

Chemotherapy Protocol

Sarcoma

IRINOTECAN - TEMOZOLOMIDE

[Regimen](#)

- Sarcoma – Irinotecan-Temozolomide

[Indication](#)

- Recurrent or progressive Ewings sarcoma
- Performance status 0, 1, 2

[Toxicity](#)

Drug	Adverse Effect
Irinotecan	Acute cholinergic syndrome, diarrhoea (may be delayed)
Temozolomide	Hepatic injury, thrombocytopenia, nausea and vomiting, <i>Pneumocystis jirovecii</i> infection

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

[Monitoring](#)

Drugs

- FBC, LFT's, U&E's prior to day 1 of the cycle and FBC on day 8.

[Dose Modifications](#)

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Prior to cycle one of treatment the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 10g/dL.

For subsequent cycles if the neutrophils are less than $1.5 \times 10^9/L$ and / or the platelets are less than $100 \times 10^9/L$ then delay treatment for seven days. The full blood count should be repeated at this time. If the neutrophils and platelets have recovered to these levels continue treatment.

If it takes longer than seven days for the counts to recover, or if two consecutive cycles are delayed then wait until the counts have reached the eligible levels and continue treatment after reducing the dose of irinotecan by 20%.

In the event of febrile neutropenia reduce the dose of irinotecan by 20% for all subsequent cycles.

Hepatic Impairment

Drug	Toxicity	Action
Irinotecan	Bilirubin more than 3xULN	Do not use
Temozolomide	Bilirubin more than 1.5xULN and / or ALT more than 2.5xULN	Stop temozolomide

Renal Impairment

Drug	Action
Irinotecan	No adjustments are necessary although there is limited information
Temozolomide	No dose reductions are required. Caution in severe renal impairment

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 2 toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. For toxicity that is NCI-CTC grade 3 or above discontinue treatment.

Irinotecan

Irinotecan is associated with a number of toxic reactions. The next cycle of treatment should not be administered until all toxicities have resolved to 0 or 1 of the National Cancer Institute Common Toxicity Criteria scale (NCI-CTC) within fourteen days. Diarrhoea must have resolved completely. Where a NCI-CTC grade 2 to 4 non-haematological event has occurred the irinotecan dose must be reduced in the first instance. If a second episode occurs despite this dose reduction delay until the symptoms have resolved and consider stopping treatment.

[Regimen](#)

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Irinotecan	20mg/m ²	1, 2, 3, 4, 5	In 100ml sodium chloride 0.9% intravenous infusion over 30 minutes
Temozolomide	100mg/m ²	1, 2, 3, 4, 5	Oral

[Dose](#)

- Irinotecan will be dose banded in accordance with the national dose bands (20mg/ml)
- Temozolomide will be dose banded in accordance with the national dose bands (temozolomide oral)

[Administration Information](#)

Extravasation

Irinotecan - irritant

Other

- Temozolomide should be taken on an empty stomach
- Temozolomide to be taken with plenty of water swallowed whole, not chewed

[Additional Therapy](#)

Antiemetics

- Prior to chemotherapy
 - dexamethasone 8mg oral or intravenous
- As take home medication
 - ondansetron 8mg 15 – 30 minutes prior to temozolomide

- Subcutaneous atropine 250microgram when required for the treatment of acute cholinergic syndrome.
- Oral loperamide 2mg every two hours once first liquid stool appears and continue until 12 hours after the last liquid stool. Do not use for longer than 48 hours (maximum daily dose is 16mg). Please refer to local guidelines on treatment of irinotecan related diarrhoea
- Consider oral ciprofloxacin 500mg twice daily where diarrhoea continues for more than 24 hours. Review the patient before starting this treatment. Please refer to the local / national guidelines on treatment of irinotecan related diarrhoea
- Growth factor according to local formulary choice. For example;
 - filgrastim or bioequivalent 30million unit once a day subcutaneous for five days starting on day six of the cycle
 - lenograstim or bioequivalent 33.6million unit once a day subcutaneous for five days starting on day six of the cycle
 - pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day six of the cycle
- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

[Additional Information](#)

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to oral temozolomide.

[Coding](#)

- Procurement – X71.1
- Delivery – X72.1, X72.4

References

1. Casey DA, Wexler LH, Merchant MS et al. Irinotecan and temozolomide for Ewings sarcoma: the Memorial Sloan Kettering experience. *Pediatr Blood Cancer* 2009; 53 (6): 1029-1034.

REGIMEN SUMMARY

Irinotecan-Temozolomide

Day 1, 2, 3, 4, 5

1. Dexamethasone 8mg oral or intravenous
2. Irinotecan 20mg/m² intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes
3. Atropine 250mcg subcutaneous when required for the relief of irinotecan cholinergic reactions

Take Home Medicines (day 1 only)

4. Temozolomide 100mg/m² oral once a day for 5 days starting on day 1 of the cycle
Administration Instructions
Take on an empty stomach, swallow whole, do not chew.
5. Ondansetron 8mg once a day 15-30 minutes prior to the temozolomide
Administration Instructions
Take 15-30 minutes prior to the temozolomide. An additional dose may be taken 12 hours later if required for the relief of nausea and vomiting
Please supply an original pack (10 tablets) or nearest appropriate equivalent
6. Growth Factor
Administration Instructions
Please supply according to local formulary choice. For example;
 - filgrastim or bioequivalent 30million unit once a day subcutaneous for five days starting on day six of the cycle
 - lenograstim or bioequivalent 33.6million unit once a day subcutaneous for five days starting on day six of the cycle
 - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once a day subcutaneous on day six of the cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	Feb 2019	Dose banding changed to national dose bands	Donna Kimber Pharmacy Technician	Dr Deborah Wright Pharmacist
1.2	April 2016	Irinotecan fluid changed to sodium chloride 0.9%	Dr Deborah Wright Pharmacist	Dr Nicola Keay Consultant Medical Oncologist
1.1	February 2016	Irinotecan dose adjusted to 20mg/m ² . Numbering in summary altered. The wording in the administration instructions for growth factors and temozolomide altered.	Dr Deborah Wright Pharmacist	Dr Nicola Keay Consultant Medical Oncologist
1	September 2015	None	Dr Deborah Wright Pharmacist	Dr Nicola Keay Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
 NHS Isle of Wight
 Portsmouth Hospitals NHS Trust
 Salisbury Hospital NHS Foundation Trust
 University Hospital Southampton NHS Foundation Trust
 Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.