Management of Radiotherapy- and Chemotherapy-Induced Diarrhoea

The Oncology Team must be informed if patients are admitted with diarrhoea whilst on chemotherapy or radiotherapy.

Diarrhoea is classified as an increase **of at least 2 to 3 stools per day** or causing waking at night or an increase in loose watery stoma output compared with before treatment. If not properly treated, diarrhoea can be life-threatening, especially in a patient who is also neutropenic.

Cytotoxic agents causing diarrhoea
Nearly all cytotoxics have the potential to induce diarrhoea.
Those cytotoxic drugs which commonly cause diarrhoea and require specific management are:

- **Capecitabine and 5-FU**
  For patients on continuous 5-FU or capecitabine, chemotherapy must be interrupted for Grade 2 or above diarrhoea. Severe diarrhoea and/or mucositis in the first cycle may be due to DPD deficiency*, in which case severe neutropenia can quickly follow.
  (*A genetic disorder in which there is significantly decreased activity of dihydropyrimidine dehydrogenase, an enzyme involved in the metabolism of active 5FU to inactive metabolites)
- **Idelalisib** – see specific management details in the R-Idelalisib protocol
- **Ipilimumab, Nivolumab, Pembrolizumab, Avelumab, Atezolizumab (or any other immunotherapies)**
  This guideline does **not** apply for these agents - any diarrhoea related to anti-cancer immunotherapy requires specialist management, in line with the Alliance "Management of Immunotherapy-related Adverse Events" guidelines document, and the treating oncologist must be notified.
- **Irinotecan** - see separate section below

- **Radiotherapy** to the abdomen or pelvis is also associated with treatment-related diarrhoea.

Differential Diagnosis
It is important to exclude other causes of diarrhoea in these patients:

- Infection
- Subacute obstruction, or constipation with overflow (abdominal X-ray if suspicious)
- Steatorrhoea in pancreatic or biliary malignancy
- Hypersecretion of 5-HIAA (carcinoid tumours)
- Previous GI surgery
- Other medicines, e.g. laxatives, bulking agents, prokinetics
- Other co-morbidities, e.g. diverticulitis, Crohn's disease
- Note that diarrhoea in neutropenic patients may indicate **C. difficile** infection requiring urgent antibiotic treatment.

Grading of Chemotherapy-Induced Diarrhoea

	Grade 1	Grade 2	Grade 3	Grade 4
Diarrhoea (without stoma)	Increase of < 4 stools/day over baseline	Increase of 4-6 stools/day over baseline, or nocturnal stools. Not interfering with daily living activities.	Increase of ≥ 7 stools/day over baseline. Interfering with daily living. Incontinence Hospitalisation	Life threatening consequences e.g. haemodynamic collapse
Diarrhoea (with stoma)	Mild increase in stoma output compared to baseline	Moderate increase in stoma output compared to baseline. Not interfering with daily living activities.	Severe increase in stoma output over baseline, interfering with daily living.	Life threatening consequences

First Report of Diarrhoea
For patient receiving chemotherapy and /or pelvic or abdominal radiotherapy

Evaluation of the Condition
Onset and duration of diarrhoea: duration > 12 hours take stool sample (**exclude C diff**)
Number of stools and stool composition (watery, blood)
Assess patient for fever, neutropenic sepsis, abdominal pain, weakness
Assess for evidence of dehydration
Medication history (laxatives, bulking agents, softeners, prokinetics)

Consider other causes (see above)

General Management
- Stop all lactose-containing products, alcohol and high osmolar supplements
- Eat frequent small meals (bananas, rice, apple sauce, toast, plain pasta)
- Drink 8-10 large glasses of clear fluids a day (e.g. water, clear soup, non-fizzy soft drinks)
- Keep a record of number of stools
- REPORT ANY NEW SYMPTOMS of life threatening potential e.g. fever, dizziness on standing
- For Grade 2+ diarrhoea, withhold cytotoxic chemotherapy and refer to relevant chemotherapy protocol

Grade 1-2 diarrhoea with no complicating signs

Consider investigations, as Grade 3 - 4

Initiate loperamide 4mg, followed by 2mg after every loose stool, up to 16mg daily (N.B. for irinotecan see **)

