MONOGRAPH

Irinotecan

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

Topoisomerase I inhibitors[1]

Irinotecan is a High Risk Medicine.

Irinotecan is a Cytotoxic Medicine.

Extravasation: Irinotecan is irritant.[2, 3] Refer to Extravasation of Antineoplastic (Cytotoxic) Agents Guideline.

Emetogenic Rating: Moderate. Refer to Anticancer Therapy Induced Nausea and Vomiting (AINV) Guideline.

INDICATIONS AND RESTRICTIONS

- Irinotecan can only be prescribed by Oncologists or Haematologists as per protocol for the treatment of malignancy.

CONTRAINDICATIONS

- Hypersensitivity to irinotecan or any component of the formulation[4]
- Interstitial pulmonary disease[4]
- Severe bone marrow failure[4]
- Eastern Cooperative Oncology Group / World Health Organization Performance Status (ECOG/WHO PS) >2[1, 4]

PRECAUTIONS

Medication errors have occurred due to confusion between irinotecan and topotecan[5].

- Severe early or late diarrhoea from irinotecan can cause severe dehydration, electrolyte imbalance and sepsis.
- Supportive care should be prescribed as per treatment protocol and/or institutional guidelines.
- **Pre-infusion:** Patients may be commenced on oral cefixime 8 mg/kg ONCE daily (max 400 mg) beginning 2 days before, during and for 3 days after the irinotecan treatment (usually total of 10 days) to reduce the incidence and severity of irinotecan associated diarrhoea.[6, 7]
    - **Special access scheme product**. SAS application(s) must be completed in accordance to the TGA regulations.
    - Cefixime is contraindicated in patients with hypersensitivity to cephalosporins, penicillins, or other beta-lactams, patients with a history of high risk allergy to cephalosporins or any component of the formulation
- Use with caution in patients:
    - of Asian ethnicity[1]
    - with prior pelvic/abdominal radiotherapy[1, 4, 5]
    - that are asthmatic or have cardiovascular conditions[1, 4]
    - with chronic inflammatory bowel disease or bowel obstruction[1, 4, 8]
    - with elevated serum bilirubin[4]
- Cytotoxic precautions are to be followed regarding the handling of patient waste. See Cytotoxic Biotherapy Agents Safety guidelines.

FORMULATIONS

Listed below are products available at PCH. Other formulations may be available, check with pharmacy if required:

- Vial for injection: 100 mg/5 mL (20 mg/mL)

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Dosage as per treatment protocol in the OIMS (Oncology Information Management System).

Hepatic impairment:

- Dose adjustment as per treatment protocol.[4, 5, 8, 9]

Treatment related toxicity:

- Dose adjustment as per treatment protocol.[4, 5, 8, 9]

Gene related toxicity (UGT1A1 Genetic Polymorphism)**:**

- Dose adjustment as per treatment protocol.[4, 5, 8, 9]

ADMINISTRATION

- Handle as cytotoxic.
- Irinotecan must be compounded in a cytotoxic drug safety cabinet by Pharmacy Compounding Services (PCS).
    - The prescribed dose is to be drawn up and added to an appropriate volume of glucose 5% (preferred) or sodium chloride 0.9% to a final concentration of between 0.12 mg/mL and 2.8 mg/mL.[3, 4]
- **IV:** Infuse the diluted solution over 90 minutes.[3, 4] Lower doses (≤ 20 mg/m^2) can be administered over 60 minutes.[6] Higher incidence of cholinergic symptoms have been reported with more rapid infusion rates. Administration via a central line is preferred to avoid extravasation.[6]
- **Oral:** The injection solution may be given orally. The prescribed dose will be drawn up into oral syringes by PCS and refrigerated until ready to use. Dose may be diluted with cranberry-containing juice to a 1 mg/mL concentration prior to administration. (Note: irinotecan has a very unpleasant flavour).[6, 10]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Glucose 5% (preferred diluent)[3-5, 9]
- Sodium chloride 0.9%[3-5, 9]

Compatible and INCOMPATIBLE drugs:

Antineoplastic therapies are not routinely administered with other medications. Consult two or more drugs references *(Compatibilities of IV drugs)* or pharmacy when there is a requirement for medications to be given concurrently.

