Modified Roswell Park (Fluorouracil 500mg/m² and Folinic Acid 50mg weekly x 6) Regimen

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 metastatic colorectal cancer</td>
<td>C18</td>
<td>00427a</td>
<td>Hospital</td>
</tr>
<tr>
<td>Adjuvant treatment of colorectal cancer</td>
<td>C18</td>
<td>00427b</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.*

Metastatic: Folinic Acid and 5-fluorouracil are administered once weekly for 6 weeks followed by a 2 week break (1 cycle= 8weeks) until disease progression or unacceptable toxicity develops.

Adjuvant: Folinic Acid and 5-fluorouracil are administered once weekly for 6 weeks followed by a 2 week break (1 cycle= 8weeks) for 3 cycles or until disease progression or unacceptable toxicity develops.

<table>
<thead>
<tr>
<th>Order of Admin</th>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route and Method of Administration</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1, 8, 15, 22, 29, 36</td>
<td>Folinic Acid (Calcium folinate)</td>
<td>50mg</td>
<td>IV bolus</td>
<td>Every 56 days</td>
</tr>
<tr>
<td>2</td>
<td>1, 8, 15, 22, 29, 36</td>
<td>5-fluorouracil</td>
<td>500mg/m²</td>
<td>IV bolus</td>
<td>Every 56 days</td>
</tr>
</tbody>
</table>

Note: Treatment may be administered once weekly for 4 weeks followed by a 2 week break at the discretion of the prescribing Consultant.

ELIGIBILTY:
- Indication as above
- ECOG 0-2

EXCLUSIONS:
- Pregnancy
- Breast Feeding
- Severe liver impairment
- 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

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This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)
PRESCRIPTIVE AUTHORITY:
The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:
- FBC, liver and renal profile.

Regular tests:
- FBC, liver and renal profile prior to each 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
- The dose of folinic acid remains fixed at 50mg and is delayed or omitted if fluorouracil bolus is delayed or omitted

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>and ≥100</td>
<td>100% Dose</td>
</tr>
<tr>
<td>0.5 - 0.99</td>
<td>or 50 - 99</td>
<td>Delay treatment until recovery*</td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>or &lt;50</td>
<td>Delay treatment until recovery* and consider reducing fluorouracil by 25% for subsequent cycles</td>
</tr>
</tbody>
</table>

Febrile neutropenia

*Missed doses will not be made up

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>&lt;85 or &gt;85</td>
<td>&lt;180 or &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.

NCCP Regimen: Modified Roswell Park Regimen
Published: 07/07/2017
Review: 10/07/2021
Version number: 3

Tumour Group: Gastrointestinal
NCCP Regimen Code: 00427
ISMO Contributor: Prof Maccon Keane
Page 2 of 4

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Management of adverse events:

### Table 3: Dose modification schedule based on adverse events

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucositis or Stomatitis</td>
<td>Delay treatment until resolved to Grade ≤1 and reduce the dose for subsequent cycles as follows:</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>• No dose reduction</td>
</tr>
<tr>
<td></td>
<td>• Reduce 5-fluorouracil by 25%</td>
</tr>
<tr>
<td></td>
<td>• Reduce 5-fluorouracil by 50%</td>
</tr>
<tr>
<td></td>
<td>• Omit 5-fluorouracil</td>
</tr>
<tr>
<td>Hand and foot syndrome (Palmar-plantar erythrodysesthesia syndrome)</td>
<td>Delay treatment until resolved to Grade ≤1 and reduce the dose for subsequent cycles as follows:</td>
</tr>
<tr>
<td></td>
<td>• Reduces 5-fluorouracil by 50%</td>
</tr>
<tr>
<td></td>
<td>• Omit 5-fluorouracil</td>
</tr>
</tbody>
</table>

### SUPPORTIVE CARE:

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

**PREMEDICATIONS:** None

**OTHER SUPPORTIVE CARE:** No specific recommendations.

### ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

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

- **Gastrointestinal toxicity:** Patients treated with fluorouracil should be closely monitored for diarrhea and managed 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 stabilised 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-Fluorouracil - L01BC02

REFERENCES:


Version | Date     | Amendment                                                                 | Approved By     |
--- | --- | --- | --- |
1  | 14/06/2017 | Update of exclusion criteria. Removal of INR testing. Update of drug interactions. | Prof Maccon Keane |
2  | 10/07/2019 | Update of exclusions | Prof Maccon Keane |
3  | 09/10/2019 | Update of exclusions | Prof Maccon Keane |

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

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