Thames Valley Chemotherapy Regimens
Colorectal Cancer
Notes from the editor

These regimens are available on the Network website www.tvscn.nhs.uk.

Any correspondence about the protocols should be addressed to:
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Acknowledgements
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Thames Valley
Chemotherapy Regimens
Colorectal Cancer

The regimens listed below are in use across the Thames Valley for the treatment of colorectal cancer.

Date published: October 2015
Date of review: October 2017

Chemotherapy Regimens

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<tr>
<td>Name of regimen</td>
<td>Indication</td>
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<td>Oxaliplatin + capecitabine 21 day</td>
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<td>Mitomycin + Fluorouracil (MF) during RT continuous infusion</td>
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<td>Mitomycin + Fluorouracil (MF) with RT &lt; 70 years infusion (Inpt)</td>
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<td>Mitomycin + Fluorouracil (MF) with RT &gt; 70 years infusion (Inpt)</td>
<td>Anal</td>
<td>69</td>
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<tr>
<td>Mitomycin + Fluorouracil (MF) with RT &gt; 70 years infusor (Daypt)</td>
<td>Anal</td>
<td>71</td>
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<td>Relapsed anal</td>
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<tr>
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<td>Relapsed anal</td>
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<td>Intra hepatic (double lumen) Mitomycin + 5Fluorouracil (MF)</td>
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<td></td>
<td>86</td>
</tr>
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</table>
List of amendments in this version

Regimen type: Colorectal Tumours
Date due for review: October 2017
Previous Version number: 3.3
This version number: 3.4

Table 1 Amendments

<table>
<thead>
<tr>
<th>Page</th>
<th>Action Type</th>
<th>Amendment</th>
<th>Made/ asked by</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Cetuximab</td>
<td>2 weekly dose changed to 500mg/m2 as per CDF</td>
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Table 2 New regimens to be added to and or approved and checked by PODG for inclusion in this version

<table>
<thead>
<tr>
<th>Name of regimen</th>
<th>Indication</th>
<th>Reason / Proposer</th>
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<tbody>
<tr>
<td>Cisplatin capecitabine</td>
<td>Anal</td>
<td>PODG</td>
</tr>
<tr>
<td>Mitomycin capecitabine RT</td>
<td>Anal</td>
<td>PODG</td>
</tr>
</tbody>
</table>
**FLUOROURACIL AND FOLINIC ACID (Weekly) with concurrent radiotherapy**

*Indication: Adjuvant colorectal*

**DRUG REGIMEN**

<table>
<thead>
<tr>
<th>Week</th>
<th>DRUGS</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CALCIUM FOLINATE</td>
<td>30mg IV bolus</td>
</tr>
<tr>
<td></td>
<td>FLUOROURACIL</td>
<td>300mg/m² IV bolus</td>
</tr>
<tr>
<td>2</td>
<td>CALCIUM FOLINATE</td>
<td>30mg IV bolus</td>
</tr>
<tr>
<td></td>
<td>FLUOROURACIL</td>
<td>300mg/m² IV bolus</td>
</tr>
<tr>
<td>3</td>
<td>CALCIUM FOLINATE</td>
<td>30mg IV bolus</td>
</tr>
<tr>
<td></td>
<td>FLUOROURACIL</td>
<td>300mg/m² IV bolus</td>
</tr>
<tr>
<td>4</td>
<td>CALCIUM FOLINATE</td>
<td>30mg IV bolus</td>
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<tr>
<td></td>
<td>FLUOROURACIL</td>
<td>300mg/m² IV bolus</td>
</tr>
<tr>
<td>5</td>
<td>CALCIUM FOLINATE</td>
<td>30mg IV bolus</td>
</tr>
<tr>
<td></td>
<td>FLUOROURACIL</td>
<td>300mg/m² IV bolus</td>
</tr>
</tbody>
</table>

**NB** Calcium folinate (calcium leucovorin) is not the same as Calcium levofolinate. Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of Calcium folinate.

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

*Fluorouracil:*

Consider dose reductions in severe renal impairment only

Bilirubin > 85micromol/L or AST >180 omit

Treatment delay.

The 5FU/FA course should be delayed for a week or until completely recovered in the event of either low blood counts (granulocytes <1.5x10⁹ or platelets <100x10⁹) or any persistent mucositis or diarrhoea.

<table>
<thead>
<tr>
<th>Haematological toxicity: Platelets (P), Neutrophils (N)</th>
<th>CTC grade</th>
<th>0-1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2 (P=50 and N=1.0)</td>
<td>100%</td>
<td>80%</td>
<td>50%</td>
<td></td>
<td>No further treatment (NFT)</td>
</tr>
<tr>
<td>3 (P=25-49 or N=0.5-0.9)</td>
<td>80%</td>
<td>70%</td>
<td>50%</td>
<td></td>
<td>NFT</td>
</tr>
<tr>
<td>4 (P&lt;25 or N&lt;0.5)</td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
<td></td>
<td>NFT</td>
</tr>
</tbody>
</table>
INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th></th>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
<td>≥100</td>
<td>&lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
<td>&lt; 1.5</td>
</tr>
</tbody>
</table>

2) Non urgent blood tests
Tests relating to disease response/progression

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouthcare
Diarrhoea – treat with codeine or loperamide
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
FLUOROURACIL (96hr infusion) with concurrent radiotherapy

**Indication:** Adjuvant colorectal

**DRUG REGIMEN**

**Day 1** FLUOROURACIL 1000mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours

**Day 2** FLUOROURACIL 1000mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours

**Day 3** FLUOROURACIL 1000mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours

**Day 4** FLUOROURACIL 1000mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours

**NB** For patients over 70 years give FLUOROURACIL at 750mg/m²/day instead.

**Note:** Fluorouracil may be given via an infusor through a central line instead.

**Cycle Frequency:** Repeat day 29

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant

**Fluorouracil:**

GFR < 30ml/min give 80% dose

Bilirubin > 50micromol/L give 50% dose

Bilirubin > 85micromol/L or AST >180 omit

The 5FU course should be delayed for a week or until completely recovered in the event of either low blood counts (neutrophils <1.5x10^9 or platelets <100x10^9) or any persistent mucositis or diarrhoea.

| Non-haematological toxicity (diarrhoea, stomatitis) |
|-----------------|-------|-------|-------|-------|
| CTC Grade       | 0-1   | 2     | 3     | 4     |

**Haematological toxicity:**

0-2 (P=or>50 & N=or>1.0) 100% 80% 50% No further treatment (NFT)

**Platelets (P),**

3 (P=25-49 or N=0.5-0.9) 80% 70% 50% NFT

**Neutrophils (N)**

4 (P<25 or N<0.5) 50% 50% 50% NFT

**INVESTIGATIONS**

**Routine Blood test**

1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th></th>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
<td>≥100</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5</td>
<td>&lt;1.5</td>
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</tbody>
</table>

2) Non urgent blood tests

Tests relating to disease response/progression

5FU + RT infusion  Colorectal PODG Chair Authorisation: Date: Page 1 of 1 Published: October 2015 Review: October 2017 Version 3.4

Chemotherapy Regimens – Colorectal Cancer 8
CONCURRENT MEDICATION

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
**FLUOROURACIL (96hr infusor) with concurrent radiotherapy**

*Indication: Adjuvant colorectal*

**DRUG REGIMEN**  
**Day 1** FLUOROURACIL 4000mg/m² in infusor over 96 hours  

**NB** For patients over 70 years give FLUOROURACIL at 3000mg/m² via an infusor instead.  

**Cycle Frequency: Repeat day 29**

**Note:** Fluorouracil may be given peripherally via daily infusion if required.

**DOSE MODIFICATIONS**  
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant  

**Fluorouracil:**  
Consider dose reductions in severe renal impairment only  
Bilirubin > 85micromol/L or AST >180 omit

The 5FU course should be delayed for a week or until completely recovered in the event of either  
low blood counts (neutrophils <1.5x10^9 or platelets <100x10^9) or any persistent mucositis or  
diarrhoea.

<table>
<thead>
<tr>
<th>Non-haematological toxicity (diarrhoea, stomatitis)</th>
<th>CTC Grade</th>
<th>0-1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematological toxicity: 0-2 (P=or&gt;50 &amp; N=or&gt;1.0)</td>
<td>100%</td>
<td>80%</td>
<td>50%</td>
<td>No further treatment</td>
<td></td>
</tr>
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</table>

| Platelets (P), 3 (P=25-49 or N=0.5-0.9) | 80% | 70% | 50% | NFT |
| Neutrophils (N), 4 (P<25 or N<0.5) | 50% | 50% | 50% | NFT |

**INVESTIGATIONS**  
Routine Blood test  
1) Blood results required before chemotherapy administration  

<table>
<thead>
<tr>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
<td>≥100</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
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2) Non urgent blood tests  
Tests relating to disease response/progression

**CONCURRENT MEDICATION**

<table>
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<th>5FU + RT infusor</th>
<th>Colorectal PODG Chair Authorisation:</th>
<th>Page 1 of 2</th>
<th>Published: October 2015</th>
<th>Review: October 2017</th>
<th>Version 3.4</th>
</tr>
</thead>
</table>
ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
MODIFIED DE GRAMONT infusion

**Indication:** Metastatic and advanced colorectal

**DRUG REGIMEN**

Day 1  
- **CALCIUM LEVOFOLINATE*** 175mg in 250ml glucose 5% infusion over 2 hours  
- **FLUOROURACIL** 400mg/m² IV bolus  
- **FLUOROURACIL** 1400mg/m² in 1000ml sodium chloride 0.9% infusion over 23 hours  
- **FLUOROURACIL** 1400mg/m² in 1000ml sodium chloride 0.9% infusion over 23 hours  
  (both infusions of fluorouracil are to run consecutively to make a continuous 46 hour infusion)

**Cycle Frequency:** Every 14 days for 12 cycles (review after 6 cycles)

**NB** Calcium levofolinate is not the same as calcium folinate (calcium leucovorin). Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of calcium folinate. If calcium levofolinate is not available calcium folinate (leucovorin) 350mg may be used instead.

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Fluorouracil:**

Consider dose reductions in severe renal impairment only

Bilirubin > 85micromol/L or AST >180 omit

If neutrophils<1.5x10⁹/L or platelets<100x10⁹/L delay 1 week, only treat when neutrophils and platelets are above these limits.

If >1 delay or 1 delay ≥ 2 weeks give 80% 5FU doses for future cycles. A further dose reduction may be made at the Clinician’s discretion.

**INVESTIGATIONS**

Routine Blood test

1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th></th>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
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<td>&lt; 100</td>
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<td>Neutrophils x 10⁹/L</td>
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</table>

2) Non urgent blood tests

Tests relating to disease response/progression
CONCURRENT MEDICATION

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
MODIFIED DE GRAMONT infusor

**Indication:** Metastatic and advanced colorectal

**DRUG REGIMEN**

Day 1  
CALCIUM LEVOFOLINATE* 175mg in 250ml glucose 5% infusion over 2 hours  
FLUOROURACIL 400mg/m² IV bolus  
FLUOROURACIL 2800mg/m² continuous infusion over 46 hours

**Cycle Frequency:** Every 14 days for 12 cycles (review after 6 cycles)

**NB** Calcium levofolinate is not the same as calcium folinate (calcium leucovorin). Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of calcium folinate.  
If calcium levofolinate is not available calcium folinate (leucovorin) 350mg may be used instead.

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant

**Flourouracil:**

Consider dose reductions in severe renal impairment only  
Bilirubin > 85micromol/L or AST >180 omit

If neutrophils <1.5x10⁹/L or platelets <100x10⁹/L delay 1 week, only treat when neutrophils and platelets are above these limits.

If >1 delay or 1 delay ≥ 2 weeks give 80% 5FU doses for future cycles. A further dose reduction may be made at the Clinician’s discretion.

**INVESTIGATIONS**

Routine Blood test

1) Blood results required before chemotherapy administration  

<table>
<thead>
<tr>
<th></th>
<th>Give</th>
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<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
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<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
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2) Non urgent blood tests  
Tests relating to disease response/progression
CONCURRENT MEDICATION

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
BEVACIZUMAB 14 day

Indication: In combination with a fluoropyrimidine-based chemotherapy for metastatic colorectal cancer [1]

NB: may only be given where individual funding has been approved.

DRUG REGIMEN
Day 1 BEVACIZUMAB 5mg/kg IV in 100ml sodium chloride 0.9% infusion over 90* minutes.

