renal and multi-organ failure.

Drug interactions: ketoconazole, chlortetracycline, demeclocycline, doxycycline, minocycline, tetracycline, oral contraceptives, vitamin A preparations

Information for patients (counselling points):

Missed dose: Take capsules as soon as remember and inform doctor. Do not double dose.

Post dose vomiting: Do not take another tablet without consulting doctor.

Side effects: (similar to isotretinoin - Roaccutane®)

- Dry skin
- Dry mouth
- Rash
• Gastrointestinal disturbances (nausea, vomiting)
• Bone pain

**Storage:** Between 5-30°C.

**Disposal of medicine/spoons:** Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines

**Advice for patients:**
• Dizziness/severe headache may impair driving ability.
• Swallow whole with water/non-alcoholic drink with meal or eat shortly after taking medication.
VINORELBINE (NAVELBINE®)

Information for Nursing and Pharmacy Staff:

Available as: 20mg and 30mg capsules (pack size 1)

Used for: Stage 3 or 4 NSCLC (lung cancer)

Metastatic Breast Cancer

Common regimens:

- **Single agent**: First three doses 60 mg/m² once weekly then increase to 80mg/m² depending on toxicities and response.

- **In combination with carboplatin or cisplatin**: 60 /80 mg/m² on day 1 and 8 of a 21 day cycles. Note IV vinorelbine may be given on day 1 (at 25-30mg/m²)

- **In combination with trastuzumab**: 60mg/m² of day 1, 8 and 15 of a 21 day cycle.

Emetogenic potential: Low to moderate, however to reduce risk of vomiting the dose – consideration should be given to using a 5HT3 anti-emetic.

Safe handling/spillages: If a capsule becomes damaged, avoid contact of the powder contents with skin or mucous membrane. If contact does occur, wash the affected area.

Storage: Refrigerate. Stable for up to 72 hours at room temperature.

Pharmaceutical Care Issues:

- Conversions: 80mg/m² orally is equivalent to 30mg/m² IV, 60mg/m² orally is equivalent to 25mg/m² IV

- Maximum 160mg as a single dose.

- Dose reduction required in significant hepatic impairment.

- In patients with massive liver metastases it is suggested that the dose be reduced by 25 % and the haematological parameters closely monitored.

- Should not be given concurrently with radiotherapy if the treatment area includes the liver.

- Patients should usually be prescribed a 5HT3 anti-emetic at least 30 minutes before treatment to reduce the risk of vomiting the dose.
**Drug Interactions:** Caution with inhibitors/inducers of CYP3A4. E.g. omeprazole & fluoxetine

**Information for patients (counselling points):**

**Missed dose:** If the scheduled days dosing is missed, contact the prescriber as a blood test may be needed to confirm if taking the missed dose is appropriate. It may be necessary that the patient has supervised consumption the next day but this is a local decision. Do not take double dose the next week.

**Post dose vomiting:** In the case of vomiting within a few hours after drug intake, never repeat the administration of this dose. Absorption is not affected by early vomiting.

**Side effects:**

- Nausea and vomiting
- Diarrhoea
- Anorexia
- Stomatitis
- Neutropenia – reversible (beware of warning signs)
- Progressive alopecia with treatment (usually mild)
- Fatigue, muscle pain, jaw pain

**Storage:** Refrigerate between 2 to 8°C

**Disposal of medicine/spoons:** Return to hospital pharmacy to be disposed of in a manner appropriate for disposal of cytotoxic & cytostatic medicines.

**Advice for patients:**

- Swallow whole with a glass of cold water. If capsule is chewed or sucked in error, rinse mouth with water or preferably a normal saline solution.
- The liquid content of the capsule is an irritant and may cause damage if comes into contact with skin, mucosa or eyes.
• Damaged or cut capsules should not be swallowed and should be returned to the pharmacy or to the doctor in order to be properly destroyed.

• If any contact occurs, immediate thorough washing with water or preferably with normal saline solution should be undertaken.

• Food does not affect absorption but it is advised to take with a light snack to reduce gastro-intestinal upset.

• Patient’s ability to drive or operate machinery may be affected however this is unlikely.

• A blood test will be performed prior to each administration. The dose will then be confirmed to be taken or not (depending on local practice this dose will be given in the hospital unit or be taken by the patient at home after confirmation)

• Advise patient about the need to take an anti-emetic 30 minutes before taking the vinorelbine to reduce the risk of vomiting the capsules.
SECTION THREE:

ORAL ANTICANCER
REGIMEN SUMMARY

Version 3: Issued 25th July 2008: Readers are advised to check NECN website www.cancernorth.nhs.uk to ensure they are using most up to date version
### ABCM (Multiple Myeloma)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ondansetron</td>
<td>8mg</td>
<td>IV bolus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Doxorubicin</td>
<td>30mg/m²</td>
<td>IV bolus</td>
<td>via 0.9% Sodium Chloride Drip</td>
</tr>
<tr>
<td></td>
<td>Carmustine (BCNU)</td>
<td>30mg/m²</td>
<td>IV infusion</td>
<td>500ml Sodium Chloride 0.9%/1 hour</td>
</tr>
<tr>
<td>22 to 25</td>
<td>Cyclophosphamide</td>
<td>100mg/m²</td>
<td>ORAL</td>
<td>Once daily For 4 days</td>
</tr>
<tr>
<td>22 to 25</td>
<td>Melphalan</td>
<td>6mg/m²</td>
<td>ORAL</td>
<td>Once Daily For 4 days</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**

42 Day cycle, usually given for a maximum of 6 cycles

**APPROVED INDICATIONS**

Multiple Myeloma

**RECOMMENDED TAKE HOME MEDICATION**

- Allopurinol 300mg Once Daily with first cycle of treatment
- Ondansetron 8mg Twice Daily for 2 days after doxorubicin.
- Metoclopramide 10mg Three Times Daily, if required, for 5 days starting on day 22

**INVESTIGATIONS / MONITORING REQUIRED**

- **Prior to first cycle:** FBC, U&Es, LFTs, Paraprotein
- **Prior to each cycle:** FBC, U&Es, LFTs, Paraprotein

**ASSESSMENT OF RESPONSE**

Bone Marrow & Paraprotein (serum/urine) every 2 cycles. Assess symptoms.
REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework.

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework.

ADMINISTRATION NOTES

- Doxorubicin is cardio-toxic. Lifetime maximum dose is 450 - 550mg/m². Patients with pre-existing cardiac disease or previous exposure to anthracyclines should be considered for ECHO.
- Cyclophosphamide is supplied as 50mg tablets – dose should be rounded to the nearest measurable dose
- Melphalan is supplied as 2mg tablets – dose should be rounded to the nearest measurable dose
- Patients should drink 2-3 litres (8 – 12 tumblers) of water on days when taking cyclophosphamide.
- Doxorubicin may discolour urine: red.

TOXICITIES

Common: Myelosupression (moderate risk), Nausea/Vomiting, Fatigue, Immunosuppressant

Less Common: Flushing, Rash, Allergic Reaction, Pulmonary Toxicity, Cardiac Toxicity, SiADH, Haemorrhagic Cystitis

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 and Day 22 if ANC < 1.3 x 10⁹ cells/l or PLT < 75 x 10⁹ cells/l. If patients recurrently have low counts consider switching to C-Weekly Regimen.
Patients at risk of fluid overload:
Consider reducing dose of (or omitting) dexamethasone in patients with a risk of fluid overload e.g. patients with cardiac involvement of amyloidosis, or nephritic syndrome.

Renal Function:

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Melphalan Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50 ml/min</td>
<td>100%</td>
</tr>
<tr>
<td>30 – 50ml/min</td>
<td>50%</td>
</tr>
<tr>
<td>&lt; 30ml/min</td>
<td>Uncertain. Clinical decision required</td>
</tr>
</tbody>
</table>

TREATMENT LOCATION
Suitable for administration in chemotherapy day units, under the supervision of haematology teams from Level 1 to 4 Haematology Services.

REFERENCES:

BUSULPHAN

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 28</td>
<td>Busulfan</td>
<td>2 to 8mg</td>
<td>ONCE Daily</td>
<td>(variable see below)</td>
</tr>
</tbody>
</table>

CYCLE LENGTH AND NUMBER OF DAYS

Busulphan is usually given in courses or administered continuously. The dose must be adjusted for the individual patient under close clinical and haematological control.

DOSE FORM

2 mg tablets

APPROVED INDICATIONS

Myeloproliferative disorders in the elderly including:

- Primary Thrombocytosis, Essential Thrombocytosis
- Chronic Myeloid Leukaemia
- Primary Proliferative Polycythaemia (Polycythaemia Vera)
- Myelofibrosis

As conditioning regimen prior to bone marrow transplant

RECOMMENDED TAKE HOME MEDICATION

No routine anti-emetic cover is usually required, if anti-emetic cover is required metoclopramide would normally be adequate

INVESTIGATIONS / MONITORING REQUIRED

Full blood count, U+E, LFT, Uric acid at each review

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework.
NURSE / PHARMACIST LED REVIEW
As per locally agreed framework.

ADMINISTRATION NOTES
- Busulphan should be prescribed to the nearest 2mg dose.
- Dose should be swallowed with a glass of water
- Drug interactions: paracetamol, phenytoin, itraconazole, clozapine
- Aplastic anaemia (sometimes irreversible) has been reported rarely, typically following long-term conventional doses and also high doses of busulfan

TOXICITIES
Common: Moderate myelosuppression, pulmonary toxicity following high dose or long term dosing, hepatic disturbance
Rarely nausea, diarrhoea, mucositis or hyperpigmentation

Haematological Toxicity:
(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)
Delay treatment on Day 1 if ANC < 1.5 x 10^9 cells/l or PLT < 100 x 10^9 cells/l.

Renal Function:
No dose adjustment for renal impairment normally required.

TREATMENT LOCATION
Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services

REFERENCES
C-WEEKLY
(Multiple Myeloma, Non Hodgkins Lymphoma)

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ondansetron</td>
<td>8mg</td>
<td>Oral</td>
<td>Twice Daily</td>
</tr>
<tr>
<td>1</td>
<td>Cyclophosphamide</td>
<td>400mg/m²</td>
<td>ORAL</td>
<td>Once Weekly For 1 day each week</td>
</tr>
<tr>
<td>Alt Days</td>
<td>Prednisolone EC</td>
<td>40mg/m²</td>
<td>ORAL</td>
<td>On Alternate Days For 4 weeks, then reduce</td>
</tr>
</tbody>
</table>

CYCLE LENGTH AND NUMBER OF DAYS
Usually for a total of 8 to 12 weeks (until disease plateaux or progression)

APPROVED INDICATIONS
- Relapsed Multiple Myeloma or
- Non-Hodgkins Lymphoma

ELIGIBILITY CRITERIA
- Particularly suited for patients with underlying bone marrow suppression from disease.
- Able to maintain a fluid intake of 3 litres per day

RECOMMENDED TAKE HOME MEDICATION
Allopurinol 300mg once daily for 28 days.
Ondansetron 8mg Twice Daily on day of cyclophosphamide.
Consider prescribing Gastro Prophylaxis (Proton Pump Inhibitor) for cover with prednisolone.

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: FBC, U&Es, LFTs, LDH, β2-MicroGlobulin, Para-protein (Urine & Serum), Calcium, Bone Marrow, Skeletal Survey

Prior to each week: U&Es, LFTs, FBC, Calcium,

Monthly: Para-protein (Urine & Serum), Immunoglobulin,
ASSESSMENT OF RESPONSE
Myeloma: Para-protein, Bone Marrow Biopsy and Symptom Control.

REVIEW BY CLINICIAN
Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW
As per locally agreed framework

ADMINISTRATION NOTES
- Prednisolone: should be taken on alternate days, before 4pm with food. After 4 weeks the dose should be gradually tapered down over the next two weeks.
- Patients unable to tolerate oral cyclophosphamide can receive intravenous cyclophosphamide (300mg/m²) instead.
- Cyclophosphamide is supplied as 50mg tablets, doses should be rounded to the nearest 50mg
- Patients should aim to maintain a fluid intake of 3 litres per day (12 tumblers of water)

TOXICITIES
Common: Gastric Irritation, Alopecia, Mild Emesis, Myelosupression, Fatigue, Dyspepsia, Increased Glucose, Insomnia, Agitation, Mucositis
Less Common: Flushing or Rash, Allergic Reaction, Mood Disturbances

DOSE MODIFICATION / TREATMENT DELAYS
Haematological Toxicity:
(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)
Delay treatment on Day 1 if ANC < 1.0 x 10⁹ cells/l or PLT < 50 x 10⁹ cells/l.
Renal Function:
Cyclophosphamide dose should be reduced if serum Cr is raised:

<table>
<thead>
<tr>
<th>Serum Cr</th>
<th>Oral Cyclophosphamide Dose</th>
<th>IV Cyclophosphamide Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 300 µmol/l</td>
<td>400 mg/m²</td>
<td>300 mg/m²</td>
</tr>
<tr>
<td>300 – 600 µmol/l</td>
<td>300 mg/m²</td>
<td>200 mg/m²</td>
</tr>
<tr>
<td>&gt; 600 µmol/l</td>
<td>Clinical Decision</td>
<td>Clinical Decision</td>
</tr>
</tbody>
</table>

Hepatic Function:
No dose adjustment normally required

TREATMENT LOCATION
Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES:
MRC – Myeloma VIII Protocol
Capecitabine (Breast and Colorectal)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 14</td>
<td>Capecitabine</td>
<td>1250mg/m²</td>
<td>Oral</td>
<td>Twice Daily for Fourteen days</td>
</tr>
</tbody>
</table>

**DOSE FORM**

Capecitabine is supplied as 150mg and 500mg tablets, therefore calculated doses must be rounded to the nearest 150mg.

**CYCLE LENGTH AND NUMBER OF DAYS**

- 21 day cycle Capecitabine taken from Day 1 to 14 then 1 week off treatment
- 8 cycles for adjuvant & advanced disease
- Is also given in combination with Oxaliplatin (XELOX) and at a reduced dose as part of ECX regimen

**APPROVED INDICATIONS**

- Adjuvant Dukes C colon cancer
- Advanced/ metastatic colorectal cancer – for patients unsuitable for FOLFOX/FOLFIRI
- Advanced/ metastatic breast cancer

**ELIGIBILITY CRITERIA**

- Colorectal cancer patients with adequate renal function.

**EXCLUSION CRITERIA**

- Patients incapable of managing oral chemotherapy themselves or with the assistance of a carer
- Patients with swallowing difficulties

**PREMEDICATION**

None

**RECOMMENDED TAKE HOME MEDICATION**

Metoclopramide 10 to 20mgs TDS to QDS as required
Loperamide 2mg when required, max 8 in 24 hours
INVESTIGATIONS / MONITORING REQUIRED

Pre treatment: Assessment of renal function, FBC, Cardiac history

Prior to each cycle FBC, U&E, LFT’s & tumour markers as appropriate

FBC on the day of treatment

Where CEA is elevated this should be measured before each cycle.

ASSESSMENT OF RESPONSE

Assessed radiologically after 4th cycle.

Metastatic: Tumour size and patient symptomatic response

Adjuvant: No visible disease to monitor for adjuvant treatment.

REVIEW BY CLINICIAN

To be reviewed by either; a nurse, pharmacist or clinician before each cycle.

NURSE / PHARMACIST LED REVIEW

On cycles where not seen by clinician.

ADMINISTRATION NOTES

- Advise patients of the risk of Hand-and-foot skin-reaction
- Diarrhoea is common, provide loperamide.

TOXICITIES

- Palmar/Plantar Erythrodysesthesia - Can be severe, patients must be forewarned
- Diarrhoea, abdominal pain
- Nausea and vomiting
- Pyrexia, fatigue, asthenia, anorexia
- Myelosupression
- Hyperbilirubinemia
- Stomatitis
- Cardiotoxicity - Occasionally patients may experience coronary artery spasm. Stop Treatment with fluoropyrimidine therapy if this occurs.
- Contra-indicated in patients with severe hepatic impairment, a history of severe and unexpected reactions to fluoropyrimidine therapy, DPD deficiency, hypersensitivity. Avoid concomitant use with allopurinol
DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

- ANC < 1-1.5 and/or platelets <100, delay for 1 week
- >1 week recovery, dose reduce by 20-25%
- Following 2 delays for toxicity, all subsequent doses should be dose reduced by 20-25%
- If further delays necessary consider further dose reduction (discuss with SpR/Consultant) or consider stopping treatment

Non-Haematological Toxicity:

Manufacturer recommends treatment interruption followed by dose reduction where indicated in the Data Sheet. Once the dose has been reduced, it should not be increased at a later time. Omitted doses are not replaced or restored, instead the patient should resume the planned treatment cycle.

Table of dose adjustments according to CTC toxicity (Not PPE/hand/foot))

<table>
<thead>
<tr>
<th>Grade 2</th>
<th>Grade3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st appearance</td>
<td>Interrupt treatment until resolved to grade 0/1, then continue at 100% of original dose with prophylaxis where possible</td>
<td>Interrupt treatment until resolved to grade 0/1, then continue at 75% of original dose with prophylaxis where possible</td>
</tr>
<tr>
<td>2nd appearance</td>
<td>Interrupt treatment until resolved to grade 0/1, then continue at 75% of original dose</td>
<td>Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose</td>
</tr>
<tr>
<td>3rd appearance</td>
<td>Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose</td>
<td>stop treatment</td>
</tr>
<tr>
<td>4th appearance</td>
<td>stop treatment</td>
<td></td>
</tr>
</tbody>
</table>
Table of hand/foot toxicity grading for capecitabine only

<table>
<thead>
<tr>
<th>Grade</th>
<th>Clinical</th>
<th>Functional</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Numbness, dysesthesia/parathesia, tingling, painless swelling or erythema</td>
<td>Discomfort but no interruption Of normal activities</td>
</tr>
<tr>
<td>2</td>
<td>Painful erythema with swelling</td>
<td>Discomfort which affects activities of daily living</td>
</tr>
<tr>
<td>3</td>
<td>Moist desquamation, ulceration, Blistering, severe pain</td>
<td>Severe discomfort, unable to work or perform activities of daily living</td>
</tr>
</tbody>
</table>

Table of Diarrhoea toxicity grading for capecitabine only

<table>
<thead>
<tr>
<th>CTC Grade</th>
<th>Toxicity</th>
<th>% Capecitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diarrhoea (watery stool 2-3 times/day)</td>
<td>Hold until recovery, then resume at 100% dose for remainder of course</td>
</tr>
<tr>
<td>2</td>
<td>Diarrhoea (watery stool 4-6 times/day)</td>
<td>Hold until recovery, then resume at 75% dose for remainder of course</td>
</tr>
<tr>
<td>3 or 4</td>
<td>Diarrhoea (watery stool &gt;7 times/day)</td>
<td>Following grade 3 or 4 diarrhoea, subsequent doses of capecitabine should be decreased or treatment discontinued permanently (grade 4).</td>
</tr>
</tbody>
</table>

*see manufacturer’s datasheet for full details

Renal Function:

Capecitabine is renally excreted; therefore dose requires adjustment for patients with moderate renal impairment (≤50ml-30ml/min) require a 25% dose reduction.

