ACUTE ONCOLOGY INITIAL MANAGEMENT GUIDELINES

National guidelines for the initial management of adult patients, who have a cancer diagnosis, and present as an emergency or unplanned admission with a complication of their disease or cancer treatment.

Review date: 01.03.2020
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Disclaimer

The information contained in these guidelines are a consensus of the development and consultation groups’ views on current treatment. They should be used in conjunction with any local policies/procedures/guidelines and should be approved for use according to the trust clinical governance process. Care has been taken in the preparation of the information contained in the guidelines. Nevertheless, any person seeking to consult the guideline, apply its recommendations or use its content is expected to use independent, personal medical and/or clinical judgment in the context of the individual clinical circumstances, or to seek out the supervision of a qualified clinician. The United Kingdom Oncology Nursing Society makes no representation or guarantee of any kind whatsoever regarding the guidelines content or its use or application and disclaim any responsibility for its use or application in any way.

Introduction

These guidelines relate to the initial assessment and immediate management of Acute Oncology patients, i.e. patients presenting with an acute problem, demonstrating symptoms deemed as having been caused by:
  - Systemic Anti-Cancer Therapy (SACT),
  - Radiotherapy,
  - Malignant disease,
  - A previously undiagnosed cancer where an urgent oncology/haematology assessment is required.

It is emphasised that these guidelines focus on initial assessment at presentation and management for the first 24 hours. Patients should be referred to, or discussed with the Acute Oncology Team as soon as possible following presentation. The Acute Oncology team will provide further advice and on-going management guidance.

To aid in this urgent initial assessment, each protocol follows a RAG (red, amber, green) format and quick reference assessment, which is in line with the UKONS Oncology/Haematology 24-Hour Triage Tool (V2, 2016). The Common Terminology Criteria for Adverse Events (CTCAE Version 4.3) an international standard set of criteria for defining adverse events (AE) and their grading within clinical trials and the routine management of Oncology/Haematology patients has been applied to assist with recognition and management of Adverse Events:


Intended Audience

These guidelines are intended for use by all health care professionals who assess and/or manage acute oncology patients at presentation. The guidelines may also be useful as an adjunct to the UKONS Triage tool when providing care advice following telephone triage (Appendix 1, P.56). They are mostly single-page "see-and-treat" guides. Whilst drug names may be referenced within each protocol, this is offered as a guide only; it is acknowledged that local variation may apply.

Please be aware of NICE National Guidelines/Pathways for the management of:
  - Neutropenic Sepsis: http://pathways.nice.org.uk/pathways/neutropenic-sepsis
  - Metastatic malignant disease of unknown primary origin in adults: diagnosis and management: https://www.nice.org.uk/guidance/cg104

The development and consultation group worked to provide a set of generic guidelines based on national guidance and clinical expertise. They have now been reviewed and updated to ensure that they remain applicable and cover current best practice in the management of treatment induced toxicity and acute disease related complications. The authors request that the original source is acknowledged in all copies or adaptations.
• **Please consider drug toxicity as a possible cause of presenting problem.** Systemic Anti-Cancer Therapy (SACT) includes cytotoxic chemotherapy, monoclonal antibodies, targeted agents, immunotherapy and new and novel therapies.

• **SACT toxicities can cause acute deterioration but are often reversible if managed rapidly and appropriately.** All patients on SACT may develop toxicities and are at risk; they may also have or develop additional toxicities to the one they are complaining of. Patients may be on new, novel or trial therapy, and may present with unexpected or unknown side effects.

• **Patient’s should know what treatment they are receiving, and have written information about their SACT and an alert card with their 24-hour advice line telephone number.** These advice lines provide telephone triage and assessment for patients receiving treatment and will advise regarding the need for urgent assessment or review and follow up. In most cases, if a patient or carer telephones your department for advice it would be wise to redirect their call to the specialist advice line. However, if you are worried about the patient or their ability to give an accurate history, or you think that this may be a medical emergency then urgent medical review is essential.

• **If a patient sounds unwell from SACT toxicities, it is sensible to arrange oncological/haematological review or assessment in hospital.** If asking a GP or member of the primary health care team to review, it is essential to speak to them outlining what is required, what to look for and who to contact if further advice is needed.

• **All licensed anticancer drugs have specific toxicities and the length of time that side effects can occur following completion of treatment varies.** Most cytotoxic chemotherapies can cause side effects for up to 6 to 8 weeks after the last treatment is given. The newer immunotherapies and targeted agents can cause side effects for up to 2 years after the last treatment is administered – please ask for details and/or advice from the acute oncology team, the site specific specialist team, the hospital pharmacy or see the Summary of Product Characteristics: [https://www.medicines.org.uk/emc/browse-medicines](https://www.medicines.org.uk/emc/browse-medicines)

• Please see specific toxicity guideline and manage the patient according to their condition, severity, concomitant medications and other medical problems.

• **Aggressive management (usually including HDU/ITU) is appropriate if unstable, sometimes, even in the context of advanced cancer.** Escalate care (e.g. HDU/ITU) if patient becoming haemodynamically compromised/drowsy/shut down, discuss with specialist team if unsure of appropriateness.

• **Organisations should consider using a standard triage and assessment format, such as the UKONS Triage Tool, for the assessment of patient’s with cancer.** Assessment should include as standard the following questions:

  - Is the patient on active treatment (including radiotherapy) at present or have they received SACT treatment in the previous 2 years?
  - Names of SACT drugs and last date of treatment (NB may be on tablets)?
  - Performance status, general condition, ability to carry out normal function at home? Has this changed recently? (Eastern Cooperative Oncology Group¹ or Karnofsky Performance Status²)
  - It is important to ask about all SACT related toxicities/problems in addition to the initial complaint, as several occurring together elevate risk and need closer management.
  - Reversible toxicities and/or problems can be treated even in the presences of any DNACPR orders, decisions should be made on an individual basis: please discuss with acute oncology/haematology team or on call oncology/haematology consultant.


General Information and Management Principles - continued

- Neutropenia can occur:
  - At any time during a course of certain SACT or up to 6 weeks after
  - With certain radiotherapy treatment
  - At any time in a patient with disease-related immunosuppression

Patient’s with a suspected neutropenic sepsis will require IV antibiotics within 1 hour of presentation for assessment.

- Review concomitant medications and consider stopping those that may affect renal function/ potentiate hypotension (e.g. ACE-inhibitors, diuretics) if unwell or hypotensive and benefits outweigh the risks of doing so.
- Establish intravenous access, or utilise indwelling lines if appropriately trained to do so, and hydrate according to clinical condition. Monitor fluid balance closely.
- Patient’s require daily medical review and daily bloods may also be required (watch for neutropenic sepsis/dehydration). Be aware that administering paracetamol/antipyretics to neutropenic patients may mask signs of sepsis.
- Rectal examination. Due to the risk of damage to rectal mucosa, it is recommended that in patients receiving SACT rectal examination is not performed. If it is deemed necessary to conduct rectal examination, this should be undertaken with caution.
- The patient’s site-specific specialist team providing cancer treatment must be informed of any admission/assessment, as adjustments to the subsequent cycle may be required. If patient is in a clinical trial, the trials team should be contacted about the admission.
- Consider the involvement of the palliative care team for symptom control advice if the problem is disease related.

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 1. ANAPHYLAXIS/ALLERGIC REACTION/HYPERSENSITIVITY Requires IMMEDIATE medical assessment!

Hypersensitivity or an allergic reaction is an inappropriate and excessive reaction to an allergen; severity ranges from mild allergy to severe systemic reactions leading to anaphylactic shock if left untreated.

Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity reaction. It is characterised by rapidly developing, life-threatening problems involving: the airway (pharyngeal or laryngeal oedema) and/or breathing (bronchospasm with tachypnoea) and/or circulation (hypotension and/or tachycardia). In most cases, there are associated skin and mucosal changes.

Treat as an emergency according to Resuscitation Council Anaphylaxis Guidelines.
https://www.resus.org.uk/anaphylaxis/emergency-treatment-of-anaphylactic-reactions/

**Signs and symptoms:**
- Bronchospasm
- Cough
- Dizziness
- Dyspnoea
- Headache
- Hypertension
- Hypotension
- Nausea, vomiting
- Urticaria
- Tachycardia
- Pruritus/itching
- Arthralgia
- Myalgia
- Asthenia
- Rash
- Swelling of tongue/throat

**Assessment:** ABCDE approach

**Observations:** Calculate and monitor NEWS score. ECG Cardiac monitoring

**Questions:**
- What treatment/drug is the patient receiving?
- Cancer diagnosis/primary disease?
- Concurrent medications?

Differential diagnosis includes: infusion reaction; cytokine release syndrome, asthma, septic shock, and transfusion reaction.

If this occurs during administration of treatment - STOP infusion/transfusion immediately

**Grade 1 (Green)**
Mild transient reaction: intervention or infusion interruption not required.

- Treat reaction in line with local guidelines/policy.
- Prophylactic medications indicated for 24 hours.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

**Grade 2 (Amber)**
Intervention or infusion interruption indicated; all symptoms respond promptly to treatment (E.g. antihistamines; NSAIDS, IV Fluids).

- Patients with a good response to initial treatment should be warned about recurrence of symptoms and in some circumstances be kept under observation for 24 hours. This includes the following:
  - Severe reactions with slow onset
  - Individuals with severe asthma or a severe asthmatic component
  - Patients with a history of biphasic reactions

**Grade 3 (Red)**
Prolonged signs and symptoms not rapidly responsive to medication and/or brief interruption of infusion or recurrence of symptoms following initial improvement

- Treat as an emergency according to Resuscitation Council Anaphylaxis Guidelines – Page 7.
  - Patients who have had a suspected anaphylactic reaction should be treated and observed for at least 6 hours in a clinical area with facilities for treating ABC problems
  - Patient should be reviewed by a senior clinician and a decision made about the need for further treatment or a longer period of observation
  - Manage in accordance with trust local guidelines depending upon differential diagnosis.
  - Check that the patient is not neutropenic – if sepsis suspected manage accordingly

**Grade 4 (Red)**
Anaphylaxis – Airway, Breathing, Circulation problem - Life threatening consequences; urgent intervention required.

- Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.
- Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
- WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Anaphylactic reaction?