* The initial dose should be administered over 90 minutes, if tolerated well the second infusion may be administered over 60 minutes. If the 60 minute infusion is well tolerated all subsequent infusions may be administered over 30 minutes.

Cycle frequency: Repeat every 14 days

DOSE MODIFICATIONS
Renal impairment no studies have been conducted to investigate bevacizumab in renal impairment since the kidneys are not a major organ for bevacizumab metabolism or excretion. Clinical decision

Hepatic impairment no studies have been conducted to investigate bevacizumab in hepatic impairment since the liver is not a major organ for bevacizumab metabolism or excretion. Clinical decision

INVESTIGATIONS
Routine Blood tests
1. Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Value 1</th>
<th>Value 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb g/dL</td>
<td>≥10</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
<td>≥100</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5</td>
<td>&lt;1.5</td>
</tr>
</tbody>
</table>

2. Non-urgent Blood tests
Tests relating to disease response/progression.
CONCURRENT MEDICATIONS

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Gastrointestinal perforation
Haemorrhage
Arterial thromboembolism

ANTI-EMETIC POLICY
Minimal emetic risk

REFERENCES
BEVACIZUMAB 21 day

*Indication: In combination with a fluoropyrimidine-based chemotherapy for metastatic colorectal cancer [1]*

NB: may only be given where individual funding has been approved.

**DRUG REGIMEN**

Day 1  **BEVACIZUMAB** 7.5mg/kg IV in 100ml sodium chloride 0.9% infusion over 90* minutes.

* The initial dose should be administered over 90 minutes, if tolerated well the second infusion may be administered over 60 minutes. If the 60 minute infusion is well tolerated all subsequent infusions may be administered over 30 minutes.

**Cycle frequency: Repeat every 21 days**

**DOSE MODIFICATIONS**

Renal impairment no studies have been conducted to investigate bevacizumab in renal impairment since the kidneys are not a major organ for bevacizumab metabolism or excretion. Clinical decision

Hepatic impairment no studies have been conducted to investigate bevacizumab in hepatic impairment since the liver is not a major organ for bevacizumab metabolism or excretion. Clinical decision

**INVESTIGATIONS**

Routine Blood tests
1. Blood results required before chemotherapy administration
  - Give
  - Discuss
  - Hb x g/dL
    - ≥10
    - <10
  - Plt x 10^9/L
    - ≥100
    - <100
  - Neutrophils x 10^9/L
    - ≥1.5
    - <1.5

2. Non-urgent Blood tests
   Tests relating to disease response/progression.
CONCURRENT MEDICATIONS

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Gastrointestinal perforation
Haemorrhage
Arterial thromboembolism

ANTI-EMETIC POLICY
Minimal emetic risk

REFERENCES
CAPECITABINE metastatic (1250)

**Indication:** For first line monotherapy of metastatic colorectal cancer
Unknown primary if appropriate

**DRUG REGIMEN**
Day 1 CAPECITABINE 1250mg/m² twice daily (2500mg/m²/day) for 14 days followed by a 7 day rest
Tablets available as strengths of 150 mg and 500 mg.

**Cycle Frequency:** Every 21 days for 8 cycles (review after 4 cycles)

**DOSE MODIFICATIONS**

**Capecitabine:**
Check CrCl prior to every cycle
CrCl (ml/min) > 50 give 100% dose
CrCl (ml/min) 30 - 50 give 75% dose
CrCl (ml/min < 30 contraindicated
Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur.
Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.
Please refer to summary of product characteristics for detailed guidance on dose modification due to toxicity (including plantar palmar, erythema and gastrointestinal toxicity).

Brief guidance on initial dose modifications at the first appearance of toxicity is given below. Users of these guidelines should also refer to the more detailed guidance contained within the Summary of Product Characteristics (SPC) which can be viewed at [www.medicines.org.uk](http://www.medicines.org.uk). This includes details on how to manage 2nd and subsequent appearance of toxicities.
Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.
**Toxicity Grades**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Dose changes within a treatment cycle</th>
<th>Dose adjustment for next cycle/dose (% of starting dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Maintain dose level</td>
<td>Maintain dose level</td>
</tr>
<tr>
<td>Grade 2</td>
<td>- 1st appearance: Interrupt until resolved to grade 0-1</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>- 2nd appearance: Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>- 3rd appearance: Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>- 4th appearance: Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Grade 3</td>
<td>- 1st appearance: Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>- 2nd appearance: Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>- 3rd appearance: Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Grade 4</td>
<td>- 1st appearance: Discontinue permanently OR if physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>- 2nd appearance: Discontinue permanently</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

**INVESTIGATIONS**

Routine Blood test

1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL ≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Pt x 10^9/L ≥100</td>
<td>&lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L ≥1.5</td>
<td>&lt; 1.5</td>
</tr>
</tbody>
</table>

Serum creatinine - GFR should be calculated or measured using EDTA

**CONCURRENT MEDICATION**

Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin. Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

**ANTIEMETIC POLICY**

Low emetogenic risk

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS**

Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds

Diarrhoea – treat with loperamide or codeine

Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with capecitabine.
CAPECITABINE (5 day) with RT

Indication: Neo-adjuvant Chemo-radiation Treatment of Locally Advanced Rectal Cancer

DRUG REGIMEN
CAPECITABINE 900mg/m² twice daily (1800mg/m²/day) for 5 days per week
Tablets available as strengths of 150 mg and 500 mg.

Cycle Frequency: for duration of radiotherapy (i.e. 5 or 6 weeks in total)

DOSE MODIFICATIONS
Capecitabine
Consider giving 75% dose of capecitabine for patients >70 years depending on performance status

In the event of haematological and non-haematological toxicities dose modification should be based on the worst toxicity grade recorded.

Capecitabine
When a dose modification is made for the development of grade 2 (lasting more than 24 hours) or grade 3 toxicity this modification remains in place for the remainder of the planned treatment course.

Dose modifications for haematological toxicity based on weekly blood counts

<table>
<thead>
<tr>
<th>Grade</th>
<th>Toxicity</th>
<th>Neutrophils &lt;LLN-1.5x10⁹/L</th>
<th>Platelets &lt;LLN-75x10⁹/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>Continue 100%</td>
<td>Continue 100%</td>
</tr>
<tr>
<td>2</td>
<td>Neutrophils &lt;1.5-1.0x10⁹/L</td>
<td>Continue 100%</td>
<td>Perform FBC x 2 per week</td>
</tr>
<tr>
<td></td>
<td>Platelets &lt;75-50x10⁹/L</td>
<td>Interrupt until grade 0-1</td>
<td>Interrupt until grade 0-1 then 100%</td>
</tr>
<tr>
<td></td>
<td>Perform FBC x 2 per week</td>
<td>Interrupt until grade 0-1</td>
<td>Interrupt until grade 0-1 then 75%</td>
</tr>
<tr>
<td>3</td>
<td>Neutrophils &lt;1.0-0.5x10⁹/L</td>
<td>Continue 100%</td>
<td>Neutrophenic sepsis with grade 3 or 4 diarrhoea</td>
</tr>
<tr>
<td></td>
<td>Platelets &lt;50-25x10⁹/L</td>
<td>Interrupt until grade 0-1</td>
<td>Discontinue treatment permanently</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interrupt until grade 0-1</td>
<td>Discontinue treatment permanently</td>
</tr>
</tbody>
</table>

In the event of a second grade 3 episode of the same toxicity, treatment should discontinue permanently.

Capecitabine 5 day RT
Colorectal PODG Chair Authorisation:

Date:

Page 1 of 4
Published: October 2015
Review: October 2017
Version 3.4

Chemotherapy Regimens – Colorectal Cancer 22
Dose modifications for palmar-plantar syndrome

Grade | Toxicity                                                                 | Capecitabine
1     | Minimal skin changes or dermatitis (eg erythema, oedema, or hyperkeratosis) without pain | Continue
2     | Skin changes (eg peeling, blisters, bleeding, oedema or keratosis) with pain limiting instrumental ADL | Interrupt until 0-1 then resume at 75%
3     | Skin changes (eg peeling, blisters, bleeding, oedema or keratosis) with pain limiting self care ADL | Interrupt until 0-1 then resume at 75%

In the event of a second grade 3 episode of the same toxicity, treatment should discontinue permanently.

Dose modifications for renal function

The GFR should be calculated weekly - if less than 50ml/min then the capecitabine dose should be reduced as below and an EDTA clearance requested - when this result is available the capecitabine dose should be reduced as below (ie if the EDTA result is higher than the GFR the EDTA result should be used). The EDTA can guide capecitabine dosing in subsequent weeks providing creatinine does not rise by >10%.

<table>
<thead>
<tr>
<th>CrCl or EDTA result</th>
<th>Capecitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50ml/min</td>
<td>Continue</td>
</tr>
<tr>
<td>30-50ml/min</td>
<td>75% dose</td>
</tr>
<tr>
<td>&lt;30ml/min</td>
<td>Stop capecitabine</td>
</tr>
</tbody>
</table>

Dose modification for non-haematological toxicity

Diarrhoea

Grade | Toxicity                                                                 | Radiotherapy | Capecitabine
1     | Increase <4 stools per day over baseline, mild increase in ostomy output | Continue     | 100%
2     | Increase 4-6 stools per day over baseline, mild increase in ostomy output. Moderate cramping (>12 hrs or <12 hours) | <12hrs duration continue. | Omit evening dose at onset and reassess 24 hours later. If <12 hrs duration continue. Interrupt until grade 0-1 then 75%.
3     | Increase >=7 stools per day over baseline, severe increase in ostomy output. Severe cramping or peritonism | >12hrs duration interrupt until grade 0-1 then resume. | Interrupt until grade 0-1 then 75%. If neutropenic sepsis stop permanently.
4     | Life threatening consequences urgent intervention indicated | Discontinue treatment permanently |
Dose modifications for deranged hepatic function and grade 3 fatigue and vomiting

Grade  Toxicity  Radiotherapy  Capecitabine
2  Elevated bilirubin  Continue  75%
    >1.5-3.0 x ULN
3  Elevated bilirubin  Continue  stop
    >3.0-10.0 x ULN
    ALT or AST > 3xULN  Continue  stop
3  Fatigue, vomiting or lethargy  omit until Interrupt until grade
    grade 0-1 0-1 then 75%

Management of non-haematological toxicity eg mucositis and stomatitis

Grade  Radiotherapy  Capecitabine
1  Continue  100%
2  Continue  Interrupt until grade 0-1 then 75%
3  Continue but treat  Interrupt until grade 0-1 with supportive therapy then 75%
4  Stop  stop

Continue radiotherapy for grade 3 mucositis or stomatitis

In the event of a second grade 3 episode of the same toxicity, treatment should discontinue permanently.

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
<td>≥100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5</td>
</tr>
</tbody>
</table>

Serum creatinine - GFR should be calculated or measured using EDTA
Blood tests should be done routinely once weekly during radiotherapy.

CONCURRENT MEDICATION

Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin.
Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.
ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with capecitabine.

REFERENCES
4. Aristotle study version 2.0 December 2011
CAPECITABINE adjuvant (1250)

Indication: For first line monotherapy of adjuvant colorectal cancer

**DRUG REGIMEN**
Day 1 CAPECITABINE 1250mg/m² twice daily (2500mg/m²/day) for 14 days followed by a 7 day rest
Tablets available as strengths of 150 mg and 500 mg.

**Cycle Frequency: Every 21 days for 8 cycles**

**DOSE MODIFICATIONS**

*Capecitabine:*
Check CrCl prior to every cycle
CrCl (ml/min) >50 give 100% dose
CrCl (ml/min 30 - 50 give 75% dose
CrCl (ml/min <30 contraindicated
Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur.
Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.
Please refer to summary of product characteristics for detailed guidance on dose modifications due to toxicity (including plantar palmar, erythema and gastrointestinal toxicity).