Contra-indicated in severe renal failure (CrCl <30ml/min) (Cockroft & Gault)

TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit
REFERENCES:

- Randomised phase 3 trial (XACT) comparing capecitabine with Mayo (bolus 5-FU and folinic acid) in Dukes C colon cancer demonstrated equivalence (primary end point Disease Free Survival); statistically significant advantage in terms of Relapse Free Survival; and a trend towards a survival advantage. (Cassidy et al J Clin Oncol 22:247, 2004 suppl; abs 3509)

Cyclophosphamide Thalidomide Dexamethasone [CTD]
(Multiple Myeloma) 21day schedule

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 3</td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>ORAL</td>
<td>Three Times Daily</td>
</tr>
<tr>
<td>1, 8 &amp; 15</td>
<td>Cyclophosphamide</td>
<td>500mg</td>
<td>ORAL</td>
<td>Once WEEKLY</td>
</tr>
<tr>
<td>1 to 4</td>
<td>Dexamethasone</td>
<td>40mg</td>
<td>ORAL</td>
<td>Once Daily for Four (4) days only</td>
</tr>
<tr>
<td>12 to 15</td>
<td>Dexamethasone</td>
<td>40mg</td>
<td>ORAL</td>
<td>Once Daily for Four (4) days only</td>
</tr>
<tr>
<td>1 to 21</td>
<td>Thalidomide</td>
<td>100-200mg*</td>
<td>ORAL</td>
<td>Once Daily (at Night) (continuous)</td>
</tr>
</tbody>
</table>

*Starting dose 100mg escalating to 200mg on subsequent cycles depending on toxicity.

**CYCLE LENGTH AND NUMBER OF DAYS**

21 Day cycle, usually given for up to 6 cycles (until best response achieved)

**APPROVED INDICATIONS**

Multiple Myeloma

**EXCLUSION CRITERIA**

- Pregnancy / Breast Feeding
- Serum Creatinine > 300µmol/l at baseline
- Current Grade III – IV Peripheral Neuropathy
- Active thrombo-embolism
RECOMMENDED TAKE HOME MEDICATION

Allopurinol 300mg once daily on first cycle only
Metoclopramide 10mg Three Times Daily on days 1 to 3
Consider if thrombo-prohylaxis with thalidomide is required (using aspirin, warfarin or LMWH as indicated)
Proton Pump Inhibitor/H$_2$ Antagonist (e.g. Omeprazole 20mg once daily) on same days as Dexamethasone

Patients should, normally, also be receiving bisphosphonate therapy (orally or intravenously) in combination with CTD.

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH, β2-MicroGlobulin, Bone Marrow & Cytogenetics, Skeletal Survey, Bone Profile. Pregnancy Test (Women of Child Bearing Potential)

Prior to each cycle: U&Es, LFTs, FBC, Pregnancy Test (Women of Child Bearing Potential)

ASSESSMENT OF RESPONSE

Paraprotein, Urinary Light Chains, Immunoglobulins & Bone Marrow Biopsy as appropriate..

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Patients must not become or attempt to become pregnant during thalidomide treatment. For women of child bearing potential, a negative pregnancy test during the 24 hours prior to each cycle of thalidomide will be required.
- Thalidomide Pharmion™ is licensed for the first-line treatment of multiple myeloma in the UK by Celgene, who have developed a risk management programme, ‘Thalidomide Pharmion™ Pregnancy Prevention Programme’
• In the Pregnancy Prevention Programme prescribers must:
  o Communicate the risks and benefits of Thalidomide Pharmion™ therapy to their patients
  o Prescribers must complete a ‘Treatment Initiation Form’ along with your patient (this only needs to be done once).
  o Provide the patient with a ‘Health Card’
  o Provide pregnancy prevention measures and counselling
  o Perform a pregnancy test (as appropriate) prior to each prescription
  o Supply a ‘Prescription Authorisation Form’ with each prescription to show confirmation that your patient has received counselling and pregnancy test date and result (if appropriate).
  o Remind your patient of the safe use of Thalidomide Pharmion™

• In the Pregnancy Prevention Programme pharmacists must
  o Register the Pharmacy with the Pregnancy Prevention Programme
  o Obtain a copy of the patient’s ‘Treatment Initiation Form’ before the first dispense
  o Dispense Thalidomide Pharmion™ only if the prescriber has annotated the ‘Prescription Authorisation Form’ correctly
  o Remind all patients of the safe use of Thalidomide Pharmion™, each time a prescription is dispensed

• Blood glucose tolerance may be affected by high dose dexamethasone, patients with diabetes should increase frequency of glucose monitoring

• Thalidomide is sedating and so should be taken at night.

• Dexamethasone dose will normally require administration of 20 tablets, which some patients may find difficult to take at one time. The dose can be divided but the last dose should not be taken after 4pm to avoid insomnia.

• Thalidomide may cause venous thromboembolism – patients should be encouraged to report calf pain early.

• Cyclophosphamide metabolites (acreolin) can cause haemorrhagic cystitis patients should be encouraged to drink 2 to 3 litres of water on days when taking cyclophosphamide.

• This is a complex regimen: patients will need time and assistance to understand when and how they should take this treatment.
TOXICITIES

Common: Moderate Emesis, Myelosupression, Fatigue, Dyspepsia, Constipation, Rash, Sedation,
Less Common: Thromboembolism, Increased blood glucose, Peripheral Neuropathy.

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:
(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Withhold cyclophosphamide from 7 to 21 days, on Day 1 if ANC < 1.5 x 10^9 cells/l or PLT < 100 x 10^9 cells/l, but continue with other drugs. Some clinicians may choose to introduce low dose (105 micrograms/day) lenograstim for 2-3 days each week, otherwise re-introduce cyclophosphamide at 300-400mg.

Non Haematological Toxicity:
Dose reduction of steroids may be warranted if patient experiences significant side effects.

Grade III – IV Toxicity: interrupt treatment for the remainder of current cycle and reintroduce at 50mg when toxicity resolves. Dose escalation may be appropriate if 50mg is tolerated.

Thromboembolism: In the event of an embolic event, thalidomide should be stopped. Once adequate anti-coagulant control has been established consideration can be given to re-introduction of thalidomide at 50mg escalating to a maximum of 100mg.

Renal Function:
Withhold cyclophosphamide if Serum Creatinine is > 300 µmol/l.

TREATMENT LOCATION
Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES:
• Myeloma IX Trial Protocol
**Cyclophosphamide Thalidomide Dexamethasone (attenuated) [CTD(a)] (Multiple Myeloma)**

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 3</td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>ORAL</td>
<td>Three Times Daily</td>
</tr>
<tr>
<td>1, 8, 15 &amp; 22</td>
<td>Cyclophosphamide</td>
<td>500mg</td>
<td>ORAL</td>
<td>Once WEEKLY</td>
</tr>
<tr>
<td>1 to 4</td>
<td>Dexamethasone</td>
<td>20mg</td>
<td>ORAL</td>
<td>Once Daily for Four (4) days only</td>
</tr>
<tr>
<td>15 to 18</td>
<td>Dexamethasone</td>
<td>20mg</td>
<td>ORAL</td>
<td>Once Daily for Four (4) days only</td>
</tr>
<tr>
<td>1 to 28</td>
<td>Thalidomide</td>
<td>50-200mg*</td>
<td>ORAL</td>
<td>Once Daily (at Night) (continuous)</td>
</tr>
</tbody>
</table>

*Starting dose 50mg escalating in 50mg increments each cycle to a maximum 200mg.

**CYCLE LENGTH AND NUMBER OF DAYS**

28 Day cycle, usually given for up to 6 cycles (until best response achieved)

**APPROVED INDICATIONS**

Multiple Myeloma

**EXCLUSION CRITERIA**

- Pregnancy / Breast Feeding
- Serum Creatinine > 300µmol/l at baseline
- Current Grade III – IV Peripheral Neuropathy
- Active thrombo-embolism

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Version 3: Issued 25th July 2008: Readers are advised to check NECN website www.cancernorth.nhs.uk to ensure they are using most up to date version
RECOMMENDED TAKE HOME MEDICATION

Allopurinol 300mg once daily on first cycle only

Metoclopramide 10mg Three Times Daily on days 1 to 3

Consider if thrombo-prophylaxis is required (Aspirin, Warfarin or LMWH)

Proton Pump Inhibitor/H₂ Antagonist (e.g. Omeprazole 20mg once daily) on same days as Dexamethasone

Patients should, normally, also be receiving bisphosphonate therapy (orally or intravenously) in combination with CTD(a).

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH, β2-MicroGlobulin, Bone Marrow & Cytogenetics, Skeletal Survey, Bone Profile. Pregnancy Test (Women of Child Bearing Potential)

Prior to each cycle: U&Es, LFTs, FBC, Pregnancy Test (Women of Child Bearing Potential)

ASSESSMENT OF RESPONSE

Paraprotein, Urinary Light Chains, Immunoglobulins & Bone Marrow Biopsy as appropriate.

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

• Patients must not become or attempt to become pregnant during thalidomide treatment. For women of child bearing potential, a negative pregnancy test during the 24 hours prior to each cycle of thalidomide will be required.

• Thalidomide Pharmion™ is licensed for the first-line treatment of multiple myeloma in the UK by Celgene, who have developed a risk management programme, ‘Thalidomide Pharmion™ Pregnancy Prevention Programme’
• In the Pregnancy Prevention Programme prescribers must:
  o Communicate the risks and benefits of Thalidomide Pharmion™
    therapy to their patients
  o Prescribers must complete a ‘Treatment Initiation Form’ along with
    your patient (this only needs to be done once).
  o Provide the patient with a ‘Health Card’
  o Provide pregnancy prevention measures and counselling
  o Perform a pregnancy test (as appropriate) prior to each prescription
  o Supply a ‘Prescription Authorisation Form’ with each prescription
    to show confirmation that your patient has received counselling
    and pregnancy test date and result (if appropriate).
  o Remind your patient of the safe use of Thalidomide Pharmion™

• In the Pregnancy Prevention Programme pharmacists must
  o Register the Pharmacy with the Pregnancy Prevention Programme
  o Obtain a copy of the patient’s ‘Treatment Initiation Form’ before
    the first dispense
  o Dispense Thalidomide Pharmion™ only if the prescriber has
    annotated the ‘Prescription Authorisation Form’ correctly
  o Remind all patients of the safe use of Thalidomide Pharmion™,
    each time a prescription is dispensed

• Blood glucose tolerance may be affected by high dose dexamethasone,
  patients with diabetes should increase frequency of glucose monitoring

• Thalidomide is sedating and so should be taken at night.

• Dexamethasone dose will normally require administration of 20 tablets,
  which some patients may find difficult to take at one time. The dose
  can be divided but the last dose should not be taken after 4pm to avoid
  insomnia.

• Thalidomide may cause venous thromboembolism – patients should be
  encouraged to report calf pain early.

• Cyclophosphamide metabolites (acreolin) can cause haemorrhagic
  cystitis patients should be encouraged to drink 2 to 3 litres of water on
  days when taking cyclophosphamide.

• This is a complex regimen: patients will need time and assistance to
  understand when and how they should take this treatment.
TOXICITIES

Common: Moderate Emesis, Myelosupression, Fatigue, Dyspepsia, Constipation, Rash, Sedation,

Less Common: Thromboembolism, Increased blood glucose, Peripheral Neuropathy.

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Withhold cyclophosphamide from 7 – 21 days, on Day 1 if ANC < 1.5 x 10^9 cells/l or PLT < 100 x 10^9 cells/l, but continue with other drugs. Some clinicians may choose to introduce low dose (105 micrograms/day) lenograstim for 2-3 days each week, otherwise re-introduce cyclophosphamide at 300-400mg.

Non Haematological Toxicity:

Dose reduction of steroids may be warranted if patient experiences significant side effects.

Grade III – IV Toxicity: interrupt treatment for the remainder of current cycle and reintroduce at 50mg when toxicity resolves. Dose escalation may be appropriate if 50mg is tolerated.

Thromboembolism: In the event of an embolic event, thalidomide should be stopped. Once adequate anti-coagulant control has been established consideration can be given to re-introduction of thalidomide at 50mg escalating to a maximum of 100mg.

Renal Function:

Withhold cyclophosphamide if Serum Creatinine is > 300 µmol/l.

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES:

Myeloma IX Trial Protocol.
Chlorambucil [3 Day Schedule]
(CLL, Waldenstroms, Non-Hodgkins Lymphoma)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Days</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 4</td>
<td>Phenytoin (See Note*)</td>
<td>300mg</td>
<td>ORAL</td>
<td>At Night For five (5) days</td>
</tr>
<tr>
<td>1 to 3</td>
<td>Chlorambucil</td>
<td>20mg/m²</td>
<td>ORAL</td>
<td>Once Daily For three (3) days</td>
</tr>
<tr>
<td>1 to 5</td>
<td>Dexamethasone</td>
<td>8mg</td>
<td>ORAL</td>
<td>Once Daily For five (5) days</td>
</tr>
</tbody>
</table>

*Caution:* There are other chlorambucil schedules given at different doses / for different lengths of time. *Select Protocol with Care!*

**CYCLE LENGTH AND NUMBER OF DAYS**
21 to 28 day cycle, for 4 – 6 cycles

**APPROVED INDICATIONS**
- Non-Hodgkins Lymphoma (NHL)
- Chronic Lymphocytic Leukaemia (CLL)
- Waldenstroms

**EXCLUSION CRITERIA**
- Inability to swallow tablets

**RECOMMENDED TAKE HOME MEDICATION**
No routine anti-emetic cover is usually required; if anti-emetic cover is required metoclopramide would normally be adequate.

Gastro prophylaxis (H2 Antagonist, or Proton Pump Inhibitor) should be considered with the dexamethasone

Consider Allopurinol 300mg once daily during the first cycle.
*Note:* There is some evidence that high doses of chlorambucil may induce seizures in susceptible individuals. The risk appears to be dose related and related to the age of the patient. Prescribers should consider the risk of seizures in individual patients and if necessary pre-medicate (starting the night before and continuing until the day after chlorambucil) with phenytoin.

**INVESTIGATIONS / MONITORING REQUIRED**

**Prior to first cycle:** CT-Scan, Chest X-Ray, LDH, Bone Marrow FBC, U&Es, LFTs, Protein Electrophoresis, UEP, IgG, Calcium, Uric Acid, WM Patients: β2-MicroGlobulin, CLL Patients: DAT

**Prior to each cycle:** U&Es, LFTs, FBC

**ASSESSMENT OF RESPONSE**

Blood parameter monitoring

**REVIEW BY CLINICIAN**

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

**NURSE / PHARMACIST LED REVIEW**

As per locally agreed framework

**ADMINISTRATION NOTES**

- Chlorambucil should be prescribed to the nearest 2mg dose.
- Dose should be swallowed with a glass of water
- Phenytoin has numerous drug interactions – check when prescribing.

**TOXICITIES**

Common: Gastric Irritation, Mild Emesis, Myelosupression (Mild)

Less Common: Rash (particularly if cross sensitive to melphalan), Seizures in older patients
DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.5 x 10^9 cells/l or PLT < 100 x 10^9 cells/l.

Renal Function:

No dose adjustment for renal impairment normally required.

Hepatic Function:

No dose adjustment normally required.

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.
Chlorambucil [4 Day Schedule]
(CL, Waldenstroms, Non-Hodgkins Lymphoma)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 5</td>
<td>Phenytoin (See Note*)</td>
<td>300mg</td>
<td>Oral</td>
<td>At Night For six (6) days</td>
</tr>
<tr>
<td>1 to 4</td>
<td>Chlorambucil</td>
<td>30mg</td>
<td>Oral</td>
<td>Once Daily for Four (4) days (or in 3 divided doses)</td>
</tr>
</tbody>
</table>

_Caution:_ There are other chlorambucil schedules given at different doses / for different lengths of time. _Select Protocol with Care!_

**CYCLE LENGTH AND NUMBER OF DAYS**

7 days for first 4 cycles then 14 days for 4 cycles

**APPROVED INDICATIONS**

- Non-Hodgkins Lymphoma (NHL)
- Chronic Lymphocytic Leukaemia (CLL)
- Waldenstroms

**EXCLUSION CRITERIA**

- Inability to swallow tablets

**RECOMMENDED TAKE HOME MEDICATION**

Metoclopramide 10mg Three Times Daily when required.

Consider Allopurinol 300mg once daily during the first cycle.

*Note:* There is some evidence that high doses of chlorambucil may induce seizures in susceptible individuals. The risk appears to be dose related and related to the age of the patient. Prescribers should _consider_ the risk of seizures in individual patients and if necessary pre-medicate (starting the night before and continuing until the day after chlorambucil) with phenytoin.
INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT-Scan, Chest X-Ray, LDH, Bone Marrow FBC, U&Es, LFTs, Protein Electrophoresis, UEP, IgG, Calcium, Uric Acid, WM Patients: β2-MicroGlobulin, CLL Patients: DAT

Prior to each cycle: U&Es, LFTs, FBC

ASSESSMENT OF RESPONSE

Blood parameter monitoring

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Chlorambucil should be prescribed to the nearest 2mg dose.
- Dose should be swallowed with a glass of water
- Phenytoin has numerous drug interactions – check when prescribing.

TOXICITIES

Common: Gastric Irritation, Mild Emesis, Myelosupression (Mild)

Less Common: Rash (particularly if cross sensitive to melphalan), Seizures in older patients

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.5 x 10⁹ cells/l or PLT < 100 x 10⁹ cells/l.

Renal Function:

No dose adjustment for renal impairment normally required.
**Hepatic Function:**

No dose adjustment normally required.

**TREATMENT LOCATION**

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.
Chlorambucil [7 Day Schedule]
(Chronic Lymphocytic Leukaemia, Non-Hodgkins Lymphoma, Waldenstrom’s)

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 7</td>
<td>Chlorambucil</td>
<td>10mg/m²</td>
<td>ORAL</td>
<td>Once Daily For Seven (7) days</td>
</tr>
</tbody>
</table>

_Caution:_ There are other chlorambucil schedules given at different doses / for different lengths of time. _Select Protocol with Care!_

CYCLE LENGTH AND NUMBER OF DAYS

28 day cycle, for 4 – 6 cycles

APPROVED INDICATIONS

- Chronic Lymphocytic Leukaemia (CLL)
- Non-Hodgkins Lymphoma (NHL)
- Waldenstrom’s (WM)

ELIGIBILITY CRITERIA

- Some CLL Patients (Stage C) will require a debulking regimen on Prednisolone EC 30mg/m² daily for 21 days prior to commencement of chlorambucil. Tail of prednisolone when starting chlorambucil.

