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>Day 1</td>
<td>Glucose 5%</td>
<td>500ml</td>
<td>Infusion</td>
<td>Fast Running for Line Flush</td>
</tr>
<tr>
<td>Day 1</td>
<td>Ondansetron</td>
<td>8mg</td>
<td>IV bolus</td>
<td>Via glucose drip</td>
</tr>
<tr>
<td>Day 1</td>
<td>Dexamethasone</td>
<td>8mg</td>
<td>Oral/Slow bolus/15 min infusion</td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>Calcium Leucovorin (folinic acid)</td>
<td>200mg/m² (max. 350mg)</td>
<td>Infusion</td>
<td>250ml Glucose 5% over 2 hours concurrent with irinotecan</td>
</tr>
<tr>
<td>Day 1</td>
<td>Irinotecan</td>
<td>180mg/m²</td>
<td>Iv Infusion</td>
<td>250ml Glucose 5% over 2 hours concurrent with folinic acid</td>
</tr>
<tr>
<td>Day 1</td>
<td>Dextrose 5%</td>
<td>500ml</td>
<td>Infusion</td>
<td>Line Flush</td>
</tr>
<tr>
<td>Day 1</td>
<td>5 Fluorouracil</td>
<td>400 mg/m²</td>
<td>IV bolus</td>
<td>Over 5 minutes</td>
</tr>
<tr>
<td>Day 1</td>
<td>5 Fluorouracil</td>
<td>2400 mg/m²</td>
<td>via infusor device</td>
<td>Sodium Chloride 0.9% over 46 hours</td>
</tr>
<tr>
<td>Day 3</td>
<td>Attend ward/clinic for removal of 5-FU infusor device</td>
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<td></td>
<td></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
First line for advanced colorectal cancer

PREMEDICATION
*If acute cholinergic syndrome appears atropine sulphate should be administered unless clinically contraindicated. The manufacturer recommends the use of prophylactic atropine sulphate with subsequent doses of Irinotecan

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
Loperamide as required (4mg after first loose stool and 2mgs every 2 hours, to a maximum of 16 (2mg) tablets in 24 hours.

INVESTIGATIONS / MONITORING REQUIRED
Blood Pressure ½ hourly during and post administration of irinotecan for ½ hour
FBC, U&E, 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.

ASSESSMENT OF RESPONSE
Assessed radiologically after 4th cycle.
Metastatic: Tumour size and patient symptomatic response
NECN CHEMOTHERAPY HANDBOOK PROTOCOL
FOLFIRI- IRINOTECAN / DE GRAMONT

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
- Irinotecan must only be given in units where clear arrangements are made to manage possible toxicity related out of hour’s admissions. Patients must be made aware of the risk of delayed diarrhoea occurring 24 hours after the administration of Irinotecan and at any time before the next cycle. This means supplying information sheets to the patient and if appropriate to their GP.
- Early onset diarrhoea (within the first 24 hours) can be a result of acute cholinergic syndrome and may occur in 9% of patients. Symptoms are short lasting and respond within minutes to administration of atropine (0.25-1mg subcutaneously)
- Delayed diarrhoea must be treated immediately with high dose Loperamide (4mg after first loose stool and 2mgs every 2 hours, to a maximum of 16 (2mg) tablets in 24 hours. Hospitalise if condition not resolved in 48 hours.
- For diarrhoea lasting greater than 24 hours add ciprofloxacin 250mg BD. Note many units give patient a supply of loperamide and ciprofloxacin at the start of treatment.
- **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.

EXTRAVASATION See NECN / local Policy

TOXICITIES
- Acute cholinergic syndrome (defined as early diarrhoea and various other symptoms such as sweating, abdominal cramping, lacrimation, myosis and salivation)
- Diarrhoea –risk of severe delayed diarrhoea – can be life threatening
- Myelosuppression
- Alopecia
- Dizziness during treatment
- Anaphylaxis
- Nausea and Vomiting
- Allergic reaction
- Diarrhoea
- Stomatitis
- Palmar/Plantar Erythrodysthesia
- Darkening/discoloration of veins
- Cardiotoxicity - Occasionally patients may experience coronary artery spasm
- Laryngopharyngeal dysesthesia
Haematological toxicity:

• Delay 1 week if ANC < 1-1.5 and Platelets < 75-100
• No dose reduction for CTC grade I/II ANC
• Grade III/IV ANC → delay chemotherapy until recovered, then proceed at 20% 5FU and Irinotecan dose reduction
• If delay > 1 week or delay 2 weeks or greater occurs, reduce the 5FU dose (bolus & infusional) and Irinotecan 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:

• Diarrhoea grade 2 during course of treatment → delay until recovered and give full dose
• Diarrhoea grade 3/ 4 during a course of treatment → delay until recovered and resume treatment at 20% reduced dose of Irinotecan and 5FU
• Hepatic - bilirubin rising consider 50% dose reduction.
• Omit if bilirubin 3 x ULN
• Renal - rising creatinine and GFR < 30ml/min, consider 50% dose reduction.

TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit

REFERENCE


• Tournigand C et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: A randomized GERCOR study. JCO 2004 22:1.