Brief guidance on initial dose modifications at the first appearance of toxicity is given below. Users of these guidelines should also refer to the more detailed guidance contained within the Summary of Product Characteristics (SPC) which can be viewed at [www.medicines.org.uk](http://www.medicines.org.uk). This includes details on how to manage 2nd and subsequent appearance of toxicities. Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.
Toxicity Grades | Dose changes within a treatment cycle | Dose adjustment for next cycle/dose (% of starting dose)
--- | --- | ---
* Grade 1 | Maintain dose level | Maintain dose level
* Grade 2 | | 
- 1st appearance | Interrupt until resolved to grade 0-1 | 100%
- 2nd appearance | Interrupt until resolved to grade 0-1 | 75%
- 3rd appearance | Interrupt until resolved to grade 0-1 | 50%
- 4th appearance | Discontinue treatment permanently | Not applicable
* Grade 3 | | 
- 1st appearance | Interrupt until resolved to grade 0-1 | 75%
- 2nd appearance | Interrupt until resolved to grade 0-1 | 50%
- 3rd appearance | Discontinue treatment permanently | Not applicable
* Grade 4 | | 
- 1st appearance | Discontinue permanently OR if physician deems it to be in the patient’s best interest to continue, interrupt until resolved to grade 0-1 | 50%
- 2nd appearance | Discontinue permanently | Not applicable

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

Give | Discuss
--- | ---
Hb x g/dL | ≥10 | < 10
Plt x 10^9/L | ≥100 | < 100
Neutrophils x 10^9/L | ≥1.5 | < 1.5
Serum creatinine - GFR should be calculated or measured using EDTA

CONCURRENT MEDICATION
Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin. Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with capecitabine.
CETUXIMAB

*Indication: EGFR expressing advanced / metastatic colorectal cancer, in combination with other chemotherapy e.g. irinotecan*

NB: may only be given where individual funding has been approved.

Results: for use as a single agent or in combination with irinotecan is indicated for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing metastatic colorectal cancer after failure of irinotecan—including cytotoxic therapy. It is recommended that cetuximab treatment be continued until progression of the underlying disease.

**DRUG REGIMEN**

**Day 1:** Loading dose (once only)
- **CHLORPHENAMINE** 10mg IV injection
- **CETUXIMAB** 400mg/m² IV infusion over 120 minutes.
  Flush with sodium chloride 0.9% after infusion

**Day 8:** Maintenance dose
- **CHLORPHENAMINE** 10mg IV injection
- **CETUXIMAB** are 250mg/m² IV infusion over 60 minutes
  Flush with sodium chloride 0.9% after infusion

*Cycle frequency: Repeat maintenance dose (day 8) every 7 days for 12 cycles (then review)*

Or

**Day 1:** **CHLORPHENAMINE** 10mg IV injection
- **CETUXIMAB** 500mg/m² IV infusion over 60 minutes.
  Flush with sodium chloride 0.9% after infusion

*Cycle frequency: Repeat maintenance dose every 14 days for 12 cycles (then review)*

**Note:** The maximum infusion rate must not exceed 5 ml/min. Close monitoring is required during the infusion and for *at least* 1 hour after the end of the infusion. Filters may occasionally clog up during the infusion. If there is evidence of filter clogging, the filter must be replaced [1]

**DOSE MODIFICATIONS**

Previous neutropenic sepsis, discuss with Consultant or Registrar.
Only patients with adequate renal and hepatic function have been investigated to date (serum creatinine <or=1.5 fold, transaminases <or=5 fold and bilirubin <or=1.5 fold the upper limit of normal). Unlikely to require dose reductions.
INVESTIGATIONS
Routine Blood tests
1. Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>if &gt; or = 9</td>
</tr>
<tr>
<td>Plt x 109/L</td>
<td>if &gt; or = 100</td>
</tr>
<tr>
<td>Neutrophils x 109/L</td>
<td>if &gt; or = 5</td>
</tr>
</tbody>
</table>

- GFR assessed using 51Cr-EDTA result or calculated creatinine clearance at the Consultant’s discretion.
- LFTs

2. Non-urgent Blood tests
Tests relating to disease response/progression.

CONCURRENT MEDICATIONS
Premedication prior to cetuximab with an antihistamine is recommended.

Note 2 Side effects: Hypersensitivity reactions if the patient experiences a mild or moderate hypersensitivity reaction, the infusion rate may be decreased. It is recommended to maintain this lower infusion rate in all subsequent infusions.

Severe hypersensitivity reactions (~4%) Symptoms usually occurred during the initial infusion and up to 1 hour after the end of infusion, but may occur after several hours (It is recommended to warn patients of this). Occurrence of a severe hypersensitivity reaction requires immediate and permanent discontinuation of cetuximab therapy and may necessitate emergency treatment

Dyspnoea may occur as part of a hypersensitivity reaction, but has also been reported after several weeks of therapy. Patients with high age, impaired performance status and underlying pulmonary disorders may be at increased risk for dyspnoea, which may be severe and/or long-standing. It is recommended to investigate patients for signs of progressive pulmonary disorders as appropriate

Skin reactions If a patient experiences a severe skin reaction therapy must be interrupted. Treatment may only be resumed, if the reaction has resolved. With the second occurrence of a severe reaction, treatment may only be resumed at 200 mg/m² after interruption. With the third occurrence of a severe reaction, treatment may only be resumed at 150 mg/m² after interruption. If severe skin reactions occur a fourth time or do not resolve during interruption of treatment, permanent discontinuation of cetuximab treatment is required. [1]
ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Gastrointestinal perforation
Haemorrhage
Arterial thromboembolism

ANTI-EMETIC POLICY
Minimal emetic risk

REFERENCES
Cetuximab October 2004 www.medicines.org.uk
IRINOTECAN 350 21 day

Indication: Metastatic and relapsed colorectal

DRUG REGIMEN
Day 1 PREMEDICATION at least 30 mins prior to treatment
  ATROPINE 250microgram subcutaneously
  IRINOTECAN 350mg/m² in 250ml glucose 5% over 30 minutes

Cycle Frequency: Every 21 days for 6 cycles

DOSE MODIFICATIONS
If neutrophils<1.5x10⁹/L or platelets<100x10⁹/L delay 1 week, only treat when neutrophils and platelets are above these limits.

Irinotecan
Bilirubin 25 -50micromol/L give 200mg/m2
Bilirubin > 51 Clinical decision

If patients suffer from severe diarrhoea, which required IV rehydration or neutropenic fever dose should be reduced to 300mg/m² in subsequent cycles, discuss with SpR or Consultant
If symptoms recur reduce dose to 250mg/m², discuss with SpR or Consultant.

If 2 consecutive cycles are delayed or 1 cycle is delayed by ≥ 2 weeks due to myelosuppression give 80% dose.
In the event of febrile neutropenia give 80% dose for all subsequent cycles.

INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration
  Give                Discuss
  Hb x g/dL           ≥10 < 10
  Plt x 10⁹/L         ≥100 < 100
  Neutrophils x 10⁹/L ≥1.5 < 1.5

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
Patients who experience delayed diarrhoea will require loperamide 2 mg every 2 hours to continue for 12 hours after the last loose stool. This high dose should be discontinued after 48 hours.
ANTIEMETIC POLICY
Moderate emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Acute Diarrhoea – delayed diarrhea occurring more than 24 hours after administration. Drink large volumes of fluid containing electrolytes and an appropriate antidiarrhoal therapy e.g. loperamide 4mg initially then 2mg every 2 hours, continuing for 12 hours after the last liquid stool (maximum of 48 hours in total). Take prophylactic broad spectrum antibiotics.

REFERENCES
1. Piccolo study
IRINOTECAN and MODIFIED DE GRAMONT

**Indication:** Advanced colorectal cancer

**DRUG REGIMEN**

**Day 1** PREMEDICATION at least 30 mins prior to treatment
- **ATROPINE** 250 microgram subcutaneously
- **IRINOTECAN** 180mg/m² infusion in 250ml glucose 5% over 30 minutes
- **CALCIUM LEVOFOLINATE** 175mg infusion in 250 ml glucose 5% over 2 hours
- **FLUOROURACIL** 400mg/m² IV bolus
- **FLUOROURACIL** 2400mg/m² continuous infusion over 46 hours via an infusor

**Cycle Frequency:** Every 14 days for 6 cycles

**NB** Calcium levofolinate is not the same as calcium folinate (calcium leucovorin).
Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of calcium folinate.
If calcium levofolinate is not available calcium folinate (leucovorin) 350mg may be used instead.

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Fluorouracil:**
Consider dose reductions in severe renal impairment only
Bilirubin > 85 micromol/L or AST > 180 omit

If neutrophils < 1.5x10⁹/L or platelets < 100x10⁹/L delay 1 week, only treat when neutrophils and platelets are above these limits.
If > 1 delay or 1 delay ≥ 2 weeks give 80% 5FU for future cycles. A further dose reduction may be made at the Clinician’s discretion

**Irinotecan:**
Bilirubin 25 - 50 micromol/L dose reduce
Bilirubin > 51 Clinical decision

If patients suffer from severe diarrhoea, which required IV rehydration or neutropenic fever, consider reduction in subsequent cycles, discuss with SpR or Consultant.
INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

<table>
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<tr>
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</tr>
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<tr>
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<td>Plt x 10⁹/L</td>
<td>≥100</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
</tr>
</tbody>
</table>

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

ANTIEMETIC POLICY
Moderately emetogenic.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Diarrhoea – delayed diarrhea occurring more than 24 hours after administration.
Drink large volumes of fluid containing electrolytes and an appropriate antidiarrhoeal therapy e.g. loperamide 4mg initially then 2mg every 2 hours, continuing for 12 hours after the last liquid stool (maximum of 48 hours in total). Take prophylactic broad spectrum antibiotics.
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Cardiototoxicity - special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil.
**IRINOTECAN and MODIFIED DE GRAMONT and Cetuximab**

**Indication: Advanced colorectal cancer**

Nice guidance: Cetuximab in combination with Fluorouracil (5-FU), folinic acid and irinotecan is recommended for the first-line treatment of metastatic colorectal cancer, for up to 16 weeks treatment, when all of the following criteria are met: and the patient is intolerant to oxaliplatin or it is contraindicated:

- The primary colorectal tumour has been resected or is potentially operable.
- The metastatic disease is confined to the liver and is unresectable.
- The patient is fit enough to undergo surgery to resect the primary colorectal tumour and to undergo liver surgery if the metastases become resectable after treatment with cetuximab.

Cetuximab in combination with 5-FU, folinic acid and irinotecan is recommended for the first-line treatment of metastatic colorectal cancer only when the above criteria are met and

- The patient is unable to tolerate or has contraindications to oxaliplatin.

**DRUG REGIMEN**

**Day 1**  
PREMEDICATION at least 30 mins prior to treatment  
**ATROPINE** 250microgram subcutaneously  
Loading dose (Cycle 1 only)  
**CHLORPHENAMINE** 10mg IV injection  
**CETUXIMAB** 400mg/m² IV infusion over 120 minutes.  
Maintenance dose (Cycle 2 onwards)  
**CETUXIMAB** 250mg/m² IV infusion over 60 minutes  
**IRINOTECAN** 180mg/m² infusion in 250ml glucose 5% over 30 minutes  
**CALCIUM LEVOFOLINATE*** 175 mg infusion in 250 ml glucose 5% over 2 hours  
**FLUOROURACIL** 400mg/m² IV bolus  
**FLUOROURACIL** 2400mg/m² continuous infusion over 46 hours via an infusor

**Day 8**  
**CETUXIMAB** 250mg/m² IV infusion over 60 minutes

**Cycle Frequency: Every 14 days for 6 cycles**

**NB** Calcium levofolinate is not the same as calcium folinate (calcium leucovorin). Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of calcium folinate. If calcium levofolinate is not available calcium folinate (leucovorin) 350mg may be used instead.
DOSE MODIFICATIONS
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Fluorouracil:**
Consider dose reductions in severe renal impairment only
Bilirubin > 85micromol/L or AST >180 omit
If neutrophils<1.5x10^9/L or platelets<100x10^9/L delay 1 week, only treat when neutrophils and platelets are above these limits.
If >1 delay or 1 delay ≥ 2 weeks give 80% 5FU for future cycles. A further dose reduction may be made at the Clinician’s discretion

**Irinotecan:**
Bilirubin 25 -50micromol/L give 200mg/m2
Bilirubin > 51 Clinical decision
If patients suffer from severe diarrhoea, which required IV rehydration or neutropenic fever, consider reduction in subsequent cycles, discuss with SpR or Consultant.

**Cetuximab:**
Previous neutropenic sepsis, discuss with Consultant or Registrar.
Only patients with adequate renal and hepatic function have been investigated to date (serum creatinine <or=1.5 fold, transaminases <or=5 fold and bilirubin <or=1.5 fold the upper limit of normal).

INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
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</tr>
<tr>
<td>Plt x 10^9/L</td>
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</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5</td>
<td>&lt; 1.5</td>
</tr>
</tbody>
</table>

2) Non urgent blood tests
Tests relating to disease response/progression

ANTIEMETIC POLICY
Moderately emetogenic.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Diarrhoea – delayed diarrhea occurring more than 24 hours after administration.
Drink large volumes of fluid containing electrolytes and an appropriate antidiarrhoeal therapy e.g. loperamide 4mg initially then 2mg every 2 hours, continuing for 12 hours after the last liquid stool (maximum of 48 hours in total). Take prophylactic broad spectrum antibiotics.
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care

---

Irinotecan +
Mod De
Gramont +
cetuximab

Colorectal PODG Chair Authorisation:

Page 2 of 2

Published: October 2015
Review: October 2017
Version 3.4

Chemotherapy Regimens – Colorectal Cancer 36
IRINOTECAN and CAPECITABINE 21 day

**Indication:** Advanced colorectal cancer

**NICE guidance:** Oral therapy with either capecitabine or tegafur with uracil (in combination with folinic acid) is recommended as an option for the first-line treatment of metastatic colorectal cancer. Capecitabine monotherapy is recommended as an option for the adjuvant treatment of stage III (Dukes’ C) colon cancer following surgery. Capecitabine is recommended as monotherapy for adjuvant treatment post surgery for stage III (Dukes’ C) colon cancer.

**DRUG REGIMEN**

Day 1 PREMEDICATION at least 30 mins prior to treatment
- ATROPINE 250microgram subcutaneously
- IRINOTECAN 250mg/m² infusion in 250ml glucose 5% over 30 minutes
- CAPECITABINE 1000mg/m² twice daily (2000 mg/m²/day) for 14 days followed by a 7 day rest

*Cycle Frequency: Every 21 days for 8 cycles (review after 4 cycles)*

NB Capecitabine tablets available as strengths of 150 mg and 500 mg.

**DOSE MODIFICATIONS**

*Irinotecan:*
Bilirubin 25 -50micromol/L give 200mg/m2
Bilirubin > 51 Clinical decision

*Capecitabine:*
Check CrCl prior to every cycle
CrCl (ml/min) > 50 give 100% dose
CrCl (ml/min 30 -50 give 75% dose
CrCl (ml/min < 30 contraindicated

Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur.
Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.

Please refer to summary of product characteristics for detailed guidance on dose modification due to toxicity (including plantar palmar, erythema and gastrointestinal toxicity).
Brief guidance on initial dose modifications at the first appearance of toxicity is given below. The Summary of Product Characteristics (SPC) which can be viewed at [www.medicines.org.uk](http://www.medicines.org.uk). This includes details on how to manage 2nd and subsequent appearance of toxicities. Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction).

Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

### Toxicity Grades

<table>
<thead>
<tr>
<th>Toxicity Grades</th>
<th>Dose changes within a treatment cycle</th>
<th>Dose adjustment for next cycle/dose (% of starting dose)</th>
</tr>
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<tbody>
<tr>
<td>* Grade 1</td>
<td>Maintain dose level</td>
<td>Maintain dose level</td>
</tr>
<tr>
<td>* Grade 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 1st appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>100%</td>
</tr>
<tr>
<td>- 2nd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td>- 3rd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td>- 4th appearance</td>
<td>Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
<tr>
<td>* Grade 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 1st appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td>- 2nd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td>- 3rd appearance</td>
<td>Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
<tr>
<td>* Grade 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 1st appearance</td>
<td>Discontinue permanently OR if physician deems it to be in the patient’s best interest to continue, interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td>- 2nd appearance</td>
<td>Discontinue permanently</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

### INVESTIGATIONS

**Routine Blood test**

1) Blood results required before chemotherapy administration

<table>
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<tr>
<th>Give</th>
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<td>≥100</td>
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<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
</tr>
</tbody>
</table>

Serum creatinine - GFR should be calculated or measured using EDTA

### CONCURRENT MEDICATION

Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin.

Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.
ANTIEMETIC POLICY
Moderately emetogenic day 1
Low emetogenic risk days 2 to 14

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Diarrhoea – delayed diarrhea occurring more than 24 hours after administration.
Drink large volumes of fluid containing electrolytes and an appropriate antidiarrhoeal therapy e.g.
loperamide 4mg initially then 2mg every 2 hours, continuing for 12 hours after the last liquid stool
(maximum of 48 hours in total). Take prophylactic broad spectrum antibiotics.
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or
those who develop chest pain during treatment with capecitabine.

REFERENCE
1. A phase I/II and pharmacokinetic study of irinotecan in combination with capecitabine as first-
line therapy for advanced colorectal cancer. Rea DW, Nortier JW, Ten Bokkel Huinink WW,
Falk S, Richel DJ, Maughan T, Groenewegen G, Smit JM, Steven N, Bakker JM, Semiond D,
Kerr DJ, Punt CJ. CR UK Institute for Cancer Studies, University of Birmingham, Birmingham,
UK. Br J Cancer. 2006 Mar 27;94(6):935-6
**OXALIPATIN with MODIFIED DE GRAMONT**

*Indication: Metastatic and adjuvant colorectal cancer
Unknown primary if appropriate*

NICE guidance: Oxaliplatin should be considered for use as first line therapy, in combination with 5FU/FA as first line or subsequent therapy. Oxaliplatin in combination with 5FU/FA is recommended as an option for the adjuvant treatment of stage III (Dukes’ C) colon cancer following surgery. Oxaliplatin is recommended with 5-fluorouracil and folinic acid for adjuvant treatment post surgery for stage III (Dukes’ C) colon cancer.

**DRUG REGIMEN**

Day 1  **OXALIPLATIN** 85mg/m$^2$ in 500ml glucose 5% infusion over 2 hours
Flush with glucose 5% after infusion
**CALCIUM LEVOFOLINATE*** 175mg in glucose 5% infusion over 2 hours concurrently with oxaliplatin via a Y site placed immediately before the injection site.
**FLUOROURACIL** 400mg/m$^2$ IV bolus
**FLUOROURACIL** 2400mg/m$^2$ continuous infusion over 46 hours via an infusor

*Cycle Frequency: Every 14 days for 12 cycles (review after 6 cycles)*

**NB** Calcium levofolinate is not the same as calcium folinate (calcium leucovorin). Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of calcium folinate.
If calcium levofolinate is not available calcium folinate (leucovorin) 350mg may be used instead.

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Fluorouracil:**
Consider dose reductions in severe renal impairment only
Bilirubin > 85micromol/L or AST >180 omit

If neutrophils$<1.5\times10^9$/L or platelets$<75\times10^9$/L delay 1 week, only treat when neutrophils and platelets are above these limits.
If >1 delay or 1 delay $\geq$ 2 weeks give 80% 5FU dose for future cycles. A further dose reduction may be made at the Clinician’s discretion.
**Oxaliplatin:**
If persistent peripheral sensory symptoms occur, withdraw treatment
GFR > 20ml/min give 100% dose and adjust according to toxicity
GFR < 20ml/min dose reduce
Hepatic impairment
Probably no dose reduction necessary. Clinical decision

If patients develop acute laryngopharyngeal dysesthesia infuse the next cycle over 6 hours.
If symptoms persist reduce dose to 65 mg/m²

**INVESTIGATIONS**
Routine Blood test 1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
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<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
<td>≥75</td>
<td>&lt; 75</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
<td>&lt; 1.5</td>
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Serum creatinine - GFR should be calculated or measured using EDTA

2) Non urgent blood tests
Tests relating to disease response/progression

**CONCURRENT MEDICATION**

**ANTIEMETIC POLICY**
Moderately emetogenic day 1
Low emetogenic risk day 2

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS**
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Diarrhoea – treat with loperamide or codeine
Peripheral sensory neuropathy and laryngeal spasm – avoid cold drinks and touching cold items.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
**Indication: Metastatic and adjuvant colorectal cancer**

NICE guidance: Oxaliplatin should be considered for use as first line therapy, in combination with 5FU/FA as first line or subsequent therapy. Oxaliplatin in combination with 5FU/FA is recommended as an option for the adjuvant treatment of stage III (Dukes’ C) colon cancer following surgery. Oxaliplatin is recommended with 5-fluorouracil and folinic acid for adjuvant treatment post surgery for stage III (Dukes’ C) colon cancer. Cetuximab in combination with Fluorouracil (5-FU), folinic acid and oxaliplatin is recommended for the first-line treatment of metastatic colorectal cancer, for up to 16 weeks treatment, when all of the following criteria are met:

- The primary colorectal tumour has been resected or is potentially operable.
- The metastatic disease is confined to the liver and is unresectable.
- The patient is fit enough to undergo surgery to resect the primary colorectal tumour and to undergo liver surgery if the metastases become resectable after treatment with cetuximab.

The manufacturer rebates 16% of the amount of cetuximab used on a per patient basis.

**DRUG REGIMEN**

**Day 1** Loading dose (Cycle 1 only)

- **CHLORPHENAMINE** 10mg IV injection
- **CETUXIMAB** 400mg/m² IV infusion over 120 minutes.

Maintenance dose (Cycle 2 onwards)

- **CETUXIMAB** 250mg/m² IV infusion over 60 minutes
  - Flush with sodium chloride 0.9% after infusion
- **OXALIPLATIN** 85mg/m² in 500ml glucose 5% infusion over 2 hours
  - Flush with glucose 5% after infusion
- **CALCIUM LEVOFOLINATE** 175mg in glucose 5% infusion over 2 hours concurrently with oxaliplatin via a Y site placed immediately before the injection site.
- **FLUOROURACIL** 400mg/m² IV bolus
- **FLUOROURACIL** 2400mg/m² continuous infusion over 46 hours via an infusor

**Day 8** CETUXIMAB 250 mg/m² IV infusion over 60 minutes

**Cycle Frequency: Every 14 days for 12 cycles (review after 6 cycles)**

**NB** Calcium levofolinate is not the same as calcium folinate (calcium leucovorin). Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of calcium folinate. If calcium levofolinate is not available calcium folinate (leucovorin) 350mg may be used instead.
DOSE MODIFICATIONS
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Fluorouracil:**
Consider dose reductions in severe renal impairment only
Bilirubin > 85micromol/L or AST >180 omit
If neutrophils<1.5x10⁹/L or platelets<75x10⁹/L delay 1 week, only treat when neutrophils and platelets are above these limits.
If >1 delay or 1 delay ≥ 2 weeks give 80% 5FU dose for future cycles. A further dose reduction may be made at the Clinician’s discretion.

**Oxaliplatin:**
If persistent peripheral sensory symptoms occur, withdraw treatment
GFR > 20ml/min give 100% dose and adjust according to toxicity
GFR < 20ml/min dose reduce
Hepatic impairment
Probably no dose reduction necessary. Clinical decision

If patients develop acute laryngopharyngeal dysaesthesia infuse the next cycle over 6 hours.
If symptoms persist reduce dose to 65mg/m²

**Cetuximab:**
Previous neutropenic sepsis, discuss with Consultant or Registrar.
Only patients with adequate renal and hepatic function have been investigated to date (serum creatinine <or=1.5 fold, transaminases <or=5 fold and bilirubin <or=1.5 fold the upper limit of normal).

INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

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</tr>
</tbody>
</table>

Serum creatinine - GFR should be calculated or measured using EDTA

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
ANTIEMETIC POLICY
Moderately emetogenic day 1
Low emetogenic risk day 2

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Diarrhoea – treat with loperamide or codeine
Peripheral sensory neuropathy and laryngeal spasm – avoid cold drinks and touching cold items.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
MITOMYCIN and MODIFIED DE GRAMONT

**Indication:** Advanced colorectal [1]

**DRUG REGIMEN**

**Day 1**
- **MITOMYCIN** 6mg/m² IV bolus.
- **CALCIUM LEVOFOLINATE** 175mg in 250ml glucose 5% over 2 hours
- **FLUOROURACIL** 400mg/m² IV bolus
- **FLUOROURACIL** 2400mg/m² continuous infusion over 46 hours

**Day 15**
- **CALCIUM LEVOFOLINATE** 175mg in 250ml glucose 5% over 2 hours
- **FLUOROURACIL** 400mg/m² IV bolus
- **FLUOROURACIL** 2800mg/m² continuous infusion over 46 hours via an infusor

**Cycle Frequency:** Repeat every 28 days for 6 cycles (review after 3 cycles)

**NB** Calcium levofolinate is NOT the same as Calcium folinate, folinic acid, leucovorin, calcium leucovorin which are equivalent. Calcium levofolinate is the single isomer of folinic acid and the dose is generally half that of calcium folinate. [2]

**DOSE MODIFICATIONS**

**Fluorouracil:**
- Symptoms including diarrhea, mucositis and leucopenia, discuss with Registrar or Consultant
- Consider dose reductions in severe renal impairment only
- Bilirubin > 85micromol/L or AST >180 omit

**Mitomycin:**
- GFR > 10ml/min give 100% dose
- GFR < 10ml/min give 75% dose
- Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min
- AST >2xULN Clinical decision

**INVESTIGATIONS**

**Routine Blood test**
1) Blood results required before chemotherapy administration

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<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
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</tbody>
</table>

GFR assessed using $^{51}$Cr-EDTA result or calculated creatinine clearance at the Consultant’s discretion.