EXCLUSION CRITERIA

- Inability to swallow tablets

RECOMMENDED TAKE HOME MEDICATION

No routine anti-emetic cover is usually required

Consider prescribing Gastro Prophylaxis (Proton Pump Inhibitor) if patient has dyspepsia

INVESTIGATIONS / MONITORING REQUIRED

**Prior to 1st cycle:** FBC, U&Es, LFTs, Protein Electrophoresis, UEP, IgG, Calcium, Uric Acid, WM Patients: β2-Microglobulin, CLL Patients: DAT

**Prior to each cycle:** U&Es, LFTs, FBC, Calcium,
ASSESSMENT OF RESPONSE

Blood parameter monitoring

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Chlorambucil should be prescribed to the nearest 2mg dose.
- Dose should be swallowed with a glass of water
- Patients may divide dose during the day if they find this easier or causes less side effects.

TOXICITIES

Common: Gastric Irritation, Mild Emesis, Myelosupression (Moderate)

Less Common: Rash (particularly if cross sensitive to melphalan)

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.5 x 10^9 cells/l or PLT < 100 x 10^9 cells/l.

Renal Function:

No dose adjustment for renal impairment normally required.

Hepatic Function:

No dose adjustment normally required

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES: CLL IV Protocol
Chlorambucil [14 Day Schedule]
(Low Grade Non-Hodgkins Lymphoma)

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Days</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 14</td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>ORAL</td>
<td>Three Times Daily If required</td>
</tr>
<tr>
<td>1 to 14</td>
<td>Chlorambucil</td>
<td>2mg</td>
<td>ORAL</td>
<td>Once Daily For fourteen (14) days</td>
</tr>
<tr>
<td>1 to 5*</td>
<td>Dexamethasone*</td>
<td>4mg*</td>
<td>ORAL</td>
<td>Once Daily For five (5) days*</td>
</tr>
</tbody>
</table>

*Note: The steroid component of this regimen is often varied to use varying doses, and course lengths of up to 14 days. Some clinicians may also substitute prednisolone.

CYCLE LENGTH AND NUMBER OF DAYS

28 day cycle, for 4 to 6 cycles

APPROVED INDICATIONS

- Low Grade Non-Hodgkins Lymphoma (NHL)

EXCLUSION CRITERIA

- Inability to swallow tablets

RECOMMENDED TAKE HOME MEDICATION

No routine anti-emetic cover is usually required; however some patients may require metoclopramide 10mg three times daily.

Allopurinol 300mg once daily for first cycle.

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH

Prior to each cycle: U&Es, LFTs, FBC, LDH

Caution: There are other chlorambucil schedules given at different doses / for different lengths of time. Select Protocol with Care!
ASSESSMENT OF RESPONSE

Blood parameter monitoring

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

• Chlorambucil should be prescribed to the nearest 2mg dose.
• Dose should be swallowed with a glass of water

TOXICITIES

Common: Gastric Irritation, Mild Emesis, Myelosupression (Mild)
Less Common: Rash (particularly if cross sensitive to melphalan)

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.5 x 10⁹cells/l or PLT < 100 x 10⁹cells/l.

Renal Function:

No dose adjustment for renal impairment normally required.

Hepatic Function:

No dose adjustment normally required

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES:

Northern Regional Haematology Handbook (2004)
ChlVPP (Hodgkin’s Lymphoma)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 and  8</td>
<td>Ondansetron</td>
<td>8mg</td>
<td>IV bolus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vinblastine</td>
<td>6mg/m² (Max: 10mg)</td>
<td>IV bolus</td>
<td>via 0.9% Sodium Chloride Drip</td>
</tr>
<tr>
<td>1 to 14</td>
<td>Chlorambucil</td>
<td>6mg/m² (Max: 10mg)</td>
<td>ORAL</td>
<td>Once daily For 14 days</td>
</tr>
<tr>
<td>1 to 14</td>
<td>Procarbazine</td>
<td>100mg/m²</td>
<td>ORAL</td>
<td>In up to three divided doses daily For 14 days</td>
</tr>
<tr>
<td>1 to 14</td>
<td>Prednisolone</td>
<td>40mg</td>
<td>ORAL</td>
<td>Once Daily For 14 days</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**

28 Day cycle, usually given for a maximum of 6 cycles

**APPROVED INDICATIONS**

Non Hodgkin’s Lymphoma (Induction Therapy)

Hodgkin’s Lymphoma

**RECOMMENDED TAKE HOME MEDICATION**

Allopurinol 300mg Once Daily with first cycle of treatment

Metoclopramide 10mg Three Times Daily, if required, for 14 days

Gastro prophylaxis (Proton Pump Inhibitor or H2 Antagonist) should be considered with the steroid.

**INVESTIGATIONS / MONITORING REQUIRED**

Prior to first cycle: FBC, U&Es, LFTs, Ca, Uric Acid, LDH

Prior to each cycle: FBC, U&Es, LFTs, Ca, Uric Acid, LDH

**ASSESSMENT OF RESPONSE**

Measure palpable disease. CT scan at mid point of treatment and after completion of therapy.
REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Vinblastine is for intravenous use only. Administration by other routes may be fatal. To reduce the risk of error, vinblastine should be diluted to 20ml.

- Procarbazine dose can be taken in three divided doses. (Total daily dose: 100mg/m²)

- Patients must not drink alcohol while taking procarbazine (risk of disulfiram type reaction)

- Patients requiring blood transfusion will require irradiated blood products.

- Some clinicians may choose to substitute vindesine in patients who develop peripheral neuropathies with vinblastine.

TOXICITIES

Common: Myelosupression (moderate risk), Nausea/Vomiting, Fatigue, Immunosuppression

Less Common: Numbness, Paraesthesias, Neuropathy, Constipation, Flushing/Rash, Allergic Reaction

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity: (Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

- Delay treatment on Day 1 if ANC < 1.5 x 10⁹ cells/l or PLT < 100 x 10⁹ cells/l.

- Consider a 20% dose reduction for Grade IV neutropenia (ANC < 0.5 cells x10⁹/l) or thrombocytopenia (PLT < 25 cells x10⁹/l) lasting more than 7 days.
Neuropathies:
Some clinicians may substitute vindesine for vinblastine. Alternatively reduce dose by 50% or withhold dose altogether.

Renal Function:
If Serum Cr > 177 µmol/l – reduce procarbazine by 50%.
If CrCl < 10ml/min – withhold procarbazine

Hepatic Function:

<table>
<thead>
<tr>
<th>AST</th>
<th>Bilirubin</th>
<th>Vinblastine</th>
<th>Chlorambucil</th>
<th>Procarbazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60 iu</td>
<td>&lt; 26 µmol/l</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>60 to 180 iu/l</td>
<td>26 – 51 µmol/l</td>
<td>50%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Normal</td>
<td>&gt; 51 µmol/l</td>
<td>50%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>&gt; 180 iu/l</td>
<td>&gt; 51 µmol/l</td>
<td>Omit</td>
<td>Consider reduction</td>
<td>100%</td>
</tr>
<tr>
<td>&gt; 180 iu/l or &gt; 85 µmol/l</td>
<td>Omit</td>
<td>Contraindicated</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TREATMENT LOCATION
Suitable for administration in chemotherapy day units, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES:
CIDEX (Multiple Myeloma)

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 5</td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>Oral</td>
<td>Three Times Daily</td>
</tr>
<tr>
<td>1</td>
<td>Ondansetron</td>
<td>8mg</td>
<td>Oral</td>
<td>Twice Daily</td>
</tr>
<tr>
<td>1</td>
<td>Lomustine (CCNU)</td>
<td>40mg</td>
<td>ORAL</td>
<td>Once Only For 1 day</td>
</tr>
<tr>
<td>1 to 3</td>
<td>Idarubicin</td>
<td>10mg/m²</td>
<td>ORAL</td>
<td>Once Daily For 3 days only</td>
</tr>
<tr>
<td>1 to 4</td>
<td>Dexamethasone</td>
<td>10mg</td>
<td>ORAL</td>
<td>Twice Daily For 4 days only</td>
</tr>
</tbody>
</table>

CYCLE LENGTH AND NUMBER OF DAYS
Minimum 28 Day cycle, usually given for up to 6 cycles

APPROVED INDICATIONS
- Relapsed Multiple Myeloma
- Prior to auto transplant for consolidation

EXCLUSION CRITERIA
- Patients with significant reduction in Left Ventricular Ejection Fraction
- Patients having reached a maximum lifetime cumulative dose of Idarubicin or any other Anthracycline

RECOMMENDED TAKE HOME MEDICATION
Allopurinol 300mg once daily for 7 days, during first cycle if appropriate.
Metoclopramide 10mg Three Times Daily.
Ondansetron 8mg Twice Daily on day 1.
Consider prescribing Gastro Prophylaxis (Proton Pump Inhibitor) for cover with dexamethasone.
INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH, ß2-MicroGlobulin, Para-protein (Urine & Serum), Calcium, Group & Save depending on Hb. Bone Marrow, Skeletal Survey, Uric Acid, CRP, ECG

Prior to each cycle: U&Es, LFTs, FBC, Para-protein (Urine & Serum), Calcium, Group & Save depending on Hb.

ASSESSMENT OF RESPONSE

Para-protein, Bone Marrow Biopsy and Symptom Control.

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Idarubicin is available as 5mg, 10mg and 25mg capsules.
- Lomustine is a 40mg capsule.
- Patients with pre-existing cardiac disease should be considered for ECHO Cardiogram.
- Maximum Lifetime Dose of Idarubicin: 400mg/m²
- Diabetic patients should increase monitoring on blood glucose
- May discolour urine red for 1-2 days after treatment
- Capsules should ideally be taken with a light meal (e.g. Breakfast)
- Patients should not consume alcohol for at least 2 hours after taking lomustine.

TOXICITIES

- Common: Gastric Irritation, Alopecia, Moderate Emesis, Myelosupression, Fatigue, Dyspepsia, Increased Glucose, Insomnia, Agitation, Mucositis
- Less Common: Flushing or Rash, Allergic Reaction, Cardiac Toxicity, Mood Disturbances

Version 3: Issued 25th July 2008: Readers are advised to check NECN website www.cancernorth.nhs.uk to ensure they are using most up to date version
DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity: (Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

- Delay treatment for 7 days on Day 1 if ANC < 1.0 x 10^9 cells/l or PLT < 75 x 10^9 cells/l.
- Dose reduction based on nadir blood counts are recommended:

<table>
<thead>
<tr>
<th>ANC (cells x10^9/l)</th>
<th>PLT (cells x10^9/l)</th>
<th>Idarubicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.0</td>
<td>&gt; 75</td>
<td>Leave at 3 Days</td>
</tr>
<tr>
<td>0.5 – 1.0</td>
<td>50 – 75</td>
<td>Reduce to 2 days</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>&lt; 50</td>
<td>Reduce to 1 day</td>
</tr>
</tbody>
</table>

Renal Function:

Based on the dosage protocol adopted in a number of Phase III clinical trials of idarubicin, dose modification is required according to the following schedule:

<table>
<thead>
<tr>
<th>Serum Cr (µmol/l)</th>
<th>Idarubicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100</td>
<td>100%</td>
</tr>
<tr>
<td>100-175</td>
<td>50%</td>
</tr>
<tr>
<td>&gt; 175</td>
<td>Clinical Decision</td>
</tr>
</tbody>
</table>

Lomustine is renally excreted. Dose reduction may be appropriate when CrCl < 60ml/min – however as Lomustine is only available as 40mg capsules this is not possible. If CrCl < 30ml/min lomustine is not recommended.

Hepatic Function:

The following dose reductions are recommended for idarubicin when Bilirubin is increased:

<table>
<thead>
<tr>
<th>Bilirubin (µmol/l)</th>
<th>Idarubicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>100%</td>
</tr>
<tr>
<td>21 – 51</td>
<td>50%</td>
</tr>
<tr>
<td>51 – 85</td>
<td>25%</td>
</tr>
<tr>
<td>86 µmol/l</td>
<td>Contra-indicated</td>
</tr>
</tbody>
</table>

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.
ERLOTINIB (TARCEVA ®) FOR NSCLC

ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Cycle length</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 28</td>
<td>Continuous</td>
<td>Erlotinib</td>
<td>150 mg</td>
<td>Oral</td>
<td>ONCE daily</td>
</tr>
</tbody>
</table>

DOSE FORM

Presented as 25mg, 100mg and 150mg Tablets

CYCLE LENGTH AND NUMBER OF DAYS

One 150mg dose orally, taken ONCE daily until disease progression.

APPROVED INDICATION(S)

Patients with locally advanced or metastatic non-small cell lung cancer after failure of first line chemotherapy regimen.

- In the NECN Erlotinib can **ONLY** be used as an alternative 2nd line treatment to Docetaxel (Taxotere),
- In the NECN Erlotinib it is **NOT** approved as a third line treatment after failure of Docetaxel (Taxotere).

ELIGIBILITY CRITERIA

- Locally advanced or metastatic non-small cell lung cancer after failure of one prior chemotherapy regime
- PS 0, 1, 2.
- Radiologically or clinically evaluable disease
- Able to take oral medication
- Using effective contraception if of reproductive potential
EXCLUSION CRITERIA

- Chemotherapy naïve patients
- Pregnant or lactating women
- Concurrent uncontrolled medical illness
- Impaired renal function (Serum creatinine > 5 x ULN)
- Impaired hepatic function (Bilirubin > 2 x ULN, ALT > 2 x ULN in absence of liver metastases and > 5 x ULN with liver metastases)

PREMEDICATION

None

RECOMMENDED TAKE HOME MEDICATION

- Metoclopramide 10 to 20 mgs TDS to QDS as required (not usually needed)
- Loperamide 2 mg when required (max 16 mg in 24 hours) for diarrhoea as required
- Emollients (for skin rash) e.g. Diprobase, Epaderm, E45 Neutrogena * encourage patients to use regularly to prevent skin dryness.

INVESTIGATIONS / MONITORING REQUIRED

Baseline chest X-ray/ CT scan, FBC, U&E, LFT’s & tumour markers as appropriate prior to starting treatment and at appropriate intervals during treatment.

ASSESSMENT OF RESPONSE

Radiological and clinical assessment will be performed at baseline and then 8 weeks following commencement of erlotinib. Erlotinib will only be continued if response is documented. Assessment will thereafter be at 3 monthly intervals

REVIEW BY CLINICIAN

Assessment of response at 8 weeks and then at 3 monthly intervals or sooner as appropriate to individual patient.

NURSE / PHARMACIST LED REVIEW

Each cycle as applicable according to local practice.
ADMINISTRATION NOTES

- Taken with water 1 hour prior to or 2 hours after food
- Avoid strong sunlight or use a good sunscreen SPF 15 or higher
- Hepatic cytochrome CYP3A4 is involved in the metabolism of erlotinib. Potent inducers of CYP3A4 may reduce the efficacy of erlotinib whereas potent inhibitors of CYP3A4 may lead to increased toxicity. Concomitant treatment with these types of agents should be avoided.
- Drugs that are CYP3A4 inhibitors include systemic anti-fungals e.g. ketoconazole, itraconazole, voriconazole; ciprofloxacin, protease inhibitors, erythromycin and SSRI’s e.g. fluoxetine, fluvoxamine. If necessary the dose of erlotinib should be reduced, particularly if toxicity is observed.
- Drugs that are CYP3A4 inducers such as rifampicin, phenytoin, carbamazepine, rifampin, phenobarbital or Hypericum perforatum (St Johns Wort) may increase metabolism and decrease erlotinib plasma concentrations and hence potentially decrease efficacy.
- As bleeding events were observed in the BR21 study when patients were taking concurrent warfarin it has been suggested that there may be a possibility of an interaction, however no formal interaction studies with warfarin have been performed. Patients taking warfarin or other coumarin-derivative anticoagulants should be monitored regularly for changes in prothrombin time or INR.
- Proton Pump Inhibitor and other drugs affecting gastric pH may affect absorption of erlotinib. Dose escalation of erlotinib does not overcome this.

TOXICITIES

- Skin Reactions (see under dose modification below)
- Diarrhoea (see under dose modification below)
- Fatigue
- Nausea & vomiting (Note if the patient vomits after taking a erlotinib tablet, the patient should NOT take another tablet, until the next dose is due.)
DOSE MODIFICATION / TREATMENT DELAYS

All dose modifications must be made by an oncology specialist following the recommended dose reduction strategy below.

<table>
<thead>
<tr>
<th>Level</th>
<th>Erlotinib (Tarceva) dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting dose</td>
<td>150mg daily</td>
</tr>
<tr>
<td>1st reduction</td>
<td>100mg daily</td>
</tr>
<tr>
<td>2nd reduction</td>
<td>50mg daily</td>
</tr>
</tbody>
</table>

All toxic events will be graded according to NCI CTCAE v3.0 criteria plus the following scale for describing rash.

| Grade 1                                      | asymptomatic, macular or papular erythematous eruption in acneiform distribution; |
| Grade 2                                      | like grade 1 but with symptoms such as pruritus; |
| Grade 3                                      | extension of the eruption beyond the acneiform distribution of head, chest and back or the development of confluent lesions, painful lesions, or minor ulceration; |
| Grade 4                                      | exfoliative or ulcerating dermatitits. |

In the event of any grade 3 or 4 toxicity that is not controlled by optimal supportive care (see below for guidelines) then dose reduce to the next dose level. Toxicity must improve by at least 1 NCI CTCAE grade within 2 weeks or further dose reduction by 1 level will be required. Once a patient has had a dose reduction the dose will not be re-escalated except after resolution of the skin rash.

Dose adjustment for skin rash

Typical erlotinib rash has the following appearance:

- Pustular/ papular appearance and usually involves the face, head and upper torso.