Airway, Breathing, Circulation, Disability, Exposure

Diagnosis - look for:
- Acute onset of illness
- Life-threatening Airway and/or Breathing and/or Circulation problems
- And usually skin changes

- Call for help
- Lie patient flat
- Raise patient’s legs

Adrenaline

When skills and equipment available:
- Establish airway
- High flow oxygen
- IV fluid challenge
- Chlorpheneramine
- Hydrocortisone

Monitor:
- Pulse oximetry
- ECG
- Blood pressure

1 Life-threatening problems:
Airway: swelling, hoarseness, stridor
Breathing: rapid breathing, wheeze, fatigue, cyanosis, SpO2 < 92%, confusion
Circulation: pale, clammy, low blood pressure, faintness, drowsy/coma

2 Adrenaline (give IM unless experienced with IV adrenaline)
IM doses of 1:1000 adrenaline (repeat after 5 min if no better)
- Adult: 500 micrograms IM (0.5 mL)
- Child more than 12 years: 500 micrograms IM (0.5 mL)
- Child 6 -12 years: 300 micrograms IM (0.3 mL)
- Child less than 6 years: 150 micrograms IM (0.15 mL)

Adrenaline IV to be given only by experienced specialists
Titrate: Adults 1 microgram/kg

3 IV fluid challenge:
Adult: 500 – 1000 mL
Child: crystalloid 20 mL/kg

Stop IV colloid if this might be the cause of anaphylaxis

4 Chlorphenamine (IM or slow IV)
- Adult or child more than 12 years: 10 mg
- Child 6 - 12 years: 5 mg
- Child 6 months to 6 years: 2.5 mg
- Child less than 6 months: 250 micrograms/kg

5 Hydrocortisone (IM or slow IV)
- Adult: 200 mg
- Child: 100 mg
- Child: 50 mg
- Child: 25 mg
Guideline 2. **ARTHRALGIA/MYALGIA**

*Initial triage assessment within 15 minutes*

Normally a symmetrical widespread joint pain but can also be associated with muscle pain (myalgia). Certain drugs can cause arthralgia, including: Taxanes, BRAF inhibitors, GCSF, Immunotherapies.

**Identify:** patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant, they may be myelosuppressed/ neutropenic and at risk of sepsis. If present, this should be managed according to guidelines.

**Observations:** Calculate NEWS score.

**Investigations:** Urgent FBC, U&E and Ca²⁺.

For patients receiving or received **immunotherapy** consider:
- Endocrine function panel - TSH, Free T4, Free T3, ACTH, LH, FSH and Cortisol, Prolactin, Blood Glucose, +/- Testosterone/Oestrogen and refer to endocrinopathy guidelines on pages 27 to 36
- CK and ESR to rule out Autoimmune Arthritis/Myositis

**Questions:**
- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Has the patient taken anything for pain?
- Where is the pain? (If not widespread then consider other causes of joint pain e.g. localised pain in isolated joint/back/spine may be related to metastatic deposit and need investigation and discussion)
- How long has the patient had the pain? Is the pain affecting what they can do?
- Has/is the patient receiving GCSF, filgrastim/pegfilgrastim injections? Some patients receiving GCSF may experience severe muscle pain commonly in the pelvic area, lower back and/or shoulders, which will usually improve after stopping GCSF. When was the last injection?
- Are there any comorbidities that may cause arthralgia/myalgia e.g. autoimmune Rheumatoid Arthritis or Systemic Lupus Erythaematosis
- Is the patient on any blood thinning drugs or steroids?

<table>
<thead>
<tr>
<th>Grade 1(Green)</th>
<th>Grade 2(Amber)</th>
<th>Grade 3(Read)</th>
<th>Grade 4(Read)</th>
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<tbody>
<tr>
<td>Mild Pain - not interfering with daily activities</td>
<td>Moderate pain - Interfering with some normal activities</td>
<td>Severe pain - and/or loss of ability to perform some activities</td>
<td>Bedridden or disabling</td>
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- Reassure the patient that this is normal, generally nothing to worry about and associated with treatment.
- Advise to observe temperature closely - if patient develops temperature they must phone helpline immediately for advice.
- Review current analgesia and consider paracetamol, non steroidal (with caution as may not then develop a temperature in response to infection) or opiate if pain severity merits it
- Heat - a heat pad, covered hot water bottle or regular warm baths. Advise patient to get plenty of rest and plan activities to include rest periods
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

- Advice and support measures as Grade 1 & 2.
- You must check that the patient is not neutropenic if discharge home is being considered
- Review analgesia – consider codeine or opiate based or non steroidal if not contraindicated, or neuropathic agent if appropriate
- Advise to observe temperature closely - if patient develops an abnormal temperature they must phone immediately for advice.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

- Ensure the patient is not neutropenic.
- Review analgesia – consider codeine or opiate based or non steroidal if not contraindicated, or neuropathic agent if appropriate
- Seek specialist oncology advice if pain is not settling.

**Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.**

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
**Guideline 3. BLEEDING AND/OR BRUISING - Requires **IMMEDIATE** medical assessment.**

**Bleeding** can occur secondary to injury, disease, or as a side effect of treatment. It can be a life-threatening event if massive blood loss or spontaneous bleeding occurs.

**Thrombocytopenia** - is a reduction in the number of platelets in the blood. If platelet count is < 50 bleeding and or bruising may occur with minor trauma.

Intracranial haemorrhage is more likely if there is **sepsis** and a platelet count of < 20

In a **non-septic** patient a platelet count of 10 or above may be adequate in the absence of additional risk factors for bleeding

**Coagulation abnormalities** - due to disease e.g. liver metastases or disseminated intravascular coagulation (DIC) or treatment e.g. anti-coagulation therapy.

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**Identify:** patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant, they may be myelosuppressed / neutropenic and at risk of sepsis. If present, manage accordingly.

Many haematological disorders (malignant and non-malignant) can cause thrombocytopenia. Some patients, e.g. those with chronic lymphocytic leukaemia (CLL) or lymphoma may develop idiopathic thrombocytopenic purpura (ITP).

Patients who are receiving certain systemic anti-cancer treatment are at risk of thrombocytopenia

If present, these conditions should be managed according to approved guidelines.

**Observations:** Calculate and monitor NEWS score.

**Investigations:** Urgent FBC, U&E, LFTs. Consider group and cross match. Coagulation screen. INR (if on Warfarin). APTT ratio (if on IV Heparin). Anti-Xa level if on low molecular weight (LMW) heparin, as it can accumulate in the presence of renal failure. Fibrinogen if considering DIC.

**Examination:**

-associated symptoms: Light headed, pallor, clammy, thirst, rash (petechial/purpura/ punctate)

**Questions:**

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Is the patient actively bleeding? Site of active bleeding? Injury related or spontaneous?
- How much blood has the patient lost?
- Onset and duration – when did bleeding and/or bruising start and how long has it persisted?
- Have they had similar bleeding and/or bruising before?
- Allergies/ current medications? - Anticoagulants, aspirin, clopidogrel, NSAIDS, DOACs (new anticoagulants e.g. rivaroxaban /apixaban) - **NB** Heparin can cause thrombocytopenia.
- Relieving factors – Is it stopped via direct pressure or other measures?

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**Grade 1 (Amber)**

- Bleeding - mild self limiting, controlled by conservative measures, ecchymosis, occult blood in secretions
- Bruising - petechiae or bruising in a localised or dependent area, with or without trauma.

**Grade 2 (Red)**

- Bleeding - loss of 1-2 units
- Bruising - moderate petechiae, purpura and/or generalised bruising, with or without trauma.

**Grade 3 (Red)**

- Bleeding - loss of 3-4 units.
- Bruising - generalised petechiae, purpura and/or bruising.
- New bruises, without significant trauma.

**Grade 4 (Red)**

- Massive bleeding loss of > 4 units.
- Life threatening haemorrhage.

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- Review blood results
- Manage neutropenia as per guideline **12 on P.19-20**
- Discuss abnormalities with on call haematologist or oncologist
- Do not discharge a patient without prior discussion with on call haematology or oncologist
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

**Always make sure that the Acute Oncology Team are informed of the patient’s assessment and/or admission as soon as possible.**

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Identify: Patients within 6/52 of chemotherapy specifically patients currently receiving 5 fluorouracil (5FU) or capecitabine, which can cause coronary artery spasm. Patients may be taking these drugs orally at home or via continuous infusion. Other chemotherapy drugs/monoclonal antibodies can cause reduction in heart function but this is not usually an acute presentation.

All cancer patients have an increased risk of pulmonary embolism.

Observations: Calculate and monitor NEWS score.

Investigations: Urgent FBC, U&E, Cardiac markers. Urgent ECG. Consider ABGs, CTPA.

Questions:
- Is there a cancer diagnosis/primary disease?
- Is the patient currently receiving 5FU/capecitabine?
- Does the patient have a history of angina, or other heart disease?
- Exacerbating / relieving factors, and characteristics of pain?
- Associated symptoms, e.g. SOB, syncope, oedema, palpitations
- Consider is this pain cardiac? Differentials for chest pain in oncology/haematology patients include cardiac cause, pulmonary embolism (PE), indigestion, disease progression or metastases

Advise Urgent A&E assessment for all symptoms of chest pain

Action: Treat chest pain as ‘Red’ until proven to be non-cardiac/life threatening

The aim is to exclude a life-threatening cause, which needs immediate treatment, from other causes of chest pain.

! If PE strongly suspected and same day CTPA not possible, consider commencing treatment with LMWH pending definitive investigation/diagnosis

! Is the patient connected to an ambulatory intravenous infusion pump of 5 fluorouracil (SACT)? – If so arrange urgent disconnection.

! Is the patient taking oral SACT such as capecitabine? - If so ensure patient does not continue with this medication

! These patients may also be myelosuppressed/ neutropenic and at risk of sepsis. If present, this should be managed according to approved guidelines
  - Admit for monitoring and on going assessment and management in accordance with local trust guidelines.

Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 5. **CONSTIPATION**

*Initial triage assessment within 15 minutes*

Irregular and infrequent or difficult evacuation of the bowels; can be a symptom of intestinal obstruction or diverticulitis.

**Identify:** Patients who have received/receiving SACT or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20

**Observations:** Calculate NEWS score. Presence of bowel sounds.

**Investigations:** Urgent FBC, U&E, CRP, Ca²⁺, and LFTs. Consider abdominal X-ray.

**Questions:**
- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- When did the patient’s bowels/stoma move last? Are they passing wind?
- What is normal bowel habit? Any recent changes? N.B. loose runny stools could be overflow.
- What medication are they taking and has there been any recent changes? Certain medication can cause constipation e.g. anti-emetics (5HT3 Antagonists), opioids, SACT including vinca-alkaloids
- What food and fluids have they been taking over last few days? Decreased fluid and/or food intake can be significant factors in constipation
- Is there any nausea or vomiting?
- Is there any abdominal pain? Is it getting worse
- Are they passing water/urine normally?

**Examination:** PR Examination (with caution in haematology patients). Presence and nature of bowel sounds. Rule out signs and symptoms of bowel obstruction.

**N.B.** Constipation may be a presenting symptom of MSCC or hypercalcaemia. Ascites can often aggravate constipation – if present consider drainage.

**Differential diagnosis includes:** Drug related e.g. SACT, opiates, anti-emetics. Bowel obstruction/ileus secondary to disease or ascites. Hypercalcaemia.