LFTs

2) Non urgent blood tests
- Tests relating to disease response/progression

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MITOMYCIN &
de Gramont

Colorectal PODG Chair Authorisation:

Date:

Page 1 of 2

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Version 3.4

Chemotherapy Regimens – Colorectal Cancer 45
CONCURRENT MEDICATION
Hickman line pack with cycle ONE only

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.

REFERENCES
1. FOCUS (CR08) clinical protocol 2001
2. Calcium levofolinate SPC 06/2002 [website]
MITOMYCIN and CAPECITABINE 42 day

**Indication: Advanced colorectal**

NICE guidance: Oral therapy with either capecitabine or tegafur with uracil (in combination with folinic acid) is recommended as an option for the first-line treatment of metastatic colorectal cancer. Capecitabine monotherapy is recommended as an option for the adjuvant treatment of stage III (Dukes' C) colon cancer following surgery. Capecitabine is recommended as monotherapy for adjuvant treatment post surgery for stage III (Dukes' C) colon cancer.

**DRUG REGIMEN**

**Day 1** CAPECITABINE 1250mg/m² twice daily (2500 mg/m²/day) for 14 days followed by a 7 day rest

**Day 22** MITOMYCIN 7mg/m² IV bolus.

CAPECITABINE 1250mg/m² twice daily (2500 mg/m²/day) for 14 days followed by a 7 day rest

**Cycle Frequency: Every 42 days for 4 cycles (review after 2 cycles)**

NB Capecitabine tablets available as 150 mg and 500 mg strengths.

**DOSE MODIFICATIONS**

**Mitomycin:**
GFR > 10ml/min give 100% dose
GFR < 10ml/min give 75% dose
AST >2xULN Clinical decision

**Capecitabine:**
Check CrCl prior to every cycle
CrCl (ml/min) > 50 give 100% dose
CrCl (ml/min) 30 - 50 give 75% dose
CrCl (ml/min) < 30 contraindicated
Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur.
Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.
Please refer to summary of product characteristics for detailed guidance on dose modification due to toxicity (including plantar palmar, erythema and gastrointestinal toxicity).
Brief guidance on initial dose modifications at the first appearance of toxicity is given below the Summary of Product Characteristics (SPC) which can be viewed at www.medicines.org.uk. This includes details on how to manage 2nd and subsequent appearance of toxicities. Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

### Toxicity Grades

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<td>Interrupt until resolved to grade 0-1</td>
<td>100%</td>
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<td>- 1st appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td>- 2nd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td>- 3rd appearance</td>
<td>Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
<tr>
<td>- 4th appearance</td>
<td>Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

| * Grade 3       | Interrupt until resolved to grade 0-1 | 75%                                                   |
| - 1st appearance| Interrupt until resolved to grade 0-1 | 50%                                                   |
| - 2nd appearance| Discontinue treatment permanently     | Not applicable                                         |

| * Grade 4       | Discontinue permanently OR if physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1 | 50%                                                   |
| - 1st appearance| Discontinue permanently               | Not applicable                                         |
| - 2nd appearance| Discontinue permanently               | Not applicable                                         |

### INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

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Serum creatinine - GFR should be calculated or measured using EDTA

### CONCURRENT MEDICATION

Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.
Capecitabine enhances the anticoagulant effects of warfarin.
Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.
ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Diarrhoea – treat with loperamide or codeine
Mucositis – use routine mouth care
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with capecitabine.

REFERENCES
**OXALIPLATIN** and **CAPECITABINE 21 day**

*Indication: Adjuvant and advanced colorectal
Unknown primary if appropriate*

**NICE Guidance:** Oral therapy with either capecitabine or tegafur with uracil (in combination with folinic acid) is recommended as an option for the first line treatment of metastatic colorectal cancer. Oxaliplatin should be considered for use as first line therapy, in combination with 5FU/FA as first line or subsequent therapy.

Oxaliplatin in combination with 5FU/FA is recommended as an option for the adjuvant treatment of stage III (Dukes' C) colon cancer following surgery.

Oxaliplatin is recommended with 5-fluorouracil and folinic acid for adjuvant treatment post surgery for stage III (Dukes' C) colon cancer.

**DRUG REGIMEN**

**Day 1** OXALIPLATIN 130mg/m² in 500ml glucose 5% infusion over 2 hours
Flush with glucose 5% after infusion
CAPECITABINE 1000mg/m² twice daily (2000mg/m²/day) po for 14 days followed by a 7 day rest

*Cycle frequency: Every 21 days for 8 cycles*

**Note:** Tablets are only available as 150mg and 500mg tablets therefore dose must be rounded appropriately Oxaliplatin should always be administered before fluoropyrimidines.

**DOSE MODIFICATIONS**

Previous neutropenic sepsis, discuss with SpR or Consultant
Symptoms including diarrhoea, mucositis and leucopenia, discuss with SpR or Consultant.

**Capecitabine:**
Check CrCl prior to every cycle
CrCl (ml/min) > 50 give 100%
CrCl (min/min) 30 - 50 give 75% dose
CrCl (ml/min) < 30 capecitabine is contraindicated

Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur.

Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.

Please refer to summary of product characteristics for detailed guidance on dose modification due to toxicity (including plantar palmar, erythema and gastrointestinal toxicity).
Brief guidance on initial dose modifications at the first appearance of toxicity is given below. Users of these guidelines should also refer to the more detailed guidance contained within the Summary of Product Characteristics (SPC) which can be viewed at [www.medicines.org.uk](http://www.medicines.org.uk).

Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

<table>
<thead>
<tr>
<th>Toxicity Grades</th>
<th>Dose changes within a treatment cycle</th>
<th>Dose adjustment for next cycle/dose (% of starting dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Grade 1</td>
<td>Maintain dose level</td>
<td>Maintain dose level</td>
</tr>
<tr>
<td>* Grade 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>100%</td>
</tr>
<tr>
<td>2nd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td>3rd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td>4th appearance</td>
<td>Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
<tr>
<td>* Grade 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td>2nd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td>3rd appearance</td>
<td>Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
<tr>
<td>* Grade 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st appearance</td>
<td>Discontinue permanently OR</td>
<td>50%</td>
</tr>
<tr>
<td>2nd appearance</td>
<td>If physician deems it to be in the patient’s best interest to continue, interrupt until resolved to grade 0-1</td>
<td></td>
</tr>
</tbody>
</table>

**Oxaliplatin:**

If persistent sensory symptoms occur, withdraw treatment
GFR > 20ml/min give 100% dose and adjust according to toxicity
GFR < 20ml/min dose reduce

Hepatic impairment
Probably no dose reduction necessary. Clinical decision

If patients develop acute laryngopharyngeal dysesthesia infuse the next cycle over 6 hours. If symptoms persist reduce dose by 20%.
INVESTIGATIONS
Routine Blood tests
1. Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Required Levels</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>Discuss</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
<td>≥75</td>
<td>Give</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5</td>
<td>Discuss</td>
</tr>
</tbody>
</table>

2. GFR assessed using $^{51}$Cr-EDTA result or calculated creatinine clearance the Consultant’s discretion.
3. LFTs

Non-urgent Blood tests
Tests relating to disease response/progression.

CONCURRENT MEDICATIONS
Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin.
Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

ANTI-EMETIC POLICY
Moderately emetogenic day 1
Low emetogenic risk all other days

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds.
Diarrhoea – treat with loperamide or codeine
Peripheral sensory neuropathy and laryngeal spasm – avoid cold drinks and touching cold items
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with capecitabine.

REFERENCES
1. Twelves C Oncology 2002; 16:23-26
RALTITREXED

Indication: Relapsed colorectal

Colorectal PODG recommendation –
raltitrexed is reserved for patients in whom fluorouracil is contraindicated
i.e. cardiac arrhythmias or appropriately designed studies.

DRUG REGIMEN
Day 1 RALTITREXED 3mg/m² in 100ml sodium chloride 0.9% infusion over 15 minutes

Cycle Frequency: Every 21 days for 6 cycles

DOSE MODIFICATIONS

\[
\begin{array}{ccc}
\text{CrCl ml/min} & \text{Dose} & \text{Interval} \\
> 65 & 100\% & 3 \text{ weekly} \\
55 -65 & 75\% & 4 \text{ weekly} \\
25 -54 & 50\% & 4 \text{ weekly} \\
< 25 & \text{No therapy} & \\
\end{array}
\]

AST/ALT < 5 x ULN, 100% dose
Bilirubin < 10xULN give 100% dose

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

\[
\begin{array}{ccc}
\text{Hb x g/dL} & \text{Give} & \text{Discuss} \\
\geq 10 & < 10 & \\
\text{Pit} \times 10^9/L & \geq 100 & < 100 \\
\text{Neutrophils} \times 10^9/L & \geq 1.5 & < 1.5 \\
\end{array}
\]

2) Non urgent blood tests
Tests relating to disease response/progression

ANTIEMETIC POLICY
Moderately emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
RALTITREXED and OXALIPLATIN

**Indication:** Metastatic and relapsed colorectal cancer, patients unable to tolerate Capecitabine / Fluorouracil treatment due to cardiac toxicity

Colorectal PODG recommendation – raltitrexed is reserved for patients in whom fluoropyrimidines are contraindicated i.e. cardiac arrhythmias or appropriately designed studies.

**DRUG REGIMEN**

**Day 1**
- **OXALIPLATIN** 130mg/m² IV infusion in 500ml 5% glucose over 2 hours
- **RALTITREXED** 3mg/m² in 100ml sodium chloride 0.9% infusion over 15 minutes

There must be a 45 minute gap between the administration of the 2 drugs.

**Cycle Frequency:** Every 21 days for 6 cycles (restage after 3 cycles)

**DOSE MODIFICATIONS**

Previous neutropenic sepsis, discuss with SpR or Consultant
Symptoms including diarrhoea, mucositis and leucopenia, discuss with SpR or Consultant

**Raltitrexed:**

<table>
<thead>
<tr>
<th>CrCl ml/min</th>
<th>Dose</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 65</td>
<td>100%</td>
<td>3 weekly</td>
</tr>
<tr>
<td>55 -65</td>
<td>75%</td>
<td>4 weekly</td>
</tr>
<tr>
<td>25 -54</td>
<td>50%</td>
<td>4 weekly</td>
</tr>
<tr>
<td>&lt; 25</td>
<td>No therapy</td>
<td></td>
</tr>
</tbody>
</table>

AST/ALT < 5 x ULN, 100% dose
Bilirubin < 10xULN give 100% dose

**Oxaliplatin:**

GFR > 20ml/min give 100% dose and adjust according to toxicity
GFR < 20ml/min dose reduce
Hepatic impairment
Probably no dose reduction necessary. Clinical decision
If persistent sensory symptoms occur, withdraw treatment
If patients develop acute laryngopharyngeal dysesthesia infuse the next cycle over 6 hours. If symptoms persist reduce dose by 20%.
INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration
   
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<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL ≥10 &lt; 10</td>
<td></td>
</tr>
<tr>
<td>Plt x 10⁹/L ≥100 &lt; 100</td>
<td></td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L ≥1.5 &lt; 1.5</td>
<td></td>
</tr>
</tbody>
</table>

2) Non urgent blood tests
   Tests relating to disease response/progression
   Also Performance status and assess for neuropathy

ANTIEMETIC POLICY
Moderately emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

REFERENCES
Capecitabine Cisplatin

*Indication: Metastatic or locally advanced anal cancer*

**DRUG REGIMEN**

Day 1

PREHYDRATION

CISPLATIN 60mg/m² in 1000ml sodium chloride 0.9% IV infusion over 1 hour

POSTHYDRATION

Days 1 to 21 CAPECITABINE 625mg/m² twice daily

Tablets available as strengths of 150 mg and 500 mg.