Erlotinib rash may be secondarily infected as diagnosed by:

- A tan/brown crust overlying inflammatory lesions, with significant oozing of fluid
- And/or an abrupt change in the appearance of lesions (particularly if they differ from those in other areas).
## Erlotinib Rash

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Symptoms</th>
<th>Dose modification</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 2</td>
<td>Generally localised Minimally Symptomatic No sign of infection</td>
<td>none</td>
<td>Topical hydrocortisone 1% and/or topical clindamycin 1% lotion/gel (non-alcoholic basis),</td>
</tr>
<tr>
<td>3</td>
<td>Generalised moderate symptoms No sign of infection</td>
<td>Dose reduction and re-escalate when rash less than grade 2</td>
<td>Topical hydrocortisone 1% or eumovate (clobetasol butyrate 0.05%) or short course of oral prednisolone and/or topical clindamycin 1% lotion/gel (non-alcoholic basis) plus oral, Minocycline or doxycycline 100mg BD for 10 to 14 days</td>
</tr>
<tr>
<td>4</td>
<td>Generalised Severe symptoms Potential for infection Significant impact on daily life.</td>
<td>Dose reduce as for 3 or dose interruption or discontinue</td>
<td>Topical eumovate (clobetasol butyrate 0.05%) or short course of oral Prednisolone and/or topical clindamycin 1% lotion/gel (non-alcoholic basis) plus oral, Minocycline or doxycycline 100mg BD for 10 to 14 days</td>
</tr>
</tbody>
</table>

- Consider adding in antihistamines e.g. chlorphenamine/ hydroxyzine and painkillers, paracetamol/ibuprofen if itching and or painful.
- Topical retinoids and other acne medications (e.g. benzyl peroxide) are NOT recommended since rash is not acne. Their skin drying effects may exacerbate rash.
**Dose adjustment for Diarrhoea**

Diarrhoea has occurred in 50% of patients on erlotinib.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Dose modification</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>Loperamide (4mg at first onset followed by 2mg after each loose stool (max 16 mg/day))</td>
</tr>
<tr>
<td>2</td>
<td>none</td>
<td>Loperamide (4mg at first onset followed by 2mg after each loose stool (max 16 mg/day))</td>
</tr>
<tr>
<td>3</td>
<td>If unresponsive to antidiarrhoeal medication for 24 hours then stop drug until resolution to grade &lt;1, then restart at next dose level down</td>
<td>Loperamide (4mg at first onset followed by 2mg after each loose stool (max 16 mg/day))</td>
</tr>
<tr>
<td>4</td>
<td>If unresponsive to antidiarrhoeal agent for &gt;24 hours then discontinue drug</td>
<td>Loperamide (4mg at first onset followed by 2mg after each loose stool (max 16 mg/day))</td>
</tr>
</tbody>
</table>

**Note:** In more severe or persistent cases of diarrhoea leading to dehydration erlotinib treatment must be stopped and appropriate measures should be taken to intensively rehydrate the patients intravenously.

**TREATMENT LOCATION**

Cancer Centre and Cancer Units

**REFERENCES:**

Etoposide for Ovarian Cancer

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>SCHEDULE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 14</td>
<td>Etoposide</td>
<td>50mg BD</td>
<td>Oral</td>
<td>7 to 14 days</td>
</tr>
</tbody>
</table>

**DOSE FORM**

Soft gelatin capsules containing 50 mg or 100 mg etoposide

**CYCLE LENGTH AND NUMBER OF DAYS**

21 day cycle for up to 6 cycles

Consider 7-10 days therapy for cycle one, then can dose escalate to 14 days cycle length or as directed by Oncology specialist

**APPROVED INDICATIONS**

Relapsed ovarian cancer

**EXCLUSION CRITERIA**

In patients who have a history of hypersensitivity reactions to etoposide

**PREMEDICATION**

**RECOMMENDED TAKE HOME MEDICATION**

Metoclopramide 10 to 20mgs QDS as required

**INVESTIGATIONS / MONITORING REQUIRED**

FBC, U&E, LFT, tumour markers as appropriate pre each cycle

D8 & D15 FBC, U&E, LFT

**ASSESSMENT OF RESPONSE**

Metastatic: Tumour size and patient symptomatic response

Adjuvant: There will be no visible disease to monitor for adjuvant treatment.

**REVIEW BY CLINICIAN**

Every other cycle
NURSE / PHARMACIST LED REVIEW

Alternate cycles

ADMINISTRATION NOTES

• Administer on an empty stomach
• Oral etoposide is poorly tolerated in this group of patients as most will have either advanced disease or have been heavily pre-treated with chemotherapy.
• There is no liquid form of etoposide, the injection can be potentially be given orally but is very unpleasant and not recommended.

TOXICITIES

• Rarely, allergic or anaphylactic reactions.
• Nausea & Vomiting
• Mucositis
• Constipation
• Alopecia
• Bone Marrow Depression; anaemia, neutropenia, thrombocytopenia
• Nephrotoxicity, monitor U&E
• Alteration in LFT’s (infrequent and transient)
• Leukaemic transformation

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

• Delay 1 week if WBC<3.0, ANC <1.0 Platelets <100
• No dose modification for CTC grade I/II ANC
• Grade III/IV ANC → delay chemotherapy until recovered. On recovery give 20% to 25% dose reduction
Non-Haematological Toxicity:

Renal Function

No dose reduction needed for mild renal failure. Avoid in moderate to severe renal failure, e.g. CrCl < 20ml/min.

Hepatic Function:

If pre-treatment LFT are abnormal or if bilirubin is raised, proceed with caution and discuss etoposide dosage with an Oncology specialist.

Suggested dose modifications

<table>
<thead>
<tr>
<th>Serum bilirubin (μmol/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 25</td>
<td>100 %</td>
</tr>
<tr>
<td>25 to 50</td>
<td>50 %</td>
</tr>
<tr>
<td>50 to 85</td>
<td>25 %</td>
</tr>
<tr>
<td>&gt; 85</td>
<td>Do not administer</td>
</tr>
</tbody>
</table>

Impaired hepatic function may be a risk factor for increased toxicities.

TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit

REFERENCES:

Oral Etoposide - Paediatrics

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 21</td>
<td>Etoposide</td>
<td>25mg/m² BD As injection solution</td>
<td>Oral</td>
<td>Repeat every 28 days</td>
</tr>
</tbody>
</table>

**DOSE FORM**

Injection 20mg/ml solution can be used orally

Soft gelatin capsules containing 50 mg or 100 mg etoposide

If capsules are used instead of injection solution the following dose conversion should be used:

Injection : Capsules

70mg : 100mg

**CYCLE LENGTH AND NUMBER OF DAYS**

28 day cycle.
Repeated until disease progression, unacceptable toxicity or patient choice.

**APPROVED INDICATIONS**

Relapsed Solid Tumours in Children

**EXCLUSION CRITERIA**

In patients who have a history of hypersensitivity reactions to etoposide

**RECOMMENDED TAKE HOME MEDICATION**

Metoclopramide QDS as required

**INVESTIGATIONS / MONITORING REQUIRED**

FBC, U&E, LFT,

**ASSESSMENT OF RESPONSE**

Metastatic: Tumour size and patient symptomatic response

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REVIEW BY CLINICIAN

Every cycle

NURSE / PHARMACIST LED REVIEW

Not applicable

ADMINISTRATION NOTES

- Administer on an empty stomach
- Ensure the patients know the treatment is not continuous and when they have finished they should never get a repeat prescription from their own GP.
- Etoposide liquid is supplied in glass bottles. Each bottle contains one dose.
- The bottles should be stored in a cool, dry place, below 25°C.
- The dose of etoposide should be added to a preferred drink (e.g. orange juice) and taken immediately.
- Patients supplied with oral etoposide liquid should receive an information leaflet explaining how the dose is to be taken.

TOXICITIES

- Rare - allergic or anaphylactic reactions.
- Nausea & Vomiting
- Mucositis
- Constipation
- Alopecia
- Bone Marrow Depression; anaemia, neutropenia, thrombocytopenia
- Nephrotoxicity, monitor U&E
- Alteration in LFT’s (infrequent and transient)
- Leukaemic transformation
DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

• Delay 1 week if WBC < 3.0, ANC < 1.0 Platelets < 100

Non-Haematological Toxicity:

Renal Function

No dose reduction needed for mild renal failure. Avoid in moderate to severe renal failure, e.g. CrCl < 20 ml/min)

Hepatic Function:

If pre-treatment LFT are abnormal or if bilirubin raised, proceed with caution and discuss etoposide dosage with an Oncology specialist.

Suggested dose modifications

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<td>100 %</td>
</tr>
<tr>
<td>25 to 50</td>
<td>50 %</td>
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<tr>
<td>50 to 85</td>
<td>25 %</td>
</tr>
<tr>
<td>&gt; 85</td>
<td>Do not administer</td>
</tr>
</tbody>
</table>

Impaired hepatic function may be a risk factor for increased toxicities.

TREATMENT LOCATION

Cancer Centre Only.

REFERENCES:

Fludarabine (Chronic Lymphocytic Leukaemia)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 5</td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>ORAL</td>
<td>Three Times Daily</td>
</tr>
<tr>
<td></td>
<td>Fludarabine</td>
<td>40mg/m²</td>
<td>ORAL</td>
<td>Once Daily for Five (5) days only</td>
</tr>
</tbody>
</table>

Tablets are supplied as 10mg tablets, suggested dose bands:

<table>
<thead>
<tr>
<th>Body Surface Area:</th>
<th>Dose (at 40mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.39 – 1.63m²</td>
<td>60mg</td>
</tr>
<tr>
<td>1.64 – 1.88m²</td>
<td>70mg</td>
</tr>
<tr>
<td>1.89 – 2.13m²</td>
<td>80mg</td>
</tr>
<tr>
<td>2.14 – 2.38m²</td>
<td>90mg</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**

28 Day cycle, usually given for up to 6 cycles (until best response achieved)

**APPROVED INDICATIONS**

Second Line Treatment of B-Chronic Lymphocytic Leukaemia (CLL).

**ELIGIBILITY CRITERIA**

- Failure of first line chemotherapy (CHOP, COP or CVP) *or*
- Intolerance or unsuitability for first line combination chemotherapy (CHOP, COP or CVP)

**EXCLUSION CRITERIA**

- Inadequate renal function (CrCl < 30ml/min)
- Pregnancy / Breast Feeding
- Decompensated haemolytic anaemia.

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Version 3: Issued 25th July 2008: Readers are advised to check NECN website [www.cancernorth.nhs.uk](http://www.cancernorth.nhs.uk) to ensure they are using most up to date version
RECOMMENDED TAKE HOME MEDICATION

All patients must have PCP Prophylaxis with Co-Tiramoxazole 960mg Three Times per Week (Mon, Wed, Fri) continuing for 6 months post chemotherapy.

Allopurinol 300mg once daily on days 1 to 5.

Metoclopramide 10mg Three Times Daily on days 1 to 5.

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH, β2-MicroGlobulin

Prior to each cycle: U&Es, LFTs, FBC

ASSESSMENT OF RESPONSE

CT scan at mid-point of treatment and after completion of treatment if appropriate. Palpable disease should be measured.

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Patients requiring blood transfusion will require irradiated blood.
- Tablets can be taken on an empty stomach or with food
- Tablets must be swallowed whole, with plenty of water.
- Ensure adequate contraception will be used if appropriate
- Ensure current CrCl has been assessed, and that any dose reduction necessary has been taken into account in prescribing
- May cause tumour lysis syndrome in susceptible patients
- Will cause amenorrhea / testicular atrophy
TOXICITIES
Common: Myelosupression, Fatigue, Immunosupression.

DOSE MODIFICATION / TREATMENT DELAYS
Haematological Toxicity:
(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)
Delay treatment on Day 1 if ANC < 1.5 x 10^9 cells/l or PLT < 100 x 10^9 cells/l

If treatment is delayed for more than 14 days:

<table>
<thead>
<tr>
<th>ANC</th>
<th>PLT</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 - 1.5</td>
<td>50 - 100</td>
<td>30mg/m^2/day</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>&lt; 50</td>
<td>20mg/m^2/day</td>
</tr>
</tbody>
</table>

Renal Function:
Fludarabine is extensively renally excreted and significant dose reduction is required for patients with mild renal failure:

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 70 ml/min</td>
<td>100%</td>
</tr>
<tr>
<td>30 – 70ml/min</td>
<td>50%</td>
</tr>
<tr>
<td>&lt; 30ml/min</td>
<td>Contra-indicated</td>
</tr>
</tbody>
</table>

TREATMENT LOCATION
Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES:
- NICE Technology Appraisal No 29, September 2001
- Summary of Product Characteristics, Bayer Schering, Feb 08.
Fludarabine – Cyclophosphamide (3 day schedule)  
(Chronic Lymphocytic Leukaemia)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 3</td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>ORAL.</td>
<td>Three Times Daily</td>
</tr>
<tr>
<td>1 to 3</td>
<td>Cyclophosphamide</td>
<td>250mg/m²</td>
<td>ORAL</td>
<td>Once Daily at Breakfast Time for Three (3) days only</td>
</tr>
<tr>
<td>1 to 3</td>
<td>Fludarabine</td>
<td>40mg/m²</td>
<td>ORAL</td>
<td>Once Daily at Lunch Time Three (3) days only</td>
</tr>
</tbody>
</table>

Caution: There is also an intravenous and oral schedule with different doses but a similar protocol over 5 days used for CLL. Select Protocol with Care!

Fludarabine Tablets are supplied as 10mg tablets, and Cyclophosphamide is supplied as 50mg tablets - suggested dose bands:

<table>
<thead>
<tr>
<th>Body Surface Area:</th>
<th>Cyclophosphamide Dose (at 250mg/m²)</th>
<th>Fludarabine Dose (at 40mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.40 – 1.50m²</td>
<td>350mg</td>
<td>60mg</td>
</tr>
<tr>
<td>1.51 – 1.62m²</td>
<td>400mg</td>
<td>60mg</td>
</tr>
<tr>
<td>1.63 – 1.70m²</td>
<td>400mg</td>
<td>70mg</td>
</tr>
<tr>
<td>1.70 – 1.87m²</td>
<td>450mg</td>
<td>70mg</td>
</tr>
<tr>
<td>1.88 – 1.90m²</td>
<td>450mg</td>
<td>80mg</td>
</tr>
<tr>
<td>1.91 – 2.10m²</td>
<td>500mg</td>
<td>80mg</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**

28 Day cycle, usually given for up to 6 cycles (until best response achieved)

**APPROVED INDICATIONS**

Non Hodgkins Lymphoma
EXCLUSION CRITERIA
- Inadequate renal function (CrCl < 30ml/min)
- Pregnancy / Breast Feeding
- Decompensated haemolytic anaemia.
- Hepatic Enzymes or Bilirubin greater than twice the upper limit of normal, not related to NHL.

RECOMMENDED TAKE HOME MEDICATION
All patients must have PCP Prophylaxis with Co-Trimoxazole 960mg Three Times per Week (Mon, Wed, Fri) continuing for 6 months post chemotherapy.
Allopurinol 300mg once daily on days 1 to 5.
Metoclopramide 10mg Three Times Daily on days 1 to 5.

INVESTIGATIONS / MONITORING REQUIRED
Prior to first cycle: CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH, β2-MicroGlobulin
Prior to each cycle: U&Es, LFTs, FBC

ASSESSMENT OF RESPONSE
CT scan at mid-point of treatment and after completion of treatment if appropriate. Palpable disease should be measured.

REVIEW BY CLINICIAN
Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW
As per locally agreed framework
ADMINISTRATION NOTES

- Patients requiring blood transfusion will require irradiated blood.
- Fludarabine tablets can be taken on an empty stomach or with food
- Fludarabine tablets must be swallowed whole, with plenty of water.
- Ensure adequate contraception will be used if appropriate
- Ensure current CrCl has been assessed, and that any dose reduction necessary has been taken into account in prescribing
- May potentiate cardiotoxicity
- May cause tumour lysis syndrome in susceptible patients
- Will cause amenorrhea / testicular atrophy

TOXICITIES

Common: Myelosuppression, Fatigue, Immunosupression.

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.5 x 10⁶ cells/l or PLT < 100 x 10⁹ cells/l

If treatment is delayed for more than 14 days:

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.5 x 10⁶ cells/l or PLT < 100 x 10⁹ cells/l

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Renal Function:
Fludarabine is extensively renally excreted and significant dose reduction is required for patients with mild renal failure:

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<td>&lt; 30ml/min</td>
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</tr>
</tbody>
</table>

TREATMENT LOCATION
Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES:
- NICE Technology Appraisal No 29, September 2001
Fludarabine – Cyclophosphamide (5 day schedule)  
(Chronic Lymphocytic Leukaemia)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 5</td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>ORAL</td>
<td>Three Times Daily</td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide</td>
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<td>ORAL</td>
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</tr>
<tr>
<td></td>
<td>Fludarabine</td>
<td>24mg/m²</td>
<td>ORAL</td>
<td>Once Daily at Lunch Time for Five (5) days only</td>
</tr>
</tbody>
</table>

*Caution: There is also an intravenous and oral schedule with different doses but a similar protocol over 3 days used for Lymphoma. Select Protocol with Care!*  

Fludarabine is supplied as 10mg tablets, and Cyclophosphamide are supplied as 50mg tablets - suggested dose bands:

<table>
<thead>
<tr>
<th>Body Surface Area:</th>
<th>Cyclophosphamide Dose (at 150mg/m²)</th>
<th>Fludarabine Dose (at 24mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.50 – 1.87m²</td>
<td>250mg</td>
<td>40mg</td>
</tr>
<tr>
<td>1.88 – 2.16m²</td>
<td>300mg</td>
<td>50mg</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**

28 Day cycle, usually given for up to 6 cycles (until best response achieved)

**APPROVED INDICATIONS**

First Line Treatment of B-Chronic Lymphocytic Leukaemia (CLL).

**ELIGIBILITY CRITERIA**

- Stage A – C, B-cell CLL

Version 3: Issued 25th July 2008: Readers are advised to check NECN website [www.cancernorth.nhs.uk](http://www.cancernorth.nhs.uk) to ensure they are using most up to date version
EXCLUSION CRITERIA

- Inadequate renal function (CrCl < 30ml/min)
- Pregnancy / Breast Feeding
- Decompensated haemolytic anaemia.
- Hepatic Enzymes or Bilirubin greater than twice the upper limit of normal, not related to CLL.

RECOMMENDED TAKE HOME MEDICATION

All patients must have PCP Prophylaxis with Co-Ttrimoxazole 960mg Three Times per Week (Mon, Wed, Fri) continuing for 6 months post chemotherapy.

Allopurinol 300mg once daily on days 1 to 5.

Metoclopramide 10mg Three Times Daily on days 1 to 5.

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH, β2-MicroGlobulin

Prior to each cycle: U&Es, LFTs, FBC

ASSESSMENT OF RESPONSE

CT scan at mid-point of treatment and after completion of treatment if appropriate. Palpable disease should be measured.

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Patients requiring blood transfusion will require irradiated blood.
- Fludarabine tablets can be taken on an empty stomach or with food
- Fludarabine tablets must be swallowed whole, with plenty of water.

