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.

ICD-10 codes

Codes with a prefix C18-C20

Regimen details

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

Cycle frequency

21 days

Number of cycles

Adjuvant: 8 cycles
Palliative: 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 low emetogenic potential.

Additional supportive medication

Mouthwashes as per local policy.
Loperamide if required.

Extravasation

Raltitrexed is an inflammatant (Group 2)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U + E (including creatinine)	14 days
LFTs	14 days

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U + E (including creatinine)	7 days
LFTs	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
Platelets	≥ 100 x 10^9/L
Creatinine clearance	> 65 mL/min
AST/ALT	< 5 x ULN
Bilirubin	< 10 x ULN

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	

- **Hepatic impairment**

Transient elevations of liver transaminase occur with raltitrexed. No dose modification is needed in mild or moderate hepatic impairment, but liver enzymes should be monitored carefully.
Raltitrexed is not recommended in severe hepatic impairment (Bilirubin > 10 x ULN and/or AST/ALT > 5 x ULN).

- **Other toxicities**

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.

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 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

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.

There is no clinically proven antidote available. In the case of inadvertent or accidental overdose, consider the use of folinic acid at a dose of 25mg/m^2 IV every 6 hours. As the time interval between raltitrexed administration and folinic acid rescue increases, its effectiveness in counteracting toxicity may diminish.

References

- Summary of Product Characteristics - Raltitrexed (Hospira) accessed 10 Sept 2014 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.

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