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<tr>
<td>Mild-no bowel movement for 24 hours over pre-treatment normal</td>
<td>Moderate-no bowel movement for 48 hours over pre-treatment normal</td>
<td>Severe-no bowel movement for 72 hours over pre-treatment normal</td>
<td>No bowel movement for &gt; 96 hours -consider paralytic ileus or bowel obstruction</td>
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**ACTION: Grade 1 and Grade 2**
- Dietary advice including good fluid intake
- Stop or change constipating drugs
- Consider use of laxatives, faecal softener or stimulant
- If patient is discharged they should be encouraged to make contact if symptoms persist or worsen.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

**Grade 3 (Red)**

**Grade 4 (Red)**

**Patients may also have:**
- Severe abdominal pain and/or distension
- Nausea and Vomiting
- Faecal smelling vomit
- Rigid abdominal distension
- History of abdominal Surgery

Admit for: -
- Further management and investigation
- Senior medical and/or surgical review
- I.V. access and fluid replacement
- Consider nil by mouth instructions and naso-gastric tube placement
- Analgesia
- Emesis control
- Monitoring

Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20

Observations: Calculate and monitor NEWS score.

Investigations: Urgent FBC, U&E + magnesium, LFTs, CRP, abdominal X-ray.

Stool sample for C&S/ova/cysts/parasites to rule out infective causes of diarrhoea-e.g. Campylobacter/salmonella and CDT screen. DO NOT assume this is infective it is most likely to be drug induced in this group of patients.

Questions:
- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Is the patient receiving radiotherapy to the abdomen or pelvis and when was their last treatment?
- How many stools a day above normal amount? or how much stoma output is there above normal amount? Have they had any nocturnal movements? For how many days have they had diarrhoea? Is it interfering with activities of daily living?
- Are stools/stoma outputs formed, loose or watery? Any faecal incontinence or urgency? Any blood or mucous in the stool?
- Is there any abdominal pain e.g., cramping pains coming in waves?
- Is the patient able to eat and drink normally? Are they passing plenty of clear urine?
- Does the patient have any other SACT related toxicities, e.g. mouth ulcers, mucositis, nausea/vomiting, red hands/feet?
- Has the patient taken any antibiotics recently or been in hospital recently?
- What medication have they taken? Have they taken any laxatives or anti-sickness medication or any anti-diarrhoal medication in the last 24 hours? If so what?

Differential diagnosis includes:
- Graft versus host disease in stem transplant patients – contact transplant haematologist urgently
- Secondary to SACT e.g. 5FU or CAPECITABINE, IRINOTECAN, any TKI, please see next page and specific DRUG INFORMATION SHEET for further management guidance. Consider DPD deficiency
- Gastrointestinal symptoms due to IMMUNOTHERAPY - proceed to guideline 21 on page 30 for further guidance
- Infection
- Constipation with overflow
- Radiotherapy – secondary to treatment

<table>
<thead>
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<tr>
<td>Increase up to 3 bowel movements a day over pre-treatment baseline or mild increase in ostomy output</td>
<td>Increase up to 4-6 episodes a day over baseline or moderate increase in ostomy output or nocturnal movement or moderate cramping</td>
<td>Increase up to 7-9 episodes a day or severe increase in ostomy output * and/or incontinence * and/or severe cramping * and/or bloody diarrhoea</td>
<td>Increase &gt; 10 episodes a day or grossly bloody diarrhoea</td>
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</table>

Review medication WITHHOLD DRUGS including any SACT that may be contributing until Acute Oncology or Site Specific team review

ESCALATE TO RED for any of the following:
- Grade 2 and receiving or received immunotherapy treatment in the last 12 months
- Grade 2 for >24 hours despite anti-diarrhoal medication
- Other symptoms e.g. temperature, nausea/vomiting, mouth ulcers, or clinical concerns
- Haematology patient
- Oncology - Consider loperamide initially. If ineffective consider Codeine Phosphate. Reduce and then stop antidiarrheal after 12-24 hours free of diarrhoea.
- Review any other SACT toxicities according to guidelines.
- Review all medications and stop prokinetics and laxatives once constipation with overflow has been ruled out. Avoid domperidone and metoclopramide anti-emetics.

Patients with grade 3 or 4 diarrhoea require specialist secondary care to manage symptoms - IV resuscitation may be required. They should be admitted further assessment and active management. WITHHOLD SACT until Acute Oncology Team review and review all other medication as they may be contributing – if receiving Capcitabine or 5FU consider DPD deficiency

If receiving or received immunotherapy treatment in the last 12 months - follow guideline 21 on page 30

Haematology patients – discuss with haematology team, urgently.

Further management detail on the page 13.

Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 6 continued.  

**DIARRHOEA**

**Initial Management**

1. Consider infective diarrhoea:  
   Isolate until infection excluded  
   • Send stool sample urgently - Inform microbiology and discuss management with microbiologist  
   • If haematology patient or strong suspicion of infective diarrhoea, withhold anti-diarrhoeal medication until stool result available  
   • Give antibiotics according to local policy (e.g. for C.Difficile or neutropenic sepsis) **Consider** administering antibiotics empirically if not settling.

2. **Consider graft versus host disease** in stem transplant patients – contact transplant haematologist **urgently**

3. **Secondary to SACT** e.g. 5FU or CAPECITABINE, IRINOTECAN, ERLOTINIB any TKI or Targeted Therapy please see specific **DRUG INFORMATION SHEET** for specific management guidance.

4. **Gastrointestinal symptoms due to IMMUNOTHERAPY** - proceed to guideline 21 on page 30 for further guidance

5. **Neutropenic Sepsis** – if there is suspicion of, or potential for neutropenic sepsis start antibiotic management immediately as per policy (guideline 12 on pages 19-20) – **do not wait for FBC**.

6. **IV fluid resuscitation**. Replace fluid and electrolyte losses. Adjust on-going fluids according to fluid balance status and renal function.

7. **Full medication review** - **Stop** ACE-inhibitors/ diuretics/ NSAIDs. NB Folic Acid can potentiate and increase side effects of some SACT drugs

8. **Nil by mouth** (except sips) if abdominal pain or distension or abnormal abdominal X-ray

9. **Antidiarrhoeal** -  
   • **Haematology** - Discuss with haematology team on call before commencing antidiarrhoeal
   • **Oncology**:  
     • Consider loperamide 4mg initially then 2mg after each loose stool (maximum16mg per 24 hours) **N.B. Caution with high doses or prolonged use of loperamide as it can cause paralytic ileus**  
     • If loperamide ineffective, then consider codeine phosphate instead of or in addition  
     • Reduce/stop antidiarrhoeal after 12-24 hours free of diarrhoea.  
     • If Grade 4 – consider the use of octreotide by sc injection and immediate IV broad-spectrum antibiotic (even if afebrile). Withhold if not on maximal antidiarrhoeal prior to admission but review every 24 hours.  
     • Do not withhold antidiarrhoeal for more than 12-24 hours without thorough senior medical review.

10. **Consider hyoscine butylbromide if abdominal spasms**
Guideline 7. **DYSPNOEA/SHORTNESS OF BREATH.** Requires **IMMEDIATE** medical assessment.
Difficulty breathing may include symptoms such as wheezing, choking, and a feeling of not getting enough air into lungs. Dyspnoea indicates a conscious appreciation of increased work done during breathing; principal factors in SOB are an increased work of breathing, increased ventilatory drive, impaired muscle function.

**Identify:** Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed/neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20

**Observations:** Calculate NEWS score.

**Investigations:** Urgent FBC, U&E, Sputum C&S, blood cultures and CRP if pyrexial. ECG and CXR. Risk assess for VTE. Consider ABGs and troponin. Consider CTPA/VQ investigations to rule out pulmonary embolism, pneumonitis. Consider D-dimer.

**Questions:**
- Is there a cancer diagnosis/primary disease?
- Is the patient taking anti-cancer treatment at the moment or recently? If so what treatment and when did it stop?
- Cardinal questions related to breathlessness including history of underlying chest complaint, asthma, COPD, ischaemic heart disease
- Is there any chest pain?
- What is the patients current medication?
- Is there a history of dyspnoea? What is their normal level? Is this a new symptom?
- Are there any exacerbating/relieving factors?
- Is there any pain or swelling in legs? – assess for signs of DVT

**Differential diagnosis includes:**
- Chest Infection
- Pulmonary embolism (PE)
- Anaemia
- Disease progression
- Consolidation
- Pneumonitis
- New cancer diagnosis or metastases
- Superior vena cava obstruction (SVC0)
- Exacerbation of respiratory condition e.g. Asthma
- Pleural effusion
- Cardiac ischaemia
- Lymphangitis

**Grade 1 (Amber)**
New onset dyspnoea with moderate exertion

- Assess for signs of sepsis: such as productive cough, pyrexia, generally unwell (Escalate to Red as appropriate)
- Anaemia – consider correction
- A history of underlying chest complaints e.g. asthma, COPD: advise patients around usual management of exacerbations and advise to discuss with GP or health professional managing this condition
- You must check that the patient is not neutropenic prior to discharge
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

**Grade 2 (Red)**
New onset dyspnoea with minimal exertion

- Ensure the patient is not neutropenic – **If present, this should be managed as per guideline 12 on P.19-20** - immediate antibiotics if sepsis suspected
- Admit if evidence of:
  - Desaturation
  - Infection
  - Other chemotherapy toxicities
  - SVCO - see guideline 40 on P.51
  - Pleural effusion - see guideline 37 on P.48
  - Carcinomatous Lymphangitis – see guideline 29 on P.38
  - Pneumonitis may be drug or radiation related:
    - Radiation pneumonitis - see guideline 39 on P.50
    - Immunotherapy induced pneumonitis – see guideline 24 on P.33
  - Discuss with Acute Oncology Team
  - Manage all other causes in accordance with trust local guidelines depending upon differential diagnosis:
    - COPD - https://www.nice.org.uk/guidance/CG101

**Grade 3 (Red)**
New onset dyspnoea at rest

**Grade 4 (Red)**
Life threatening symptoms requiring ventilatory support

Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
**Guideline 8. FATIGUE**

Initial triage assessment within 15 minutes

Fatigue is a subjective unpleasant symptom, which incorporates total body feelings ranging from tiredness not relieved by rest or sleep to total exhaustion creating an unremitting overall condition that interferes with the individual ability to function to their normal capacity.

**Identify:** Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20 - immediate antibiotics if sepsis suspected

**Observations:** Calculate NEWS score.

**Investigations:** Urgent FBC, U&E, group and save, CRP, blood glucose, consider blood cultures, Ca$^{2+}$; If the patient is receiving or has received immunotherapy in the past 12 months, check random cortisol, TSH, T4, T3.

**Questions:**
- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- How many days have they been feeling like this?
- Do they have any pain? Have they taken any painkillers? If so, what?
- Are they able to eat and/or drink?
- Are they short of breath?
- Are they able to mobilise – ambulant – performance status?
- Are they passing usual amounts of urine and are bowels functioning normally?
- Patient mood? Has their mood changed recently? Are they receiving any psychological support?

