CCC Chemotherapy Protocols

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Haematological Malignancies

Hodgkins disease
Early HD  PET/CT as part of staging

Group I  Involved field XRT

Group II  ABVD x 3 + IF XRT

Group III  Three cycles full dose chemotherapy + IF XRT
          or
          6 cycles full dose chemotherapy + IF XRT if residual abnormality

Advanced HD
Stages III / IV or I / II with mediastinal bulk + / - B symptoms

ABVD  
Doxorubicin  25mg/m² IV  day 1 and 15
Bleomycin  10000iu/m² IV  day 1 and 15
Hydrocortisone  100mg IV  day 1 and 15
Vinblastine  6mg/m² IV  day 1 and 15 (max 10mg)
Dacarbazine  350mg/m² IV  day 1 and 15

Repeat at 28 day intervals to CR + 2, min 6 max 8 cycles

Laboratory Investigations
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

ChlVPP  
Vinblastine  6mg/m² IV  days 1 and 8 (max 10mg)
Chlorambucil  6mg/m² po  days 1-14
Prednisolone  40mg po  days 1-14
Procarbazine  50mg oral tds  days 1-14

Repeat 28 days from day 1 x 6 cycles)
Laboratory Investigations

- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply
Non-Hodgkins Lymphoma
Low grade
First line

CVP-R
- Cyclophosphamide 600mg/m² IV day 1
- Vincristine 1.4mg/m² IV day 1 (maximum 2mg)
- Prednisolone 50mg orally days 1-5
- Rituximab 375mg/m² IV day 1

Repeat at 21 day intervals to a maximum of 6-8 cycles.

Laboratory Investigations
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

*Bendamustine 120mg/m² IV days 1 and 2
Repeat at 21 day intervals to a maximum of 8 cycles

Laboratory Investigations
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

*NB available via the Cancer Drug Fund

CHOP-R
- Cyclophosphamide 750mg/m² IV day 1
- Doxorubicin 50mg/m² IV day 1
- Vincristine 1.4mg/m² IV day 1
- Prednisolone 50mg po days 1-5
- Rituximab 375mg/m² IV day 1

Repeat at 21 day intervals for 6 cycles

Criteria: fit patients with bulky disease
Laboratory Investigations
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

*Maintenance Rituximab

Rituximab 375mg/m\(^2\) IV every 3 months for 2 years

Criteria  CR or PR following first line therapy
           Must commence within 2 months of completion of first line therapy

*Maintenance Bendamustine

Bendamustine 120mg/m\(^2\) IV days 1 and 2

Repeat at 21 day intervals to a maximum of 8 cycles

Criteria  Option for first line therapy

Laboratory Investigations
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

*NB available via the Cancer Drug Fund

Second Line

*Bendamustine 120mg/m\(^2\) IV days 1 and 2
Repeat at 21 day intervals to a maximum of 8 cycles

Laboratory Investigations
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

Criteria
- Unable to receive R-CHOP
- Unable to receive high dose therapy

*NB available via the Cancer Drug Fund

Second / third line

Chlorambucil +/- Prednisolone

Chlorambucil 10mg daily orally for 14 days
+ Prednisolone 20mg oral daily for 14 days

Repeat at 28 day intervals for up to 6 cycles

Laboratory Investigations
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

Fludarabine Fludarabine 40mg/m² orally days 1-5 (only 3 days if heavily pre-treated)
Repeat at 28 day intervals max 6 cycles

Criteria     Progressed after alkylating agents and anthracyclines  
Age < 75yrs                    PS 0-1
Normal marrow function

NB: patients receiving fludarabine should have all blood products irradiated

Laboratory Investigations
• Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
• Where renal / hepatic function are abnormal treatment is at physician discretion
• FBC prior to each cycle
• Normal FBC limits for administration apply

Rituximab
Rituximab 375mg/m$^2$ in 500ml Sodium chloride 0.9% IV weekly x 4

Criteria     Stage III / IV follicular / Mantle cell NHL
Chemoresistant (prior alkylating agent and anthracycline chemotherapy)
Normal renal / hepatic function
Anticipated survival > 3 months
Age < 65yrs                    PS 0-2
Not eligible for a clinical trial

Intermediate / High grade

Stage I
CHOP x 3 + involved field XRT

Laboratory Investigations
• Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
• Where renal / hepatic function are abnormal treatment is at physician discretion
• FBC prior to each cycle
• Normal FBC limits for administration apply

**Stage II-IV**

CHOP-R

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>750mg/m² IV</td>
<td>day 1</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>50mg/m² IV</td>
<td>day 1</td>
<td></td>
</tr>
<tr>
<td>Vincristine</td>
<td>1.4mg/m² IV</td>
<td>day 1 (max. 1mg &gt;70)</td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td>50mg po</td>
<td>days 1-5</td>
<td></td>
</tr>
<tr>
<td>Rituximab</td>
<td>375mg/m² IV</td>
<td>day 1</td>
<td></td>
</tr>
</tbody>
</table>