MONITORING

Monitor as per treatment protocol.

- Signs of diarrhoea, dehydration and dyselectrolytaemia[1, 5]
- Fever and infection[1]
- Signs of bleeding and bruising[1]
- Serum electrolytes[5]

- Serum creatinine and creatinine clearance[5]
- Complete blood count with differentials and platelets[1, 5, 9]
- Liver function tests[1, 5, 9]
- Blood urea nitrogen (BUN)[5]
- Infusion site for signs of inflammation[5]

ADVERSE EFFECTS

Common: anaemia, thrombocytopenia, neutropenia, nausea, vomiting, constipation, anorexia, fever, asthenia, acute diarrhoea, delayed diarrhoea, cholinergic symptoms such as rhinitis, miosis, sweating, salivation, abdominal cramps, lacrimation and miosis, severe infections, mucositis, pain, weight loss, cough[1, 4, 9, 11]

Infrequent: fainting, pulmonary infiltrates, ascites, jaundice, alopecia, mucositis, bilirubinaemia hypovolaemia, febrile neutropenia[1, 4, 9, 11]

Rare: anaphylaxis, bradycardia, transient speech disorders, acute renal failure, ileus, colitis, pancreatitis, syncope, malaise, sepsis, urinary tract infection, breast pain, abnormal gait, pneumonitis[1, 4, 9, 11]

Supportive care instructions for late diarrhoea: Instruct parents about the possibility of late diarrhoea (starting more than 24 hours after irinotecan administration), which can lead to serious dehydration and/or electrolyte imbalances if not managed promptly. Ensure that a prescription of anti-diarrhoea medication (loperamide) is given to parents with instructions for use. Warn patient and parents against taking laxatives while on therapy.[7]

Loperamide dosing recommendations for late diarrhoea which occurs 24 hours after irinotecan (based on body weight):

< 13 kg: Take 0.5 mg after the first loose bowel movement, followed by 0.5 mg every 3 hours. During the night, the patient may take 0.5 mg every 4 hours. Do not exceed 4 mg per day.

≥ 13 kg to < 20 kg: Take 1 mg after the first loose bowel movement, followed by 1 mg every 3 hours. During the night the patient may take 1 mg every 4 hours. Do not exceed 6 mg per day.

≥ 20 kg to < 30 kg: Take 2 mg after the first loose bowel movement, followed by 1 mg every 3 hours. During the night, the patient may take 2 mg every 4 hours. Do not exceed 8 mg per day.

≥ 30 kg to < 43 kg: Take 2 mg after the first loose bowel movement, followed by 1 mg every 2 hours. During the night, the patient may take 2 mg every 4 hours. Do not exceed 12 mg per day.

≥ 43kg: Take 4 mg after the first loose bowel movement, followed by 2 mg every 2 hours. During the night the patient may take 4 mg every 4 hours. Do not exceed 16 mg per day.[7]

STORAGE

Vial: Store below 25ºC. Do not Freeze. Protect from light.[3]

Compounded product: Refrigerate. Do not Freeze. Protect from light. Stable for up to 28 days when stored at 2-8°C. Solutions in sodium chloride 0.9% may precipitate if refrigerated.[3, 11]

INTERACTIONS

Irinotecan is a major substrate for UGT1A1, CYP2B6 and CYP3A4. Patients on inhibitors or inducers of CYP3A4, CYP2B6 and UGT1A1 should be monitored closely for toxicity or reduced efficacy.[5, 8, 9]

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **Irinotecan**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Cytotoxic Biotherapy Agents Administration

Extravasation of Antineoplastic (Cytotoxic) Agents

Cytotoxic Biotherapy Agents Safety

Anti-Cancer Therapy Induced Nausea and Vomiting Management

References

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