Irinotecan (colorectal)

Indication

Monotherapy for metastatic colorectal cancer in patients who have failed first-line fluoropyrimidine-based therapy.

(NICE CG131)

ICD-10 codes

Codes prefixed with C18-20.

Regimen details

Day	Drug	Dose	Route
1	Irinotecan	350mg/m^2 (max 700mg)*	IV infusion

* For patients with WHO PS 2 or > 70 years old, reduce dose to 300mg/m^2.
Reduce dose to 200mg/m^2 in patients with Gilberts Syndrome or in patients with a baseline bilirubin 1.5-3 x ULN.

Cycle frequency

21 days

Number of cycles

Usual maximum of 6 cycles

Administration

Irinotecan is administered in 250-500mL sodium chloride 0.9% over 30 – 90 minutes. The first dose must be administered over 90 minutes. If this is well tolerated subsequent doses may be administered over 30 minutes.

Pre-medication

Atropine 250microgram SC 30 minutes prior to irinotecan administration to control anticholinergic syndrome. An additional dose may be given if this develops.

Emetogenicity

This regimen has a moderate-high emetogenic potential.

Additional supportive medication

Mouthwashes as per local policy.
Loperamide if required.

Extravasation

Irinotecan is an irritant (Group 3).

Investigations – pre first cycle

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

*FBC should be monitored weekly for the first 2 cycles

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	≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Bilirubin	< 1.5 x ULN
AST/ALT	< 1.5 x ULN
Creatinine Clearance (CrCl)	≥ 30mL/min

Dose modifications

- **Haematological toxicity**

Defer treatment for 1 week if neutrophil count <1.0 x 10^9/L and/or platelets <100 x 10^9/L. If there is > 1 week delay due to haematological toxicity reduce irinotecan dose to 80%.

If febrile neutropenia (neutrophils < 0.5 x 10^9/L and fever requiring IV antibiotics) – reduce all subsequent doses of irinotecan to 80% and start prophylactic ciprofloxacin 250mg BD.

- **Renal impairment**

CrCl (mL/min)	**Irinotecan dose**
≥ 30	100%
< 30	50%

- **Hepatic impairment**

Bilirubin (x ULN)		**AST/ALT** (x ULN)	**Irinotecan dose**
< 1.5	and	< 1.5	100%
1.5 - 3	or	1.5 – 5	50%
> 3	or	> 5	Contraindicated

Note that significantly impaired hepatic function may be a sign of disease progression and require cessation of, or change in, treatment.

- **Other toxicities**

Diarrhoea:

If diarrhoea > grade 2 on day 1, withhold treatment.

If resolved to grade 2 or less within 2 weeks continue treatment at a dose of 300mg/m^2.

If diarrhoea persists after 2 weeks at grade 3 or 4 discontinue treatment.

Diarrhoea may be life-threatening and requires prompt, aggressive treatment:

• Early diarrhoea or abdominal cramps occurring within the first 24 hours should be treated with atropine 0.3 - 1.2 mg IV or SC. DO NOT ADMINISTER LOPERAMIDE DURING THIS 24 HOUR PERIOD.

• Late diarrhoea (diarrhoea occurring >24 hours after treatment) must be treated with loperamide; 4mg at the first loose stool and then 2mg every 2 hours until diarrhoea-free for 12 hours after last loose stool (4 mg every 4 hours may be taken over night). Note: this dose is higher than recommended by the manufacturer. If diarrhoea persists for >24 hours ciprofloxacin 500 mg BD should be commenced. Loperamide must not be administered for more than 48 consecutive hours at these doses without appropriate medical supervision due to the risk of paralytic ileus.

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

- **Serious side effects**

Myelosuppression
Infertility
Hypertension
Anaphylaxis
Severe diarrhoea

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Diarrhoea
Stomatitis and mucositis
Palmar-plantar erythema
Alopecia
Electrolyte disturbances
Acute cholinergic syndrome

- **Other side effects**

Confusion

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.

Irinotecan is a major substrate of **cytochrome P450 CYP2B6 and CYP3A4** and as such levels of irinotecan may be reduced by medicines that induce levels of these enzymes. Conversely, levels of irinotecan may be increased by medicines that inhibit these enzymes.

Prochlorperazine should be avoided on the same day as irinotecan treatment due to the increased incidence of akathisia.

Additional comments

Use with caution in patients with Gilbert's Syndrome (due to the increased risk of irinotecan-induced toxicity).

References

- National Institute for Health and Clinical Excellence. Clinical Guidance 131 accessed 3 Sept 2014 via www.nice.org.uk
- Summary of Product Characteristics Irinotecan (Pfizer) accessed 3 Sept 2014 via www.medicines.org.uk
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.

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