Repeat at 21 day intervals for 6 cycles

**Laboratory Investigations**

- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

**Relapsed Intermediate / High grade**

A proportion of patients with relapsed intermediate / high grade NHL may be salvaged with high dose chemotherapy + marrow / PBSC rescue. Patients in this situation should be discussed with the NHL MDT at the Royal Liverpool Hospital.
Head and Neck Cancer

Locally advanced disease

XRT + Cisplatin/5FU

Cisplatin 80mg/m² IV day 1
Fluorouracil 1g/m² over 24hrs IV days 1-4

Repeat at 21 day intervals for 2-4 cycles prior to XRT

Laboratory investigations

• Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
• Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
• Where renal / hepatic function are abnormal treatment is at physician discretion
• FBC prior to each cycle
• Normal FBC limits for administration apply

or

XRT + Cisplatin

Cisplatin 100mg/m² IV days 1, 22, and 43 with concomitant XRT

Laboratory investigations

• Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
• Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
• Where renal / hepatic function are abnormal treatment is at physician discretion
• FBC prior to each cycle
• Normal FBC limits for administration apply

or

XRT + Cisplatin / 5FU / Docetaxel

Cisplatin 80mg/m² IV day 1
Fluorouracil 1000mg/m² over 24hrs IV days 1-4
Docetaxel 75mg/m² IV day 1

Repeat at 21 day intervals for 3 cycles prior to CTX/XRT
Criteria  Locally advanced SCC suitable for CTX/XRT
PS 0/1
Creatinine clearance > 50mls/min

Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

XRT + Cetuximab

Cetuximab  400mg/m$^2$ IV loading dose 1 week prior to XRT
250mg/m$^2$ IV weekly during XRT

Criteria  Locally advanced SCC suitable for CTX/XRT
Unsuitable for cisplatin eg creatinine clearance < 50mls/min
PS 0/1

Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

Recurrent or Metastatic Disease

Cisplatin/5FU

Cisplatin  80mg/m$^2$ IV  day 1
Fluorouracil  1g/m$^2$ IV over 24hrs  days 1-4

or

Cisplatin

Cisplatin  100mg/m$^2$ IV
Repeat at 21 day intervals max 6 cycles

Laboratory investigations
- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

*Cisplatin or Carboplatin + /5FU + Cetuximab

**Cisplatin/5FU**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Route</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>80mg/m² IV</td>
<td>day 1</td>
<td></td>
</tr>
<tr>
<td>5Fluorouracil</td>
<td>1g/m² IV over 24hrs</td>
<td>days 1-4</td>
<td></td>
</tr>
</tbody>
</table>

Repeat at 21 day intervals max 6 cycles

Or

**Carboplatin/5FU**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Route</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>AUC 5</td>
<td>Day 1</td>
<td></td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>1g/m² IV over 24hrs</td>
<td>Days 1-4</td>
<td></td>
</tr>
</tbody>
</table>

Repeat at 21 day intervals max 6 cycles

**Cetuximab**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>400mg/m² IV</td>
<td>loading dose week 1</td>
</tr>
<tr>
<td></td>
<td>250mg/m² IV</td>
<td>weekly during chemotherapy and may be continued until progression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Criteria 1st line chemotherapy for advanced disease

PS 0/1

No prior treatment with cetuximab

**Laboratory investigations**

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

*Available via the cancer drugs fund

**2nd Line Chemotherapy for advanced disease**
Paclitaxel  
135-175mg/m^2 IV over 3hrs

Dose depends on PS and extent of prior therapy

Premedication
Chlorphenamine 10mg IV
Dexamethasone 20mg IV
Ranitidine 50mg IV

Repeat at 21 day intervals, max 6 cycles

Criteria PS 0-1

Nasopharyngeal Carcinoma

Chemoradiation + Adjuvant Chemotherapy
Criteria Nasopharyngeal carcinoma Stage III/IV
Creatinine clearance > 50ml/min

Chemoradiation
Cisplatin 100mg/m^2 days 1, 22, 43 to start prior to XRT

Laboratory investigations
- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply followed by:

Adjuvant chemotherapy
Commencing 21 days after 3rd cycle of cisplatin

Cisplatin 80mg/m^2 IV day 1
Fluorouracil 1g.m^2 IV over 24 hrs days 1-4

Repeat at 21 day intervals for 3 cycles

Laboratory investigations
- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
• Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
• Where renal / hepatic function are abnormal treatment is at physician discretion
• FBC prior to each cycle
• Normal FBC limits for administration apply
Thyroid Cancer

Medullary Thyroid Cancer

*Vandetanib
Continue until disease progression

Criteria  PS  0-2
Locally advanced unresectable / metastatic
First line

Laboratory investigations
- FBC, U/Es, LFTs prior to each cycle
- Where renal / hepatic function are abnormal treatment is at physician discretion
- Discontinue if deteriorating renal or liver function
Normal FBC limits for administration apply

