

**Systemic Anti Cancer Treatment Protocol**

**FOLFOX**

**PROTOCOL REF: MPHAFOLFO  
(Version No: 1.0)**

**Approved for use in:**

Adjuvant colorectal cancer stage 3 or high risk stage 2

Advanced colorectal cancer first line

Advanced colorectal cancer second or third line after irinotecan based therapies

**Dosage:**

Drug	Dosage	Route	Frequency
Oxaliplatin	85mg/m <sup>2</sup>	IV	Every 14 days
Folinic Acid	350mg	IV	Every 14 days
Fluorouracil	400mg/m <sup>2</sup>	IV	Every 14 days
Fluorouracil	2400mg/m <sup>2</sup>	IV	Every 14 days

Adjuvant – give for 12 cycles

Advanced – give for 6 cycles and review, continue subject to patient choice, tolerability and response

**Supportive treatments:**

Anti-emetic risk – Moderate

Domperidone 10mg oral tablets, up to 3 times a day or as required

Dexamethasone tablets 4mg twice daily for 3 days

Loperamide 2mg after each loose stool

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## Extravasation risk:

PICC line will be usually inserted. Network guidelines suggest that fluorouracil and oxaliplatin are IRRITANTS and should be treated using Network guidance

## Administration:

Day	Drug	Dosage	Route	Diluent and Rate
1	<b>Dexamethasone</b> 30 mins before chemotherapy	8mg	PO	
1	<b>Ondansetron</b> 30 mins before chemotherapy	16mg	PO	
1	<b>Oxaliplatin</b>	85mg/m <sup>2</sup>	IV	500mL Glucose 5% infusion over 2 hours
Oxaliplatin and Folinic Acid given at same time concomitantly				
1	<b>Folinic Acid</b>	350mg	IV	250mL Glucose 5% infusion over 2 hours
1	<b>Fluorouracil</b>	400mg/m <sup>2</sup>	IV	Bolus over 5 minutes
1 to 2	<b>Fluorouracil</b>	2400mg/m <sup>2</sup>	IV	46 hour continuous infusion in Sodium Chloride 0.9%

### Notes:

Caution in patients with pre-existing neurotoxicity – see below

Caution in patients with pre-existing heart disease, angina pectoris, arrhythmias

Correct any magnesium deficiency before giving oxaliplatin

Be aware of infusion related allergic reactions – see below

Sorivudine and analogues – Potentially fatal interaction – avoid completely

## Main Toxicities:

### Oxaliplatin

Infusion reactions, neuro toxicity, myelosuppression, mucositis, diarrhoea, nausea and vomiting

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### **Fluorouracil**

Diarrhoea, nausea and vomiting, conjunctivitis / sore eyes, skin rashes, Palmar Plantar Erythema (PPE or hand foot syndrome), stomatitis, chest pain (myocardial ischaemia or angina), ovarian failure / infertility, nail ridges, taste changes

DPD deficiency – leads to severe early fluorouracil toxicity, affects approximately 3% of population, may be life threatening

### **Investigations and treatment plan**

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X		X		X	Alternate cycles
Nursing Assessment	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
CT scan	X					
Informed Consent	X					
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	Every cycle

## Dose Modifications and Toxicity Management:

### Haematological toxicity

Proceed on day 1 if:-

ANC $\geq 1.0 \times 10^9/L$	Platelets $\geq 75 \times 10^9/L$
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Delay 1 week on day 1 if:-

ANC $\leq 0.9 \times 10^9/L$	Platelets $\leq 74 \times 10^9/L$
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If WCC, platelets or ANC still below required levels for treatment at week 2, delay treatment again and patient will need assessment and chemotherapy dose reduction as follows.

