### Drug Administration Schedule

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Glucose 5%</td>
<td>500ml</td>
<td>Infusion</td>
<td>Fast Running for Line Flush</td>
</tr>
<tr>
<td></td>
<td>Ondansetron</td>
<td>8mg</td>
<td>Oral /Slow bolus/15 min infusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>8mg</td>
<td>IV bolus</td>
<td>Via glucose drip</td>
</tr>
<tr>
<td>Day 1</td>
<td>Calcium Leucovorin (folinic acid)</td>
<td>200mg/m²* (See Note)</td>
<td>Infusion</td>
<td>250ml Glucose 5% over 2 hours concurrent with oxaliplatin</td>
</tr>
<tr>
<td>Day 1</td>
<td>Oxaliplatin</td>
<td>85 mg/m²</td>
<td>Iv Infusion</td>
<td>250ml Glucose 5% over 2 hours concurrent with folinic acid</td>
</tr>
<tr>
<td></td>
<td>Glucose 5%</td>
<td>500ml</td>
<td>Infusion</td>
<td>Line Flush</td>
</tr>
<tr>
<td>Day 2</td>
<td>Fluorouracil 5 F</td>
<td>400 mg/m²</td>
<td>IV bolus</td>
<td>Over 5 minutes</td>
</tr>
<tr>
<td>Day 3</td>
<td>Fluorouracil 5 F</td>
<td>2400 mg/m²</td>
<td>via infusor device</td>
<td>0.9% Sodium Chloride over 46 hours</td>
</tr>
</tbody>
</table>

*Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.

### Cycle Length and Number of Days

Every 14 days

### Approved Indications

- adjuvant treatments after surgery for stage III (Dukes’ C) colon cancer
- Advanced/ metastatic colorectal cancer

### Eligibility Criteria

*Details as per key trial submission based upon as appropriate*

### Exclusion Criteria

Patients with baseline renal function less than 30ml/min (Creatinine Clearance)

### Premedication

As above

### Recommended Take Home Medication

- Ondansetron 8mg twice daily for 2 to 3 days
- Dexamethasone 4mg twice daily for 1 to 3 days
- Metoclopramide 10mg three times daily as required

### Investigations / Monitoring Required

- FBC, U&E’s, LFT’s & tumour markers as appropriate prior to each course of chemotherapy
- FBC on the day of chemotherapy
- Where CEA is elevated this should be measured before each cycle.

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FOLFOX-CNTW-protocol-CRP09-CR007 V1.3  
Issue Date 29/05/2014  
Expiration Date May 2016
ASSESSMENT OF RESPONSE
Assessed radiologically after 4th cycle.
Metastatic: Tumour size and patient symptomatic response
Adjuvant There will be no visible disease to monitor for adjuvant treatment.

REVIEW BY CLINICIAN
To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

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

ADMINISTRATION NOTES
- Patient needs to attend on day 3 for removal of infusor
- If diarrhoea is a problem give loperamide 2-4 mg QDS prn or codeine phosphate.
- **Oxaliplatin is incompatible with saline.** Must use 5% dextrose as diluent and line flush
- Bronchospasm can occur. * If severe laryngeal spasm occurs consider increasing Oxaliplatin infusion to 6 hours
- Two forms of folinic Acid are available. The doses given above refer to 'standard' calcium folinate only. If the disodium salt, calcium levofoamate (Isovorin®) is used the dose will generally be half that of the 'standard' folinate.
- *Note: A variety of calcium folinate doses have been previously used and there is no hard and fast rule that requires a specific dose. Some trials have used 175mg Calcium LevoFolinate or 350mg Calcium Folate as a fixed dose. Other trials have used 200mg/m² with max dose 350mg. To use a convenient vial size, other centres have adopted 300mg as a fixed dose. A consistent strategy for dosing of folinic acid through an individual organisation will reduce risk of errors.
- As with all platinum based chemotherapy, patients may experience allergic reaction during administration. The following table is intended to help differentiate between Platinum Hypersensitivity and Laryngo-pharyngeal Dyesthesia.

<table>
<thead>
<tr>
<th>Clinical Symptoms</th>
<th>Laryngo-pharyngeal Dyesthesia</th>
<th>Platinum Hypersensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>O₂ saturation</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Difficulty swallowing</td>
<td>Present (loss of sensation)</td>
<td>Absent</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Cold induced symptoms</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Normal or Increased</td>
<td>Normal or Decreased</td>
</tr>
<tr>
<td>Treatment</td>
<td>Anxiolytics; observation in a controlled clinical setting until symptoms abate or at physician's discretion</td>
<td>Oxygen, steroids, epinephrine, bronchodilators; Fluids and vasopressors if appropriate</td>
</tr>
</tbody>
</table>
• Patients who have previously experienced Grade I or II Platinum Hypersensitivity should be pre-medicated with
  45 minutes prior to Oxaliplatin:
  • Dexamethasone 20 mg IV in 50 mL NS over 15 minutes (or Hydrocortisone 100mg)
  30 minutes prior to Oxaliplatin:
  • Chlorphenamine 10 mg IV and Ranitidine 50 mg IV in 50 mL NS over 20 minutes

EXTRAVASATION  See NECN / local Policy

TOXICITIES
• Peripheral neurotoxicity very common with Oxaliplatin. (dose limiting toxicity)
• Myelosuppression
• Cold induced parathesia
• Nausea and Vomiting
• Allergic reaction
• Diarrhoea
• Stomatitis
• Palmar/Plantar Erythrodysesthesia
• Darkening/discholoration of veins
• Cardiotoxicity - Occasionally patients may experience coronary artery spasm
• Laryngopharyngeal dysesthesia

DOSE MODIFICATION / TREATMENT DELAYS

Haematological toxicity:
• Delay 1 week if ANC < 1-1.5 and Platelets < 75
• No dose reduction for CTC grade I/II ANC
• Grade III/IV ANC → delay chemotherapy until recovered, then proceed at 20% 5FU and Oxaliplatin dose reduction
• If delay > 1 week or delay 2 weeks or greater occurs, reduce the 5FU dose (bolus & infusional) and oxaliplatin by 20%. Continue at the reduced dose for subsequent cycles unless other toxicity occurs.
• If further delay(s) for bone marrow suppression occur despite a 20% dose reduction, consider a further 20% dose reduction.

Non –Haematological toxicity:
• No dose reduction should apply to oxaliplatin in case of PPE
• In case of Grade III/IV stomatitis or diarrhoea despite a 20% reduction of 5FU, Oxaliplatin should be reduced by 20%

Neurotoxicity:
• Cold related paraesthesia of hands/feet or dysesthesia/laryngeal spasm syndrome last a few hours and do not require treatment or dose reduction.
• If severe laryngeal spasm occurs consider increasing Oxaliplatin infusion to 6 hours
• If symptoms persist for 14 days and/or there is pain, functional loss, omit Oxaliplatin and continue with 5FU/FA until fully recovered, then restart Oxaliplatin at 20% dose reduction
TREATMENT LOCATION
Can be given at Cancer Centre or Cancer Unit

REFERENCES:

- NICE TA100: Capecitabine and oxaliplatin in the adjuvant treatment of stage III (Dukes' C) colon cancer: April 2006