*NB available via the Cancer Drug

Papillary or Follicular Thyroid Cancer

Sorafenib  400mg bd oral continuously
Continue until disease progression

Criteria  PS  0-2
Refractory to radioiodine

Laboratory investigations
- FBC, U/Es, LFTs prior to each cycle
- Where renal / hepatic function are abnormal treatment is at physician discretion
- Discontinue if deteriorating renal or liver function
- Normal FBC limits for administration apply

*NB available via the Cancer Drugs fund
Sarcomas

Soft Tissue Sarcoma

Adjuvant

There is no proven role for adjuvant chemotherapy for soft tissue sarcomas. However, treatment may be considered when chemo-sensitive tumours such as rhabdomyosarcoma, synovial sarcoma are resected with close margins.

Neo-adjuvant

Suggested protocol for downsizing prior to surgery

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>20mg/m²</td>
<td>1,2,3</td>
</tr>
<tr>
<td>Mesna prior to ifosfamide</td>
<td>3g/m²</td>
<td>1,2,3</td>
</tr>
<tr>
<td>Ifosfamide + Mesna</td>
<td>3g/m² / 3g/m²</td>
<td>1,2,3</td>
</tr>
<tr>
<td>Mesna post ifos/mesna infusion</td>
<td>3g/m²</td>
<td>1,2,3</td>
</tr>
</tbody>
</table>

Advanced

There is no evidence that combinations are superior to single agents as palliative chemotherapy

First line

**Doxorubicin**

- Doxorubicin 75mg/m² IV q 21 days x 6 cycles

Laboratory Investigations

- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

Second line

**Ifosfamide**

- Mesna prior to ifosfamide 3g/m² days 1,2,3
- Ifosfamide/Mesna 3g/m² days 1,2,3
- Mesna post ifos/mesna infusion 3g/m² days 1,2,3

Repeat at 21 day intervals for up to 6 cycles

Laboratory Investigations

- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
• Where renal / hepatic function are abnormal treatment is at physician discretion
• FBC prior to each cycle
• Normal FBC limits for administration apply

**Dacarbazine** 800mg/m² IV day 1

Repeat at 21 day intervals for up to 6 cycles

**Laboratory Investigations**

• Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
• Where renal / hepatic function are abnormal treatment is at physician discretion
• FBC prior to each cycle
• Normal FBC limits for administration apply

*Trabectedin*

Consider in select cases of advanced STS- Failure after treatment with anthracyclines and ifosfamide or intolerant/contraindications to anthracyclines and ifosfamide.

Consider in Myxoid liposarcomas and leiomyosarcomas.

PS 0-2

1.5 mg/m² as IV infusion over 24 hours every 21 days.

*NB Available via the off-protocol mechanism*
Osteosarcoma / MFH of bone / Leiomyosarcoma of Bone

Neoadjuvant / Post operative schedule

PAM x 2 -> Surgery (week 10) -> PAM x 2 -> Doxorubicin - Methotrexate x 2

<table>
<thead>
<tr>
<th>PAM</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>60mg/m² IV</td>
<td>day 1, 2</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>25mg/m² IV</td>
<td>days 1, 2, 3</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>12g/m² IV</td>
<td>days 22 and 29</td>
<td></td>
</tr>
</tbody>
</table>

Folinic acid rescue
- Start 24 hrs post start of Methotrexate infusion with 30mg IV 6 hourly
- Switch to oral after 6 doses if not vomiting
- Methotrexate levels at 24, 48, 72 hrs etc.
- Continue until Methotrexate undetectable ie <0.1M usually 4-5 days

<table>
<thead>
<tr>
<th>Methotrexate level</th>
<th>Folinic acid dose 6hrly</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.1M</td>
<td>Stop rescue</td>
</tr>
<tr>
<td>&lt;0.5-5M</td>
<td>15-30mg 6hrly</td>
</tr>
<tr>
<td>5-50M</td>
<td>200mg/m² 6hrly</td>
</tr>
<tr>
<td>&gt;50M</td>
<td>1000mg/m² 6hrly</td>
</tr>
</tbody>
</table>

In addition patients urinary pH should be >7 prior to starting Methotrexate infusion

NB: do not give methotrexate if renal function is abnormal or in the presence of a third space. Also avoid all non-steroidal anti-inflammatory agents prior to treatment and until Methotrexate undetectable.

Doxorubicin / Methotrexate

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>37.5mg/m² IV</td>
<td>days 1, 2</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>12g/m² IV</td>
<td>days 15 and 22</td>
</tr>
</tbody>
</table>

Folinic acid rescue – see above

Criteria
- Age < 40yrs
- PS 0-2
Cisplatin/Doxorubicin  

Cisplatin  100mg/m² IV day 1  
Doxorubicin 25mg/m² IV days 1, 2, 3 (20mg/m² days 1-3 age > 60yrs)

Repeat at 21 days x 3 cycles then surgery then 3 further cycles.