**Differential diagnosis includes:**
- Anaemia
- Side effect of treatment
- Disease progression
- Patient entering the dying phase
- Immunotherapy induced endocrinopathy
- Depression/psychological problems
- Hormone disturbance e.g. thyroid dysfunction

**Grade 1 (Green)**
Increased fatigue but not affecting normal level of activity

- Check all blood results prior to discharge and escalate any abnormalities:
  - Neutropenia/pancytopenia
  - Endocrine disturbance in immunotherapy
- Advice: Encourage diet and fluids
- Consider psychological support measures
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

**Grade 2 (Amber)**
Moderate or interfering with some normal activities

- Check all blood results and escalate any abnormalities:
  - Neutropenia/pancytopenia
  - Endocrine disturbance in immunotherapy
- Escalate if evidence of:
  - Dehydration
  - Infection
  - Poor oral intake
  - SACT toxicities
- Consider possible disease progression.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

**Grade 3 (Amber)**
Severe or loss of ability to perform some activities

- Check all blood results and act on abnormalities e.g.
  - Neutropenia/pancytopenia
  - Endocrine disturbance in immunotherapy
  - Hormone disturbance e.g. thyroid dysfunction
- Consider possible disease progression.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

**Grade 4 (Red)**
Bedridden or disabling

- Check all blood results and act on abnormalities e.g.
  - Neutropenia/pancytopenia
  - Endocrine disturbance in immunotherapy
  - Hormone disturbance e.g. thyroid dysfunction
- Admit for:
  - Monitoring and continued assessment
  - Management according to symptoms/blood results.
  - Contact the acute oncology team for advice on continuing anti-cancer therapy and consider possible disease progression.

Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
### Guideline 9. METASTATIC SPINAL CORD COMPRESSION (MSCC) / Cauda Equina Syndrome.

**IMMEDIATE medical assessment.**

MSCC is due to a pathological vertebral body collapse or direct tumour growth causing compression of the spinal cord. Irreversible neurological damage ensues with resulting paraplegia. Early diagnosis and treatment is essential.

**Identify:**
- Patients with known diagnosis/history of, or suspected cancer. Please note to rule out spinal cord compression, MRI scan must be performed within 24 hours of clinical suspicion.
- Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and are at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20 - immediate antibiotics if sepsis suspected.
- **Observations:** Calculate and monitor NEWS score. **Examination:** Full neurological assessment and on-going review
- **Investigations:** Urgent MRI whole spine within 24 hours of clinical suspicion. Urgent FBC, U&E, LFT, Group & Save, Ca²⁺. If considering myeloma/plasmacytoma then Immunoglobulins/electrophoresis, serum light chains and urine bence jones protein. If considering lymphoma then LDH. If new diagnosis of cancer consider appropriate tumour markers to aid diagnosis.

**Key signs/symptoms:**
- The patient may or may not have a cancer diagnosis/primary disease
- Referred back pain that is multi segmental or band like
- Escalating pain which is poorly responsive to treatment, including medication
- Different character or site to previous symptoms
- Funny feeling, odd sensations or heavy legs (multi segmental), pins and needles
- Lying flat increases back pain
- Pain, worsening on coughing or sneezing
- Agonising pain causing anguish and despair
- Gait disturbance, unsteadiness, especially on stairs (not just limp)
- Sleep grossly disturbed due to pain being worse at night
- Established motor/sensory/bladder / bowel disturbances incontinence are late signs

If you have suspicion of MSCC then contact the Acute Oncology team and/or MSCC coordinator for advice regarding management.

### Grade 1 (Amber)
- Mild paraesthesia, subjective weakness; no objective findings
- **Rule out spinal cord compression – full neurological examination**
- **Discuss with the Acute Oncology Team and/or MSCC Coordinator**
- MRI whole spine to be performed within 1 week of clinical suspicion
- **Advise on pain control**
- **DO NOT discharge the patient** until you are sure they do not have MSCC.
- If you do discharge the patient:
  - Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen/persist.

### Grade 2 (Red)
- Mild or moderate sensory loss, moderate paraesthesia, mild weakness with no loss of function
- **Rule out spinal cord compression/cauda equine - Urgent MRI whole spine**
- **Treat as unstable spine until MRI results reported or oncology/neurosurgical assessment**
- **Admit for monitoring and ongoing assessment**
- **Commence:**
  - Dexamethasone 16mg stat dose followed by 16mg daily
  - Analgesia
  - Thromboprophylaxis

**N.B. Note:** need for caution in patients with no previous known malignancy and lymphoma suspected steroids might cause rapid resolution of the tumour, which may make histological diagnosis very difficult. If possible, steroids should be avoided before biopsy if lymphoma suspected.

- **Contact MSCC coordinator or oncologist on call to assess and plan treatment – radiotherapy or surgery if required**
- All patients should start definitive treatment within 24 hours once MRI confirms a diagnosis of MSCC.
- See your trust/network agreed algorithm for more detailed local guidance including contact details for the specialist team.
- Please consider Cancer of Unknown Primary (CUP), guideline 38 for patients who present with metastatic disease without a previous diagnosis of cancer


### Grade 3 (Red)
- Severe sensory loss, paraesthesia or weakness that interferes with function
- **Urgent MRI whole spine within 24 hours of clinical suspicion.**
- **Inpatient management / treatment as per guideline 12 on P.19-20**
- **Admit for monitoring and on-going assessment**
- **Commence:**
  - Dexamethasone 16mg stat dose followed by 16mg daily
  - Analgesia
  - Thromboprophylaxis
  - Early radiotherapy

### Grade 4 (Red)
- Paralysis
- **Admit for monitoring and on-going assessment**
- **Commence:**
  - Dexamethasone 16mg stat dose followed by 16mg daily
  - Analgesia
  - Thromboprophylaxis
  - Early radiotherapy

**Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.**

**Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.**

**WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.**
Identify: Patients who have received/receiving SACT or are at risk of disease related immunosuppression or a history of stem cell transplant (PBSCT). These patients may be myelosuppressed/neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20 - immediate antibiotics if sepsis suspected.

Observations: Calculate NEWS score.

Investigations: Urgent FBC, U&Es, LFTs, CRP, Lactate and Blood Cultures (Oncology patients - consider the need for pathology investigations in grade 1 and 2 presentations on an individual basis and in light of any other presenting symptoms or risk factors)

Examination and questions:
- Is there a cancer diagnosis/primary disease?
- Is this a haematology patient? If so please contact haematology team as soon as possible.
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Is there evidence of super added infection? Does the patient have any blisters, ulcers or white patches on tongue/lips mouth?
- Is there any pain or bleeding from the mouth?
- Are they able to eat and/or drink?
- Does eating or swallowing make the pain worse?
- Are they using any mouthwashes, painkillers or other treatments within the mouth?
- Do they also have diarrhoea?
- Is there any dryness, pain, inflammation of genitals and/or rectum – consider rectal mucositis
- Are they passing usual amounts of urine?
- Have they had any recent radiotherapy treatment to the head and/or neck?

Differential diagnosis includes:
- Radiotherapy reaction
- SACT related
- Viral/bacterial infection
- Candidiasis

Grade 1 (Green)
Painless ulcers, erythema or mild soreness, able to eat and drink normally

Grade 2 (Amber)
- Painful ulcers and/or erythema, mild soreness but able to eat and drink normally

Grade 3 (Red)
Painful erythema, and difficulty with eating and drinking

Grade 4 (Red)
Significant pain, minimal intake and/or reduced urinary output

Consider the following mouth care advice:
- Ice chips for symptomatic relief
- If painful: an anti-inflammatory mouthwash
- Consider the use of a mucosal barrier gel
- Analgesia: use care if advising antipyretic as it may mask signs of neutropenic sepsis
- Assess for thrush/candidiasis and arrange for an antifungal agent to be prescribed if required
- You must check that the patient is not neutropenic prior to discharge
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

Check all blood results and act on abnormalities e.g.
- Neutropenia or pancytopenia
- Assess for evidence of:
  - Dehydration
  - Poor oral intake
- Other SACT toxicities
- If receiving Capecitabine or 5FU consider DPD deficiency
- Admit for monitoring and management
- Consider parenteral hydration
- Analgesia, consider:
  - Dispersible analgesics e.g. soluble paracetamol/co codamol
- If no improvement consider opiates
- Assess for thrush/candidiasis and arrange for an antifungal agent to be prescribed if required
- Consider referral to the SALT team and dietician for management support
- Consider the following mouth care advice:
  - Ice chips for symptomatic relief
  - If painful: anti-inflammatory mouthwash
  - Consider the use of a mucosal barrier gel

Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
**Guideline 11. NAUSEA**

Initial triage assessment within 15 minutes

Nausea is the sensation of being about to vomit. Acute chemotherapy induced nausea usually presents within the first 24 hours of receiving treatment. Delayed nausea may present any time after the first 24 hours and continues for up to 6 or 7 days after treatment.

**Identify:** Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20 - immediate antibiotics if sepsis suspected.

**Observations:** Calculate NEWS score.

**Investigations:** Urgent FBC, U&Es, LFTs, Ca^{2+}, blood cultures and CRP, (consider the need for pathology investigations in grade 1 and 2 presentations on an individual basis and in light of any other presenting symptoms or risk factors)

**Questions:**
- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- How often are they feeling sick/nauseous?
- Have they been sick/vomited?
- Assess bowel movements, any symptoms that suggest constipation? Any diarrhoea? Bowel obstruction?
- What food and fluids have they been taking over last few days?
- Any evidence of reflux/gastritis?
- Any signs of dehydration e.g. decreased urine output, fever, thirst, dry mucous membranes etc.
- What is the extent of the disease? – e.g. known metastases to brain, bone, liver etc.
- Are they taking any medication and has there been any recent change?
- Are they currently receiving radiotherapy? (Especially to brain, liver, GI Tract)
- Do they have any abdominal pain? Is this a new symptom?

**Differential diagnosis includes:**
- Medication related e.g. SACT
- Gastric stasis
- Hypercalcaemia
- CNS disease
- Gastro intestinal infection
- Disease related

Grade 1 (Green)
Able to eat and drink with a reasonable intake

- Review prescribed antiemetic medication make sure dose / route and frequency are appropriate and assess patient compliance and understanding
- Fully investigate cause:
  - Disease related e.g. brain or liver metastases, electrolyte imbalance, and obstruction.
  - Medication related e.g.SACT, opiates etc.
- When cause has been clearly identified, change antiemetic in line with local policy directions
- Advise self help measures:
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

Grade 2 (Amber)
Able to eat and drink but intake is significantly reduced

- Admit for further assessment and management.
- IV fluids and electrolyte replacement as appropriate
- Fully investigate cause:
  - Disease related e.g. brain or liver metastases, electrolyte imbalance, and obstruction.
  - Medication related e.g.SACT, opiates etc.
- Prescribe antiemetic as appropriate to cause in line with local policy
- Consider alternative route of administration of antiemetic’s e.g. syringe driver especially if associated with vomiting

Grade 3 - 4 (Red)
Inadequate or no oral caloric and/or fluid intake

- Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 12. (2-page guideline)  
**Suspected Neutropenic Sepsis**  
**IMMEDIATE assessment**  
(Photocopy of image not provided)

**Clinical suspicion of infection and potential for neutrophils <0.5x10^9 L** (NICE)  
(Patients who have received or receiving SACT or have a history of myelosuppression or known bone marrow failure have the potential for neutropenia)

**Initial assessment:**  
- Identify patients with clinical suspicion of infection and potential for neutrophils <0.5x10^9 L (received or receiving SACT or history of myelosuppression or known bone marrow failure)  
- Patients may appear well initially but if untreated can rapidly progress to septic shock + death. Early diagnosis will normally prevent death.