Version 3: Issued 25th July 2008: Readers are advised to check NECN website www.cancernorth.nhs.uk to ensure they are using most up to date version
• Ensure adequate contraception will be used if appropriate
• Ensure current CrCl has been assessed, and that any dose reduction necessary has been taken into account in prescribing
• May potentiate cardiotoxicity
• May cause tumour lysis syndrome in susceptible patients
• Will cause amenorrhea / testicular atrophy

**TOXICITIES**

*Common*: Myelosupression, Fatigue, Immunosuppression.


**DOSE MODIFICATION / TREATMENT DELAYS**

**Haematological Toxicity:**

(Nota: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.5 x 10⁹ cells/l or PLT < 100 x 10⁹ cells/l

If treatment is delayed for more than 14 days:

<table>
<thead>
<tr>
<th>ANC</th>
<th>PLT</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 - 1.5</td>
<td>50 - 100</td>
<td>50%</td>
</tr>
</tbody>
</table>

**Renal Function:**

Fludarabine is excreted by the kidneys and significant dose reduction is required for patients with mild renal failure:

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Fludarabine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 70 ml/min</td>
<td>100%</td>
</tr>
<tr>
<td>30 – 70ml/min</td>
<td>50%</td>
</tr>
<tr>
<td>&lt; 30ml/min</td>
<td>Contra-indicated</td>
</tr>
</tbody>
</table>

Version 3: Issued 25th July 2008: Readers are advised to check NECN website [www.cancernorth.nhs.uk](http://www.cancernorth.nhs.uk) to ensure they are using most up to date version
TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.

REFERENCES:

- NICE Technology Appraisal No 29, September 2001
- CLL4 Trial Protocol (Chronic Lymphocytic Leukaemia Trial 4: A Randomised Comparison of Chlorambucil, Fludarabine and Fludarabine Plus Cyclophosphamide.). Accessed at: 
  http://www.icr.ac.uk/research/research_sections/haemato_oncology/4459.pdf
Hydroxycarbamide [Hydroxyurea]  
(Myeloproliferative Disorders)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
</table>
| 1 to 28 | Hydroxycarbamide | A: 20-30mg/kg  
B: 15-20mg/kg | ORAL  | Once Daily  
(continuous) |

**Dose schedule A:** (20-30mg/kg) is the starting dose for CML. 20mg/kg is more appropriate where WBC < 20 x 10^9 cells/l.

**Dose schedule B:** (15-20mg/kg) is the starting dose for Polycythaemia, for Essential Thrombocytosis start at 15mg/kg

Doses should be based on actual or ideal body weight whichever is the lower value. Ideal body weight is calculated from:

\[ IBW[kg] = F + (0.905 \times (Ht[cm] - 152)) \]

\( F = 45.5 \) for women, and 50 for men. This equation is only valid for adults over 152 cm (5 feet tall)

Normal doses may range from 500mg once per week to a maximum of 3000mg daily.

**CYCLE LENGTH AND NUMBER OF DAYS**

Minimum 28 Day cycle (continuous treatment)

**APPROVED INDICATIONS**

Myeloproliferative Disorders including:

- Essential Thrombocytthaemia
- Chronic Myeloid Leukaemia
- Primary Proliferative Polycythaemia (Polycythaemia Vera)
- Myelofibrosis
- Myeloproliferative disorder unclassified
EXCLUSION CRITERIA

- Leukopenia (WBC < 2.5 x 10^9 cells/l)*
- Thrombocytopenia (PLT < 100 x 10^9 cells/l)*
- Severe Anaemia
- Previous hypersensitivity to hydroxycarbamide
- Patients currently receiving anti-retroviral therapy with: didanosine and/or stavudine,
- Pregnancy & Breast Feeding

Where these are the result of bone marrow suppression secondary to haematological disease, at the discretion of a consultant haematologist treatment may commence cautiously.

RECOMMENDED TAKE HOME MEDICATION

Allopurinol 300mg once daily on for 1 -2 months.
Essential Thrombocythaemia: Aspirin 75mg daily.

INVESTIGATIONS / MONITORING REQUIRED

**Prior to first cycle:** CT Scan, Chest X-Ray, FBC (including differential), B12, Folate, Uric Acid, U&Es, LFTs, LDH, Bone Marrow including Cytogenetics, JAC II

**During & following first cycle of treatment:** FBC every 1-2 weeks during first 6 weeks of treatment.

**Prior to each cycle:** U&Es (minimum 6 monthly when stable), LFTs (minimum 6 monthly when stable), FBC (minimum of 3 monthly when stable).

**Following dose escalation/reduction:** FBC to be rechecked after 2 weeks if dose of hydroxycarbamide is changed.

ASSESSMENT OF RESPONSE

Response should be assessed after 6 weeks. If response is achieved treatment should continue (with appropriate monitoring) indefinitely.

For CML:

To maintain WCC between 5 -10 cells x10^9/l
For Essential Thycaemia:
To maintain PLT < 600 cells x10^9/l and WCC > 4 cells x10^9/l.

For Polycythaemia:
To maintain Haematocrit at < 45% and PLT < 400 cells x 10^9/l

**REVIEW BY CLINICIAN**
Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework. Minimum consultant review annually.

**NURSE / PHARMACIST LED REVIEW**
As per locally agreed framework, or under share care with GP. 3 monthly review when stable.

**ADMINISTRATION NOTES**
- Patients should be advised to report unexplained bruising, bleeding, purpura (or other skin changes), sore throat, fever or malaise immediately to their GP. Their GP will suspend hydroxycarbamide treatment pending FBC result.
- To reduce the risk of elevated uric acid levels patients should be instructed to maintain an adequate fluid intake (usually around 2 litres per day [8 tumblers of water]).
- Patients (Men and Women) must use appropriate contraception, during and for 3 months after treatment.
- Hydroxycarbamide capsules are available as 500mg strengths only. Doses should be expressed to the nearest 500mg. Doses *should not* be written in grams.
- Large doses (e.g. 2000mg daily) may be divided if easier for patient.

**TOXICITIES**
Common: Bone Marrow Suppression (Usually mild), Anaemia, Leucopenia, Thrombocytopenia, Megaloblastosis (Raised MCV).
Less Common: Thrombocytopenia, Anaemia, Nausea, Vomiting, Anorexia, Stomatitis, Fever, Chills, Malaise, Maculopapular Rash, Facial Erythema,
Peripheral Erythema, Altered LFTs, Reduction in renal tubular function, Diarrhoea, Constipation, Leg Ulceration.

**DOSE MODIFICATION / TREATMENT DELAYS**

**Haematological Toxicity:**

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment (withhold for 3 days) on Day 1 if WCC < 4 x 10^9 cells/l, ANC < 2.5 x 10^9 cells/l or PLT < 100 x 10^9 cells/l, or a sequential fall in these results by 10% over the last 3 results.

If MCV significantly abnormal and/or patient becomes anaemic – repeat B12 and Folate and initiate appropriate supplementation if necessary. (NB. MCV is always raised in patients on hydroxycarbamide)

Rapid fall in counts, or consistent downward trends indicate for increased monitoring.

**Non-Haematological Toxicity:**

Leg Ulcers, Squamous or Basal Cell Carcinomas: Stop Treatment & Discuss with Consultant Haematologist.

**Renal Function:**

If creatinine is greater than twice the upper limit of normal withhold treatment until discussed with a consultant haematologist. The following dose reductions (with appropriate dose adjustments for response) may act as a guide to dosing in renal impairment:

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60 ml/min</td>
<td>100%</td>
</tr>
<tr>
<td>45 – 60 ml/min</td>
<td>85%</td>
</tr>
<tr>
<td>30 – 44 ml/min</td>
<td>80%</td>
</tr>
<tr>
<td>&lt; 30 ml/min</td>
<td>50%</td>
</tr>
</tbody>
</table>
Hepatic Function:

If ALT or ALP is greater than twice the upper limit of normal, withhold treatment until discussed with consultant haematologist. There is no definitive guidance that dose reduction is warranted with hepatic impairment for hydroxycarbamide.

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services, including with Shared Care with Primary Care where a formal Shared Care Protocol is in place.
Imatinib (Chronic Myeloid Leukaemia)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 28</td>
<td>Imatinib</td>
<td>400 to 800mg*</td>
<td>ORAL</td>
<td>Once Daily (continuous)</td>
</tr>
</tbody>
</table>

*See Administration Notes for advice regarding dose selection

**CYCLE LENGTH AND NUMBER OF DAYS**

Continuous treatment

**APPROVED INDICATIONS**

- First Line Treatment of Chronic Phase Chronic Myeloid Leukaemia (Chronic, Accelerated, Blast Phase)
- Treatment of Chronic Myeloid Leukaemia (Accelerated & Blast Phase) in patients who have previously not received imatinib.
- Some cases of Philadelphia positive Acute lymphoblastic Leukaemia
- Gastro-Intestinal Stromal Tumour

**ELIGIBILITY CRITERIA**

- Chronic Phase CML: Chronic phase CML is defined when all of the following criteria are met: blasts < 15% in blood and bone marrow, peripheral blood basophils < 20%, platelets > 100 cells x10^9/l
- Accelerated Phase CML: Accelerated phase CML is defined by the presence of any of the following: blasts ≥15% but < 30% in blood or bone marrow, blasts plus promyelocytes ≥30% in blood or bone marrow (providing < 30% blasts), peripheral blood basophils ≥20%, platelets < 100 x 10^9/l unrelated to therapy.
- Blast Crisis CML: Blast crisis is defined as blasts ≥30% in blood/bone marrow or extramedullary disease other than hepatosplenomegaly.
- Gastro-Intestinal Stromal Tumour as first-line management of KIT (CD117)-positive unresectable and/or KIT (CD117)-positive metastatic gastro-intestinal stromal tumours (GISTs).
EXCLUSION CRITERIA

- Philadelphia Chromosome (BCR-ABL) Negative CML

RECOMMENDED TAKE HOME MEDICATION

No anti-emetic cover is usually required.

Consider Allopurinol 300mg once daily during the first cycle.

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: LDH, Bone Marrow FBC, U&E, LFTs, Calcium, Uric Acid,

Prior to each cycle: U&E, LFT, FBC

ASSESSMENT OF RESPONSE

May include repeat bone marrow test for G banding, FISH analysis or peripheral blood monitoring for BCR/ABL PCR. Appropriate test decided by physician responsible.

GIST: Assessment of response at least every 12 weeks. Response to imatinib treatment should be assessed on the basis of the results of diagnostic imaging to assess size and density of the tumour(s), patients’ symptoms and other factors, in accordance with the Southwest Oncology Group (SWOG) criteria or standard RECIST Criteria as clinically appropriate.

REVIEW BY CLINICIAN

Prior to each cycle.

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Starting dose - Chronic Phase: 400mg daily. Patients who fail to respond after may benefit from dose escalation to 600mg or 800mg daily. Discuss with Regional CML Team (Newcastle).
- **Starting Dose – Accelerated Phase & Blast Crisis:** 600mg daily. Patients who fail to respond may benefit from dose escalation to 400mg twice daily. Discuss with the Regional CML Team (Newcastle).

- **Starting Dose – GIST:** 400mg daily.

- Imatinib should be taken with food with a large glass of water.

- 100mg and 400mg tablets are available in pack sizes of 30 tablets. Tablets can be dissolved in mineral water or apple juice (400mg in 200ml), stirred and drunk as soon as possible after disintegration of the tablet.

- CY3A-P450 metabolised drugs such as warfarin, simvastatin, rifampicin, St Johns Wort, Dexamethasone, phenytoin, and erythromycin may have clinically significant drug interactions with imatinib – exercise caution in prescribing.

- Patients should be encouraged to report severe oedema early to their haematology team.

### TOXICITIES

**Common:** Headache, GI disturbances (nausea, vomiting, diarrhoea, dyspepsia, abdominal pain), muscle cramps, oedema, rash, blurred vision, Liver enzyme abnormalities

### DOSE MODIFICATION / TREATMENT DELAYS

**Haematological Toxicity:**

(\textit{Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.})

**Chronic Phase or GIST:**

Interrupt treatment if at any time ANC < 1.0 \times 10^9 \text{cells/l} or PLT < 50 \times 10^9 \text{cells/l}. Stop until ANC \geq 1.5 \text{cells} \times 10^9 /l and PLT \geq 75 \text{cells} \times 10^9 /l. Resume at previous dose. In event of recurrence of Myelosupression, repeat delay and resume at 300mg daily.
**Accelerated Phase / Blast Crisis:**

If at least one month after treatment started ANC < $0.5 \times 10^9$ cells/l or PLT < $10 \times 10^9$ cells/l. Check if related to disease (via Bone Marrow Aspirate)

- If unrelated to disease reduce dose to 400mg daily. If cytopenia continues for 2 weeks, reduce to 300mg daily. If cytopenia continues for further 2 weeks interrupt treatment until ANC $\geq 1.0$ cells $\times 10^9$/l and PLT $\geq 20$ cells $\times 10^9$/l and resume treatment at 300mg daily.

- If related to disease, continue with current dose

**Renal Function:**

No dose adjustment for renal impairment normally required, however patients should normally start at 400mg daily, and in patients with severe renal impairment caution should be exercised.

**Hepatic Function:**

Patients with hepatic impairment (Bilirubin > $1.5 \times$ ULN or AST > ULN) should normally start at 400mg daily. Frequency of monitoring should be increased and if toxicity occurs dose should be reduced.

**TREATMENT LOCATION**

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

GIST: Suitable for administration in patients own homes, under the supervision of an oncologist with experience treating GIST. Can be given at either cancer units (subject to local funding & governance arrangements) or cancer centres.

**REFERENCES:**

Melphalan and Prednisolone (Myeloma)

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 4</td>
<td>Melphalan</td>
<td>7mg/m²</td>
<td>ORAL</td>
<td>Once Daily for Four days</td>
</tr>
<tr>
<td>1 – 5</td>
<td>Prednisolone EC</td>
<td>40mg</td>
<td>ORAL</td>
<td>Once Daily for Five days</td>
</tr>
</tbody>
</table>

CYCLE LENGTH AND NUMBER OF DAYS

28 day cycle

APPROVED INDICATIONS

- Multiple Myeloma

ELIGIBILITY CRITERIA

- Patients unsuitable for allogeneic/autologous stem cell transplant

RECOMMENDED TAKE HOME MEDICATION

No anti-emetic cover is usually required.

Consider Allopurinol 300mg once daily during the first cycle.

Consider gastro protection (proton pump inhibitor) with steroid.

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT-Scan, Chest X-Ray, LDH, Bone Marrow, FBC, U&Es, LFTs, Protein Electrophoresis, Uric Acid, Calcium, β2-MicroGlobulin.

Prior to each cycle: U&Es, LFTs, FBC, Protein Electrophoresis, Calcium

ASSESSMENT OF RESPONSE

Protein Electrophoresis

REVIEW BY CLINICIAN

Prior to each cycle

NURSE / PHARMACIST LED REVIEW

As per local practice
ADMINISTRATION NOTES

• Melphalan is supplied as 2mg tablets. Doses should be rounded to the nearest 2mg.

• Melphalan interacts with nalidixic acid, ciclosporin, phenytoin, and clozapine.

• Patients should take their prednisolone with meals. They can divide the dose if desired but should avoid taking a dose after 6pm.

TOXICITIES

Common: Nausea; Alopecia; Dermatitis/Rash; Constipation/Diarrhoea

Less Common: Pulmonary fibrosis; Acute Leukaemia following long-term use.

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on day 1 if ANC < 1.0 x 10^9 cells/l or PLT < 75 x 10^9 cells/l.

Dose reduction based on nadir blood counts (Day 10-14) are recommended:

<table>
<thead>
<tr>
<th>ANC</th>
<th>or</th>
<th>PLT</th>
<th>Melphalan</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.0 cells x10^9/l</td>
<td>&gt; 75 cells x10^9/l</td>
<td>Leave at 4 Days</td>
<td></td>
</tr>
<tr>
<td>0.5 – 1.0 cells x10^9/l</td>
<td>50 – 75 cells x10^9/l</td>
<td>Reduce to 3 days</td>
<td></td>
</tr>
<tr>
<td>&lt; 0.5 cells x10^9/l</td>
<td>&lt; 50 cells x10^9/l</td>
<td>Reduce to 2 day</td>
<td></td>
</tr>
</tbody>
</table>

Renal Function:

Melphalan is excreted by the kidney. Explicit dose modifications are not available for melphalan, however, melphalan should not be given if Serum Cr > 300 µmol/l. For patients who are frail, or have co-existing medical illness or mild renal impairment dose reduction may be advisable from the outset – adjusted on subsequent cycles to account for toxicity. The Myeloma IX Study reduced the melphalan dose to 5mg/m² in patients with Cr > 200µmol/l.
Hepatic Function:
No dose modification is normally required.

TREATMENT LOCATION
Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.

REFERENCES:
• Myeloma IX Protocol
MP-T Melphalan, Prednisolone and Thalidomide  
(Myeloma)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 to 21</td>
<td>Thalidomide</td>
<td>200mg</td>
<td>Oral</td>
<td>ONCE Daily for 28 days</td>
</tr>
<tr>
<td>Days 1 to 7</td>
<td>Melphalan*</td>
<td>4 mg/m²</td>
<td>Oral</td>
<td>ONCE Daily for SEVEN days</td>
</tr>
<tr>
<td>Days 1 to 7</td>
<td>Prednisolone*</td>
<td>40 mg/m²</td>
<td>Oral</td>
<td>ONCE Daily for SEVEN days</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**

28 day cycle

**APPROVED INDICATIONS**

- Multiple Myeloma

**ELIGIBILITY CRITERIA**

- Patients unsuitable for allergenic-autologous stem cell transplant

**RECOMMENDED TAKE HOME MEDICATION**

No anti-emetic cover is usually required.

Consider Allopurinol 300mg once daily during the first cycle.

Consider gastro protection (proton pump inhibitor) with steroid.

Consider if thrombo-prophylaxis with thalidomide is required (using aspirin, warfarin or LMWH as indicated)

**INVESTIGATIONS / MONITORING REQUIRED**

Prior to first cycle: CT-Scan, Chest X-Ray, LDH, Bone Marrow, FBC, U&Es, LFTs, Protein Electrophoresis, Uric Acid, Calcium, β2-MicroGlobulin,

Prior to each cycle: U&Es, LFTs, FBC, Protein Electrophoresis, Calcium

**ASSESSMENT OF RESPONSE**

Protein Electrophoresis
REVIEW BY CLINICIAN

Prior to each cycle

NURSE / PHARMACIST LED REVIEW

As per local practice

ADMINISTRATION NOTES

- Patients must not become or attempt to become pregnant during thalidomide treatment. For women of child bearing potential, a negative pregnancy test during the 24 hours prior to each cycle of thalidomide will be required.