Criteria  
Not suitable for PAM schedule.  
PS 0-2

Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply
Advanced Osteosarcoma
Cisplatin/Doxorubicin  
Cisplatin  100mg/m² IV  day 1  
Doxorubicin  25mg/m² IV  days 1, 2, 3

Repeat at 21 days x 6 cycles

Laboratory investigations
- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- LV ejection fraction prior to cycle 1 if history of cardiac problems
- FBC prior to each cycle
- Normal FBC limits for administration apply
Ewings Sarcoma
Non-metastatic Ewings Sarcoma/PNET/Askin tumour / Rhabdomyosarcoma

Laboratory Investigations
FBC/Biochemistry/Ca/Mg/Ci/HCO3 each cycle
Early morning urine PO4, Creatinine, osmolarity at baseline and repeat every other cycle of VIDE
Echo/MUGA baseline/cycle 4 if indicated/cycle 6/ end Rx / pregnant
Bone scan/CT chest/MRI primary/Marrow biopsy at baseline
MRI primary after cycles 2, 4, 6(omit after 2 if good response)

Neoadjuvant

VIDE (cycles 1-6)

- Vincristine  1.5mg/m$^2$  (max 2mg) IV day 1
- Doxorubicin  20mg/m$^2$  IV days 1-3
- Mesna  1g/m$^2$  IV day 1
- Etoposide  150mg/m$^2$  IV days 1-3
- Ifosfamide/Mesna 1.5g/m$^2$ / 1.5g/m$^2$  IV days 1-3
- Mesna  1.5g/m$^2$  IV days 3
- Pegfilgrastim  6mg subcutaneous injection day 4

Evaluation after cycle 4:
- If surgical resection likely proceed to cycles 5 and 6
- If radiotherapy to be definitive local therapy proceed to cycles 5 and 6
- If disease progression discontinue and consider surgery or radiotherapy
- If pre-surgery XRT planned proceed to cycles 5 and 6 omitting doxorubicin

Dose modifications

Haematological toxicity
Delayed recovery of wbc / platelets > 6 days reduce etoposide 20%
Neutropenic sepsis grade 3 or 4 reduce etoposide 20%
Further episodes – repeat etoposide 20% reductions

GI / Mucositis
Graded 3 or 4 reduce etoposide by 20%

Cardiac function
LVEF < 40% omit doxorubicin and substitute Dactinomycin 1.5mg/m²
Repeat echo after next cycle and consider reintroducing doxorubicin if LVEF has recovered.

Definitive local treatment
- Surgery should occur 21 days after cycle 6 or as soon as recovery allows.
- Radiotherapy should commence concurrent with cycle 7 omitting Dactinomycin from concurrent cycles.
- If radiation is required following surgery it should commence after cycle 8 omitting Dactinomycin from concurrent cycles.

VIA (cycles 7-14)
- **Vincristine**: 1.5mg/m² (max 2mg) IV day 1
- **Dactinomycin**: 0.75mg/m² (max 1.5mg) IV days 1-2
- **Mesna prior to ifosfamide**: 1g/m² days 1-2
- **Ifosfamide/Mesna**: 1.5g/m² / 1.5g/m² IV days 1-2
- **Mesna post ifos/mesna infusion**: 1.5g/m² days 1-2

**NB**: omit Dactinomycin during radiotherapy

**Haematological toxicity**
- Delayed recovery of wbc/platelets > 6 days reduce Dactinomycin & Ifosfamide by 20%
- Neutropenic sepsis grade 3/4 reduce Dactinomycin & Ifosfamide by 20% + add GCSF
- Further episodes should be managed with serial 20% reductions

**GI / Mucositis**
- Grade 3 or 4 reduce Ifosfamide + Dactinomycin by 20%

**Renal Toxicity**
- GFR > 60 no change
- GFR 40-59 reduce Ifosfamide by 30%, reduce etoposide by 30%
- GFR < 40 switch Ifosfamide to cyclophosphamide 1500mg/m² on day 1 only reduce etoposide by 30%

**Cardiac function**
- LVEF < 40% or 10% decrease from previous level, delay chemotherapy and repeat in 7 days. If recovered proceed with chemotherapy. If still impaired consider omission or dose reduction of Ifosfamide.
VAC

Vincristine 1.5mg/m² IV (max 2mg) day 1
Dactinomycin 0.75mg/m² IV (max 1.5mg) day 1-2
Mesna prior to cyclophosphamide 500mg/m² IV pre-cyclophosphamide day 1
Cyclophosphamide/Mesna 1500mg/m² /1500mg/m² IV day 1
Mesna post cyclo/mesna infusion 1500mg/m² IV post cyclophosphamide/mesna day 1

Repeat at 21 days for 4 – 6 cycles

Laboratory Investigations
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

VACA (In patients unsuitable for VIDE previously NOT exposed to anthracyclines. Dactinomycin and doxorubicin on alternate cycles)