**Cycle Frequency: Every 21 days for 8 cycles**

**DOSE MODIFICATIONS**

*Cisplatin:*

GFR >60ml/min give 100% dose  
GFR 45-59ml/min give 75% dose  
GFR <45ml/min consider carboplatin [1]

If patient complains of tinnitus, tingling of fingers and/or toes discuss with SpR or Consultant before administration.

*Capecitabine:*

Check CrCl prior to every cycle  
CrCl (ml/min) >50 give 100% dose  
CrCl (ml/min 30 - 50 give 75% dose  
CrCl (ml/min <30 contraindicated

If hepatic toxicity occurs and the transaminases are <3.0 x ULN then treatment can be continued as per INTERAACT protocol without any dose modifications or delays. If the transaminases become elevated to 3.0–5.0 x ULN, 5-FU should be reduced by one dose level and cisplatin can still be administered at the same dose. If the transaminases are elevated to >5.0 x ULN then treatment with all drugs should be withheld until resolution to ≤ grade 1 for patients without liver metastases or to ≤ grade 2 for patients with liver metastases and elevated transaminases at baseline (i.e. 3.0–5.0 x ULN). On recovery, 5-FU should be reduced by 1 dose level.

**Neurotoxicity**

If grade 2 sensory or motor neuropathy occurs cisplatin treatment should be interrupted until neuropathy has resolved to ≤ grade 1. On recovery, cisplatin should be reduced by 1 dose level INTERAACT protocol. If this requires a delay of more than three weeks then the cisplatin should be omitted from subsequent cycles. If grade ≥3 sensory or motor neuropathy occurs cisplatin should be omitted from subsequent cycles. Anti-neuropathic medications can be used upon investigators discretion.
INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Required Range</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10 &lt; 10</td>
<td>Give</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
<td>≥100 &lt; 100</td>
<td>Discuss</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5 &lt; 1.5</td>
<td></td>
</tr>
</tbody>
</table>

Serum creatinine - GFR should be calculated or measured using EDTA

CONCURRENT MEDICATION
Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin.
Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR. Ensure adequate pre-and post-hydration prescribed as per inpatient schedule at the end of the TVCN protocols. If patient gains >2kg in weight or urine output <100ml/hour during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV Hickman line pack with cycle ONE only if using an infusor device

ANTIEMETIC POLICY
Highly emetogenic day 1
Low emetogenic risk all other days

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Diarrhoea – treat with loperamide or codeine
Mucositis – use routine mouthcare
Diarrhoea – treat with codeine or loperamide
Nephrotoxicity- ensure adequate pre and post hydration
Ototoxicity- assess patient for tinnitus or hearing abnormalities
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil.
Mitomycin Capecitabine + RT

Indication: Anal with radiotherapy

DRUG REGIMEN
Day 1  MITOMYCIN 12mg/m² IV bolus.
Days 1 to 5, 8 to 12, 15 to 19, 22 to 26, 29 to 33 and 36 to 38 (on each day of radiotherapy)
   CAPECITABINE 825mg/m² oral twice daily

Cycle Frequency: 1 cycle

DOSE MODIFICATIONS
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

Mitomycin:
GFR > 10ml/min give 100% dose
GFR < 10ml/min give 75% dose

Capecitabine:
Capecitabine
Check CrCl prior to every cycle
CrCl (ml/min) > 50  give 100% dose
CrCl (ml/min) 30 - 50 give 75% dose
CrCl (ml/min) < 30 contraindicated

Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur.
Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.
Please refer to summary of product characteristics (SPC) for detailed guidance on dose modifications due to toxicity (including plantar palmar, erythema and gastrointestinal toxicity).

Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.
Toxicity Grades | Dose changes within a treatment cycle | Dose adjustment for next cycle/dose (% of starting dose)
--- | --- | ---
* Grade 1 | Maintain dose level | Maintain dose level
* Grade 2 |  |  
- 1st appearance | Interrupt until resolved to grade 0-1 | 100%
- 2nd appearance | Interrupt until resolved to grade 0-1 | 75%
- 3rd appearance | Interrupt until resolved to grade 0-1 | 50%
- 4th appearance | Discontinue treatment permanently | Not applicable
* Grade 3 |  |  
- 1st appearance | Interrupt until resolved to grade 0-1 | 75%
- 2nd appearance | Interrupt until resolved to grade 0-1 | 50%
- 3rd appearance | Discontinue treatment permanently | Not applicable
* Grade 4 |  |  
- 1st appearance | Discontinue permanently OR | 50%
If physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1
- 2nd appearance | Discontinue permanently | Not applicable

CONCURRENT MEDICATION
Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.
Capecitabine enhances the anticoagulant effects of warfarin. Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10 &lt; 10</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
<td>≥100 &lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5 &lt; 1.5</td>
</tr>
</tbody>
</table>

Creatinine clearance at each cycle
Serum creatinine - GFR should be calculated or measured using EDTA

2) Non urgent blood tests
Tests relating to disease response/progression
CONCURRENT MEDICATION
Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.
Capecitabine enhances the anticoagulant effects of warfarin. Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
Mitomycin and Fluorouracil (MF)

Indication: Anal and metastatic colorectal

**DRUG REGIMEN**

Day 1  **MITOMYCIN** 7mg/m² IV bolus,  
          **FLUOROURACIL** 300mg/m²/24 hours continuous infusion for 7 days via an infusor

Day 8  **FLUOROURACIL** 300mg/m²/24 hours continuous infusion for 7 days via an infusor

Day 15 **FLUOROURACIL** 300mg/m²/24 hours continuous infusion for 7 days via an infusor

**Cycle Frequency:** Mitomycin – repeat every 3 to 6 weeks according to blood count  
Fluorouracil – Repeat day 21  
for 3 cycles (maximum 6 cycles)

**NB** Some Clinicians may prefer to cap mitomycin dose at 12mg.  
**NB** during radiotherapy Fluorouracil to be given at a dose of 225mg/m²/24 hours with mitomycin  
once only see alternative regimen. Prior to and after completion of radiotherapy Fluorouracil to be  
given at the dose above.

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Fluorouracil;**  
Consider dose reductions in severe renal impairment only  
Bilirubin > 85micromol/L or AST >180 omit

**Mitomycin:**  
GFR > 10ml/min give 100% dose  
GFR < 10ml/min give 75% dose  
Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min  
AST >2xULN Clinical decision

**INVESTIGATIONS**

Routine Blood test  
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th></th>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
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<td>&lt; 10</td>
</tr>
<tr>
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<tr>
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<td>≥1.5</td>
<td>&lt; 1.5</td>
</tr>
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2) Non urgent blood tests  
Tests relating to disease response/progression

---

Chemotherapy Regimens – Colorectal Cancer 61
CONCURRENT MEDICATION

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
Mitomycin + Fluorouracil (MF) with Radiotherapy

Indication: Anal and metastatic colorectal

DRUG REGIMEN
Day 1  MITOMYCN 7mg/m² IV bolus (cycle 1 only).
        FLUOROURACIL* 225mg/m²/24 hours continuous infusion for 7 days via an infusor
Day 8  FLUOROURACIL* 225mg/m²/24 hours continuous infusion for 7 days via an infusor
Day 15 FLUOROURACIL* 225mg/m²/24 hours continuous infusion for 7 days via an infusor

*NB Fluouracil to be given at a dose of 300mg/m²/24 hours prior to and after completion of
radiotherapy see alternative regimen.
NB Some Clinicians may prefer to cap mitomycin dose at 12mg.

Cycle Frequency: Mitomycin cycle 1 only
        Fluorouracil – continue fluorouracil for a total of 12 weeks

DOSE MODIFICATIONS
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

Fluorouracil:
Consider dose reductions in severe renal impairment only
Bilirubin > 85micromol/L or AST >180 omit

Mitomycin:
GFR > 10ml/min give 100% dose
GFR < 10ml/min give 75% dose
Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min
AST >2xULN Clinical decision

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

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</tbody>
</table>

2) Non urgent blood tests
Tests relating to disease response/progression
CONCURRENT MEDICATION

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
Mitomycin and Fluorouracil (MF) with concurrent Radiotherapy for patients < 70 years infusion

Indications: Anal cancer

DRUG REGIMEN

Day 1 MITOMYCIN 12mg/m² IV bolus. Max 20mg (Cycle 1 only)

   FLUOROURACIL 1000mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours

Day 2 FLUOROURACIL 1000mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours

Day 3 FLUOROURACIL 1000mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours

Day 4 FLUOROURACIL 1000mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours

Cycle Frequency: Repeat fluorouracil days 29 to 32

NB If a patient is 70 years old it is a clinical decision by the doctor based on specific patient factors whether the patient is treated with the <70 or >70 regimen.

DOSE MODIFICATIONS

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

Fluorouracil:
Consider dose reductions in severe renal impairment only
Bilirubin > 85micromol/L or AST >180 omit

Mitomycin:
GFR > 10ml/min give 100% dose
GFR < 10ml/min give 75% dose
Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min
AST >2xULN Clinical decision

INVESTIGATIONS

Routine Blood test 1) Blood results required before chemotherapy administration

<table>
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<td>≥1.5</td>
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</tbody>
</table>

2) Non urgent blood tests
Tests relating to disease response/progression
CONCURRENT MEDICATION
Prophylactic antibiotics ciprofloxacin 250mg bd for 6 weeks during chemoradiotherapy

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
Mitomycin and Fluorouracil (MF) with concurrent Radiotherapy for patients < 70 years infusor

**Indications:** Anal cancer

**DRUG REGIMEN**

**Day 1 MITOMYCIN** 12mg/m² IV bolus. Max 20 mg (Cycle 1 only)

**FLUOROURACIL** 4000mg/m² over 96 hours via an infusor

**Cycle Frequency:** Repeat fluorouracil days 29 to 32

NB if a patient is 70 years old it is a clinical decision by the doctor based on specific patient factors whether the patient is treated with the <70 or >70 regimen.

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Fluorouracil:**

Consider dose reductions in severe renal impairment only

Bilirubin > 85micromol/L or AST >180 omit

**Mitomycin:**

GFR > 10ml/min give 100% dose

GFR < 10ml/min give 75% dose

Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min

AST >2xULN Clinical decision

**INVESTIGATIONS**

Routine Blood test 1) Blood results required before chemotherapy administration

<table>
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<td>&lt; 10</td>
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<tr>
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<td>&lt; 100</td>
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<td>&lt; 1.5</td>
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</table>

2) Non urgent blood tests

Tests relating to disease response/progression

**CONCURRENT MEDICATION**

Prophylactic antibiotics ciprofloxacin 250mg bd for 6 weeks during chemoradiotherapy
ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
Mitomycin and Fluorouracil (MF) with concurrent Radiotherapy used for patients > 70 years infusion

Indications: Anal cancer

DRUG REGIMEN
Day 1  MITOMYCIN 10mg/m² IV bolus. Max 20 mg (Cycle 1 only)
       FLUOROURACIL 750mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours
Day 2  FLUOROURACIL 750mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours
Day 3  FLUOROURACIL 750mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours
Day 4  FLUOROURACIL 750mg/m² in 1000ml sodium chloride 0.9% infusion over 24 hours

Cycle Frequency: Repeat fluorouracil days 29 to 32

NB if a patient is 70 years old it is a clinical decision by the doctor based on specific patient factors whether the patient is treated with the <70 or >70 regimen.

DOSE MODIFICATIONS
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

Fluorouracil:
Consider dose reductions in severe renal impairment only
Bilirubin > 85micromol/L or AST >180 omit

Mitomycin:
GFR > 10ml/min give 100% dose
GFR < 10ml/min give 75% dose
Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min
AST >2xULN Clinical decision

INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

Give  Discuss
Hb x g/dL  ≥10  < 10
Plt x 10⁹/L  ≥100  < 100
Neutrophils x 10⁹/L  ≥1.5  < 1.5

2) Non urgent blood tests
Tests relating to disease response/progression
CONCURRENT MEDICATION
Prophylactic antibiotics ciprofloxacin 250mg bd for 6 weeks during chemoradiotherapy

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
Mitomycin + Fluorouracil (MF) with concurrent Radiotherapy used for patients > 70 years infusor

**Indications:** Anal cancer

**DRUG REGIMEN**

Day 1  **MITOMYCIN** 10mg/m² IV bolus. Max 20 mg (Cycle 1 only)

**FLUOROURACIL** 3000mg/m² infusion over 96 hours via an infusor

**Cycle Frequency:** Repeat fluorouracil days 29 to 32

NB if a patient is 70 years old it is a clinical decision by the doctor based on specific patient factors whether the patient is treated with the <70 or >70 regimen.