**START TREATMENT AT POINT OF SUSPICION**

**Immediately: Take bloods and administer 1st IV antibiotics** (DON'T wait for FBC result)

*Door to needle time for first antibiotics should be less than one hour.*

- **Urgent:** FBC, U&Es, LFT's include albumin, Coagulation screen, G+S, Ca^2+, PO_4^-, Mg^2+, Urate, CRP, and Lactate peripheral and central line blood cultures  
- **Observations:** Calculate NEWS score. Assess urine output  
- **Commence:** NEWS chart – patients can deteriorate rapidly and should be monitored closely. Monitor urine output

**Clinical assessment:**  
- Full history (consider current or recent SACT) + examination  
- Assess urine output  
- Urine, sputum + stool cultures  
- Consider: throat swab, central line swab, wound swab and CXR

**Signs of SEVERE sepsis - YES**

- Altered mental state or  
- Hypoxia (O_2 sat < 94%) or  
- Shock (Systolic BP < 90 mmHg)  
- Cold/clammy/ Hyper/hypothermic; Tachycardic; Short of breath

**Resuscitation Management:**

- Resuscitation room or outreach team  
- Optimise haemodynamics & O_2 delivery  
- ENSURE that 1st line intra-venous antibiotics have been administered  
- Transfer to HDU/ICU

**Further management guidance: proceed to page 20**

**Early signs of SIGNIFICANT sepsis - YES**

- Temp > 38°C or < 36°C or  
- HR > 90 and/or RR > 20 or  
- Generally unwell. Infective symptoms; Shivering/rigors; Diarrhoea  
- Raised lactate

**Commence Neutropenic sepsis management:**

- ENSURE that 1st line antibiotics have been administered, **DO NOT DELAY** for lab confirmation  
- Supplemental O_2  
- 1L 0.9% sodium chloride over 1-2 hours  
- Differentiate between sepsis and neutropenic sepsis  
- Supportive measures  
- **Admit to appropriate area**

**Identify:** Potential sources of infection  
Rx: Presenting complaint/co-morbidity  
Tx: ECG, ABGs, Urinalysis, and Swabs  
Do not perform a CXR unless clinically indicated

**1st line IV antibiotics in neutropenic sepsis as per NICE guideline:**

- Beta lactam monotherapy with piperacillin with tazobactam as initial empiric antibiotic therapy for patients with suspected neutropenic sepsis if there are no patient-specific or local microbiological contraindications.  
- Patients with penicillin allergy should be discussed with the on call microbiologist  
- Avoid aminoglycoside therapy in patients who have received platinum based chemotherapy in the last week  
- Consider adding vancomycin /teicoplanin if CVAD is the suspected focus of infection


Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible. Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.  
**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
**Guideline 12 continued. Suspected Neutropenic Sepsis**

- Subsequent treatment should occur in an environment where appropriate skills and expertise are available.
- The patient should be closely monitored and the patient’s risk of septic complications frequently reassessed using a validated risk scoring system (NICE 2012).
- If the patient continues to deteriorate despite initial treatment their condition should be discussed urgently with a senior clinician.

<table>
<thead>
<tr>
<th>DAY ONE – Day of Admission</th>
<th>Monitoring</th>
<th>DAY TWO</th>
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</thead>
<tbody>
<tr>
<td>National Early Warning Score Chart (NEWS)</td>
<td>NEWS Chart x 6 daily (every 4 hours)</td>
<td>Daily FBC and U&amp;E blood tests.</td>
</tr>
<tr>
<td>Every 15 minutes initially then regular monitoring according to patients condition.</td>
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**Chemotherapy drugs**

Discontinue on admission; ensure safe disposal of unused chemotherapy

**Antimicrobials**

**1st line antibiotics in neutropenic sepsis as per NICE guideline:** Offer beta lactam monotherapy with piperacillin with tazobactam as initial empiric antibiotic therapy to patients with suspected neutropenic sepsis who need intravenous treatment unless there are patient-specific or local microbiological contraindications.

- Do not offer an aminoglycoside, either as monotherapy or in dual therapy, for the initial empiric treatment of suspected neutropenic sepsis unless there are patient-specific or local microbiological indications.
- Blood culture from central lines and peripherally, sputum, urine, swabs-throat & skin lesions.
- Liaise with microbiology prior to altering regimen.
- **Do not** remove CVADs as part of initial empiric management of suspected neutropenic sepsis.
- **NB.** CVADs may need to be removed in cases of severe sepsis, if unsure seek senior clinical support.
- Aggressive fluid replacement in dehydration.
- Hourly urine output measurement. Replace Na⁺ and K⁺ judiciously.
- Early critical care management if deterioration, severe sepsis (any evidence of organ failure) or suspected invasive fungal infection.

**Improving?**

Assess if all antibiotics still required and route of administration. Discontinue empiric antibiotic therapy in patients whose neutropenic sepsis has responded to treatment, irrespective of neutrophil count.

**Unresponsive fever 48 hours?**

Do not switch initial empiric antibiotics in patients with unresponsive fever unless there is clinical deterioration or a microbiological indication. Continue inpatient therapy in all patients who have unresponsive fever unless an alternative cause of fever is likely.

**Additional antimicrobials: Therapeutic monitoring/dose adjustment - Liaise with Pharmacy & Microbiology.**

- Consider viral and fungal infections, liaise with microbiology.

**Cultures**

Liaise with microbiology re interim results
Re-culture patient before changing antimicrobials.

**Fluid and Electrolyte Balance**

Monitor fluid intake and output

Assess the patient’s risk of septic complications according to NICE guidelines and MASCC score
Discharge only if:
- Low risk
- Physiologically stable
- When co-morbidity treated
- Neutropenic sepsis advice has been reinforced
- Discussed with a member of the acute oncology team prior to discharge
Skin rash can be a side effect of:

- Systemic Anti Cancer Therapy; Rash can be frequent and sometimes severe with:  
  Targeted- agents: EGFR antagonists, BRAF and MEK inhibitors  
  Immunotherapies  
  Radiotherapy- radiation toxicity  
- Graft versus host disease in a patient who has undergone allogeneic stem cell transplant (Contact haematology team)  
- Illnesses or infection e.g. shingles, chicken pox, impetigo, cellulitis, allergic reaction, meningitis.

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of allogeneic stem cell transplant. These patients may be myelosuppressed / neutropenic and are at risk of neutropenic sepsis and/or thrombocytopenia due to reduced marrow production or marrow infiltration and/or graft versus host disease: If present, this should be managed as per guideline 12 on P.19-20 - immediate antibiotics if sepsis suspected.

Observations: Calculate NEWS score.

Investigations: Urgent FBC, U&Es, LFTs, CRP, blood cultures if signs of systemic sepsis

Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop? Is skin rash a commonly associated and sometimes serious toxicity of their treatment, please see specific DRUG INFORMATION SHEET.
- Have they received immunotherapy proceed to guideline 26 page 35
- Have they received oral targeted agents: EGFR antagonists, BRAF and MEK inhibitors; see guideline 14 page 23
- Have they received radiotherapy recently: see guideline 15 on P.24
- Have they had a stem cell/ bone marrow transplant? If yes contact the haematology team.
- If the patient has received 5FU,Capcitabine see guideline 16 on P.25
- Are they otherwise well? Does the patient have any signs of infection e.g. pain, swelling, pustules, fever, discharge?
- Has the patient recently started any other medication including antibiotics?
- Does the patient have a history of skin complaints?
- Where is the skin rash, what % BSA does it cover and what does it look like?
- Does the rash itch? Itch only, consider liver/kidney problems/ dry skin/ allergy.
- Has the patient been in recent contact with infectious disease e.g. shingles/chicken pox?
- Does the patient have any other SACT toxicity related symptoms; if so please symptom specific guideline

Differential diagnosis includes:

- Side effect of medication
- Allergic reaction
- Infection
- Thrombocytopenia

**Grade 1 (Green)**
- Rash covering <10% BSA, Macular/Papular eruption. Asymptomatic
- Provide appropriate skin care advice and emphasise the importance of skin care regimen (See P 22)
- Treat with emollient creams and antihistamines if required
- Ask patient to contact 24-hour advice line if symptoms worsen or persist

**Grade 2 (Amber)**
- If any of the following are present:
  - Pruritus, burning tightness
  - Rash covering 10-30% BSA
  - Bleeding with trauma
  - Affecting ADL or sleep
- Check all blood results and act on abnormalities
- Discuss with Haematology /Acute Oncology Team prior to discharge
- Treat symptomatically with emollient creams, antihistamines and consider topical or oral steroids. (See P.22)
- IMMUNOTHERAPY see guideline 26 on P.35
- Telephone/review patient within 24 hours ask patient to contact the 24-hour advice line if symptoms worsen/persist.

**Grade 3/4 (Red)**
- If any of the following are present:
  - Pruritic symptoms >30% skin surface
  - Generalised
  - Exfoliative
  - Ulcerative
  - Bullous dermatitis
  - Spontaneous bleeding or signs of associated infection.
- Check all blood results and act on abnormalities
- For unusual, severe or persistent rash, particularly if the patient is unwell-urgent referral to dermatology
- Urgent admission if symptoms suggestive of Steven Johnson Syndrome or Toxic Epidermal Nekrolysis
- Analgesia, fluid balance monitoring and skin care support and advice (see P.22)
- Consider admission for support and assessment.
- Determine cause and treat appropriately, this may include I.V. /oral or topical steroids.
- IMMUNOTHERAPY see guideline 26 on P.35
- Oral targeted agents see guideline 15 on P.24

Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
SKIN RASH

Initial management:
Assessment of fluid balance status, establish IV access if any signs of dehydration or sepsis
Intravenous fluids according to fluid balance status and renal function
Treat any infected lesions as appropriate and adjust antibiotics according to clinical condition, myelosuppression, swab results and local antibiotic guidelines
Delineate and record area affected area - photograph
Check platelet count – rash may be secondary to thrombocytopenia
If ulcers: Topical acyclovir for lips/oral acyclovir for herpes infection in mouth.