Vincristine 1.5mg/m² IV (max 2mg) day 1
Mesna prior to cyclophosphamide 500mg/m² IV day 1
Cyclophosphamide/Mesna 1200mg/m² /1200mg/m² IV day 1
Mesna post cyclo/mesna infusion 1200mg/m² IV day 1
Dactinomycin 0.5mg/m² IV (max 1mg) days 1-3

Alternating with
Doxorubicin 20mg/m² IV days 1-3

Etopside / Ifosfamide
Etoposide 120mg/m² IV days 1-3
Mesna prior to ifosfamide 500mg/m2 days 1-3
Ifosfamide/Mesna 3g/m² / 3g/m² IV days 1-3
Mesna post ifos/mesna infusion 1.5g/m² IV days 1-3
Laboratory Investigations
• Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
• Where renal / hepatic function are abnormal treatment is at physician discretion
• FBC prior to each cycle
• Normal FBC limits for administration apply

Palliative Ewings

Etoposide / cisplatin
Etoposide 120mg/m² IV days 1-3
Cisplatin 50mg/m² IV days 1-2
or
Carboplatin AUC 5 IV day 1
Etoposide 120mg/m² IV day 1
Etoposide 240mg/m² PO days 2,3

Repeat at 21 day intervals max 6 cycles

Criteria PS 0-1
Cr cl > 50ml/min for cisplatin

Laboratory investigations
• Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
• Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
• Where renal / hepatic function are abnormal treatment is at physician discretion
• FBC prior to each cycle
• Normal FBC limits for administration apply

Cyclophosphamide/ Topotecan
Relapsed Ewing’s sarcomas
Relapsed/ 2nd line rhabdomyosarcoma
Topotecan 0.75 mg/m² Days 1-5
Cyclophosphamide 250 mg/m² Days 1-5
Cycle repeated every 21 days
**Gemcitabine/Docetaxel**

Relapsed metastatic osteosarcoma

Selected metastatic soft tissue sarcomas (3rd line)/ uterine leiomyosarcoma

Relapsed Ewings (if other 2nd line is not suitable)

Day 1
- Gemcitabine 675 mg/m² IV over 90 minutes

Day 8
- Gemcitabine 675 mg/m² IV over 90 minutes followed by
- Docetaxel 75-100 mg/m² IV over 60 minutes

Dexamethasone 8 mg bd for 3 days to start 24 hours pre docetaxel (ie Days 7-9)

Cycle repeated every 21 days

**Irinotecan/Temozolomide**

Relapsed Ewing’s sarcoma

Relapsed/ 2nd line rhabdomyosarcoma

- Irinotecan 20 mg/m² IV Days 1-5, Days 8-12
- Temozolomide 100 mg/m² po Days 1-5

Cycle repeated every 21-28 days

**Paclitaxel**

Angiosarcomas

(2nd line or 1st line if not suitable for doxorubicin)

80 mg/m² weekly up to 12 weeks

175 mg/m² every 21 days (4-6 cycles, review after cycle 3)

**Oral Etoposide**

Palliative metastatic Ewings or rhabdomyosarcoma

Etoposide 50-100 mg bd 7-14 days (at clinician’s discretion)
**Aggressive fibromatosis**

1\(^{st}\) Line
Tamoxifen +/- NSAID's

2\(^{nd}\) Line
Methotrexate \(30\, \text{mg/m}^2\) (usually 50mg total dose)
Vinblastine \(6\, \text{mg/m}^2\) (usually 10mg total dose)

Every 1-2 weeks
Duration of course at clinician’s discretion

Vinorelbine can replace vinblastine if neuropathy is a problem.

**Rhabdomyosarcoma**

Baseline investigations:
- FBC, U+E’s, LFT’s Bone chemistry
- CT thorax / Abdo staging
- Bone marrow aspirate and trephine
- Bone Scan
- If paramningeal site- CSF
- Consider early morning urine for phosphate, creatinine, osmolarity for Ifosfamide containing regimes

**For patients aged < 40 years:**
IVADo regime for high risk rhabdomyosarcoma (see separate regime)

Maintenance therapy:

Vinorelbine \(25\, \text{mg/m}^2\) IV D 1, 8, 15
Cyclophosphamide \(25\, \text{mg/m}^2\) PO OD D 1-28
Every 28 days

Maintenance therapy following IVADo to be used in:

1. For Alveolar Rhabdomyosarcoma maintenance therapy following IVADo for 6 cycles (i.e. 6 months)
2. For metastatic disease on intensive treatment, if no residual disease or limited residual disease, IVADo to be followed by maintenance treatment for 12 cycles
For patients > 40 years:

**IVAD**

Vincristine 1.4 mg/m² (max dose 2mg) D1  
Doxorubicin 30 mg/m² D1, D2  
Mesna 1.2g/m² pre ifosfamide D1,D2  
Ifosfamide 3g/m² D1,D2  
Mesna 2.4g/m² post ifosfamide in 2 divided doses D1,D2