- Thalidomide Pharmion™ is licensed for the first-line treatment of multiple myeloma in the UK by Celgene, who have developed a risk management programme, ‘Thalidomide Pharmion™ Pregnancy Prevention Programme’

- In the Pregnancy Prevention Programme prescribers must:
  - Communicate the risks and benefits of Thalidomide Pharmion™ therapy to their patients
  - Prescribers must complete a ‘Treatment Initiation Form’ along with your patient (this only needs to be done once).
  - Provide the patient with a ‘Health Card’
  - Provide pregnancy prevention measures and counselling
  - Perform a pregnancy test (as appropriate) prior to every prescription
  - Supply a ‘Prescription Authorisation Form’ with each prescription to show confirmation that your patient has received counselling and pregnancy test date and result (if appropriate).
  - Remind your patient of the safe use of Thalidomide Pharmion™

- In the Pregnancy Prevention Programme pharmacists must
  - Register the Pharmacy with the Pregnancy Prevention Programme
  - Obtain a copy of the patient’s “Treatment Initiation Form” before the first dispense
  - Dispense Thalidomide Pharmion™ only if the prescriber has annotated the ‘Prescription Authorisation Form’ correctly
Remind all patients of the safe use of Thalidomide Pharmion™, each time a prescription is dispensed.

- Blood Glucose Tolerance may be affected by high dose dexamethasone, patients with diabetes should increase frequency of glucose monitoring.
- Thalidomide is sedating and so should be taken at night.
- Thalidomide may cause venous thromboembolism – patients should be encouraged to report calf pain early.
- Cyclophosphamide metabolites (acreolin) can cause haemorrhagic cystitis patients should be encouraged to drink 2-3 litres of water on days when taking cyclophosphamide.
- This is a complex regimen: patients will need time and assistance to understand when and how they should take this treatment.
- Melphalan is supplied as 2mg tablets. Doses should be rounded to the nearest 2mg.
- Melphalan interacts with nalidixic acid, ciclosporin, phenytoin, and clozapine.
- Patients should take their prednisolone with meals. They can divide the dose if desired but should avoid taking a dose after 6pm.

**TOXICITIES**

**Common:** Moderate Emesis, Myelosupression, Fatigue, Dyspepsia, Constipation, Rash, Sedation,

**Less Common:** Thromboembolism, Increased blood glucose, Peripheral Neuropathy, Pulmonary fibrosis; Acute Leukaemia following long-term use.

**DOSE MODIFICATION / TREATMENT DELAYS**

**Haematological Toxicity:**

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on day 1 if ANC < 1.0 x 10⁹ cells/l or PLT < 75 x 10⁹ cells/l.

Dose reduction based on nadir blood counts are recommended:
### ANC or PLT

<table>
<thead>
<tr>
<th>ANC</th>
<th>PLT</th>
<th>Melphalan</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.0 cells x10⁹/l</td>
<td>&gt; 75 cells x10⁹/l</td>
<td>Leave at 4 Days</td>
</tr>
<tr>
<td>0.5 – 1.0 cells x10⁹/l</td>
<td>50 – 75 cells x10⁹/l</td>
<td>Reduce to 3 days</td>
</tr>
<tr>
<td>&lt; 0.5 cells x10⁹/l</td>
<td>&lt; 50 cells x10⁹/l</td>
<td>Reduce to 2 day</td>
</tr>
</tbody>
</table>

**Renal Function:**

Melphalan is renally excreted. Explicit dose modifications are not available for melphalan, however, melphalan should not be given if Serum Cr > 300 µmol/l. For patients who are frail, or have co-existing medical illness or mild renal impairment dose reduction may be advisable from the outset – adjusted on subsequent cycles to account for toxicity.

**Hepatic Function:**

No dose modification is normally required.

**TREATMENT LOCATION**

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.

**REFERENCES:**

- Falcon et al. Melphalan and prednisone plus thalidomide versus melphalan and prednisone alone or reduced-intensity autologous stem cell transplantation in elderly patients with multiple myeloma (IFM 99–06): a randomised trial Lancet 2007; 370: 1209–18
- Palumbo et al: Oral melphalan and prednisone chemotherapy plus thalidomide compared with melphalan and prednisone alone in elderly patients with multiple myeloma: randomised controlled trial Lancet 2006; 367: 825–31
Nilotinib (Chronic Myeloid Leukaemia)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 28</td>
<td>Nilotinib</td>
<td>400mg</td>
<td>ORAL</td>
<td>Twice Daily</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**
Continuous treatment

**APPROVED INDICATIONS**
- Second line treatment of chronic phase Chronic Myeloid Leukaemia (CML) for patients who have resistance or intolerance to prior therapy including imatinib.

**ELIGIBILITY CRITERIA**
- Patients with Chronic Phase CML, who have resistance or intolerance to prior therapy including imatinib as defined by the following criteria.

<table>
<thead>
<tr>
<th>Time</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>No haematological response</td>
</tr>
<tr>
<td>6 months</td>
<td>Less than complete haematological response</td>
</tr>
<tr>
<td></td>
<td>No cytogenetic response (Ph&gt;95%)</td>
</tr>
<tr>
<td>12 months</td>
<td>Less than partial cytogenetic response (Ph&gt;35%)</td>
</tr>
<tr>
<td>18 months</td>
<td>Less than complete cytogenetic response (Ph&gt;0%)</td>
</tr>
<tr>
<td>After 18 months</td>
<td>Failure to achieve major molecular response (&lt;0.1% BCR-ABL/ABL transcript)</td>
</tr>
<tr>
<td>Any time</td>
<td>Loss of complete haematological response</td>
</tr>
<tr>
<td></td>
<td>Loss of complete cytogenetic response</td>
</tr>
<tr>
<td></td>
<td>Sustained or progressive loss of major molecular response</td>
</tr>
<tr>
<td></td>
<td>Mutation (e.g. T315I)</td>
</tr>
</tbody>
</table>

Patients with one of the following will be considered to have developed imatinib intolerance:
- any non-haematologic toxicity of grade 3 or higher severity
- any non-haematologic toxicity of grade 2 severity lasting more than one month
• any non-haematologic toxicity of grade 2 or higher recurring more than 3 times despite dose reduction and maximal supportive care
• haematologic toxicity of grade 4 severity persisting for more than seven days

EXCLUSION CRITERIA
• Philadelphia Chromosome (BCR-ABL) Negative CML
• Highly resistant ABL kinase domain mutation such as T315I
• Pregnancy. Patients younger than 18 years
• Patients with uncontrolled or significant cardiac disease (e.g. recent myocardial infarction, congestive heart failure, unstable angina or clinically significant bradycardia)

RECOMMENDED TAKE HOME MEDICATION
No anti-emetic cover is usually required.

INVESTIGATIONS / MONITORING REQUIRED
• First 2 months - every 2 weeks before each prescription: FBC, U&Es, LFTs, serum lipase
• Subsequently – every 4 weeks before each prescription: FBC, U&Es, LFTs, serum lipase
• Baseline ECG for QTc (Nilotinib should be used with caution in patients who have or who are at significant risk of developing prolongation of QTc)
• Molecular monitoring - BCR-ABL/ABL transcript monitoring every 3 months

ASSESSMENT OF RESPONSE
Haematological and cytogenetic response assessed following routine monitoring.

REVIEW BY CLINICIAN
Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework.

NURSE / PHARMACIST LED REVIEW
As per locally agreed framework.
ADMINISTRATION NOTES

- Nilotinib should be taken twice daily approximately 12 hours apart and must not be taken with food. No food should be consumed for 2 hours before and at least one hour after the dose is taken.
- The capsules should be swallowed whole with water.
- 200mg hard capsules are available in pack sizes of 112 tablets.
- Drugs that strongly inhibit CYP3A4 (e.g. ketoconazole, itraconazole, voriconazole, clarithromycin, telithromycin and ritonavir) can increase Nilotinib levels and should not be administered concurrently. Grapefruit juice and any other foods that are known CYP3A4 inhibitors should also be avoided.
- In patients for whom CYP3A4 inducers (e.g. phenytoin, rifampicin, carbamazepine, Phenobarbital and St. John’s Wort) alternative agents should with less enzyme induction potential should be considered.
- Nilotinib is a competitive inhibitor of CYP3A4, CYP2C8, CYP2C9 and CYP2D6 in vitro, potentially increasing the concentrations of drugs eliminated by these enzymes. Since warfarin is metabolized by CYP2C9 and CYP3A4 it should be given with caution. Other medications for anticoagulation should be considered.

TOXICITIES

**Very common:** headache, nausea, constipation, diarrhoea, rash, pruritus, fatigue, increased serum lipase

**Common:** neutropenia, pancytopenia, prolonged QT, anorexia, vomiting, abdominal pain, alopecia, myalgia, arthralgia, muscle spasms, bone pain, asthenia, oedema peripheral

**Uncommon:** pericardial effusion, pleural effusion

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

ANC <1x10⁹/l or platelets < 50x10⁹/l → stop nilotinib and monitor FBC. Resume within 2 weeks at prior dose if ANC > 1x10⁹/l and/or platelets > 50x10⁹/l.

If blood counts remain low, give nilotinib 400 mg ONCE DAILY.
Renal Function:
No dose adjustment for renal impairment normally required.

Hepatic Function:
For Grade 3-4 serum lipase (>2 ULN) or bilirubin (>3 ULN) elevations, doses should be reduced to 400 mg once daily or interrupted.

TREATMENT LOCATION
Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.

REFERENCES:
PECC (Non-Hodgkin’s and Hodgkin’s Lymphoma’s)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1to5</td>
<td>Ondansetron</td>
<td>8mg</td>
<td>Oral</td>
<td>Twice Daily</td>
</tr>
<tr>
<td>1</td>
<td>Lomustine (CCNU)</td>
<td>100mg/m²</td>
<td>ORAL</td>
<td>ONCE ONLY For 1 day only</td>
</tr>
<tr>
<td>1 to</td>
<td>Etoposide</td>
<td>200mg/m²</td>
<td>ORAL</td>
<td>Once Daily For 3 days only</td>
</tr>
<tr>
<td>4</td>
<td>Chlorambucil</td>
<td>20mg/m²</td>
<td>ORAL</td>
<td>In three divided doses daily For 4 days only</td>
</tr>
<tr>
<td>7</td>
<td>Prednisolone</td>
<td>40mg</td>
<td>ORAL</td>
<td>Once Daily For 7 days only</td>
</tr>
</tbody>
</table>

*Caution:* There is also a schedule called Mini-PECC which uses lower doses for frail patients. **Select Protocol with Care!**

**CYCLE LENGTH AND NUMBER OF DAYS**

Minimum 28 Day cycle, usually given for up to 6 cycles

**APPROVED INDICATIONS**

Salvage therapy for Advanced Relapsed Hodgkin’s Lymphoma

Salvage therapy for Advanced Relapsed Non-Hodgkin’s Lymphoma

**RECOMMENDED TAKE HOME MEDICATION**

Allopurinol 300mg once daily on days 1 to 5 of first cycle.

Ondansetron 8mg twice daily for 5 days. (PECC is moderately emetogenic, however, to avoid the risk of loosing the lomustine dose through vomiting relatively aggressive anti-emetic cover is recommended)

Consider prescribing Gastro Prophylaxis (Proton Pump Inhibitor or H2-antagonist) for cover with prednisolone.

**INVESTIGATIONS / MONITORING REQUIRED**

**Prior to first cycle:** CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH, β2-MicroGlobulin

**Prior to each cycle:** U&Es, LFTs, FBC
ASSSESSMENT OF RESPONSE
CT scan at mid-point of treatment and after completion of treatment if appropriate.

REVIEW BY CLINICIAN
Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW
As per locally agreed framework

ADMINISTRATION NOTES
- Etoposide should be taken on an empty stomach
- Patients requiring blood transfusions will require irradiated blood.
- Steroid dose may cause impaired glucose tolerance. Diabetic patients should increase frequency of glucose monitoring.
- Chlorambucil dose can be divided into three doses to reduce GI irritation
- There have been fatalities with this regimen when the course of lomustine and etoposide have been given for longer than recommended.
- Lomustine is supplied as 40mg capsules – the dose should be rounded to the nearest multiple of 40mg.
- Chlorambucil is supplied as 2mg tablets – the dose should be rounded to the nearest 2mg.
- Etoposide is supplied as 50mg and 100mg capsules – the dose should be rounded to the nearest 50mg.

TOXICITIES
Common: Nausea & Vomitting, Myelosuppression (Moderate to Severe), Fatigue, Glucose Intolerance, Alopecia
DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.5 x 10⁹ cells/l or PLT < 50 x 10⁹ cells/l. There will be two nadirs with this regimen. One caused by Etoposide (between day 7 and 14, and one caused by Lomustine which may not present until day 28)

Renal Function:

Lomustine and Etoposide are both renally excreted and dose modification is required in mild renal impairment:

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Lomustine</th>
<th>Chlorambucil</th>
<th>Etoposide</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60 ml/min</td>
<td>100% Dose</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>45 to 60ml/min</td>
<td>75% Dose</td>
<td>100%</td>
<td>85%</td>
</tr>
<tr>
<td>30 to 44ml/min</td>
<td>70% Dose</td>
<td>100%</td>
<td>80%</td>
</tr>
<tr>
<td>&lt; 30ml/min</td>
<td>Not Recommended</td>
<td>100%</td>
<td>75%</td>
</tr>
</tbody>
</table>

Hepatic Function:

Lomustine is partly hepatically excreted, however, no data exists on its safety in hepatic disease. In event of hepatic impairment consider dose reduction with dose escalation if no toxicity on first cycle.

Etoposide is hepatically metabolised, If Bilirubin > 26µmol/l or AST > 60iu/l reduce dose to 50%, if Bilirubin > 51µmol/l or AST > 180iu/l clinical decision required to proceed with treatment.

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.

REFERENCES:

SUNITINIB (SUTENT®)

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 28</td>
<td>Sunitinib*</td>
<td>50 mg</td>
<td>Oral</td>
<td>ONCE daily</td>
</tr>
</tbody>
</table>

- Presented as 12.5mg, 25mg and 50mg Hard Capsules
- Can be taken with regard to meals

CYCLE LENGTH AND NUMBER OF DAYS

One 50mg dose orally, taken daily for four consecutive weeks followed by a two week rest period to comprise a complete cycle of 6 weeks

APPROVED INDICATIONS

- First line treatment of metastatic renal cell carcinoma (MRCC)
- Treatment of unresectable or metastatic malignant gastrointestinal stromal tumours (GIST) after failure of imatinib treatment

ELIGIBILITY CRITERIA

- For MRCC patients with Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, and adequate haematological, coagulation, hepatic, renal, and cardiac function.
- Failure of imatinib in GIST patients based either on progression of disease (according to RECIST Criteria) or on unacceptably severe toxic effects during imatinib therapy that precluded further treatment. Imatinib last administered at least 2 weeks before starting and resolution of all toxic effects of imatinib or other therapy to grade 1 or less.

RECOMMENDED TAKE HOME MEDICATION

Metoclopramide 10 to 20mgs three or four time daily as required
Loperamide 2mg when required (max 16mg in 24 hours) for diarrhoea
Emollients (for skin rash) as required
INVESTIGATIONS / MONITORING REQUIRED

- Baseline assessment of cardiac function (ECHO) for patients with cardiac risk factors or history of coronary artery disease plus ongoing monitoring of cardiac function as deemed appropriate by clinician.

- Careful monitoring of BP during first six weeks, e.g. every one or two weeks, particularly in patients with pre-existing hypertension.

- BP, Thyroid Function, FBC, U&E, LFT’s & tumour markers as appropriate prior to each cycle.

ASSESSMENT OF RESPONSE

- Scan after 2 cycles

REVIEW BY CLINICIAN

Day 14 and Day 28 of Cycle One; Day 28 for each subsequent cycle

NURSE / PHARMACIST LED REVIEW

Each cycle as applicable according to local protocols

ADMINISTRATION NOTES

- Drugs that are CYP3A4 inhibitors such as ketoconazole, and to a lesser extent itraconazole, erythromycin, clarithromycin and grapefruit juice may decrease metabolism and increase sunitinib plasma concentrations. The dose of sunitinib may be decreased to 37.5 mg in the presence of strong CYP3A4 inhibitors.

- Drugs that are CYP3A4 inducers such as rifampin and to a lesser extent dexamethasone, phenytoin, carbamazepine, rifampin, phenobarbital or Hypericum perforatum (St Johns Wort) may increase metabolism and decrease sunitinib plasma concentrations. The dose of sunitinib may be increased up to 87.5 mg in the presence of strong enzyme inducers.

- Sunitinib induced hypertension can be treated with angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, beta blockers or diuretics as per local Trust formulary/ hypertension guidelines. Avoid calcium channel blockers such as diltiazem and verapamil due to potential for drug interactions.
TOXICITIES
• Diarrhoea
• Fatigue
• Nausea & vomiting
• Myelosupression
• Hypertension
• Left Ventricular Dysfunction
• Hypothyroidism
• Use with caution in patients with pre-existing uncontrolled hypertension, left ventricular dysfunction or arrhythmias or in patients taking concomitant drugs with arrhythmic potential.
• Yellow discolouration of urine and skin
• Risk of treatment-related tumour haemorrhage

DOSE MODIFICATION
All dose modifications must be made by an oncology specialist.

Haematological toxicity
Dose delay: If ANC < 1.5 or Platelets < 100. Until counts recovered

Non-Haematological Toxicity, e.g. Diarrhoea, Skin Rash
CTC grade 0 - 1 No change.
CTC grade 2 Therapy withheld until toxicity resolves to grade 1. No change in subsequent dose.
CTC grade 3 - 4 Therapy withheld until toxicity resolves to grade 1. Decrease subsequent dose to 37.5mg. Dose reduction maintained for ongoing cycle and remainder of therapy.

TREATMENT LOCATION
Cancer Centre or Cancer Unit where there is an Oncologist with a specialisation in urology or GIST patients as appropriate.
REFERENCES:

- Demetri, G et al Efficacy and safety of sunitinib in patients with advanced gastrointestinal stromal tumour after failure of imatinib: a randomised controlled trial, Lancet 368, October 14, 2006, p1329-38
Concomitant & Adjuvant Temozolomide and Radiotherapy for Malignant Glioma

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 42</td>
<td>Temozolomide</td>
<td>75mg/m² (Rounded to nearest 10mg)</td>
<td>Oral</td>
<td>ONCE daily for 42 days</td>
<td>1 Hour before Radiotherapy (Mornings and Weekends)</td>
</tr>
<tr>
<td>Day 70 (week 10)</td>
<td>Temozolomide</td>
<td>150mg/m²</td>
<td>Oral</td>
<td>Once Daily for Five Days</td>
<td>Adjuvant cycle One</td>
</tr>
<tr>
<td>Day 98 (week 14) Then every 28 days</td>
<td>Temozolomide</td>
<td>200mg/m²</td>
<td>Oral</td>
<td>Once Daily for Five Days</td>
<td>Adjuvant Cycle 2,3,4 etc</td>
</tr>
</tbody>
</table>

* Day 1 = start day radiotherapy

**DOSE FORM**

Available as 5 mg, 20 mg, 100 mg, 140 mg, 180 mg or 250 mg capsules

**NO DAYS CYCLE**

Starting from day 70 temozolomide is given for 5 days 28 days to a maximum of 6 cycles. Note average number of cycles given in trial = 3.2.

