Guideline for the Management of Systemic Anti-Cancer Therapy (SACT) Induced Diarrhoea in Adult Haematology and Oncology Patients

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Contents **Page No.**

1. Introduction

Diarrhoea is the passage of frequent loose stools with urgency. It can be defined as the passage of more than three unformed stools within a 24 hour period but is relative to normal baseline function.

2. Area of Application

This policy applies to all adult SACT services across the North region, except for the administrative areas of Argyll and Bute in NHS Highland which are linked to the WOSCAN CEL 30 (2012) governance framework.

3. Points to Consider

The following can cause diarrhoea:

- Medication: laxatives, antacids, iron, antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), SACT, oral electrolyte supplements of potassium or magnesium (e.g. Sando K®, magnaspartate)
- Radiotherapy, particularly when involving the abdomen or pelvis
- Faecal impaction can result in diarrhoea as overflow
- Obstruction: malignant faecal impaction, narcotic bowel syndrome (severe constipation caused by opioid analgesia)
- Disease related – pancreatic carcinoma, pancreatic islet tumours, carcinoid tumours
- Concurrent disease, for example diabetes mellitus, hyperthyroidism, pancreatic insufficiency, inflammatory bowel disease such as Crohn's disease, ulcerative colitis
- Infection

4. Initial Assessment

- Document history of presenting symptoms:
    - Frequency and duration of diarrhoea
    - Normal baseline bowel function
    - Colour or any blood in stool (brown fluid is likely to be treatment related, yellow/green indicates infective and specimen should be taken)
    - Does the patient have a temperature of >37.5°C or <36°C ?
    - Any new medication?
    - Any abdominal pain, colic or recent constipation?

- Ascertain what SACT the patient is prescribed and when the last treatment was administered
- **CAPECITABINE, FLUOROURACIL, Tyrosine Kinase Inhibitors (TKIs)** – please see individual SACT protocols.
- **IRINOTECAN** and **IMMUNOTHERAPIES** require specific management – see below.
- If the patient is receiving radiotherapy, contact the radiotherapy team during working hours.
- If the patient is participating in a clinical trial – contact Clinical Trials team. Some clinical trials may need to be unblinded and notified immediately (follow local policy)
- Grade toxicity as per Table 1.

Consider infective diarrhoea:

If a patient has refractory diarrhoea, recent hospital admission, antibiotics or previous Clostridium Difficile (C.diff) infection:

- Send stool specimen urgently for culture.
- If strong suspicion of infective diarrhoea, **withhold anti-motility medication, any non-C.diff antibiotics and gastric acid suppressants (Protein pump inhibitors (PPIs) or H2 receptor antagonists), where possible, until stool result available.**
- Prescribe antibiotics for treatment of C.diff as per local policy.

Consider dehydration:

If patient reports dry mouth, fatigue, thirst, decreased urine output, headache or feeling dizzy or light headed. Patients with extreme dehydration can also have symptoms of irritability or confusion.

Table 1: Toxicity Grading

TOXICITY GRADING (Document in patient's case notes / nursing notes)			
Grade 1 Increase to 2-3 bowel movements a day over pre-treatment baseline or mild increase in stoma output	**Grade 2** Increase of 4 - 6 bowel movements per day over pre-treatment baseline; moderate increase in stoma output compared to baseline; moderate cramping; nocturnal stools	**Grade 3** Increase of 7-9 bowel movements per day over pre-treatment baseline or incontinence; severe increase in stoma output compared to baseline; severe cramping; nocturnal stools; interfering with ADL	**Grade 4** Increase to >10 bowel movements a day over pre-treatment baseline and/or grossly bloody diarrhoea and/or need for parenteral support
Antimotility drugs not normally required for Grade 1 **If patient also has associated temperature, nausea/vomiting, sore mouth/throat, dizziness, confusion or other clinical concerns – needs medical review/admission**	Initiate loperamide - if ineffective, try codeine If Grade 2 for >24hours maximal antidiarrhoeal treatment – admit for assessment/admission. **Withhold systemic anti-cancer therapy (SACT) until discussion with Haematology/oncology team.** Reduce/stop antidiarrhoeal medication after 24 hours free of diarrhoea. **If patient also has associated temperature, nausea/vomiting, sore mouth/throat, dizziness, confusion or other clinical concerns – needs medical review/admission**	**Withhold systemic anti-cancer therapy (SACT)** Admit patient urgently (unless clinical review suggests no concerns, well hydrated, has not yet had antidiarrhoeals and able to review patient daily). History to include other chemotherapy toxicities (risk of damage to rest of GI tract and skin –manage nausea/ mucositis /sepsis/hand-foot syndrome according to local guidelines) Assessment of fluid balance status (BP, pulse etc) and signs of systemic infection **Fluid resuscitation and electrolyte replacement where indicated** Review all medication and stop any drugs which may be contributing. Stop **ACE-inhibitors/ Angiotensin-II inhibitors /diuretics/ NSAIDs /metformin** Daily bloods (U&Es, FBC, CRP, magnesium, albumin, blood cultures if signs of systemic sepsis), NEWS, cumulative fluid balance Stool sample (send for urgent culture, C diff toxin and viral screen - discuss with Microbiology) Consider abdominal XR to exclude ileus/ obstruction/ perforation /megacolon Dietician review if appropriate	

5. Management

See **Table 1** for initial management according to grade of diarrhoea.