Repeat at 21 day intervals for 6 cycles

**VAC**

Vincristine 1.5mg/m² IV (max 2mg) Day 1  
Dactinomycin 0.75mg/m² IV (max 1.5mg) Day 1 and 2  
Mesna prior to cyclophosphamide 500mg/m² IV pre –cyclophosphamide Day 1  
Cyclophosphamide/Mesna 1500mg/m² / 1500mg/m² IV Day 1  
Mesna post cyclo/mesna infusion 1500mg/m² IV post cyclophosphamide/mesna Day 1

Repeat at 21 day intervals for 4-6 cycles

**IVA**

Vincristine 1.5mg/m² (max dose 2mg) Day 1  
Dactinomycin 1.5 mg/m² (max single dose 2mg) Day 1  
Mesna prior to ifosfamide 1.2g/m² day Days 1-2  
Ifosfamide/Mesna 3 g/m² / 3 g/m² Days 1-2  
Mesna post ifos/mesna infusion 2.4g/m² split into 2 doses Day 2

Repeat at 21 day intervals for 6 cycles
IVADo Regime for High Risk Rhabdomyosarcoma

<table>
<thead>
<tr>
<th>Week</th>
<th>Cycle 1</th>
<th>Cycle 2</th>
<th>Cycle 3</th>
<th>Cycle 4</th>
<th>Surgery/ \nRadiotherapy</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>IVADo V</td>
<td>V</td>
<td>IVADo V</td>
<td>V</td>
<td>IVADo</td>
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<tr>
<td>2</td>
<td>IVADo</td>
<td>V</td>
<td>IVADo</td>
<td>V</td>
<td>IVADo</td>
</tr>
<tr>
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<td>IVADo</td>
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<td>IVADo</td>
<td>V</td>
<td>IVADo</td>
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<tr>
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<td>IVADo</td>
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<td>IVADo</td>
<td>V</td>
<td>IVADo</td>
</tr>
<tr>
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<td>V</td>
<td>IVADo</td>
<td>V</td>
<td>IVADo</td>
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<tr>
<td>10</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

I = Mesna prior to ifosfamide 1.2g/m² over 1 hour
Ifosfamide/Mesna 3g/m² / 3g/m² over 3 hours Days 1-2
Mesna post ifos/mesna infusion 2.4g/m² over 8 hours (split into 2 doses)

V = Vincristine 1.5mg/m² (max single dose 2mg) Day 1

A = Dactinomycin 1.5 mg/m² (max single dose 2mg) Day 1

Do= Doxorubicin 30 mg/m² Days 1-2 for cycles 1-4

Each cycle:
WCC>2
Neutrophils> 1.0 ( or physician’s discretion)
Platelets > 80
Weekly vincristine to be given irrespective of pancytopenia unless unwell

Reassess after cycle 3. If not CR or PR > 1/3rd consider 2nd line treatment + RT
PAM Chemotherapy for Resectable Osteosarcoma

<table>
<thead>
<tr>
<th>Cycle 1</th>
<th>Cycle 2</th>
<th>SURGERY</th>
<th>Cycle 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP</td>
<td>M</td>
<td>M</td>
<td>AP</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>7</td>
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<td>9</td>
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<td>12</td>
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<tr>
<td>13</td>
<td>14</td>
<td>15</td>
<td>16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cycle 4</th>
<th>Cycle 5</th>
<th>Cycle 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>17</td>
<td>18</td>
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<tr>
<td>25</td>
<td>A</td>
<td>M</td>
</tr>
<tr>
<td>26</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>M</td>
</tr>
</tbody>
</table>

AP - Doxorubicin 25 mg/m2 Days 1-3
Cisplatin 60mg/m2 Days 1-2
M - Methotrexate 12 g/m2 (With folinic acid rescue) Day 1
A - Doxorubicin 37.5 mg/m² Days 1-2
Gastro-intestinal Stromal Tumours (GIST)

*Adjuvant*  
Imatinib po 400mg daily for 36 months

Criteria  
- Tumour > 5cm
- Mitoses > 5 mitoses/50 HPF
- SI / colonic primary

*Available via the Cancer Drugs Fund

**Imatinib (Glivec®)**  
Imatinib 400mg daily orally until progression

Criteria  
- PS 0-2
- c-Kit positive
- locally advanced / metastatic disease

**Laboratory Investigations**
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC / biochemistry prior to each visit
- Normal FBC limits for administration apply
- Dose reduce if significant toxicity / rising hepatic transaminases

**Sunitinib (Sutent®)**  
Sunitinib 50mg orally daily for 4 weeks followed by a two week break

Criteria  
- PS 0-2
- c-Kit positive
- locally advanced / metastatic disease
- previous response to imatinib

**Laboratory Investigations**
- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC / biochemistry prior to each visit
- Normal FBC limits for administration apply
*Available via the off protocol mechanism*
Germ Cell Tumours

