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 Indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of metastatic colorectal cancer</td>
<td>C18</td>
<td>00427a</td>
<td></td>
</tr>
<tr>
<td>Adjuvant treatment of colorectal cancer</td>
<td>C18</td>
<td>00427b</td>
<td></td>
</tr>
</tbody>
</table>

If a reimbursement indicator (e.g. ODMS, CDS) is not defined, the drug and its detailed indication have not gone through the formal reimbursement process as legislated for in the Health (Pricing and Supply of Medical Goods) Act 2013.

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-FU are administered once weekly for 6 weeks followed by a 2 week break (1 cycle= 8 weeks) until disease progression or unacceptable toxicity develops.

Adjuvant: Folinic Acid and 5-FU are administered once weekly for 6 weeks followed by a 2 week break (1 cycle= 8 weeks) 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-FU</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.

ELIGIBILITY:

- Indication as above
- ECOG 0-2

EXCLUSIONS:

- Pregnancy
- Breast Feeding
- Severe liver impairment
- Patients homozygotic for dihydropyrimidine dehydrogenase (DPD)

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:
- FBC, U&E, LFTs

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INR tests if patient is on warfarin as clinically indicated.

Regular tests:
- FBC, U&E, LFTs prior to each treatment
- INR tests if patient is on warfarin as clinically indicated.

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 1. Recommended dose modification for 5-FU

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x 10^9/L) (Any stage of cycle)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>0.5-0.99</td>
<td>Delay treatment until recovery*</td>
<td>50-99</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>Delay treatment until recovery* and consider reducing 5-FU by 25% for subsequent cycles</td>
<td>&lt; 50</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>Delay treatment until recovery* and consider reducing 5-FU by 25% for subsequent cycles</td>
<td></td>
</tr>
</tbody>
</table>

*Missed doses will not be made up
Renal and Hepatic Impairment:

Table 2. Recommended dose modification for 5-FU in patients with renal or 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

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><strong>Mucositis or Stomatitis</strong></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></td>
</tr>
<tr>
<td>Hand and foot syndrome (Palmar-plantar erythrodysthesia syndrome)</td>
<td></td>
</tr>
</tbody>
</table>

Grade 2
- First occurrence
- Second occurrence
- Third occurrence
- Fourth occurrence

Grade 3 or 4
- First occurrence
- Second occurrence

Delay treatment until resolved to Grade ≤1 and reduce the dose for subsequent cycles as follows
- No dose reduction
- Reduce 5-FU by 25%
- Reduce 5-FU by 50%
- Omit 5-FU

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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 stabilized on warfarin therapy following initiation of fluorouracil regimes.
- Concurrent administration of fluorouracil and phenytoin may result in increased serum levels of phenytoin.
- Caution should be taken when using fluorouracil in conjunction with medications which may affect dihydropyrimidine dehydrogenase activity.
- Current drug interaction databases should be consulted for more information.

**ATC CODE:**

5-Fluorouracil - L01BC02

**REFERENCES:**

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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/profin/profinonmedonc/cdmp/