General Advice

- **If diarrhoea lasts > 48 hours, or if the patient reports symptoms of dehydration or fever, they should be reviewed as a matter of urgency and admitted to hospital for further management if necessary.**
- Increase oral fluids (2-3 L per day), avoid caffeinated drinks and alcohol.
- Avoid milk, high-fat foods, raw fruit and vegetables, beans, fibrous vegetables, cereals.
- Suggest bananas, rice, noodles, white bread, crackers, skinned chicken, white fish.
- Ensure anal area is kept clean and intact by regular washing and application of barrier cream (for patient not undergoing concurrent chemo radiotherapy). Some barrier creams contain ingredients contraindicated in radiotherapy. Discuss with local radiotherapy team if wishing to consider a barrier cream in a radiotherapy patient.
- Stop any medication that may be contributing e.g. laxatives, domperidone, metoclopramide, magnesium containing antacids.

Pharmacological Management

- Consider oral rehydration salts (e.g. Dioralyte®) – 200-400ml of solution after every loose bowel movement.
- Where there is concern that the cause may be infective, anti-motility agents should be not be commenced until negative cultures have been obtained.

Table 2: Oral drug doses

Treatment choice	Drug	Indication	Dose
1st line	Loperamide	Anti-motility	4mg initially then 2mg after each loose stool (maximum 16mg/24 hours)*
2nd line	Codeine phosphate	Anti-motility	30-60mg every four hours when required (maximum 240mg/24hours)

* If not controlling diarrhoea rapidly, change to 2mg four times a day. This can be increased to 4mg four times a day if required.

6. Irinotecan

Irinotecan can cause both **early (acute)** and **delayed diarrhoea.** Early diarrhoea is caused by an acute cholinergic syndrome which can occur shortly after infusion of irinotecan and includes symptoms such as diarrhoea, sweating, abdominal cramping, myosis and salivation.

Management of irinotecan-induced acute diarrhoea:

- Atropine sulphate (250 micrograms subcutaneously) should be administered unless clinically contraindicated and should be used prophylactically for future cycles.

Management of irinotecan-induced delayed diarrhoea:

- At the first loose stool, loperamide should be commenced: 4mg (2 tablets), then 2mg every 2 hours until 12 hours after the last loose stool (up to a maximum of 48 hours) **(Note this exceeds licensed dose).**
- If diarrhoea lasts more than 24 hours, ciprofloxacin 500mg twice daily should be started, in addition to loperamide.

Notes:-

- **If diarrhoea lasts > 48 hours**, or if the patient reports symptoms of dehydration or fever, they should be admitted immediately to hospital for rehydration and further management, including an infection screen. Loperamide and ciprofloxacin should be supplied routinely with irinotecan chemotherapy.
- The occurrence of severe diarrhoea concomitantly with severe neutropenia is life-threatening, requiring immediate admission to hospital and the institution of supportive measures.

7. Immunotherapy

- Immunotherapy is associated with serious immune-related gastrointestinal reactions. Median time to onset of severe or fatal (grade 3-5) reactions is 8 weeks from the start of treatment. However symptoms can occur weeks or months after treatment is discontinued.
- Clinical presentation may include diarrhoea, increased frequency of bowel movements, abdominal pain, or haematochezia (bright red blood in stool), with or without fever.
- Diarrhoea or colitis occurring **after initiation of immunotherapy** must be promptly evaluated. Any patient who presents with diarrhoea who is currently receiving immunotherapy or has previously had an immunotherapy should be discussed with the Haematology / Oncology Team as soon as possible.
- **Please refer to local Immunotherapy Toxicity Management Guidelines for treatment recommendations.**

8. References

- National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE), Version 4. 28th May 2009
- NHS Highland Cancer Chemotherapy Protocol – Capecitabine 06/11/17
- NHS Highland Cancer Chemotherapy Protocol – FOLFIRI 06/11/17
- NHS Highland Formulary, 7th Edition.
- NHS TAYSIDE Cancer chemotherapy protocol- De Gramont chemotherapy
- Scottish Palliative Care Guidelines http://www.palliativecareguidelines.scot.nhs.uk/guidelines/symptom-control/Diarrhoea.aspx (Accessed 06/06/15)
- South East Scotland Cancer Network. Management of Chemotherapy Toxicity Guidelines – Diarrhoea 2010.
- Summary of Product Characteristics for individual drugs – www.medicines.org (Accessed 06/11/17)
- UKONS Acute Oncology Initial Management Guidelines 2015

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Revision History:

Revision Date	Previous Revision Date	Summary of Changes (Descriptive summary of the changes made)	Changes Marked (Identify page numbers and section heading)
06/11/17	N/A	Added Nivolumab, pembrolizumab, aztezolizumab to drugs which require specific management	Page 3 – Initial Assessment
		'SACT induced diarrhea most likely to occur in 7 days' – removed	Page 3
		Temperature defined	Page 4
		Toxicity grading updated in line with UKONS triage tool	Page 5 – Table 1
		Withhold SACT included in table for Grade 3/4. Added for Grade 2 if diarrhoea >24h despite anti-diarrhoeal medication	Page
		'Review all medication and stop any drugs which may be contributing.' Added to grade 3/4 management	Page 5 – Table 1
		Oral rehydration salts as option under pharmacological management	Page 6 – Pharmacological management
		Ipilimumab changed to immunotherapy. Removed table 4 (Management of ipilimumab-induced diarrhoea). To refer to local immunotherapy toxicity management guidelines	Page 7/8 – Ipilimumab
		Removal of specific drug recommendations – refer to local SACT protocols	

* Changes marked should detail the section(s) of the document that have been amended i.e. page number and section heading (If there is no previous document, insert N/A into the boxes in the top row of the table below)