Raltitrexed (Colorectal)

Indication

Adjuvant therapy in colorectal cancer for patients who have experienced cardiotoxicity with standard fluoropyrimidine therapy.

Palliative chemotherapy for locally advanced/metastatic colorectal cancer in patients with documented fluoropyrimidine cardiotoxicity.

Regimen details

Day	Drug	Dose	Route
1	Raltitrexed	3mg/m^2	IV infusion

Cycle frequency

21 days

Number of cycles

Neo-adjuvant/Adjuvant: 8 cycles
Metastatic: continue until disease progression or unacceptable toxicity

Administration

Raltitrexed is administered in 100mL sodium chloride 0.9% over 15minutes.

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.
Metoclopramide 10mg tds prn.

Extravasation

Raltitrexed 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
Magnesium	14 days
CEA	14 days
Hepatitis B serology (HBsAG, HBcAb)	none
HbA1c	3 months
Random glucose	14 days

Calculated Creatinine Clearance	14 days

Investigations - pre subsequent cycles

Investigation	Validity period
FBC	96 hours
U+E (including creatinine)	7 days
LFTs (including AST)	7 days
Calcium	7 days
Magnesium	7 days
CEA	7 days
Random glucose	7 days
Calculated Creatinine Clearance	7 days

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	≥ 100 x 10^9/L
Bilirubin	<5 x ULN
AST/ALT	< 5 x ULN
Creatinine Clearance (CrCl)	≥ 65mL/min (see dose modifications below)

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

Dose modifications

- **Haematological toxicity**

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Dose**
≥ 1.5	and	≥ 100	100%
1.0-1.49	or	75-99	75%
< 1.0	or	< 75	Delay until recover, then 75%

- **Renal impairment**

Creatinine Clearance (mL/min)	**Dose**	**Dosing interval**
> 65	100%	21 days
55-65	75%	28 days
25-54	50%	28 days
< 25	Contraindicated	

Changing the dosing interval in iQemo will require switching to a new regimen

- **Hepatic impairment**

Transient elevations of liver transaminases may occur with raltitrexed treatment. No dose modification is needed in mild or moderate hepatic impairment, but LFTs should be monitored carefully during treatment.
Raltitrexed is not recommended in severe hepatic impairment (Clinically jaundiced or Bilirubin > 5 x ULN and/or AST/ALT > 5 x ULN).

- **Other toxicities**

Raltitrexed:

Toxicity	Definition	Dose adjustment
Diarrhoea*	Grade 1	100%
	Grade 2	Delay until resolved then 75%
	Grade 3	Delay until resolved then 50%
	Grade 4	Discontinue
Mucositis	Grade 1	100%
	Grade 2	Delay until resolved then 75%
	Grade 3	Delay until resolved then 50%
	Grade 4	Discontinue

* Diarrhoea is often associated with myelosuppression, if grade 3-4, check FBC.

Once doses are reduced for toxicity, they must not be re-escalated.

Dose modifications should be made as per the following table:

Toxicity grade	1st occurrence	2nd occurrence	3rd occurrence	4th occurrence
0-1	100%	100%	100%	100%
2	Delay then 100%	Delay then 75%	Delay then 50%	Discontinue
3	Delay then 75%	Delay then 50%	Discontinue	
4	Delay then 50%	Discontinue		

Any delays should be until the toxicity has resolved to grade 0-1.

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

- **Serious side effects**

Myelosuppression

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Diarrhoea
Mucositis
Asthenia
Anorexia
Abdominal pain
Rash

- **Other side effects**

Elevated liver enzymes
Dysgeusia

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

Warfarin/coumarin anticoagulants: Avoid use due to elevations in INR. Switch to low molecular weight heparin or NOAC during treatment.

Folic acid, folinic acid/leucovorin (or vitamin preparations containing these agents) – may reduce efficacy of raltitrexed and should be avoided immediately before and during drug use.

Additional comments

Fertility/Contraception

Raltitrexed is mutagenic. Pregnancy should be avoided if either partner is receiving raltitrexed. It is also recommended that conception should be avoided for at least 6 months after cessation of treatment. Patients should agree to use an acceptable method of birth control to avoid pregnancy for the duration of treatment and for 6 months afterwards. Breastfeeding should be discontinued during treatment.

References

- Summary of Product Characteristics - Raltitrexed accessed 10 JUly 2025 via www.medicines.org.uk
- Cunningham D. Mature results from three large controlled studies with raltitrexed ('Tomudex'). Br J Cancer 1998; 77 (Suppl 2): 15-21.

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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