Take after 2 hour fast (ideally overnight and no food until 2 hours after)

**INDICATIONS**

Adjuvant therapy (adult or paediatric) High Grade Gliomas; for all performance status (PS) = 0 or 1 patients

*Used for 2nd line recurrent malignant glioma see separate protocol*

**INVESTIGATIONS / MONITORING REQUIRED**

Pre treatment on radiotherapy: Twice weekly FBC.

Once weekly treatment/exam – review

Prior to each cycle

Adjuvant: FBC, U & E’s, LFT’s

If toxicities re-schedule may need delay or dose reducing.

Version 3: Issued 25th July 2008: Readers are advised to check NECN website www.cancernorth.nhs.uk to ensure they are using most up to date version
PREMEDICATION
Concurrent: Pre day 1 (with radiotherapy) Ondansetron 8mg and then as required.
Adjuvant: Ondansetron 8mg BD for 5 days whilst having temozolomide.

RECOMMENDED TAKE HOME MEDICATION
Ondansetron 8mg BD for 5 days

ASSESSMENT OF RESPONSE
There will be no visible disease to monitor for adjuvant treatment.

REVIEW BY CLINICIAN
Concurrent Phase: Weekly in radiotherapy floor clinic for review and two weekly FBC.
Adjuvant Phase: Monthly for blood review and clinical review

NURSE LED REVIEW
Prior to each cycle

ADMINISTRATION NOTES
• Fasting recommended when taking tablets (see above)
• Observation haematology toxicity criteria
• Ensure prophylaxis against *Pneumocystis carinii* pneumonia PCP prophylaxis Co-trimoxazole (Septrin) x 1 tablet 3 x week during radiotherapy & until lymphocytopenia recovers.
• Oral preparation, therefore advise patients to swallow and not open the capsules. If a capsule becomes damaged, avoid contact of the powder contents with skin or mucous membrane. If contact does occur, wash the affected area.

TOXICITIES
• Nausea
• Alopecia
• Constipation
• Bone Marrow Depression; anaemia, neutropenia, thrombocytopenia
• Lethargy and Anorexia
• Headaches
DOSE MODIFICATION

Haematological Toxicity:
Delay by one week if: If ANC < 1.5 or Platelets < 100.
Reduce dose if ANC < 1.0 x 10^9 /l or platelets < 50 x 10^9 /l
- If dose is 200mg/m2 reduce to 150mg/m2
- If dose is 150mg/m2 reduce to 100mg/m2
- If dose is 100mg/m2 discontinue.

Non-Haematological Toxicity:
Any CTC Grade 3 non-haematological toxicity (except for alopecia, nausea, vomiting) reduce dose as described above
Any CTC Grade 4 Non-haematological toxicity discontinue

TREATMENT LOCATION
Can be given at Cancer Centre

REFERENCES:
- Stupp et al Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma NEJM March 2005 352;10
Temozolomide for Metastatic Malignant Glioma

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 5</td>
<td>Temozolomide</td>
<td>200mg/m²* (Can give 150mg/m² for cycle one)*</td>
<td>Oral</td>
<td>Once Daily for Five Days</td>
</tr>
</tbody>
</table>

*In patients previously treated with chemotherapy, the initial dose is 150mg/m² once daily, to be increased in the second cycle to 200 mg/m² once daily, for five days if there is no haematological toxicity

**DOSE FORM**

Available as 5 mg, 20 mg, 100 mg, 140 mg, 180 mg or 250 mg capsules

**NO DAYS CYCLE**

28 Day cycle

**INDICATIONS**

Recurrent or progressive malignant glioma (adult or paediatric)

*Used for adjuvant therapy of malignant glioma see separate protocol*

**INVESTIGATIONS / MONITORING REQUIRED**

Pre treatment and prior to each cycle FBC, U&E, LFTs.

**PREMEDICATION**

Ondansetron 8mg BD for 5 days whilst having temozolomide.

**RECOMMENDED TAKE HOME MEDICATION**

Metoclopramide 10 to 20mgs three to four times daily as required

**ASSESSMENT OF RESPONSE**

CT or MRI Scan

**REVIEW BY CLINICIAN**

Monthly for blood review and clinical review

**NURSE LED REVIEW**

Prior to each cycle
ADMINISTRATION NOTES

- Take after 2 hour fast (ideally overnight) no food until 2 hours after
- Oral preparation, therefore advise patients to swallow and not open the capsules. If a capsule damaged, avoid contact of the powder contents with skin or mucous membrane. If contact does occur, wash the affected area.

TOXICITIES

- Nausea
- Alopecia
- Constipation
- Bone Marrow Depression; anaemia, neutropenia, thrombocytopenia
- Lethargy and Anorexia
- Headaches

DOSE MODIFICATION

Haematological Toxicity:
Delay by one week if: If ANC < 1.5 or Platelets < 100.
Reduce dose if ANC< 1.0 x 10^9 /l or platelets < 50 x 10^9 /l
- If dose is 200mg/m2 reduce to 150mg/mg2
- If dose is 150mg/m2 reduce to 100mg/m2
- If dose is 100mg/m2 discontinue.

Non- Haematological Toxicity:
Any CTC Grade 3 non-haematological toxicity (except for alopecia, nausea, vomiting) reduce dose as described above
Any CTC Grade 4 Non-haematological toxicity discontinue

TREATMENT LOCATION

Can be given at Cancer Centre.

REFERENCES:

Thalidomide Maintenance (Multiple Myeloma)

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 28</td>
<td>Thalidomide</td>
<td>50-200mg*</td>
<td>ORAL</td>
<td>Once Daily at Night (Continuous)</td>
</tr>
</tbody>
</table>

*Starting dose 50mg escalating in 50mg increments each cycle to a maximum 200mg. (If patient is already on thalidomide under another protocol continue the dose from that protocol and escalate upwards from there if appropriate).

CYCLE LENGTH AND NUMBER OF DAYS

28 Day cycle, usually given for up to 6 cycles (until best response achieved)

APPROVED INDICATIONS

Multiple Myeloma

ELIGIBILITY CRITERIA

- Stable Disease

EXCLUSION CRITERIA

- Pregnancy / Breast Feeding
- Current Grade III – IV Peripheral Neuropathy
- Active thrombo-embolism

RECOMMENDED TAKE HOME MEDICATION

Consider if thrombo-prophylaxis is required (Aspirin, Warfarin or LMWH)

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH, β2-MicroGlobulin, Bone Marrow & Cytogenetics, Skeletal Survey, Bone Profile. Pregnancy Test (Women of Child Bearing Potential)

Prior to each cycle: U&Es, LFTs, FBC, Pregnancy Test (Women of Child Bearing Potential)
ASSESSMENT OF RESPONSE
Paraprotein, Urinary Light Chains, Immunoglobulins & Bone Marrow Biopsy as appropriate.

REVIEW BY CLINICIAN
Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW
As per locally agreed framework

ADMINISTRATION NOTES
• Patients must not become or attempt to become pregnant during thalidomide treatment. For women of child bearing potential, a negative pregnancy test during the 24 hours prior to each cycle of thalidomide will be required.

• Thalidomide Pharmion™ is licensed for the first-line treatment of multiple myeloma in the UK by Celgene, who have developed a risk management programme, ‘Thalidomide Pharmion™ Pregnancy Prevention Programme’

• In the Pregnancy Prevention Programme prescribers must:
  o Communicate the risks and benefits of Thalidomide Pharmion™ therapy to their patients
  o Prescribers must complete a ‘Treatment Initiation Form’ along with your patient (this only needs to be done once).
  o Provide the patient with a ‘Health Card’
  o Provide pregnancy prevention measures and counselling
  o Perform a pregnancy test (as appropriate) prior to each prescription
  o Supply a ‘Prescription Authorisation Form’ with each prescription to show confirmation that your patient has received counselling and pregnancy test date and result (if appropriate).
  o Remind your patient of the safe use of Thalidomide Pharmion™

• In the Pregnancy Prevention Programme pharmacists must
  o Register the Pharmacy with the Pregnancy Prevention Programme
  o Obtain a copy of the patient’s ‘Treatment Initiation Form’ before the first dispense
Dispense Thalidomide Pharmion™ only if the prescriber has annotated the ‘Prescription Authorisation Form’ correctly

Remind all patients of the safe use of Thalidomide Pharmion™, each time a prescription is dispensed

• Thalidomide is sedating and so should be taken at night.

• Thalidomide may cause venous thromboembolism – patients should be encouraged to report calf pain early.

TOXICITIES

Common: Sedation,

Less Common: Thromboembolism, Peripheral Neuropathy.

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Thalidomide is not normally myelosuppressive.

Non Haematological Toxicity:

• Dose reduction of steroids may be warranted if patient experiences significant side effects.

• Grade III – IV Toxicity: interrupt treatment for the remainder of current cycle and reintroduce at 50mg when toxicity resolves. Dose escalation may be appropriate if 50mg is tolerated.

• Thromboembolism: In the event of an embolic event, thalidomide should be stopped. Once adequate anti-coagulant control has been established consideration can be given to re-introduction of thalidomide at 50mg escalating to a maximum of 100mg.

Renal Function: No dose modification is recommended.

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.

REFERENCES:

Myeloma IX Trial Protocol.
Uftoral® (tegafur/uracil)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 28</td>
<td>tegafur/uracil</td>
<td>300 mg/m² and 672mg/m² *</td>
<td>Oral</td>
<td>In three divided doses</td>
</tr>
<tr>
<td>Days 1 to 28</td>
<td>calcium folinate</td>
<td>30mg</td>
<td>Oral</td>
<td>Three times Daily</td>
</tr>
</tbody>
</table>

**DOSE FORM**
Presented as capsules containing tegafur (100 mg) and uracil (224 mg).

**DOsing SCHEDULE**
Tegafur 300 mg/m²/day and 672 mg/m²/day uracil combined with 90 mg/day oral calcium folinate (calcium folinate), given in three divided doses. The daily dose per body surface area (BSA) is given below.

<table>
<thead>
<tr>
<th>BSA (m²)</th>
<th>Uftoral (capsules/day)</th>
<th>Daily schedule (number of capsules)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Morning</td>
<td>Midday</td>
</tr>
<tr>
<td>&lt; 1.17</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>1.17 - 1.49</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>1.50 - 1.83</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>&gt; 1.83</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**
Doses should be taken for 28 consecutive days. Subsequent cycles should start after 7 days without tegafur/uracil/calcium folinate (i.e. 35 days per treatment cycle).

**APPROVED INDICATIONS**
Tegafur/uracil is indicated for first-line treatment of metastatic colorectal cancer in combination with calcium folinate.
PREMEDICATION
None required

RECOMMENDED TAKE HOME MEDICATION
Metoclopramide 10 to 20mgs three to four times daily as required

INVESTIGATIONS / MONITORING REQUIRED
FBC, U&E LFT’s & tumour markers as appropriate prior to each course of chemotherapy

REVIEW BY CLINICIAN
5 weekly

NURSE / PHARMACIST LED REVIEW
Ongoing each cycle

ADMINISTRATION NOTES
• Tegafur/uracil as must be used with great care in patients who are known or suspected to have a dihydropyrimidine dehydrogenase deficiency
• Caution in patients with, renal or hepatic impairment, bowel obstruction, in patients with a history of significant cardiac disease.
• Patient compliance with oral therapy should be monitored. Checking that patients understand the prescribed administration schedule and that they can recognise adverse effects and the necessary course of action when they occur is recommended.
• Doses should be taken at least one hour before or one hour after meals for 28 consecutive days. Swallow whole with water

TOXICITIES
• Diarrhoea
• Abdominal pain
• Nausea and vomiting
• Fatigue, asthenia, anorexia
• Stomatitis
• Cardiotoxicity - Occasionally patients with heart disease may experience coronary artery spasm. Stop treatment if this occurs.
## DOSE MODIFICATION

<table>
<thead>
<tr>
<th>Common Toxicity Criteria (CTC) Grade</th>
<th>Uftoral Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Haematological Toxicity (including diarrhoea)</strong></td>
<td></td>
</tr>
<tr>
<td>0 to 1</td>
<td>No change.</td>
</tr>
<tr>
<td>2</td>
<td>Therapy withheld until toxicity resolves to grade 1. No change in subsequent dose.</td>
</tr>
<tr>
<td>3 to 4</td>
<td>Therapy withheld until toxicity resolves to grade 1. Decrease subsequent dose by 1 capsule/day. Dose reduction maintained for remainder of therapy.</td>
</tr>
<tr>
<td><strong>Haematological Toxicity (based on granulocyte or platelet count)</strong></td>
<td></td>
</tr>
<tr>
<td>0 to 1</td>
<td>No change.</td>
</tr>
<tr>
<td>2 to 4</td>
<td>Therapy withheld until granulocytes ≥ 1500/mm³ and platelets ≥ 100,000/mm³.</td>
</tr>
<tr>
<td><strong>Haematological Toxicity: Retreatment</strong></td>
<td></td>
</tr>
<tr>
<td>0 to 2</td>
<td>No change.</td>
</tr>
<tr>
<td>3 to 4</td>
<td>Decrease subsequent dose by 1 capsule/day. Dose reduction maintained for ongoing cycle and remainder of therapy.</td>
</tr>
</tbody>
</table>

† Calcium folinate dose remains unchanged, even if < 3 Uftoral capsules/day are required. If Uftoral therapy is interrupted, calcium folinate must also be stopped. When Uftoral therapy is interrupted, doses that are missed during 28 consecutive days of treatment should not be taken later.

### TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit

### References

- NICE guidance TA61 Colorectal cancer - capecitabine and tegafur uracil: Guidance: May 2003

Version 3: Issued 25th July 2008: Readers are advised to check NECN website [www.cancernorth.nhs.uk](http://www.cancernorth.nhs.uk) to ensure they are using most up to date version
VEPEMB (Hodgkin's Lymphoma)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ondansetron</td>
<td>8mg</td>
<td>IV bolus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vinblastine</td>
<td>6mg/m²</td>
<td>IV bolus</td>
<td>via 0.9% Sodium Chloride Drip</td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide</td>
<td>500mg/m²</td>
<td>IV bolus</td>
<td>via 0.9% Sodium Chloride Drip</td>
</tr>
<tr>
<td>1 to 5</td>
<td>Procarbazine</td>
<td>100mg/m²</td>
<td>ORAL</td>
<td>Once Daily For 5 days</td>
</tr>
<tr>
<td></td>
<td>Prednisolone EC</td>
<td>40mg</td>
<td>ORAL</td>
<td>Once Daily For 5 days</td>
</tr>
<tr>
<td>15</td>
<td>Ondansetron</td>
<td>8mg</td>
<td>IV bolus</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Mitoxantrone</td>
<td>6mg/m² (diluted to 50ml)</td>
<td>IV bolus</td>
<td>via 0.9% Sodium Chloride Drip</td>
</tr>
<tr>
<td>15</td>
<td>Hydrocortisone</td>
<td>100mg</td>
<td>IV bolus</td>
<td>via 0.9% Sodium Chloride Drip</td>
</tr>
<tr>
<td>15</td>
<td>Bleomycin</td>
<td>10,000 iu/m² (Max: 15,000 iu)</td>
<td>IV infusion</td>
<td>100ml 0.9% Sodium Chloride</td>
</tr>
<tr>
<td>15 to 19</td>
<td>Etoposide</td>
<td>60mg/m²</td>
<td>ORAL</td>
<td>Once Daily For 5 days</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**

28 Day cycle, usually given for a maximum of 6 cycles

**APPROVED INDICATIONS**

Hodgkin’s Lymphoma in Older Patients

**ELIGIBILITY CRITERIA**

- Over 60 years of age
RECOMMENDED TAKE HOME MEDICATION

- Allopurinol 300mg Once Daily with first cycle of treatment
- Metoclopramide 10mg Three Times Daily, if required, for 14 days
- Gastro prophylaxis (Proton Pump Inhibitor or H2 Antagonist) should be considered with the steroid.
- Co-trimoxazole 960mg three times per week to continue until 6 months after treatment stops
- Antifungal (Fluconazole) and antibiotic cover (Ciprofloxacin) may be appropriate during period while ANC < 0.5 cells $\times 10^9/l.$

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: FBC, U&Es, LFTs, LDH, Chest X-Ray, CT scan, ECG, Consider ECHO

Prior to each cycle: FBC, U&Es, LFTs

ASSESSMENT OF RESPONSE

Measure palpable disease. CT scan at mid point of treatment and after completion of therapy.

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Vinblastine is for intravenous use only. Administration by other routes may be fatal. To reduce the risk of error, vinblastine should be diluted to 20ml.
- Procarbazine dose can be taken in three divided doses. (Total daily dose: 100mg/m²)
- Patients must not drink alcohol while taking procarbazine (risk of disulfiram type reaction)
- Patients requiring blood transfusion will require irradiated blood products.
• Bleomycin can cause pulmonary fibrosis. Patients should receive pre-
medication with hydrocortisone before receiving bleomycin to
minimise the risks.
• Etoposide capsules are supplied as 50mg and 100mg. 100mg capsules
are very large and patients with swallowing difficulties would be better
prescribed multiples of 50mg. Doses should normally be rounded up
to the nearest 50mg
• Procarbazine is supplied as 50mg capsules. Dose should normally be
rounded up to the nearest 50mg.

TOXICITIES
• Common: Mild Nausea/Vomitting, Mucositis, Myelosupression,
Fatigue, Constipation, Dyspepsia, Glucose Intolerance, Alopecia
• Less Common: Fever, Flushing or Rash, Allergic Reaction, Pulmonary
Toxicity, Neurotoxicity (paraesthesia), SiADH, cardiotoxicity,
arrhythmias.

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity: (Note: where haematological disease is affecting bone
marrow function, lower treatment parameters may be acceptable. This should be clearly
documented for the specific patient.)