On-going management:
Reassess daily (close monitoring of routine observations as at risk of infection)
Observe for development of sepsis, neutropenia, or other chemotherapy toxicities
Fluid balance or daily weights
Daily full blood count
Dermatology review if concerns/uncertainty of diagnosis

Ensure general care measures:
Good fluid intake
Keep area clean and dry
Avoid hot baths/tight clothes
Mild soaps/cleansers/detergents

Consider Prescribing:
Topical creams/lotions (alcohol free, hypoallergenic e.g. E45) – apply regularly to all affected areas
Anti-histamines if rash causes itchiness
Analgesia if painful (caution with paracetamol/aspirin if risk of neutropenic sepsis)
Oral or topical steroids may be required.

Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 14. Skin Toxicities - Targeted therapy-related (Papulopustular rash)

Newer targeted anticancer therapies, particularly EGFR antagonists, BRAF, MEK and MTOR inhibitors, are frequently associated with skin toxicities, which are often seen in particular patterns and at different stages of treatment.

- **Papulopustular ("acneiform") rash:** Predominately affects the scalp, face and upper trunk. Pruritus, irritation and pain may also be present.
- **Xerosis ("dry skin"):** Usually develops gradually and may present with eczema and/or fissuring.
- **Nail changes:** Include paronychia, onycholysis, splinter haemorrhages, and nail fold pyogenic granulomas.
- **Hand-foot skin reaction:** Dyseaesthesia and paraesthesia can progress to localised, tender lesions, which may be bullous and severe. More common in plantar, pressure sites, heels and distal digits. Evolves to hyperkeratosis.
- **Hair abnormalities:** Classically a reversible inflammatory, non-scarring frontal alopecia. Hair growth is slowed and textural changes can occur. Increased hair growth is also seen, particularly of the eyelashes and eyebrows. Hypertrichosis can also involve the face and chest.

### Initial Assessment

**Observations:** Calculate NEWS score.

**Investigations:** FBC, U&E

**NB:** Isotretinoin is not indicated for the treatment of papulopustular rash.

#### Grade 1 (Green)
- Papules and/or pustules covering <10% BSA ± pruritus or tenderness
- Topical acne treatment (e.g. 1% Clindamycin lotion or gel)

#### Grade 2 (Amber)
- Papules and/or pustules covering 10-30% BSA ± pruritus or tenderness
- Limiting instrumental ADL
- Associated with psychosocial impact
- Topical emollients e.g. Aveeno, Epaderm, Hydromol
- Oral tetracyclines (e.g. Lymecycline, Doxycycline)
- Antihistamines for itch if required (Hydroxyzine)

#### Grade 3 (Red)
- Papules and/or pustules covering >30% BSA ± pruritus or tenderness
- Limiting self-care ADL
- Associated with local superinfection
- Consider delaying treatment
- As for grades 1 and 2
- If local superinfection: Oral antibiotics are indicated
- If extensive superinfection: IV antibiotics are indicated

#### Grade 4 (Red)
- Papules and/or pustules covering any BSA ± pruritus or tenderness and are associated with extensive superinfection
- Life-threatening
- Consider delaying treatment
- As for grades 1 and 2
- If local superinfection: Oral antibiotics are indicated
- If extensive superinfection: IV antibiotics are indicated

### General management and advice (and management of other skin toxicity patterns)

- For hand-foot skin reaction, see guideline 16 on palmar-plantar erythrodysesthesia (PPE)
- Patients should be advised on general skin care at the commencement of treatment
- The use of soap substitutes, light emollients, sun cream and alcohol-free lotions should be advised
- Emollient creams are preferred over ointments as they can increase acneiform eruptions, e.g. Aveeno, Epaderm, Hydromol
- Topical or oral steroids may be required
- Avoid tight footwear and damage to the nail and surrounding skin if nail changes are observed
- Trichomegaly of the eyelashes can cause discomfort and trichiasis, which should prompt referral to an Ophthalmologist

#### Xerosis
- Eczema
  - Face & Neck: 1% hydrocortisone cream
  - Body: 0.05% clobetasone butyrate cream
  - Treat secondary bacterial superinfection as guided by microbiology swabs
- Fissures
  - Greasy emollients (e.g. Hydromol ointment, 50% propylene glycol under clingfilm or plastic glove occlusion)
  - Fluorouracil impregnated tape or Zinc oxide paste with salicylic acid

#### Nail changes
- Inflammation of nail folds
- Milton sterilising solution for 20 minutes daily
- Topical steroid/antifungal (e.g. 1% hydrocortisone/miconazole cream)
- Purulent paronychia
- Oral antibiotics
- Nail fold pyogenic granuloma
- Curettage and cautery

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
**Guideline 15. Skin Rash - Radiotherapy reactions**

- A skin reaction is a common side effect following radiotherapy treatment to the breast, head and neck, perineum, and skin, but may occur for any treated area.
- Commonly there is mild erythema and pruritus similar to mild sunburn, but the skin may get sore and break down.
- Patients are told to expect this after 10-14 days and can last for 4-6 weeks after completion of treatment.
- This is usually simple to manage but for patients with treatment of the head and neck or perineum, it can be severe, very painful, and impair function.
- Development of skin reactions depends on dose, fractionation, position and size of area treated, concurrent chemotherapy, and patient specific factors such as nutritional status.

**NB. If the patient is receiving or has recently received SACT treatment please see skin rash guideline 13 on P. 21-22**

<table>
<thead>
<tr>
<th>Grade 1 (Green)</th>
<th>Grade 2 (Amber)</th>
<th>Grade 3 (Amber)</th>
<th>Grade 4 (Amber)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faint or dull erythema (RTOG1)</td>
<td>Tender or bright erythema without moist desquamation (RTOG 2a)</td>
<td>Patchy moist desquamation, moist oedema (RTOG 2b)</td>
<td>Confluent moist desquamation. (RTOG 3)</td>
</tr>
</tbody>
</table>

**Head and Neck – E45**
- Skin- E45
- Pelvis- E45
- Breast- E45
- Other- E45

Ask patient to contact the 24-hour advice line if symptoms worsen.

**Skin** - E45

**Pelvis** - E45

**Breast** - E45

**Other** - E45

Analgesia may be required
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

**Head and Neck** – E45

- Skin- Mepilex lite and E45 on surrounding areas
- Pelvis- E45
- Breast- E45
- Other- E45

- Appropriate conformable dressing as below:
  - **Head and Neck** – Mepilex Lite/Border (No Nu-Gel)
  - **Skin** - Mepilex Lite/Border
  - **Pelvis** - Nu-Gel, Sitz Bath and Fan Therapy
  - **Breast** - Mepilex Lite
  - **Other** - Mepilex Lite

- Swab area if signs of infection and prescribe antibiotics as required
- Analgesia for pain – may require opiates
- Telephone/review patient within 24 hours and arrange regular review with the radiotherapy team to assess progress.
- Ask patient to contact the 24-hour advice line if symptoms worsen.

**Breast** - Aquacel, Mepilex Lite/Border

**Other** - Mepilex Lite/Border

- Swab area if signs of infection and prescribe antibiotics as required
- Analgesia for pain – may require opiates
- Telephone/review patient within 24 hours and arrange regular review with the radiotherapy team to assess progress.
- Ask patient to contact the 24-hour advice line if symptoms worsen.

The advice above is for a guide only and each patient should be assessed individually. If unsure about products to use please seek further advice.


Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 16. Skin toxicity - PALMAR - PLANTAR ERYTHRODYSESTHESIA (Hand foot syndrome)
A distinctive localised cutaneous reaction to certain antineoplastic agents. Symptoms include: Tingling or burning, redness, flaking/dryness, swelling, small blisters, sores on palms and/or sole.

**Identify:** Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed according to guidelines.

**Observations:** Calculate NEWS score.

**Investigations:** FBC, U&Es

**Questions:**
- What SACT regimen is the patient on? When was the last dose?
- Is this a continuous intravenous administration? E.g. 5-fluorouracil (5FU)
- Is the patient still taking oral SACT? E.g. capecitabine, sunitinib.
- Is the patient otherwise well? Any other symptoms e.g. diarrhoea/stomatitis (if yes refer to specific management guidelines) and contact the Acute Oncology Team.
- Have they experienced this side effect before on previous treatment cycles?
- Any signs of infection in the affected areas? – Discuss treatment options with the acute oncology team.

**Grade 1 (Green)**
Mild numbness, tingling, swelling of hands and/or feet, with or without pain or redness.

- Reassure the patient that this is recognised treatment related complication and generally nothing to worry about.
- Emphasise the importance of skin care regimen.
- Ask patient to contact 24-hour advice line if symptoms worsen.

**Grade 2 (Amber)**
Painful redness and or swelling of hands and/or feet.

- **Stop** the SACT until discussed with acute oncology or prescribing team.
- Reassure the patient that this is recognised treatment related complication and generally nothing to worry about.
- Emphasise the importance of skin care regimen.
- Consider prescription of high urea based cream.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

**Grade 3 (Amber)**
Moist desquamation, ulceration and severe pain in hands and or feet.

- **Stop** the SACT until discussed with the Acute Oncology Team. If receiving Capecitabine or 5FU consider DPD deficiency.
- Review current analgesia (with caution as may not then develop a temperature in response to infection)
- Emphasise the importance of continuing skin care regimen.
- Consider prescription of high urea based cream.
- Consider specialist dermatology referral.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

**Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.**

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
**Identify:** Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic fever and at risk of sepsis. If present, this should be managed according to guidelines

**Observations:** Calculate NEWS score.

**Investigations:** Urgent FBC, U&Es, CRP, LFTs, Magnesium, Ca²⁺, Glucose, Blood cultures and CRP, Cortisol, (consider the need for pathology investigations in grade 1 presentations on an individual basis and in light of other presenting symptoms or risk factors)

**Questions:**
- Is there a cancer diagnosis/primary disease?
- What is the extent of the disease? – E.g. known metastases to brain, bone, liver etc.
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- How often are they being sick? And are they also feeling nauseous?
- Assess bowel movements, any symptoms that suggest constipation? Any diarrhoea? Bowel obstruction?
- What food and fluids have been taken over last few days?
- Is there any evidence of reflux/gastritis?
- Are there any signs of dehydration e.g. decreased urine output, fever, thirst, dry mucous membranes etc.
- Are there any signs of infection?
- Are they taking any medication e.g. steroids, and has there been any recent change?
- How is the patient fed? Do they have a feeding tube? Is this in the correct position?