Lowest count since previous cycle	Oxaliplatin dose	Fluorouracil dose
Grade 3 / 4 neutropenia ( $<1.0 \times 10^9/L$ ) or thrombocytopenia ( $<50 \times 10^9/L$ )	65mg/m <sup>2</sup> (metastatic) 75mg/m <sup>2</sup> (adjuvant)	80% bolus and infusion

### Non-haematological toxicity

<b>Renal</b>	Calculate CrCl using Cockcroft and Gault before each cycle.		
	<b>Creatinine Clearance (mL/min)</b>	<b>Oxaliplatin Dose</b>	<b>Fluorouracil dose</b>
	$\geq 30$	Full dose	Full dose
	$< 30$	Omit	75%
If moderate impairment monitor closely and adjust oxaliplatin dose if deterioration or toxicity appears			
<b>Hepatic</b>	<b>Liver function</b>	<b>Oxaliplatin dose</b>	<b>Fluorouracil dose</b>
	Bilirubin $> 3 \times \text{ULN}$	50%	50%
	Note that significantly impaired hepatic function might be a sign of disease progression and require cessation or change of treatment. <b>Always discuss deteriorating organ function with consultant</b>		

**Oxaliplatin**

Neurotoxicity – see notes below for specific cases	Neurotoxicity	Oxaliplatin dose
	Grade 1 any duration or grade 2 < 7days but resolving before next cycle	85mg/m <sup>2</sup>
	Grade 2 persisting for 7 days or Grade 3 resolved by next cycle	65mg/m <sup>2</sup>
	Grade 3 persisting to next cycle or any grade 4	Stop oxaliplatin
If oxaliplatin is discontinued, review the infusional dose of fluorouracil and consider increasing to 2800mg/m <sup>2</sup>		
Acute cold related dysaesthesia (CRD)	Transient paraesthesia of hands and feet as well as laryngopharyngeal dysaesthesia (unpleasant sensations in throat) is common. Onset is during or within hours of infusion and it resolves in minutes or days. Symptoms are exacerbated by cold – advise patients on suitable precautions eg avoid cold drinks. Should not require dose reduction, but if troublesome then infusion duration can be increased to 6 hours (see note below)	
Laryngopharyngeal dysaesthesia	Stop infusion, provide symptomatic treatment. Resume at slower infusion rate. Give subsequent infusions over 6 hours (see note below)	
Cumulative dose related sensory neuropathy	Usually occurs after a cumulative dose of 800mg/m <sup>2</sup> . It can occur after treatment is completed, is usually reversible taking about 3-5 months to recover	
Allergic reactions during infusion	Stop the infusion and call for help. Follow trust hypersensitivity policy. Treat with IV corticosteroid and antihistamine. Discuss continuing with fluorouracil alone or rechallenge with the consultant.	

Whilst the recommended increase in duration of infusion is to 6 hours – where the oncologist and the treating team agree, this can be reduced to 4 hours dependent on the severity of the reaction and the tolerability of the infusion over this time.

### Fluorouracil

Chest pain, coronary artery spasm	Stop fluorouracil, standard angina investigations, refer to consultant, if symptoms persist stop permanently
Stomatitis	If mouth ulcers or > grade 2 symptoms develop treat symptomatically, delay treatment until resolved to grade 1 and reduce fluorouracil doses by 20%. See table
Diarrhoea	Treat diarrhoea between cycles symptomatically. If diarrhoea has not resolved by next cycle delay treatment by 1 week. If diarrhoea remains troublesome or more than 1 delay is required reduce both fluorouracil bolus and infusion doses by 20% and continue at the lower dose unless further toxicity occurs - See table
PPE	Treat symptomatically, delay treatment until resolved to grade 1. Reduce fluorouracil doses (bolus and infusion) by 20% for subsequent doses if persistent troublesome PPE. See table

### Fluorouracil dose reductions for non haematological toxicity

	Non haematological toxicity (diarrhoea, stomatitis, PPE)			
Grade	0-1	2	3	4
1 <sup>st</sup> occurrence	100%	80%	50%	Stop treatment
2 <sup>nd</sup> occurrence	80%	70%	50%	Stop treatment
3 <sup>rd</sup> occurrence	50%	50%	50%	Stop treatment

### References:

Cheshire and Merseyside Strategic Clinical Networks. Network Guidance for the prevention and management of extravasation injuries V6.0 accessed 11.49 on 26/01/2017 on [http://nww.clatterbridgecc.nhs.uk/application/files/5814/5934/5142/Prevention\\_Management\\_of\\_Extravasation\\_Injuries\\_V6.0.pdf](http://nww.clatterbridgecc.nhs.uk/application/files/5814/5934/5142/Prevention_Management_of_Extravasation_Injuries_V6.0.pdf)

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NICE technology appraisal No 100, Capecitabine and oxaliplatin in the adjuvant treatment of stage III (Duke's C) colon cancer; Issue April 2006

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