WEEKLY 5-FLUOROURACIL AND FOLINIC ACID

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Diluent and Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Sodium Chloride 0.9%</td>
<td>500ml</td>
<td>Infusion</td>
<td>Fast Running</td>
</tr>
<tr>
<td></td>
<td>Calcium Leucovorin (folinic acid)</td>
<td>20mg/m²</td>
<td>IV bolus</td>
<td>Slow Bolus via saline drip</td>
</tr>
<tr>
<td></td>
<td>5-Fluorouracil</td>
<td>*425mg/m²</td>
<td>IV bolus</td>
<td>Slow Bolus via saline drip</td>
</tr>
</tbody>
</table>

*The 5-FU dose may be reduced to 370 mg/m² depending on patient's performance status.

If used with concurrent radiotherapy, a dose of 300 mg/m² is used.

CYCLE LENGTH AND NUMBER OF DAYS
Given ONCE a week for 30 doses (30 weeks)

APPROVED INDICATIONS
Adjuvant treatment for Duke's B & C colorectal cancer

EXCLUSION CRITERIA
Pregnancy, lactation

RECOMMENDED TAKE HOME MEDICATION
Metoclopramide 10mg three times daily as required
Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details

INVESTIGATIONS / MONITORING REQUIRED
FBC, U&E & LFT's every 2-4 weeks or pre-cycle
Where CEA is elevated this should be measured every 4 weeks.

ASSESSMENT OF RESPONSE
Adjuvant There will be no visible disease to monitor for adjuvant treatment.

REVIEW BY CLINICIAN
Every 4 to 6 weeks

NURSE / PHARMACIST LED REVIEW
On cycles where not seen by clinician.

ADMINISTRATION NOTES
- The dose of folinic acid given with 5-FU varies depending on clinician preference. The usual dose is 20mg/m² however many units use a standard dose for all patients. Doses in the range 20mg to 50mg are all acceptable.
- Two forms of folinic acid are available. The doses given above refer to 'standard' racemic calcium folinate only. If the pure active enantiomer, calcium levofolinate (Isovorin®) is used the dose will generally be half that of the 'standard' folinate.
- Diarrhoea is common, and may require intervention with fluids and electrolytes if severe. If diarrhoea is a problem, give loperamide 2 to 4 mg four times daily as required or codeine phosphate 30mg four times daily and stop 5FU infusion if diarrhoea moderate/severe.
EXTRAVASATION  See NCA / local Policy

TOXICITIES
Usually tolerated very well with few side effects
- Diarrhoea
- Occasional Nausea
- Darkening/ Discoloration of Veins
- Myelosuppression
- Stomatitis
- Palmar/Plantar Erythrodysesthesia
- Hyperpigmentation
- Dry/watery eyes
- Cardiotoxicity - Occasionally patients with heart disease may experience coronary artery spasm. Stop Treatment with 5-FU if this occurs.

DPD Deficiency and Severe Toxicity Risk
Dihydropyrimidine dehydrogenase (DPD) plays an important role in the metabolism of fluoropyrimidine drugs 5-fluorouracil (5FU) and capecitabine. Patients with DPD deficiency may be predisposed to experience increased or severe toxicity when receiving 5-FU or capecitabine, and in some cases these events can be fatal.

For all patients having capecitabine or fluorouracil, the risk of severe side effects from capecitabine or 5FU if patients have a deficiency of DPD must be mentioned and patient given a copy of the DPD toxicity information leaflet from cancer research UK.


DOSE MODIFICATION / TREATMENT DELAYS
The 5-FU dose may be reduced to 400 mg/m² or to 370 mg/m² depending on patient’s performance status.

Haematological Toxicity:
- ANC < 1.5 and/or platelets <75, delay for 1 week
- >1 week recovery, dose reduce by 20-25%
- Following 2 delays for toxicity, all subsequent doses should be dose reduced by 20-25%
- If further delays necessary, consider further dose reduction (discuss with SpR/Consultant) or consider stopping treatment.
**Non- Haematological Toxicity:**
Any patient with CTC toxicity should be prescribed the therapeutic option for grade 1 toxicity in addition to 5FU modification (see PVI 5FU modification).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
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</thead>
<tbody>
<tr>
<td><strong>Stomatitis</strong></td>
<td>Encourage good oral hygiene. Difflam mouthwash PRN as local pain relief.</td>
<td>Mouth care + Delay treatment until recovered</td>
<td>Delay chemo until recovered. Restart with a 20% 5FU dose reduction</td>
<td>Delay chemo until recovered. Restart with a 40% 5FU dose reduction</td>
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<tr>
<td><strong>PPE</strong></td>
<td>No change. Advise E45 or aqueous cream</td>
<td>Delay treatment until recovered</td>
<td>Delay chemo until recovered. Restart with a 20% 5FU dose reduction</td>
<td>Delay chemo until recovered. Restart with a 40% dose reduction</td>
</tr>
<tr>
<td><strong>Diarrhoea</strong></td>
<td>Loperamide 4mg initially, then 2mg after each motion</td>
<td>Despite correct loperamide treatment, delay treatment until recovered. Restart with a 20% 5FU dose reduction</td>
<td>Delay chemo until recovered. Restart with a 20% 5FU dose reduction</td>
<td>Delay chemo until recovered. Discontinue or restart with a 20% dose reduction (Discuss with SpR/Consultant)</td>
</tr>
</tbody>
</table>

**TREATMENT LOCATION**
Can be given at Cancer Centre or Cancer Unit

**REFERENCES:**