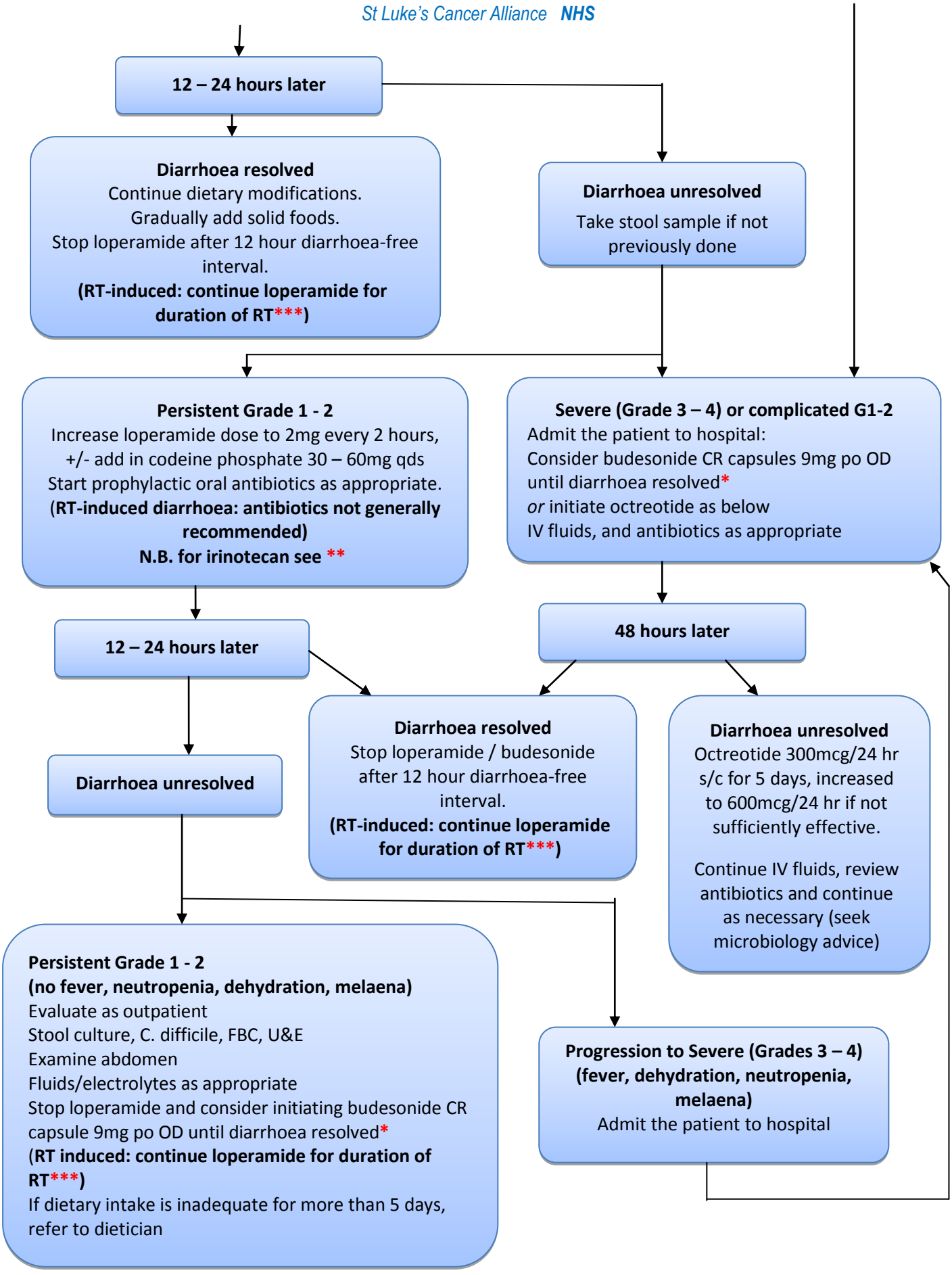
For patients with an ileostomy, loperamide often needs to be taken routinely before meals;
- *contact stoma nurse for specialist advice and management*
- *loperamide tablets or syrup may be more effective than capsules.*

Grade 3-4 diarrhoea
or
Grade 1-2, with one or more of cramping, fever, sepsis, neutropenia, frank bleeding, dehydration, nausea/vomiting, decreased PS

Investigations
FBC, U&Es, LFTs, Mg

Stool culture, C. difficile

Blood cultures (if neutropenic sepsis suspected)



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Prepared by: S Taylor	Checked by: M Chow

* Patients who achieve a positive response to budesonide may be considered for prophylactic budesonide (9mg po OD for 3 to 5 days) with subsequent chemotherapy cycles. However, this is **not** an alternative to appropriate dose reduction of chemotherapy, according to relevant protocol.

** Irinotecan-induced diarrhoea

Following treatment with irinotecan, onset of diarrhoea may be acute (< 24 hours after administration) or delayed (> 24 hours after administration).

Acute onset diarrhoea

Cholinergic syndrome occurs during administration of irinotecan and can be controlled by giving **atropine 0.25mg** subcutaneously at the time of irinotecan administration. Should the syndrome develop a further dose of atropine may be given.

Delayed onset diarrhoea

Patients must be made aware of the risks of delayed diarrhoea which can occur more than 24 hours after the administration of irinotecan and at any stage before the next administration.
The risk of diarrhoea is increased in

- Previous abdominal / pelvic radiotherapy
- Patients also receiving 5-FU or capecitabine
- Performance status > 2

As soon as the **first** liquid stool occurs, the patient should:

- Start drinking large volumes of water / electrolytes
- Take **loperamide 4mg** (2 tablets) immediately, followed by **loperamide 2mg** (1 tablet) **every 2 hours** for at least 12 hours **and** continuing for 12 hours following the last liquid stool.

After **24 hours** of persistent diarrhoea, if no other symptoms or signs of infection:

- Start prophylactic course of **ciprofloxacin 250mg po bd** for 7 days as an out-patient

Patients must be **admitted** if they have

- persistent diarrhoea, > 48 hours, despite loperamide
- severe diarrhoea requiring intravenous hydration
- diarrhoea with fever
- concomitant vomiting

*** Radiotherapy-induced diarrhoea

- Symptoms typically occur during the third week of radiotherapy (RT). They may then gradually increase in severity, with the peak reaction normally 7-10 days after the end of radiotherapy.
- Anti-motility agents should be continued until the end of treatment and should be tailed off gradually (do not stop abruptly).
- If the lower pelvis is treated (e.g. prostate only fields), patients may experience more of a sensation of tenesmus rather than a change in stool calibre. Fybogel (one sachet daily) may help to bulk the stool and improve symptoms.

References: Benson et al; JCO 2004; 22: 2918 - 2926
Wadler et al; JCO 1998; 16: 3169 – 3178
Lenfers et al; Annals of Oncology 1999; 10: 1251 – 1253
RMH Policy "Management of Chemotherapy Induced Diarrhoea" kindly supplied in 2011
NCI (National Cancer Institute) Common Toxicity Criteria version 4