**Differential diagnosis includes:**
- Medication related e.g. SACT
- Gastric stasis/ outlet obstruction
- Bowel obstruction
- Hypercalcaemia
- CNS disease
- Endocrinopathy
- Gastro intestinal infection
- Disease related
- Hyper-or-hypoglycaemia


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### Grade 1 (Green)
1-2 episodes in 24 hours

- Review prescribed antiemetic medication make sure dose / route and frequency are appropriate and assess patient compliance and understanding
- Fully investigate cause:
  - **Disease** related e.g. brain or liver metastases, electrolyte imbalance, and obstruction.
  - **Medication** related e.g SACT, opiates etc.
  - When cause is clearly identified, change antiemetic in line with local policy directions
  - Telephone / review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

### Grade 2 (Amber)
3-5 episodes in 24 hours

- Admit for further assessment and management.
- IV fluids and electrolyte replacement as appropriate
- Fully investigate cause:
  - Disease related e.g. brain or liver metastases, electrolyte imbalance, and obstruction.
  - Medication related e.g SACT, opiates etc. If receiving Capecitabine or 5FU consider DPD deficiency

**Initial advice as for grade 1**
- Consider clinical review
- Telephone / review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.
- If symptoms worsen or are associated with other toxicities consider escalation to RED.

### Grade 3 (Red)
6-10 episodes in 24 hours

- Consider alternative route of administration of antiemetic’s e.g. syringe driver
- Consider substitution, discontinuation of oral chemotherapy if appropriate.
- Telephone / review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

### Grade 4 (Red)
>10 episodes in 24 hours

- Admit for further assessment and management.
- IV fluids and electrolyte replacement as appropriate
- Fully investigate cause:
  - Disease related e.g. brain or liver metastases, electrolyte imbalance, and obstruction.
  - Medication related e.g SACT, opiates etc. If receiving Capecitabine or 5FU consider DPD deficiency
- Consider placement of naso-gastric tube and nil by mouth order in suspicion of bowel obstruction
- Prescribe antiemetic as appropriate to cause in line with local policy
- Contact Acute Oncology / Haematology Team who may consider substitution, discontinuation of oral chemotherapy if appropriate.

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Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 18. Endocrinopathies

Adrenal Crisis

Immune-Related Adverse Event (irAE)

Immune checkpoint inhibitors (ICPi) have been causatively associated with a number of endocrinopathies, including hypophysitis, hypopituitarism and adrenal insufficiency. Patients may present with nonspecific symptoms, which may resemble other causes such as brain metastasis or underlying disease.

Endocrine function panel:

TSH, Free T4, free T3, ACTH, LH, FSH & cortisol prolactin, blood glucose +/- testosterone/oestrogen.

(9am cortisol is preferable but random cortisol measurement should be performed if the patient is unwell)

NB Values will be lab assay specific.

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**Severe or Life-threatening (Grade 3 + 4)
Suspect adrenal crisis:**

Hypovolemic shock

Hypotension – SBP <90mm Hg

Postural hypotension – 20mm Hg drop

Dizziness/Collapse

Nausea/Vomiting

Abdominal pain/tenderness/guarding

Fever

Confusion/delirium/coma

Hypotension/hyperkalaemia

hypoglycaemia

Pre-renal failure

Severely unwell patient: severe dehydration, abdominal pain, or shock

Investigations:

- Send endocrine function panel bloods immediately
- Admit patient
- Immediate management with an ABCDE approach
- Immediate bolus injection of 100mg hydrocortisone i.v. or i.m. followed by continuous intravenous infusion of 200mg hydrocortisone per 24h (alternatively 50mg hydrocortisone per i.v. or i.m. injection every 6h)
- Rehydration with rapid intravenous infusion of 1000 mL of isotonic saline infusion within the first hour, followed by further intravenous rehydration as required (usually 4 – 6L in 24h; monitor for fluid overload in case of renal impairment and in elderly patients)
- Urgent Endocrinology referral for urgent review of the patient, advice on further tapering of hydrocortisone, investigation of the underlying cause of disease including diagnosis of primary vs secondary adrenal insufficiency
- Rule out superadded infections
- Withhold the next cycle of ICPi

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**Moderate – Symptomatic (Grade 2)
Suspect endocrinology based on symptoms:**

Tiredness/fatigue, headache, weight loss, susceptibility to infection.

**Investigations:**

- Endocrine function panel if outstanding
- 9am cortisol and ACTH
- MRI brain with pituitary cuts

**Actions**

Consider other causes of symptoms
Continue ICPi

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**Cortisol 100 - 450mmol/L
Investigations**

Repeat cortisol at 9am within 48 hours
Endocrine function panel if outstanding

**Actions**

Monitor regularly (before each cycle as a minimum) and act as per algorithm if serum levels fall
Continue immune checkpoint inhibitors (ICPi)

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**Cortisol <100mmol/L
Investigations**

Endocrine function panel if outstanding

**Treatment**

Commence hydrocortisone 10mg-breakfast
5mg –lunch, 5mg - dinner

**Actions**

Refer to endocrinology for advice/ further investigation
Give emergency advice/card about hydrocortisone
Continue ICPi

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**Instigation**

- If a delay in endocrinology review is anticipated then commence hydrocortisone - 10mg- breakfast, 5mg –lunch, 5mg – dinner. This will ensure patient safety until endocrinology review.
- If the patient is currently on steroids (prednisolone/dexamethasone) then serum cortisol will likely be suppressed – please discuss with the endocrinology team before commencing replacement.
- If thyroid function is also compromised within a hypopituitary picture ensure cortisol is replaced for 24 - 48 hours prior to commencing thyroid replacement (for which the grade 1 hypothyroidism guidelines should be instituted – guideline 20 P.29)

Society for Endocrinology [SIE] guidelines for adrenal crisis:

www.endocrineconnections.com/content/5/5/61


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Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHELD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Endocrine function panel:
TSH, Free T4, free T3, ACTH, LH, FSH & cortisol prolactin, blood glucose +/- testosterone/oestrogen.
(9am cortisol is preferable but random cortisol measurement should be performed if the patient is unwell)
NB Values will be lab assay specific.

Symptoms:
- Vague symptoms:
  - Mild fatigue
  - Anorexia
  - No headache or
  - Asymptomatic
- Moderate symptoms:
  - Headache but no visual disturbance or
  - Fatigue/mood alteration but haemodynamically stable, no electrolyte disturbance.
- Severe mass effect symptoms such as:
  - Severe headache
  - Any visual disturbance or
  - Severe hypoadrenalism i.e.
    - Hypotension
    - Severe electrolyte disturbance

Investigations:
- Complete endocrine function panel
- FBC, U&E, LFT
- MRI pituitary protocol to confirm diagnosis- exclude cerebral metastases
- Consider formal visual field assessment
- NEWS monitoring

Actions:
- Refer to endocrinology
- Replace cortisol and/or thyroxine according to endocrinology guidance. Refer to IrAE management guidance on treatment of hypoadrenalism and thyroid dysfunction for replacement doses and further management – Guideline 18, P.27
- Withhold ICI until symptoms controlled and consider restarting once patient stable

Guideline 19.  Endocrinopathies - Hypophysitis  Immune-Related Adverse Event (irAE)

Clinical presentation
Typically, hypophysitis presents with headache, fatigue and visual loss. There are a range of non-specific symptoms including nausea, diarrhoea, malaise and anorexia, which may represent pituitary dysfunction and a low threshold for clinical suspicion is required. However, these typical symptoms are common in patients with complications of cancer undergoing SACT and other differentials, such as CNS metastases need to be considered.

Symptoms: Resolve or Improve to Mild
See steroid tapering guidance

PERSIST > 48 hours
WORSEN or RELAPSE

Endocrine function panel:
- Complete endocrine function panel
- FBC, U&E, LFT
- MRI pituitary protocol to confirm diagnosis- exclude cerebral metastases
- Consider formal visual field assessment
- NEWS monitoring

Treatment:
- Consider oral prednisolone 0.5-1 mg/kg/day to reduce pituitary oedema, if headaches or neurological problems are present
- Start steroid therapy after sending endocrine function panel

Actions:
- Refer to endocrinology
- Replace cortisol and/or thyroxine according to endocrinology guidance. Refer to IrAE management guidance on treatment of hypoadrenalism and thyroid dysfunction for replacement doses and further management – Guideline 18, P.27
- Withhold ICI until symptoms controlled and consider restarting once patient stable

Investigations:
- Complete endocrine function panel
- FBC, U&E, LFT
- MRI pituitary protocol to confirm diagnosis- exclude cerebral metastases
- Consider formal visual field assessment
- NEWS monitoring

Treatment:
- Consider i.v. Methylprednisolone 1 mg/kg/day to reduce pituitary oedema, if headaches or neurological problems are present
- Start steroid therapy after sending endocrine function panel
- Analgesia for headache

Actions:
- Refer to endocrinology

CAUTION: If thyroid function is also compromised within a hypopituitary picture ensure cortisol is replaced for 24 - 48 hours prior to commencing thyroid replacement (for which hypothyroidism guidelines should be instituted – guideline 20 P.29)

Society for Endocrinology [SfE] guidelines for adrenal crisis:
www.endocrineconnections.com/content/5/5/G1


Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 20. Endocrinopathies - Thyroid Dysfunction

Immune checkpoint inhibitors (ICPI) have been causatively associated with a number of endocrinopathies, including hypo/hyperthyroidism. Observational studies have shown that there is a typical pattern of thyroid specific biochemical disturbance presenting with asymptomatic hyperthyroidism, before return to normal levels for a brief period. This is nearly always followed by the development of, in some cases profound, hypothyroidism that is frequently persistent and requires long-term thyroid replacement. Smaller subsets of patients develop isolated hypothyroidism over a period of weeks. Both groups appear to require long-term replacement in a majority of cases. Thyroiditis and autoimmune Grave’s disease hyperthyroidism can occur as well as primary hypothyroidism.

Endocrine function panel:
TSH, Free T4, free T3, ACTH, LH, FSH & cortisol prolactin, blood glucose +/- testosterone/oestrogen.
(9am cortisol is preferable but random cortisol measurement should be performed if the patient is unwell)
NB Values will be lab assay specific.

Hypothyroidism
TSH of >10 mULN and Free T4 < lower limit of normal (LLN)
NB Values will be lab assay specific.

Symptoms: Fatigue - Weakness - Sensitivity to cold Weight gain or difficulty losing weight - Coarse, dry hair and dry skin - Hair loss - Muscle cramps and aches - Constipation - Depression - Irritability - Memory loss - Abnormal menstrual cycles - Decreased libido - Slowed speech (severe cases) - Jaundice (severe cases) - Increase in tongue size (severe cases)

Investigations:
- Endocrine function panel if outstanding

Treatment:
- Commence Levothyroxine at 75 mcg or 25 mcg for high risk patients
- Consider starting Levothyroxine at 25 micrograms in profoundly hypothyroid patients to avoid palpitations
- Caution with high risk patients - history of/or existing cardiac conditions e.g. Atrial fibrillation and elderly patients

Actions:
- Recheck TFTs and cortisol with next cycle of treatment – note TSH will not fall for 4-6 weeks after starting levothyroxine.
- Discuss with endocrinologist to identify best pathway for long-term management and monitoring (primary/secondary care)
- Refer to endocrinologist if unable to stabilise thyroid function
- Continue ICPI

Hyperthyroidism
TSH <0.40 mULN and Free T4 > upper limit of normal (ULN)
NB Values will be lab assay specific.
(IF TSH low and T4 normal or low need to exclude pituitary dysfunction)

Check TSH receptor antibodies

Symptoms: fatigue or muscle weakness - hand tremors - mood swings - nervousness or anxiety - rapid heartbeat - heart palpitations or irregular heartbeat - skin dryness - trouble sleeping - weight loss - increased frequency of bowel movements - menstrual disturbance

Investigations:
- Endocrine function panel if outstanding

1. Asymptomatic

The majority of cases become hypothyroid within a matter of weeks.