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

*Fluorouracil:*  
Consider dose reductions in severe renal impairment only  
Bilirubin > 85micromol/L or AST >180 omit

*Mitomycin:*  
GFR > 10ml/min give 100% dose  
GFR < 10ml/min give 75% dose  
Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min  
AST >2xULN Clinical decision

**INVESTIGATIONS**

Routine Blood test 1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL ≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L ≥100</td>
<td>&lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L ≥1.5</td>
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</tr>
</tbody>
</table>

2) Non urgent blood tests  
Tests relating to disease response/progression

**CONCURRENT MEDICATION**

Prophylactic antibiotics ciprofloxacin 250mg bd for 6 weeks during chemoradiotherapy
ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
**CISPLATIN and FLUOROURACIL INFUSIONAL**

*Indication: Metastatic anal carcinoma (second line post MF)* [1]

**DRUG REGIMEN**

**Day 1** Pre hydration
- **CISPLATIN** 75mg/m² in 1000ml sodium chloride 0.9% infusion over 4 hours

Post hydration
- **FLUOROURACIL** 1000mg/m² in 1000ml sodium chloride infusion 0.9% over 24 hours

**Day 2** **FLUOROURACIL** 1000mg/m² in 1000ml sodium chloride infusion 0.9% over 24 hours

**Day 3** **FLUOROURACIL** 1000mg/m² in 1000ml sodium chloride infusion 0.9% over 24 hours

**Day 4** **FLUOROURACIL** 1000mg/m² in 1000ml sodium chloride infusion 0.9% over 24 hours

Some Clinicians may prefer to give cisplatin 60mg/m² instead.

Note: The 5FU may be given in an infusor over 4 days instead

**Cycle Frequency: Every 21 days for 6 cycles**

**DOSE MODIFICATIONS**

Previous neutropenic sepsis, discuss with Consultant or Registrar.
Discuss with consultant whether 5-FU to go ahead if cisplatin is contra- indicated/discontinued
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Fluorouracil:**
Discuss with consultant whether 5-FU to go ahead if cisplatin is contra- indicated/discontinued
Consider dose reductions in severe renal impairment only
Bilirubin > 85micromol/L or AST >180 omit

**Cisplatin:**
GFR >60ml/min give 100% dose
GFR 45-59ml/min give 75% dose
GFR <45ml/min consider carboplatin [1]
If patient complains of tinnitus, tingling of fingers and/or toes discuss with SpR or Consultant before administration.

**TREATMENT DELAYS**

If Neutrophils <1.5 x 10⁹/L and/or the platelet count < 100 x 10⁹/L delay the second course by one week, recheck blood count.
If satisfactory (>1.5 x 10⁹/L and > 100x 10⁹/L) dose give 75% dose Cisplatin and 5FU.
If not satisfactory delay by a further week and recheck blood count, if satisfactory (>1.5 x 10⁹/L and >100 x 10⁹/L) then give 50% dose Cisplatin and 5FU.
If still unsatisfactory after 2 week delay chemotherapy should be discontinued
INVESTIGATIONS
Routine Blood tests
1. Blood results required before chemotherapy administration
<table>
<thead>
<tr>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
<td>≥100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5</td>
</tr>
</tbody>
</table>
2. GFR assessed using ⁵¹Cr-EDTA result or calculated creatinine clearance at the Consultant’s discretion. (cisplatin)
3. LFTs

Non-urgent Blood tests
Tests relating to disease response / progression.

CONCURRENT MEDICATION
Ensure adequate pre-and post-hydration prescribed as per inpatient schedule at the end of the TVCN regimens. If fluid balance is > 2L positive after 8 hours post hydration OR if patient gains >2kg in weight or urine output <100ml/hour during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV

ANTI-EMETIC POLICY
Highly emetogenic day 1
Low emetogenic risk day all other days

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Nephrotoxicity – ensure adequate pre and post hydration is prescribed.
Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.

REFERENCES
1. ACT 2 trial. final protocol (v.1.20) 31/01/2002 Cancer research UK
CISPLATIN and FLUOROURACIL infusor

**Indication:** Metastatic anal carcinoma (second line post MF) [1]

**DRUG REGIMEN**

**Day 1**
- Pre hydration
  - CISPLATIN 75mg/m² in 1000ml sodium chloride 0.9% infusion over 2 hours
  - Post hydration
  - FLUOROURACIL 4000mg/m² over 96 hours via an infusor

Some Clinicians may prefer to give cisplatin 60mg/m² instead.
Note: The 5FU may be given as 4 infusions of 24 hours instead

**Cycle Frequency:** Every 21 days for 6 cycles

**DOSE MODIFICATIONS**

Previous neutropenic sepsis, discuss with Consultant or Registrar.
Discuss with consultant whether 5-FU to go ahead if cisplatin is contra-indicated/discontinued
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Cisplatin:**
- GFR >60ml/min give 100% dose
- GFR 45-59ml/min give 75% dose
- GFR <45ml/min consider carboplatin.[1]

If patient complains of tinnitus, tingling of fingers and/or toes discuss with SpR or Consultant before administration.

**Fluorouracil:**
Discuss with consultant whether 5-FU to go ahead if cisplatin is contra-indicated/discontinued
Consider dose reductions in severe renal impairment only
- Bilirubin > 85micromol/L or AST >180 omit

**TREATMENT DELAYS**
If Neutrophils <1.5 x 10⁹/L and/or the platelet count < 100 x 10⁹/L delay the second course by one week, recheck blood count.
If satisfactory (>1.5 x 10⁹/L and > 100x 10⁹/L) give 75% dose Cisplatin and 5FU.
If not satisfactory delay by a further week and recheck blood count, if satisfactory (>1.5 x 10⁹/L and >100 x 10⁹/L) then give 50% dose Cisplatin and 5FU.
If still unsatisfactory after 2 week delay chemotherapy should be discontinued
INVESTIGATIONS
Routine Blood tests
1. Blood results required before chemotherapy administration

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<td>Hb x g/dL</td>
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<td>≥1.5</td>
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</tr>
</tbody>
</table>

2. GFR assessed using ^{51}Cr-EDTA result or calculated creatinine clearance at the Consultant’s discretion. (cisplatin)
3. LFTs

Non-urgent Blood tests
Tests relating to disease response / progression.

CONCURRENT MEDICATION
Ensure adequate pre-and post-hydration prescribed as per inpatient schedule at the end of the TVCN regimens. If patient gains >2kg in weight or urine output <100ml/hour during IV administration post Cisplatin give 20 - 40 mg Furosemide PO/IV OR 200ml Mannitol 10% IV Hickman line pack with cycle ONE only if using an infusor device

ANTI-EMETIC POLICY
Highly emetogenic day 1
Low emetogenic risk all other days

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Nephrotoxicity – ensure adequate pre and post hydration is prescribed.
Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.

REFERENCES
1. ACT 2 trial. final protocol (v.1.20) 31/01/2002 Cancer research UK
Intra hepatic (single lumen) Mitomycin + Fluorouracil (MF)

*Indications: Colon and rectum*

**DRUG REGIMEN**

**Day 1**  
Calcium folinate 350mg in 250ml sodium chloride 0.9% infusion over 1 hour  
100ml Sodium chloride 0.9% intra-hepatic arterial bolus to flush off line  
DEXAMETHASONE 8mg intra hepatic arterial bolus  
FLUOROURACIL 3000mg/m² intra hepatic arterial infusion over 46 hours via an infusor

**DAY 3**  
HEPARIN 5000units to flush hepatic PORTACATH after disconnection of chemotherapy

**Day 15**  
Calcium folinate 350mg in 250ml sodium chloride 0.9% infusion over 1 hour  
100ml Sodium chloride 0.9% intra hepatic arterial bolus to flush off line  
DEXAMETHASONE 8mg intra hepatic arterial bolus  
500ml Sodium chloride 0.9% intra hepatic arterial fast running drip for chemo administration  
MITOMYCIN 6mg/m² Intra hepatic arterial bolus over 15-20 mins via arm of fast running drip.  
FLUOROURACIL 3000mg/m² intra hepatic arterial infusion over 46 hours via an infusor

**DAY 17**  
HEPARIN 5000units to flush hepatic PORTACATH after disconnection of chemotherapy

**Cycle Frequency:** Repeat every 28 days for 3 cycles

**DOSE MODIFICATIONS**

Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.  
All dose reductions discuss with Registrar or Consultant

*Fluorouracil:*

Consider dose reductions in severe renal impairment only  
Bilirubin > 85micromol/L or AST >180 omit

*Mitomycin:*

GFR > 10ml/min give 100% dose  
GFR < 10ml/min give 75% dose  
Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min  
AST >2xULN Clinical decision
INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

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2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
Intra hepatic (double lumen) Mitomycin + Fluorouracil (MF)

Indications: Colon and rectum
For use in patients with a separate left and right portocath where dose is to be split evenly between left and right hepatic artery

**DRUG REGIMEN**

Day 1  
**Calcium folinate** 350mg in 250ml sodium chloride 0.9% infusion over 1 hour  
100ml Sodium chloride 0.9% intra hepatic arterial bolus to flush off line  
**DEXAMETHASONE** 4mg LEFT ARTERY intra hepatic arterial bolus  
**DEXAMETHASONE** 4mg RIGHT ARTERY intra hepatic arterial bolus  
**FLUOROURACIL** 1500mg/m² LEFT ARTERY intra hepatic arterial infusion over 46 hours via an infusor  
**FLUOROURACIL** 1500mg/m² RIGHT ARTERY intra hepatic arterial infusion over 46 hours via an infusor

**DAY 3**  
**HEPARIN** 2500units to flush LEFT ARTERY hepatic PORTACATH after disconnection of chemotherapy  
**HEPARIN** 2500units to flush RIGHT ARTERY hepatic PORTACATH after disconnection of chemotherapy

Day 15  
**Calcium folinate** 350mg in 250ml sodium chloride 0.9% infusion over 1 hour  
100ml Sodium chloride 0.9% intra hepatic arterial bolus to flush off line  
**DEXAMETHASONE** 4mg LEFT ARTERY intra hepatic arterial bolus  
**DEXAMETHASONE** 4mg RIGHT ARTERY intra hepatic arterial bolus  
250ml Sodium chloride 0.9% IV fast running drip for chemo administration LEFT ARTERY  
250ml Sodium chloride 0.9% IV fast running drip for chemo administration RIGHT ARTERY  
**MITOMYCIN** 3mg/m² Intra LEFT ARTERY hepatic arterial bolus over 15-20 mins via arm of fast running drip.  
**MITOMYCIN** 3mg/m² Intra RIGHT ARTERY hepatic arterial bolus over 15-20 mins via arm of fast running drip.  
**FLUOROURACIL** 1500mg/m² LEFT ARTERY intra hepatic arterial infusion over 46 hours via an infusor  
**FLUOROURACIL** 1500mg/m² RIGHT ARTERY intra hepatic arterial infusion over 46 hours via an infusor

**DAY 17**  
**HEPARIN** 2500units to flush LEFT ARTERY hepatic PORTACATH after disconnection of chemotherapy  
**HEPARIN** 2500units to flush RIGHT ARTERY hepatic PORTACATH after disconnection of chemotherapy

**Cycle Frequency: Repeat every 28 days for 6 cycles**
DOSE MODIFICATIONS
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant. All dose reductions discuss with Registrar or Consultant

**Fluorouracil:**
Consider dose reductions in severe renal impairment only
Bilirubin > 85micromol/L or AST >180 omit

**Mitomycin:**
GFR > 10ml/min give 100% dose
GFR < 10ml/min give 75% dose
Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min
AST >2xULN Clinical decision

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

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2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouth care
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment with fluorouracil.
Tegafur with uracil (Uftoral)

**Indication:** an option for the first-line treatment of metastatic colorectal cancer. (Technology appraisal guidance No. 61)

**DRUG REGIMEN**

**Days 1 to 28 UFTORAL** 324mg/m² TDS orally

(Uftoral 972mg/m²/day = tegafur 300mg/m²/day plus uracil 672mg/m²/day)

**CALCIUM FOLINATE** 30mg TDS orally

NB. Each Uftoral capsule 324mg contains Tegafur 100mg and Uracil 224mg

<table>
<thead>
<tr>
<th>Surface area/m²</th>
<th>Uftoral capsules/day @ Tegafur 300mg/m²/day plus Uracil 672mg/m²/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1.17</td>
<td>3 capsules/day</td>
</tr>
<tr>
<td>1.17-1.49</td>
<td>4 capsules/day</td>
</tr>
<tr>
<td>1.50-1.83</td>
<td>5 capsules/day</td>
</tr>
<tr>
<td>&gt; 1.83</td>
<td>6 capsules/day</td>
</tr>
</tbody>
</table>

**Cycle Frequency:** Repeat every 35 days for 6 cycles

**DOSE MODIFICATIONS**

NB. Do not dose reduce Folinic Acid

Neutrophils <1.5 or Platelets <100 Stop therapy until counts above these limits. Once recovered dose according to grade. <grade 2: Full dose

>grade 3: Decrease dose by 1 capsule/day in all subsequent treatment.

