Weekly 5 Fluorouracil plus Folinic acid (colorectal)

Indication
Adjuvant chemotherapy for colorectal cancer

Regimen details

Day	Drug	Dose	Route
1	Calcium folinate	50mg	IV bolus
1	Fluorouracil	425mg/m^2	IV bolus

Cycle frequency
Weekly

Number of cycles

Adjuvant: 30 weeks

Administration
Fluorouracil is administered as an IV bolus injection.

Pre-medication
Antiemetics as per local policy.

Emetogenicity
This regimen has a low emetogenic potential

Additional supportive medication
Mouthwashes as per local policy. Loperamide if required.

Extravasation

Fluorouracil is an inflammatant (Group 2).

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFTs (including AST)	14 days
Calcium	14 days
CEA	14 days
DPYD mutation testing	none
Hepatitis B serology (HBsAG, HBcAb)	none
HbA1c	3 months

Random glucose	14 days
ECG	28 days
Calculated Creatinine Clearance	14 days

Investigations - pre subsequent cycles

FBC, U&Es, LFT (including AST), calculated creatinine clearance, calcium, magnesium, random glucose, CEA every 4 weeks

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophils	≥ 1.5 x 10^9/L (discuss with consultant ≥ 1.0- <1.5)
Platelets	≥ 75 x 10^9/L
Bilirubin	< 1.5 x ULN
AST/ALT	< 1.5 x ULN
Creatinine Clearance (CrCl)	≥ 50mL/min (see dose modifications below)

For treatment with adjuvant intent consultants may be happy to proceed with Neutrophils ≥1.0 x 10^9/L and should document this.

Dose modifications

- **DPYD variants**

All patients due to receive fluoro-pyrimidine based therapy should have a DPD test prior to starting treatment. Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism (this can present as severe diarrhoea and/or severe stomatitis early in the first cycle).

Any patient who has not had a DPD test should be discussed with the consultant prior to going ahead. Patients with variants should be considered for a dose modification following national advice for recommended dose adjustments.

https://www.uksactboard.org/_files/ugd/638ee8_4d24d37a598c485d9ef4d1ba90abccd5.pdf

Where a patient has had significant toxicities but the DPD test has shown none of the variants to be present, a further test can be conducted to test the presence of rarer variants.

- **Haematological toxicity**

Defer treatment for 1 week if neutrophil count <1.0 x 10^9/L and/or platelets < 75 x 10^9/L.

Neutrophils	Platelets	5 Fluoruracil dose
≥1.0 and	≥75	100%
0.5-0.9 or	50-74	100%
<0.5 and/or	25-49	100%
<0.5 and/or	<25	100%

If febrile neutropenia (neutrophils < 0.5 x 10^9/L and fever requiring IV antibiotics) – reduce

subsequent doses of fluorouracil to 50%

- **Renal impairment**

CrCl (mL/min)	**Fluorouracil dose**
≥ 50	100%
30-49	100%
10-29	100%
< 10	Consider dose reduction

- **Hepatic impairment**

Bilirubin (x ULN)		**AST/ALT (x**	**Fluorouracil dose**
≤ 1.5	and	≤ 1.5	100%
1.5 - 3	and	≤ 3	Consider dose reduction*
3 – 5	or	3 – 5	Consider dose reduction*
> 5	or	> 5	Contraindicated

*consultant decision

- **Other toxicities**

For all toxicities, delay treatment until resolved to ≤ Grade 1. Then reduce doses as per the following table:

Toxicity	**Definition**	**Fluorouracil dose**
Diarrhoea*	Grade 2	80%
	Grade 3	50%
	Grade 4	Discontinue treatment
Stomatitis/Mucositis	Grade 2	80%
	Grade 3	50%
	Grade 4	Discontinue treatment
Palmar-Plantar erythema	Grade 2	80%
	Grade 3/4	50%

* Patients presenting with diarrhoea must be carefully monitored until the symptoms have disappeared completely, since a rapid (sometimes fatal) deterioration can occur.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Infertility
Neurotoxicity
Coronary artery spasm*

*Coronary artery spasm is a recognised complication of fluorouracil treatment, although the evidence base regarding aetiology, management and prognosis is not particularly strong.
Coronary artery spasm is more common in patients receiving continuous infusions of fluorouracil, and is usually reversible on discontinuing the infusion. Should a patient receiving fluorouracil present with chest pains, stop the treatment. Standard investigation and treatment of angina may be required. If re-challenge is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, the fluorouracil should be permanently discontinued.

- **Frequently occurring side effects**

Nausea and vomiting
Diarrhoea
Stomatitis and mucositis
Palmar-plantar erythema
Alopecia
Fatigue
Dyspnoea

- **Other side effects**

Transient cerebellar syndrome
Confusion

Significant drug interactions – for full details consult product literature/ reference texts

Fluorouracil:
Folinates: Avoid concomitant use of folinic and folic acid – enhanced toxicity of fluorouracil.
Co-trimoxazole/trimethoprim: Avoid if possible – enhances antifolate effect. If essential, monitor FBC regularly. **Warfarin/coumarin anticoagulants:** Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.

Additional comments

Cardiotoxicity has been associated with fluoropyrimidine therapy, with adverse events being more common in patients with a prior history of coronary artery disease. Caution must be taken in patients with a history of significant cardiac disease, arrhythmias or angina pectoris.

Fertility/Contraception

Patients should agree to use an acceptable method of birth control to avoid pregnancy for the duration of treatment and for 6 months afterwards. Breast feeding should be discontinued during treatment.

References

- Colorectal NICE guideline NG151 (updated 15 Dec 2021) accessed 17 April 2025
- Summary of Product Characteristics (Fluorouracil) accessed 17 April 2025 via www.medicines.org.uk
- Personalised Medicine Approach for Fluoro-pyrimidine-based Therapies. UK Chemotherapy Board V2 September 2024 accessed 17 April 2025 via https://www.uksactboard.org/_files/ugd/638ee8_4d24d37a598c485d9ef4d1ba90abccd5.pdf

THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON DESIGNATED LEAD CLINICIAN FOR COLORECTAL CANCER
RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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