Adjuvant
Stage I Pure Seminoma

Carboplatin  Carboplatin  AUC x 7 IV - one dose only

Laboratory investigations
- EDTA clearance required to calculate AUC
- Ensure normal hepatic function prior to treatment
- Normal FBC limits for administration apply

Stage I Non-seminomatous testicular GCT

Criteria: vascular or lymphatic invasion

BEP<sub>3</sub>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleomycin</td>
<td>30000iu IV</td>
<td>day 1, 8, 15</td>
</tr>
<tr>
<td>Etoposide</td>
<td>165mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>days 1-3</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>50mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>days 1-2</td>
</tr>
</tbody>
</table>

Repeat at 21 day intervals for 2 cycles

Laboratory investigations
- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- Tumour markers: HCG, AFP, LDH where appropriate prior to each cycle
- FBC prior to each cycle
- Normal FBC limits for administration apply

Low risk – all GCT

BEP<sub>3</sub>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
<tr>
<td>Cisplatin</td>
<td>50mg/m&lt;sup&gt;2&lt;/sup&gt; IV</td>
<td>days 1-2</td>
</tr>
</tbody>
</table>

Repeat at 21 day intervals for 3 cycles.
Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- Tumour markers: HCG, AFP, LDH where appropriate prior to each cycle
- FBC prior to each cycle
- Normal FBC limits for administration apply

Intermediate / High risk – all GCT

\[
\text{BEP}_5
\]

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
<th>Cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleomycin</td>
<td>30000iu IV</td>
<td></td>
<td>1, 5, 15</td>
<td>1-3</td>
</tr>
<tr>
<td>Etoposide</td>
<td>100mg/m^2 IV</td>
<td></td>
<td>1-5</td>
<td></td>
</tr>
<tr>
<td>Cisplatin</td>
<td>20mg/m^2 IV</td>
<td></td>
<td>1-5</td>
<td></td>
</tr>
</tbody>
</table>

Repeat at 21 day intervals x 3 cycles then EP5 for a further 3 cycles (i.e. omit bleomycin)

Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- Tumour markers: HCG, AFP, LDH where appropriate prior to each cycle
- FBC prior to each cycle
- Normal FBC limits for administration apply

CNS disease

POMB / ACE + Intrathecal (IT) Methotrexate

POMB

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vincristine</td>
<td>2mg IV</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>1g/m^2 IV over 24hrs (Standard dose is 300mg/m^2)</td>
<td></td>
</tr>
</tbody>
</table>
Methotrexate

Day 2  Bleomycin  15mg IV over 24hr
Day 3  Bleomycin  15mg IV over 24hr
Day 4  Cisplatin  120mg/m² IV over 12hr

Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- Tumour markers: HCG, AFP, LDH where appropriate prior to each cycle
- FBC prior to each cycle
- Normal FBC limits for administration apply

ACE

Dactinomycin  0.5mg IV  days 1-3
Etoposide  100mg/m² IV  days 1-3
Cyclophosphamide  500mg/m² IV  day 3

Intrathecal (IT) Methotrexate  12.5mg flat dose (folinic acid rescue 15mg 6hrly x 4 start at 24hrs)

Laboratory Investigations

- Ensure normal renal and hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply

Repeat cycles at 14 days from day 1, POMB, POMB, ACE, POMB, ACE etc 4-5 cycles of POMB.

Initial organ failure

Low dose cisplatin / etoposide

Cisplatin 20mg/m² IV
Etoposide 100mg/m² IV
Repeat daily x 2-3 days depending on clinical situation
Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- Tumour markers: HCG, AFP, LDH where appropriate prior to each cycle
- FBC prior to each cycle
- Normal FBC limits for administration apply

Relapsed NSGCT

**TIP**

Paclitaxel  175mg/m² IV 3hr infusion day 1  
Ifosfamide  1000mg/m² (+mesna) IV days 1-5  
Cisplatin  20mg/m² IV  days 1-5

Premedication  
Chlorphenamine  10mg IV  
Dexamethasone  20mg IV  
Ranitidine  50mg IV

Repeat at 21 day intervals x 4 cycles

Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- Tumour markers: HCG, AFP, LDH where appropriate prior to each cycle
- FBC prior to each cycle
- Normal FBC limits for administration apply

High dose chemotherapy May be curative in selected patients with drug sensitive relapsed disease.
**Primary CNS Lymphoma**

**De Angelis (Modified)**

**Weeks 1, 5, 9**

Day -1-7 allopurinol 300mg/day

Vincristine 1.4mg/m\(^2\) (max 2mg) IV bolus weeks 2,

Methotrexate 3500mg/m\(^2\) IV over 6 hours

With adequate folinic acid rescue (see below) and urinary alkalinisation

Procarbazine 100mg/m\(^2\) oral daily for 7 days

**Weeks 3, 7**

Vincristine 1.4mg/m\(^2\) (max 2mg) IV bolus weeks 2,

Methotrexate 3500mg/m\(^2\) IV over 6 hours

With adequate folinic acid rescue (see below) and urinary alkalinisation

Dexamethasone 16mg/day week 1

12mg / day week 2

8mg/day week 3

6mg/day week 4

4mg/day week 5

2mg/day week 6

**Folinic acid rescue**

- Start 24 hrs post start of Methotrexate infusion with 30mg IV 6 hourly
- Switch to oral after 6 doses if not vomiting
- Methotrexate levels at 24, 48, 72 hrs etc.
- Continue until Methotrexate undetectable ie <0.1M usually 4-5 days