Renal and Hepatic impairment SPC states the effect of renal impairment has not been assessed. Discuss with consultant

Non-haematological toxicities e.g. stomatitis, diarrhoea, hand-foot

Grade 2 Stop chemo until recovered to grade 1 then full dose.

Grade 3-4 Stop chemo until recovered to grade 1 then restart with dose reduction: Decrease subsequent doses by 1 capsule/day for all future treatment

DPD Deficiency 1-3% of patients have markedly exaggerated uftoral toxicity due to reduced uftoral catabolism. Discuss with consultant.
INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
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<td>&lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5</td>
<td>&lt; 1.5</td>
</tr>
</tbody>
</table>

Liver function Tests (LFTs)

2) Non urgent blood tests
Tests relating to disease response/progression, tumour markers CEA, C19-9

CONCURRENT MEDICATION

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPlications
Palmar plantar (hand foot syndrome) causing red palms and soles – see dose modifications treat with pyridoxine 50mg tds
Mucositis – see dose modifications use routine mouth care
Diarrhoea – see dose modifications treat with loperamide or codeine
Cardiotoxicity uncommon. Uftoral may provoke angina or MI in patients with ischaemic heart disease. Seek specialist opinion on upgraded anti-anginal medication and consider dose reduction or alternative non uftoral treatment.
Neurotoxicity uncommon – cerebellar consider alternative non uftoral treatment

REFERENCES
1 eMC 2005 uftoral
2 WLCN protocols (colorectal) December 2005
Pre-hydration and post-hydration regimens

Ensure adequate diuresis is obtained prior to administration and maintained during and after administration.

1. **Inpatient**
   
   **Pre**
   
   1L sodium chloride 0.9% + 20mmol KCl + 8mmol MgSO₄ infusion over 4 hours
   
   *Give cisplatin in 1000ml volume over 4 hours*
   
   **Post**
   
   1L sodium chloride 0.9% + 20mmol KCl + 8mmol MgSO₄ infusion over 4 hours
   
   1L sodium chloride 0.9% + 20mmol KCl + 8mmol MgSO₄ infusion over 4 hours
   
   NB 1L sodium chloride 0.9% + 20mmol KCl + 8mmol MgSO₄ infusion over 6 hours if oral intake is inadequate

2. **Day case**
   
   **Pre**
   
   1L sodium chloride 0.9% + 20 mmol KCl + 8mmol MgSO₄ infusion over 2 hours
   
   200ml mannitol 10% infusion over 30 minutes
   
   *Give cisplatin in 1000ml volume over 2 hours*
   
   **Post**
   
   1L sodium chloride 0.9% + 20 mmol KCl + 8mmol MgSO₄ infusion over 2 hours

   NB Furosemide 40mg may be added if required
NICE Guidance for Colorectal Cancer: www.nice.org.uk

**Capecitabine**
Oral therapy with either capecitabine or tegafur with uracil (in combination with folinic acid) is recommended as an option for the first line treatment of metastatic colorectal cancer.
Capecitabine monotherapy is recommended as an option for the adjuvant treatment of stage III (Dukes’ C) colon cancer following surgery.
Capecitabine is recommended as monotherapy for adjuvant treatment post surgery for stage III (Dukes’ C) colon cancer.

**Irinotecan**
Irinotecan monotherapy is recommended in patients who have failed an established 5-fluorouracil containing treatment regimen or in combination with 5FU and folinic acid as first line therapy in metastatic disease.

**Oxaliplatin**
Oxaliplatin should be considered for use as first line therapy, in combination with 5FU/FA as first line or subsequent therapy in metastatic disease.
Oxaliplatin in combination with 5FU/FA is recommended as an option for the adjuvant treatment of stage III (Dukes’ C) colon cancer following surgery.
Oxaliplatin is recommended with 5-fluorouracil and folinic acid for adjuvant treatment post surgery for stage III (Dukes’ C) colon cancer.

**Raltitrexed**
On the balance of evidence relating to its clinical and cost effectiveness, raltitrexed is not recommended for the treatment of advanced colorectal cancer.
Its use for this patient group should be confined to appropriately designed clinical studies.
Cetuximab
Cetuximab given with other drugs called 5-fluorouracil, folinic acid and oxaliplatin is recommended as a possible first treatment for people with metastatic colorectal cancer only when:
- surgery to remove the cancer in the colon or rectum has been carried out or is possible
- the metastases are only in the liver and cannot be removed surgically before treatment
- the person is fit enough to have surgery to remove the cancer in the colon or rectum and to have liver surgery if it becomes possible to remove the metastases after cetuximab treatment
- the manufacturer refunds 16% of the amount of cetuximab used on a per patient basis.

Cetuximab given with 5-fluorouracil, folinic acid and irinotecan is recommended as a possible first treatment for people with metastatic colorectal cancer only when:
- surgery to remove the cancer in the colon or rectum has been carried out or is possible
- the metastases are only in the liver and cannot be removed surgically before treatment
- the person is fit enough to have surgery to remove the cancer in the colon or rectum and to have liver surgery if it becomes possible to remove the metastases after cetuximab treatment
- the person cannot take oxaliplatin because of its side effects or contraindications.

Treatment with cetuximab should stop after 16 weeks and the person should be assessed to see if they can have surgery to remove the metastases in their liver.
People with metastases only in the liver who receive cetuximab should have their treatment managed only by multidisciplinary teams that involve highly specialised liver surgical services.
<table>
<thead>
<tr>
<th>Toxicity</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allergic</strong></td>
<td>None</td>
<td>Transient rash, drug fever &lt;38°C (100.4°F)</td>
<td>Urticaria, drug fever ≥38°C (100.4°F) and/or asymptomatic bronchospasm</td>
<td>Symptomatic bronchospasm requiring parenteral medication(s) with or without urticaria; allergy related oedema / angioedema</td>
<td>Anaphylaxis</td>
</tr>
<tr>
<td><strong>Alopecia</strong></td>
<td>Normal</td>
<td>Mild hair loss</td>
<td>Pronounced hair loss</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Anorexia</strong></td>
<td>None</td>
<td>Loss of appetite</td>
<td>Oral intake significantly decreased</td>
<td>Requiring IV fluids</td>
<td>Requiring feeding tube or parenteral nutrition</td>
</tr>
<tr>
<td><strong>Blood counts Neutrophils</strong></td>
<td>Within normal limits</td>
<td>1.5x10⁹/l - normal</td>
<td>1.0-1.4x10⁹/l</td>
<td>0.5-0.9x10⁹/l</td>
<td>&lt;0.5x10⁹/l</td>
</tr>
<tr>
<td><strong>Blood counts Haemoglobin</strong></td>
<td>Within normal limits</td>
<td>10.0g/dl – normal</td>
<td>8.0 9.9g/dl</td>
<td>6.5-7.9g/dl</td>
<td>&lt;6.5g/dl</td>
</tr>
<tr>
<td><strong>Blood counts Platelets</strong></td>
<td>Within normal limits</td>
<td>75x10⁹/l - normal</td>
<td>50-74x10⁹/l</td>
<td>10-49x10⁹/l</td>
<td>&lt;10x10⁹/l</td>
</tr>
<tr>
<td><strong>Blood counts White blood count</strong></td>
<td>Within normal limits</td>
<td>3.0x10⁹/l - normal</td>
<td>2.0-2.9x10⁹/l</td>
<td>1.0-1.9x10⁹/l</td>
<td>&lt;1.0x10⁹/l</td>
</tr>
<tr>
<td><strong>Diarrhoea (patients with colostomy)</strong></td>
<td>None</td>
<td>Mild increase in loose, watery colostomy output compared with pre-treatment</td>
<td>Moderate increase in loose, watery colostomy output compared with pre-treatment, but not interfering with normal activity</td>
<td>Severe increase in loose, watery colostomy output compared with pre-treatment, interfering with normal activity</td>
<td>Physiologic consequences requiring intensive care, or haemodynamic collapse</td>
</tr>
<tr>
<td><strong>Diarrhoea (patients without colostomy)</strong></td>
<td>None</td>
<td>Increase of &lt;4 stools/day over pre-treatment</td>
<td>Increase of 4-6 stools/day, or nocturnal stools</td>
<td>Increase of ≥ 7 stools/day, or incontinence; or need for parenteral support for dehydration</td>
<td>Physiological consequences requiring intensive care, or haemodynamic collapse</td>
</tr>
<tr>
<td><strong>Hand-foot skin reaction</strong></td>
<td>None</td>
<td>Skin changes or dermatitis without pain</td>
<td>Skin changes with pain, not interfering with function</td>
<td>Skin changes with pain, interfering with function</td>
<td>-</td>
</tr>
<tr>
<td><strong>Hepatic – alk phos</strong></td>
<td>UNL</td>
<td>&gt;ULN – 2.5x ULN</td>
<td>&gt;2.5 – 5.0xULN</td>
<td>5.0 – 20.0xULN</td>
<td>&gt;20.0XULN</td>
</tr>
<tr>
<td><strong>Hepatic – bilirubin</strong></td>
<td>UNL</td>
<td>&gt;ULN – 1.5x ULN</td>
<td>&gt;1.5 – 3.0xULN</td>
<td>3.0 – 10.0xULN</td>
<td>&gt;10.0XULN</td>
</tr>
</tbody>
</table>

Chemotherapy Regimens – Colorectal Cancer 86
<table>
<thead>
<tr>
<th>Symptom</th>
<th>None</th>
<th>Increased fatigue over baseline, but not altering normal activities</th>
<th>Moderate (decrease in performance status by level 1) or causing difficulty performing some activities</th>
<th>Severe (decrease in performance status by ≥2 levels), or loss of ability to perform some activities</th>
<th>Bedridden or disabling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lethargy</td>
<td>None</td>
<td>oral intake significantly decreased</td>
<td>No significant intake, requiring IV fluids</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>None</td>
<td>able to eat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropathy - motor</td>
<td>Normal</td>
<td>subjective weakness but no objective findings</td>
<td>Mild objective weakness interfering with function, but not interfering with activities of daily living</td>
<td>Objective weakness interfering with activities of daily living</td>
<td>Paralysis</td>
</tr>
<tr>
<td>Neuropathy - sensory</td>
<td>Normal</td>
<td>loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function</td>
<td>Objective sensory loss or paresthesia (including tingling), interfering with function, but not interfering with activities of daily living</td>
<td>Sensory loss of paresthesia interfering with activities of daily living</td>
<td>Permanent sensory loss that interferes with function</td>
</tr>
<tr>
<td>Pain</td>
<td>None</td>
<td>mild pain not interfering with function</td>
<td>moderate pain: pain or analgesics interfering with function but not interfering with activities of daily living</td>
<td>severe pain: pain or analgesics severely interfering with activities of daily living</td>
<td>Disabling</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>None</td>
<td>painless ulcers, erythema or mild soreness</td>
<td>painful erythema, oedema or ulcers but can eat or swallow</td>
<td>painful erythema oedema, or ulcers requiring IV hydration</td>
<td>Severe ulceration or requires parenteral or enteral nutritional support or prophylactic intubation</td>
</tr>
<tr>
<td>Vomiting</td>
<td>None</td>
<td>1 episode in 24 hours</td>
<td>2-5 episodes in 24 hours</td>
<td>≥6 episodes in 24 hours, or need for IV fluids</td>
<td>Requiring parenteral nutrition, or physiological consequences requiring intensive care; haemodynamic collapse</td>
</tr>
</tbody>
</table>