**NCCP Chemotherapy Regimen**

**5-Fluorouracil (4 day) and mitoMYcin Chemoradiation Therapy**

**INDICATIONS FOR USE:**

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>Reimbursement Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of anal canal carcinoma</td>
<td>C21</td>
<td>00451a</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

**TREATMENT:**

*The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.*

mitoMYcin is administered at a dose of 10mg/m² on day 1 and day 29.

5-fluorouracil (5-FU) is administered at a dose of 1000 mg/m²/day on days 1–4 (week 1) and 29–32 (week 5) by continuous 24 h intravenous infusion with radiotherapy.

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route and Method of Administration</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 29</td>
<td>mitoMYcin</td>
<td>10mg/m² (Max single dose =20mg)</td>
<td>IV Bolus</td>
<td></td>
</tr>
<tr>
<td>1-4 29-32</td>
<td>5-Fluorouracil</td>
<td>1000mg/m²/day (Total dose = 4000mg/m² over 96hours)</td>
<td>Continuous IV infusion over 4 days</td>
<td>Infusor pump</td>
</tr>
</tbody>
</table>

*Alternative mitoMYcin schedule: 12 mg/m² IV on Day 1 ONLY

**ELIGIBLITY:**

- Indications as above
- ECOG status 0-2

**EXCLUSIONS:**

- Hypersensitivity to fluorouracil, mitoMYcin or any of the excipients
- Pregnancy
- Breast Feeding
- Fluorouracil (5-FU) should not be given to patients who are known to be homozygotic for dihydropyrimidine dehydrogenase (DPD) or in patients with a known complete absence of DPD activity.

**PRESCRIPTIVE AUTHORITY:**

The treatment plan must be initiated by a Consultant Medical Oncologist.
TESTS:

Baseline tests:
- FBC, renal and liver profile

Regular tests:
- FBC, renal and liver profile weekly throughout treatment

Disease monitoring:
Disease monitoring should be in line with the patient’s treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:
- Any dose modification should be discussed with a Consultant

Haematological:

Table 1: Dose Modification for Haematological toxicity

<table>
<thead>
<tr>
<th>ANC (x10^9/L) (on day of chemotherapy)</th>
<th>Platelets (x10^9/L) (at any stage during cycle)</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1</td>
<td>≥100</td>
<td>100%</td>
</tr>
<tr>
<td>0.5-0.99</td>
<td>50-99</td>
<td>Delay treatment until recovery</td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>&lt;50</td>
<td>Delay treatment until recovery and consider reducing fluorouracil by 25% for subsequent cycles</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Renal and Hepatic Impairment:

Table 2: Dose Modification in Renal and Hepatic Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>Consider dose reduction in severe renal impairment only</td>
<td></td>
</tr>
<tr>
<td>Mitomycin</td>
<td>CrCl (ml/min) &lt;10 I 75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consider a dose reduction for high doses of mitomycin when GFR 10-60 ml/min.</td>
<td></td>
</tr>
</tbody>
</table>

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient’s care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE’s terms of use available at http://www.hse.ie/eng/Disclaimer. This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens.
Non-Haematological Toxicity:

Table 3: Dose modification of fluorouracil for adverse events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Dose modification of 5 Fluorouracil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea or Mucositis</td>
<td>Delay treatment until toxicity has resolved to Grade 1 or less</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Delay treatment until toxicity has resolved to Grade 1 or less and</td>
</tr>
<tr>
<td>Grade ≥ 3</td>
<td>reduce fluorouracil by 50% for subsequent cycles</td>
</tr>
</tbody>
</table>

**SUPPORTIVE CARE:**

**EMETOGENIC POTENTIAL:**

- 5-Fluorouracil Low (Refer to local policy).
- mitoMYcin Low (Refer to local policy).

**PREMEDICATIONS:** Not required

**OTHER SUPPORTIVE CARE:**

- Anti-diarrhoeal treatment (Refer to local policy).
- Mouth Care (Refer to local policy)

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:**

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details

- **Extravasation:** mitoMYcin causes pain and tissue necrosis if extravasated (Refer to local policy)
- **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Myocardial ischaemia and angina:** Cardiotoxicity is a serious complication during treatment with fluorouracil. Patients, especially those with a prior history of cardiac disease or other risk factors, treated with fluorouracil, should be carefully monitored during therapy.
- **Dihydropyrimidine dehydrogenase (DPD) deficiency:** Rare, life-threatening toxicities such as stomatitis, mucositis, neutropenia, neurotoxicity and diarrhoea have been reported following administration of fluoropyrimidines (e.g. fluorouracil and capecitabine). Severe unexplained toxicities require investigation prior to continuing with treatment.

**DRUG INTERACTIONS:**

- Marked elevations of prothrombin time and INR have been reported in patients stabilized on warfarin therapy following initiation of fluorouracil regimes.
- Concurrent administration of fluorouracil and phenytoin may result in increased serum levels of phenytoin
- 5-Fluorouracil is contraindicated in combination with brivudin, sorivudin and analogues as these are potent inhibitors of the 5-fluorouracil metabolising enzyme dihydropyrimidine dehydrogenase (DPD).
Caution should be taken when using fluorouracil in conjunction with medications which may affect dihydroprimidene dehydrogenase activity.

Current drug interaction databases should be consulted for more information.

ATC CODE:

5-Fluorouracil - L01BC02
mitoMYcin - L01DC03

REFERENCES:


<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>15/11/2017</td>
<td></td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>06/11/2019</td>
<td>Reviewed. Update of exclusions, emetogenic potential and drug interactions</td>
<td>Prof Maccon Keane</td>
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</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.