On Day 1:

<table>
<thead>
<tr>
<th>ANC (cells x10⁹/l)</th>
<th>PLT (cells x10⁹/l)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2.0</td>
<td>≥ 100</td>
<td>Give 100% Doses</td>
</tr>
<tr>
<td>&lt; 2.0</td>
<td>&lt; 100</td>
<td>Delay 1 week. Consider GCSF support</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>&lt; 75</td>
<td>Delay Treatment</td>
</tr>
</tbody>
</table>

Renal Function:

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Etoposide</th>
<th>Bleomycin</th>
<th>Cyclophosphamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50 ml/min</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>30 – 50 ml/min</td>
<td>80%</td>
<td>75%</td>
<td>75%</td>
</tr>
<tr>
<td>10 – 29 ml/min</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
</tr>
<tr>
<td>&lt; 10ml/min</td>
<td>75%</td>
<td>50%</td>
<td>50%</td>
</tr>
</tbody>
</table>
Hepatic Function:

<table>
<thead>
<tr>
<th>AST (iu/l)</th>
<th>Bilirubin (µmol/l)</th>
<th>Vinblastine</th>
<th>Procarbazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60</td>
<td>and &lt; 26</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>60 – 180</td>
<td>or 26 – 51</td>
<td>50%</td>
<td>100%</td>
</tr>
<tr>
<td>Normal</td>
<td>and &gt; 51</td>
<td>50%</td>
<td>100%</td>
</tr>
<tr>
<td>&gt; 180 iu/l</td>
<td>and &gt; 51</td>
<td>Omit</td>
<td>100%</td>
</tr>
<tr>
<td>&gt; 180 iu/l</td>
<td>or &gt; 85</td>
<td>Omit</td>
<td>Contraindicated</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bilirubin (µmol/l)</th>
<th>Etoposide</th>
<th>Mitoxantrone</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>20 – 51</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>&gt; 51</td>
<td>Clinical decision</td>
<td>25%</td>
</tr>
</tbody>
</table>

Free etoposide concentration may be increased by low plasma protein, further increasing toxicity.

TREATMENT LOCATION

Suitable for administration in chemotherapy day units, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES:

- Proctor SJ et al. A phase II study VEPEMB in patients with Hodgkins Disease aged over 60 years (Shield Study)
Vinorelbine Oral

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Vinorelbine</td>
<td>60 to 80 mg/m²</td>
<td>Oral</td>
<td>ONCE ONLY For 1 day only</td>
</tr>
<tr>
<td>Day 8</td>
<td>Vinorelbine</td>
<td>60 to 80 mg/m²</td>
<td>Oral</td>
<td>ONCE ONLY For 1 day only</td>
</tr>
<tr>
<td>Day 15*</td>
<td>Vinorelbine</td>
<td>60 to 80 mg/m²</td>
<td>Oral</td>
<td>ONCE ONLY For 1 day only</td>
</tr>
</tbody>
</table>

Caution: **DAY 15 is not given as part of NECN lung cancer protocol.**

**ORAL VINORELBINE DOSAGE**

Vinorelbine oral is available as 20mg and 30mg capsules

The following table gives the dose required for range of body surface area.

<table>
<thead>
<tr>
<th>Body Surface Area (BSA)</th>
<th>60 mg/m² Dose</th>
<th>80 mg/m² Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.25 to 1.34</td>
<td>80 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>1.35 to 1.44</td>
<td>80 mg</td>
<td>110 mg</td>
</tr>
<tr>
<td>1.45 to 1.54</td>
<td>90 mg</td>
<td>120 mg</td>
</tr>
<tr>
<td>1.55 to 1.64</td>
<td>100 mg</td>
<td>130 mg</td>
</tr>
<tr>
<td>1.65 to 1.74</td>
<td>100 mg</td>
<td>140 mg</td>
</tr>
<tr>
<td>1.75 to 1.84</td>
<td>110 mg</td>
<td>140 mg</td>
</tr>
<tr>
<td>1.85 to 1.94</td>
<td>110 mg</td>
<td>150 mg</td>
</tr>
<tr>
<td>≥ 1.95</td>
<td>120 mg</td>
<td>160 mg</td>
</tr>
</tbody>
</table>

Total dose must never exceed 160 mg per week. Even for patients with BSA ≥ 2 m²

**Dose Escalation**

The manufacturer recommends escalation of oral vinorelbine dose from 60mg/m² after first three administrations to 80mg/m² except in those patients for whom the neutrophil count dropped once below 0.5 x 10⁹/l, or more than once between 0.5 and 1 x 10⁹/l during the first three administrations at 60mg/m².

When used in combination with trastuzumab, dose escalation above 60mg/m² adds limited benefit with greater toxicity.
**CYCLE LENGTH AND NUMBER OF DAYS**

**BREAST CANCER:** 21 day cycle, Day 1 & Day 8, Day 15.

**LUNG CANCER:** Every 21 days Day 1 & Day 8, omit day 15.

**APPROVED INDICATIONS**

- For the treatment of advanced breast cancer stage 3 and 4, relapsing after or refractory to an anthracycline containing regimen.
- First-line therapy for NSCLC for patients that cannot receive platinum based therapy

**PREMEDICATION**

Single oral dose of metoclopramide 10mg or ondansetron 8mg given 30 minutes before vinorelbine dose.

**RECOMMENDED TAKE HOME MEDICATION**

Metoclopramide 10 to 20mgs three to four times daily as required

**INVESTIGATIONS / MONITORING REQUIRED**

FBC, U&E, LFT & CXR prior to commencing

FBC, U&E & LFT’s prior to each cycle

**ASSESSMENT OF RESPONSE**

Metastatic: Tumour size and patient symptomatic response

**REVIEW BY CLINICIAN**

To be reviewed by either Nurse, Pharmacist or Clinician before every cycle.

**NURSE / PHARMACIST LED REVIEW**

On day 8 and /or day 15 of each cycle

**ADMINISTRATION NOTES**

- Vinorelbine IV 25 mg/m² is equivalent to Vinorelbine oral 60 mg/m²
- Vinorelbine IV 30 mg/m² is equivalent to Vinorelbine oral 80 mg/m²
- Food does not affect absorption but it is advised to take with food to reduce gastro-intestinal upset.
- Patient’s ability to drive or operate machinery may be affected however this is unlikely.
TOXICITIES

- Rare anaphylaxis
- Severe venous irritation, discoloration and/or pain during injection
- Nausea & Vomiting
- Constipation
- Peripheral Neuropathy
- Fatigue, Myalgia
- Alopecia (Rare/mild)
- Myelosupression (Neutropenia common)

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

**Day One:**

Proceed if neutrophil count > 1.5, WBC > 3.0, plts >100, unless directed by an Oncology specialist.

Delay 1 week on DAY 1 if:

<table>
<thead>
<tr>
<th>WCC</th>
<th>PLT</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3.0</td>
<td>&lt;100</td>
<td>&lt; 1.5</td>
</tr>
</tbody>
</table>

**Day Eight/Fifteen**

Proceed on if neutrophil count > 1.0, plts >100, unless directed by an Oncology specialist.

Omit treatment On DAY 8/ 15 if:

<table>
<thead>
<tr>
<th>PLT</th>
<th>ANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100</td>
<td>&lt; 1.0</td>
</tr>
</tbody>
</table>

**NB** On Day 8 of the cycle patients whose bloods are not at the required level will miss that dose and proceed to the next cycle of treatment as planned

- If WCC, Platelets or ANC still below required levels for treatment at after one week delay, delay treatment again and patient will need assessed and chemotherapy dose reduction by Oncologist
• If Hb < 10 & patient symptomatic will need blood transfusion, but may proceed with chemotherapy as planned if performance status (PS) stable.

• If pre-treatment (Day 1) U&E’s & LFT’s abnormal, delay treatment 1 week and discuss with Oncologist as may need dose reduction, On Day 8 Patient will miss that dose and proceed to next cycle of chemotherapy as planned.

Non-Haematological Toxicity:

If PS deteriorates to 3 or 4 and on assessment patient is more symptomatic withhold treatment and discuss with Oncologist

TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit

REFERENCES:


• Zelek L, Barthier S, Riofrio M et al. (2001) Weekly vinorelbine is an effective palliative regimen after failure with anthracyclines and taxanes in metastatic breast carcinoma. Cancer. 92: 2267


Z-DEX (Multiple Myeloma)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 5</td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>Oral</td>
<td>Three Times Daily</td>
</tr>
<tr>
<td>1 to 4</td>
<td>Idarubicin</td>
<td>10mg/m²</td>
<td>ORAL</td>
<td>Once Daily for Four days Only</td>
</tr>
<tr>
<td>1 to 4*</td>
<td>Dexamethasone</td>
<td>40*mg</td>
<td>ORAL</td>
<td>Once Daily for Four days Only</td>
</tr>
</tbody>
</table>

* Reduce dexamethasone dose to 20mg in patients over 60 years of age

**On the first cycle give Dexamethasone 40*mg daily on days 1 to 4, 8 to 11 and 15 to 18**

**CYCLE LENGTH AND NUMBER OF DAYS**

Minimum 21 Day cycle, usually given for up to 6 cycles

**APPROVED INDICATIONS**

- Relapsed Multiple Myeloma
- Prior to auto transplant for consolidation

**EXCLUSION CRITERIA**

- Patients with significant reduction in Left Ventricular Ejection Fraction
- Patients having reached a maximum lifetime cumulative dose of Idarubicin or any other Anthracycline

**RECOMMENDED TAKE HOME MEDICATION**

Allopurinol 300mg once daily for 7 days, during first cycle if appropriate.

Metoclopramide 10mg Three Times Daily.

Consider prescribing Gastro Prophylaxis (Proton Pump Inhibitor) for cover with dexamethasone.

Ciprofloxacin 250mg Twice Daily for 10 days may be appropriate in elderly patients

Fluconazole 100mg daily may be appropriate in patients susceptible to oral Candida infections with high dose steroids.
INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: CT Scan, Chest X-Ray, FBC, U&Es, LFTs, LDH, β2-MicroGlobulin, Para-protein (Urine & Serum), Calcium, Group & Save depending on Hb.

Prior to each cycle: U&Es, LFTs, FBC, Para-protein (Urine & Serum), Calcium, Group & Save depending on Hb.

ASSESSMENT OF RESPONSE

Para-protein, Bone Marrow Biopsy and Symptom Control.

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework

ADMINISTRATION NOTES

- Idarubicin is available as 5mg, 10mg and 25mg capsules.
- There have been fatalities with this regimen when the total dose of idarubicin was given for each of the 4 days.
- Patients with pre-existing cardiac disease should be considered for ECHO Cardiogram.
- Maximum Lifetime Dose of Idarubicin: 400mg/m²
- Diabetic patients should increase monitoring on blood glucose
- Many centres give this regimen over 28 days instead of 21 days.
- May discolour urine red for 1-2 days after treatment
- Capsules should ideally be taken with a light meal (e.g. Breakfast).

TOXICITIES

Common: Alopecia, Moderate Emesis, Myelosupression, Fatigue, Dyspepsia, Increased Glucose, Insomnia, Agitation

Less Common: Flushing or Rash, Allergic Reaction, Cardiac Toxicity, Mood Disturbances

Version 3: Issued 25th July 2008: Readers are advised to check NECN website www.cancernorth.nhs.uk to ensure they are using most up to date version
DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.3 x 10^9 cells/l or PLT < 75 x 10^9 cells/l.

Renal Function:

Based on the dosage protocol adopted in a number of Phase III clinical trials of idarubicin, dose modification is required according to the following schedule:

<table>
<thead>
<tr>
<th>Serum Cr</th>
<th>Idarubicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100 µmol/l</td>
<td>100%</td>
</tr>
<tr>
<td>100–175 µmol/l</td>
<td>50%</td>
</tr>
<tr>
<td>&gt; 175 µmol/l</td>
<td>Clinical Decision</td>
</tr>
</tbody>
</table>

Hepatic Function:

The following dose reductions are recommended for idarubicin when bilirubin is increased:

<table>
<thead>
<tr>
<th>Bilirubin</th>
<th>Idarubicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20 µmol/l</td>
<td>100%</td>
</tr>
<tr>
<td>21–51 µmol/l</td>
<td>50%</td>
</tr>
<tr>
<td>51–85 µmol/l</td>
<td>25%</td>
</tr>
<tr>
<td>86 µmol/l</td>
<td>Contra-indicated</td>
</tr>
</tbody>
</table>

TREATMENT LOCATION

Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 to 4 Haematology Services.

REFERENCES:

APPENDIX ONE ADDITIONAL REFERENCES

Note the primary references for regimen protocols are listed in the monographs but in addition the following sources were consulted during preparation of the drug monographs and reference protocols;


http://www.bccancer.bc.ca  individual drug and regimen monographs.


APPENDIX TWO: GLOSSARY OF TERMS

ANC: Absolute Neutrophil Count. Values expressed in this handbook refer to number of cells x10^9 per litre unless stated otherwise. Caution should be exercised to ensure that the neutrophil count is an absolute count rather than a percentage of reported white cells.

Cytotoxic drug: drugs which are damaging to cells. Effects are greatest on cells which are rapidly reproducing.

Emetogenic potential: the likelihood of inducing nausea or vomiting.

Hand and foot syndrome: also known as palmar plantar syndrome, soreness and redness or darkening of the palms of the hands and soles of the feet can occur. Can also manifest as a rash and dry or itchy skin. Vitamin B6 (pyridoxine) can reduce this.

Mucositis: inflammation of a mucous membrane

PCP: pneunocystis pneumonia. An opportunistic pneumonia caused by Pneumocystis carinii

PLT: Platelets. Values expressed in this handbook refer to number of cells x10^9 per litre unless stated otherwise.

SPC: Summary of Product Characteristics accessed via www.medicines.org.uk

Stomatitis: any disorder of the mouth

WCC or WBC: White Blood Cells. Values expressed in this handbook refer to number of cells x10^9 per litre unless stated otherwise.
APPENDIX THREE

SUPPLEMENTARY REGIMEN INFORMATION

This section gives brief summary of predominantly IV regimens that have an oral component and lists regimens not in current/regular use in NECN

ATRA – APML (maintenance)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATRA (tretinoin)</td>
<td>45mg/m²/day</td>
<td>oral</td>
<td>Days 1 to 15</td>
</tr>
<tr>
<td>6-Mercaptopurine</td>
<td>90mg/m²/day</td>
<td>oral</td>
<td>Days 1 to 15</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>15mg/m²/week</td>
<td>oral</td>
<td>Days 1 to 15</td>
</tr>
</tbody>
</table>

CAPOX/ XELOX

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxaliplatin</td>
<td>130mg/m²</td>
<td>IV Infusion</td>
<td>Day 1</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>1000mg/m²</td>
<td>Twice daily</td>
<td>Oral Days 1 to 14</td>
</tr>
</tbody>
</table>

CE for SCLC (4 weekly version)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>AUC 5 or 6</td>
<td>IV Infusion</td>
<td>Day 1</td>
</tr>
<tr>
<td>IV Etoposide</td>
<td>120 mg/m²</td>
<td>Once Daily</td>
<td>IV Infusion</td>
</tr>
<tr>
<td>Oral Etoposide</td>
<td>120 mg/m²</td>
<td>Twice daily</td>
<td>oral</td>
</tr>
</tbody>
</table>

CE for SCLC (3 weekly version)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>AUC 5 or 6</td>
<td>IV Infusion</td>
<td>Day 1</td>
</tr>
<tr>
<td>IV Etoposide</td>
<td>100 mg/m²</td>
<td>Once Daily</td>
<td>IV Infusion</td>
</tr>
<tr>
<td>Etoposide</td>
<td>100 mg</td>
<td>Twice daily</td>
<td>oral</td>
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C-VAD

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>16 mg/m²/day</td>
<td>IV Infusion</td>
<td>Days 1 to 4</td>
</tr>
<tr>
<td>Vincristine</td>
<td>0.4 mg/day</td>
<td>IV Infusion</td>
<td>Days 1 to 4</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>500mg Once Only</td>
<td>Oral</td>
<td>Once Weekly</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>40mg /day</td>
<td>Oral</td>
<td>Days 1 to 4</td>
</tr>
</tbody>
</table>
### ECX/EcarboX for upper GI cancers

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epirubicin</td>
<td>50 mg/m²</td>
<td>IV Bolus</td>
<td>Day 1</td>
</tr>
<tr>
<td>Cisplatin/Carboplatin</td>
<td>50 mg/m² / AUC5</td>
<td>IV Infusion</td>
<td>Day 1</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>625 mg/m² Twice daily</td>
<td>Oral</td>
<td>Days 1 to 21</td>
</tr>
</tbody>
</table>

### NP

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vinorelbine</td>
<td>25-30 mg/m² (60mg max)</td>
<td>IV bolus</td>
<td>Day 1</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>AUC 5 or 6</td>
<td>IV Infusion</td>
<td>Day 1</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>60-80 mg/m²</td>
<td>Oral</td>
<td>Day 8</td>
</tr>
</tbody>
</table>

### PVACE-BOP

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vinblastine</td>
<td>6 mg/m² (max 10mg)</td>
<td>IV Bolus</td>
<td>Day 1</td>
</tr>
<tr>
<td>Etoposide</td>
<td>100 mg/m²</td>
<td>IV Bolus</td>
<td>Day 1</td>
</tr>
<tr>
<td>Etoposide</td>
<td>200 mg/m² / day</td>
<td>oral</td>
<td>Days 2,3</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>6 mg/m² / day</td>
<td>oral</td>
<td>Days 1 to 14</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>100 mg/m² / day</td>
<td>oral</td>
<td>Days 1 to 14</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>25 mg/m²</td>
<td>IV Bolus</td>
<td>Day 8</td>
</tr>
<tr>
<td>Vincristine</td>
<td>2 mg</td>
<td>IV Bolus</td>
<td>Day 8</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>6 mg/m²</td>
<td>IV Bolus</td>
<td>Day 15</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>6 mg/m²</td>
<td>IV Bolus</td>
<td>Day 22</td>
</tr>
<tr>
<td>Prednisolone c/e</td>
<td>40mg/day</td>
<td>oral</td>
<td>Days 14 to 28</td>
</tr>
</tbody>
</table>

### P-COME

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorambucil</td>
<td>10mg / day</td>
<td>oral</td>
<td>Days 1 to 15</td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td>10 mg/m²</td>
<td>IV Infusion</td>
<td>Day 1</td>
</tr>
<tr>
<td>Vincristine</td>
<td>2 mg</td>
<td>IV Bolus</td>
<td>Day 15</td>
</tr>
<tr>
<td>Etoposide</td>
<td>100 mg/m²</td>
<td>IV Bolus</td>
<td>Day 15*</td>
</tr>
<tr>
<td>Etoposide</td>
<td>40mg/m² / day</td>
<td>oral</td>
<td>Days 16 &amp; 17</td>
</tr>
<tr>
<td>Prednisolone c/e</td>
<td>40mg / day</td>
<td>oral</td>
<td>Days 1 to 15</td>
</tr>
</tbody>
</table>

Version 3: Issued 25th July 2008: Readers are advised to check NECN website www.cancernorth.nhs.uk to ensure they are using most up to date version.
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