5-fluorouracil 225mg/m²/day and Radiotherapy (RT) - Continuous infusion (7 day)

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 locally advanced rectal cancer</td>
<td>C20</td>
<td>00421a</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

*If the reimbursement status is not defined, the indication has yet to be assessed through the formal HSE reimbursement process.

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 patient's individual clinical circumstances.

5-fluorouracil is administered by continuous infusion with concurrent radiotherapy for 6 weeks. The 5-fluorouracil infusor pump should be changed every 7 days.

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route and Method of Administration</th>
<th>Diluent &amp; Rate</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-7</td>
<td>5-fluorouracil</td>
<td>225mg/m²/day</td>
<td>Continuous IV infusion over 7 days</td>
<td>Infusor pump</td>
<td>For duration of radiotherapy (6 weeks)</td>
</tr>
</tbody>
</table>

ELIGIBILITY:

- Indications as above
- ECOG status 0-2

EXCLUSIONS:

- Hypersensitivity to 5-fluorouracil or any of the excipients
- Pregnancy
- Breast Feeding
- Fluorouracil (5-FU) should not be given to patients 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
NCCP Chemotherapy Regimen

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>
<thead>
<tr>
<th>ANC (x 10^9/L) (on day of chemotherapy)</th>
<th>Platelets (x 10^9/L) (at any stage during cycle)</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1</td>
<td>≥100</td>
<td>100% Dose</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>
</tbody>
</table>

Renal and Hepatic Impairment:

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider dose reduction in severe renal impairment only</td>
<td>Bilirubin (micromol/L)</td>
</tr>
<tr>
<td>ANC &lt;50</td>
<td>&lt;85</td>
</tr>
<tr>
<td>ANC &gt;50 but &lt;100</td>
<td>&gt;85 or &lt;180</td>
</tr>
<tr>
<td>ANC ≥100</td>
<td>&gt;180</td>
</tr>
</tbody>
</table>

Clinical decision.
Moderate hepatic impairment; reduce initial dose by 1/3. Severe hepatic impairment, reduce initial dose by 1/2. Increase dose if no toxicity

SUPPORTIVE CARE:

**EMETOGENIC POTENTIAL:** Low  (Refer to local policy).

**PREMEDICATIONS:** Not required

**OTHER SUPPORTIVE CARE:** No specific recommendations

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NCCP Chemotherapy Regimen

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

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

- **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.
- Fluorouracil (5-FU) is contraindicated in combination with brivudin, sorivudin and analogues as these are potent inhibitors of the 5-FU-metabolising enzyme dihydropyrimidine dehydrogenase (DPD). Current drug interaction databases should be consulted for more information.

ATC CODE:

5-Flourouracil L01BC02

REFERENCES:


<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>08/05/2017</td>
<td></td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>2</td>
<td>19/06/2019</td>
<td>Updated exclusions, hepatic dose modification table, drug interactions.</td>
<td>Prof Maccon Keane</td>
</tr>
<tr>
<td>3</td>
<td>09/10/2019</td>
<td>Update of exclusions</td>
<td>Prof Maccon Keane</td>
</tr>
</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

1 ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes

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Further details on the Cancer Drug Management Programme is available at:
http://www.hse.ie/eng/services/list/5/cancer/profinfomedonc/cdmp/

NCCP Regimen
S-FU and RT-Continuous Infusion-7day
Published: 11/05/2017
Review: 19/06/2021
Version number: 3

Tumour Group:
Gastrointestinal
NCCP Regimen Code: 00421

ISM0 Contributor:
Prof Maccon Keane

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