<table>
<thead>
<tr>
<th>Methotrexate level</th>
<th>Folinic acid dose 6hrly</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.1M</td>
<td>Stop rescue</td>
</tr>
<tr>
<td>&lt;0.5-5M</td>
<td>15-30mg 6hrly</td>
</tr>
<tr>
<td>5-50M</td>
<td>200mg/m(^2) 6hrly</td>
</tr>
<tr>
<td>&gt;50M</td>
<td>1000mg/m(^2) 6hrly</td>
</tr>
</tbody>
</table>
In addition patients urinary pH should be >7 prior to starting Methotrexate infusion

NB: do not give methotrexate if renal function is abnormal or in the presence of a third space. Also avoid all non-steroidal anti-inflammatory agents prior to Rx and until Methotrexate undetectable.

Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer methotrexate only if clearance is > 50mls/min
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply
Adenocarcinoma of Unknown Primary Origin

Possible GI primary  MdG / capecitabine / gemcitabine

Possible breast primary  Manage as for similar stage breast cancer

Possible ovarian primary  Carboplatin 5 x (GFR+25)

Possible lung primary  Carboplatin / Gemcitabine

Midline nodal disease  +/- lung metastases

BEP₃ x max 4 cycles depending on response

Undifferentiated carcinoma  Etoposide / platinum

Etoposide  120mg/m² days 1-3 (or oral 240mg/m²)
Cisplatin  70mg/m² days 1

Repeat at 21 day intervals max 6 cycles

Laboratory investigations

- Ensure normal hepatic function prior to cycle 1 and repeat during subsequent cycles if clinically indicated
- Calculate creatinine clearance prior to each cycle and administer cisplatin according to guidelines
- Where renal / hepatic function are abnormal treatment is at physician discretion
- FBC prior to each cycle
- Normal FBC limits for administration apply
**CCC Emergency Chemotherapy Drugs**

Likely cancers requiring treatment:
- Lymphoma
- Germ Cell Tumours
- Small Cell Lung Cancer

**Drugs Available**

- Cisplatin   30mg in 250ml Sodium chloride 0.9% x 2 doses
- Etoposide  100mg x 2 doses
- Doxorubicin  50mg
- Cyclophosphamide  800mg
- Vincristine  2mg
- Pegfilgrastim  6mg

These drugs will be stored in oncology pharmacy in the fridge in the dispensary area labelled Fridge 3. The fridge will be labelled as containing Emergency Chemotherapy Drugs. Cisplatin will be stored at room temperature on top of fridge 3.

Emergency chemotherapy should be prescribed by a consultant and entry to the pharmacy will be via the CCC bleep holder only.
**Bone Metastases**

There is increasing evidence from studies in a number of malignancies that intravenous bisphosphonate therapy can ameliorate bone pain and reduce the risk of skeletal complications in patients with bone metastases. At present for suitable patients the recommended treatment is zelodronate + Adcal D3 until progression.

**Bisphosphonates**

**Zoledronic acid**

4mg IV in 100mls Sodium chloride 0.9% over 15-30 minutes repeated at 28 day intervals.

Criteria:
- Performance status 0-2
- Symptomatic / extensive bone metastases

Calcium supplements: Patients should have their serum calcium measured every four weeks and Adcal D3 prescribed as necessary.

Renal impairment: Cr clearance  

<table>
<thead>
<tr>
<th>Cr clearance (Cockcroft-Gault)</th>
<th>Dose of zoledronic acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>4.0mg</td>
</tr>
<tr>
<td>50 - 60</td>
<td>3.5mg</td>
</tr>
<tr>
<td>40 - 49</td>
<td>3.3mg</td>
</tr>
<tr>
<td>30 –39</td>
<td>3.0mg</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>no treatment</td>
</tr>
</tbody>
</table>

Serum creatinine should be repeated every 4 weeks and if it rises significantly during treatment zoledronic acid should be withheld until the creatinine has returned to within 10% of the baseline prior to starting.

**Ibandronate (Bondranat®)**

Bondranat has yet to be shown to be as effective as zoledronic acid in reducing the incidence of skeletal events and thus we cannot recommend it as routine treatment. However for patients who have difficulties with venous access or renal impairment it may be requested via the off protocol mechanism.
*Denosumab  Denosumab 120mg sc monthly

Criteria  Patients ineligible for IV bisphosphonate due to poor venous access or renal impairment

*NB  Available via the Cancer Drugs Fund
Surface Area Nomogram