Actions:
- Recheck TFTs and cortisol within 1-2 weeks and every 1-2 weeks thereafter.
- Once hypothyroid - manage as per hypothyroidism

2. Symptomatic

The majority of cases become hypothyroid within a matter of weeks.

If persistent manage in collaboration with an endocrinologist

Added Investigations:
- TSH Receptor Ab, anti-TPO Ab, nuclear medicine thyroid uptake scan

Treatment:
- Consider B-blocker - Propranolol or Atenolol
- Painful thyroiditis - consider prednisolone 0.5mg/kg and taper
- Consider Carbimazole if TSH Receptor Ab positive – seek endocrinology advice

Actions:
- Recheck TFTs and cortisol within 1-2 weeks and every 1-2 weeks thereafter.
- Once hypothyroid - manage as per hypothyroidism
- If unwell withhold ICPI and consider restarting when symptoms controlled

CAUTION: If thyroid function is also compromised within a hypopituitary picture ensure cortisol is replaced for 24 - 48 hours prior to commencing thyroid replacement (for which hypothyroidism guidelines should be instituted – guideline 20 P.29)

Society for Endocrinology [SIE] guidelines for adrenal crisis:
www.endocrineconnections.com/content/5/5/61

ESMO Guidelines -
http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy

Always make sure that the Acute Oncology Team are informed of the patients’ assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Gastrointestinal Immune-Related Adverse Event (irAE)

Gastrointestinal (GI) irAEs are among the most common, if they are left unrecognised or untreated, they can become life threatening. These toxicities can be managed effectively in almost all patients by using established guidelines that stress vigilance and the use of corticosteroids and other immunosuppressive agents when necessary.

As with all irAEs this can be a delayed effect of treatment and can occur up to 12 months after completion of treatment.

**Guideline 21.**

**Management Plan:**

- **Mild (Grade 1)**
  - < 4 stools/day over baseline or mild increase in ostomy output
  - NO history of abdominal pain, mucous/blood in stools

- **Moderate (Grade 2)**
  - If **any** of the following symptoms are present:
    - 4-6 stools/day over baseline or moderate increase in ostomy output
    - Moderate abdominal pain/cramps/discomfort
    - Mucous in stool regardless of number of stools
    - Nocturnal stools
    - Persistent grade 1 symptoms

- **Severe or Life-Threatening (Grade 3 + 4)**
  - If **any** of the following symptoms are present:
    - ≥6 stools/day over baseline or significant increase in ostomy output
    - Severe abdominal pain
    - Fever
    - Dehydration
    - Blood in stool
    - Incontinence
    - Limiting ADLs
    - Episodes within 1 hour of eating

**Investigations:**

- Baseline bloods (FBC, U&E, LFTs, TFTs, cortisol & CRP)
- Stool microscopy and culture
- Clostridium difficile toxin
- Faecal calprotectin (if symptoms persist)
- Polymerase Chain Reaction (PCR) screen
- Abdominal X-Ray and consider CT abdomen/pelvis.

**Symptoms:**

- **PERSIST** (≥25 days) or WORSEN or are associated with deranged U & E’s
- **Assess response to treatment within 72 hours**
- **Persist ≥ 3 days IV corticosteroids**

**Actions:**

- **Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible.**
- Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
- **WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

**Admit patient**

- Baseline bloods (FBC, U&E, LFTs, TFTs, cortisol & CRP)
- Stool microscopy and culture
- Clostridium difficile toxin
- Faecal calprotectin (if symptoms persist)
- Daily bloods (FBC, U&E, LFTs & CRP)
- CT Abdomen/pelvis
- Flexible sigmoidoscopy with biopsies (inc. CMV staining)
- Screen for Infliximab administration suitability on admission to avoid delay if treatment is required (to include-TB Eli spot test, hepatitis screen, HIV, chest X-Ray (if chest CT not already performed)

**Refer and review by gastroenterologist**

- IV hydration and fluid balance
- IV Methylprednisolone 1-2 mg/kg/day + PPI cover
- Antibiotics are not required as standard
- STOP loperamide and codeine
- Use analgesia with CAUTION

**Treatments:**

- Prednisolone 0.5-1 mg/kg/day + PPI cover
- STOP Loperamide and codeine
- Fluid balance and replacement as appropriate (inc. diarolyte sachets)

**Management Plan:**

- Withhold next dose of ICPI
- Daily telephone monitoring
- Gastroenterology advice/review (consider endoscopy).

**Symptoms:**

- **PERSIST** or **WORSEN**
- **See steroid tapering guidance**
- **Relapse**
- **Evaluate**

**Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible.**

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

**Review patient daily, if no improvement within 72 hours, seek further urgent gastroenterology advice/opinion for management with infliximab.**

**http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy**
Guideline 22. Hepatotoxicities

Hepatic transaminases (ALT/AST) and bilirubin must be evaluated before each dose of immunotherapy, as early laboratory changes may indicate emerging immune-related hepatitis. Elevations in LFTs may develop in the absence of clinical symptoms. This guidance should be used in context of baseline LFTs and presence of known liver metastases.

### Mandatory investigations and actions at initial assessment:

- **LFTs**
- **Amylase**
- **AST/ALT**
- **gGT**
- **CK**
- **Clotting (INR)**
- **Lactate/acidosis**
- **Ferritin**
- **EBV/CMV**
- **HSV & parvovirus**
- **Hepatitis PCR screen**
- **Auto immune screen**
- **Hepatitis ABCE screen**
- **gGT**
- **EBV/CMV**
- **Split bilirubin if bilirubin is markedly elevated**
- **CK**
- **Ferritin**
- **Hepatitis ABCE screen**
- **gGT**
- **EBV/CMV**
- **Split bilirubin if bilirubin is markedly elevated**
- **FBC – document cytopenia especially lymphopenia and monocytopenia**
- **Ultra Sound Scan in the first 12- 24 hours to assess spleen size and include doppler to assess flow in hepatic veins and arteries**

**Observations:** Monitor and document Glasgow Coma Scale and NEWS

### Mild (Grade 1)

- **AST or ALT > ULN = 3 x ULN**
- **Continue treatment**
- **Repeat LFT's in 1 week - if rising escalate**

### Moderate (Grade 2)

- **AST or ALT > 3 to ≤5 x ULN**
- **Re-check LFTs and INR every 3 days**
- **Consider imaging for metastases/clot**
- **Consider checking paracetamol levels.**
- **Treatment:** Commence prednisolone 1mg/kg/day (max 60mg OD)

**Actions:**
- Withhold ICI treatment until the adverse reaction resolves to Grade 0-1 or returns to baseline.
- **Medications Review:** STOP regular paracetamol, NSAIDs.
- Concomitant medications can exacerbate liver toxicity in this scenario. Therefore **discontinuation of ALL non-essential medication is advisable on admission.**

### Severe or Life-Threatening (Grade 3/4)

- **AST or ALT >5 x ULN (Grade 4 >20 x ULN)**
- **Admit to hospital**
- **Early/Urgent referral to hepatologist required**

**Investigations:**
- **Daily LFTs / INR /Albumin**
- **Consider checking paracetamol levels.**

**Treatment:**
- **Steroids**
  - **Grade 3**
    - If ALT/AST <400 and normal bilirubin/INR/albumin - **oral** prednisolone 1mg/kg/day.
    - If ALT/AST >400 or raised bilirubin/INR/albumin - **IV** methylprednisolone 2mg/kg/day.
  - **Grade 4** - **IV** methylprednisolone 2mg/kg/day
- **Consider IV N-acetylcysteine (NAC 150mg/Kg as loading dose and 150mg/Kg over 24 hours for patients in grade 3 or 4 toxicity**

**Actions:**
- **Medications Review:** STOP regular paracetamol, NSAIDs.
- **Concomitant medications can exacerbate liver toxicity in this scenario. Therefore **discontinuation of ALL non-essential medication is advisable on admission.**
- **Discuss requirements for CT scan after USS with hepatologist**
- **Discuss requirements for liver biopsy with hepatologist**
- **If Grade 3 withhold next cycle of treatment**
- **If Grade 4 discontinue treatment permanently**

**Biochemical Abnormality PERSISTS (≥3 days), WORSEN or RELAPSE**

**Symptoms: Resolve or Improve to Mild**

See steroid tapering guidance – see guideline 27, P.36

**Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible. Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.**

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

**http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy**
Guideline 23. Neurological Immune-Related Adverse Event (irAE)

Neurologic irAEs can manifest as central abnormalities (e.g., aseptic meningitis, encephalitis) or peripheral sensory/motor neuropathies (e.g., Guillain-Barre Syndrome). Early recognition and treatment of neurologic irAEs is critical to its management. As neurologic symptoms can be common in subjects with cancer, it is important that an evaluation/work-up distinguish between non-drug-related causes (e.g. progression of disease, concomitant medications, infection) and a possible drug-related AE as the management can be quite different.

**Mild (Grade 1)**
- Asymptomatic;
- Loss of deep tendon reflexes or paraesthesia (including tingling);
- Not interfering with function or ADLs not concerning to patient

**Moderate (Grade 2)**
- Sensory alteration or paraesthesia (including tingling);
- Some interference with function
- Cranial nerve problem
- Symptoms concerning to patient

**Severe or Life-Threatening (Grade 3-4)**
- Severe or disabling symptoms;
- Limiting self-care ADLs
- Life-threatening (e.g. respiratory problems)

**Investigations:**
- Neurological examination
- FBC, U&E, ALT, cortisol, TFTs, glucose, B12 and folate, HIV, TSH
- Consider autoimmune and vasculitis screen
- Consider MRI/MRA brain /spine +/- CSF exam to exclude other causes e.g. CVA, brain metastases.
- Alcohol history and medications - opiates
- Special investigations guided by clinical picture of specific disorders
- Consider nerve conduction studies or EMG for lower motor neuron and/or sensory changes
- Consider pulmonary function, sniff, and diaphragmatic function tests

**Management:**
- Delay ICPI
- Daily monitoring for progression
- Consider neurology referral and review
- Treat symptoms per local guidelines
- Consider IV methylprednisolone 0.5-1mg/kg/day methylprednisolone or oral prednisolone 0.5-1mg/kg/day (max 60mg/day) + PPI
- Consider pregabalin or duloxetine for neuropathic pain
- Consider orthotic devices

**Resolved or Improved (Grade 1)**
- Continued with ICPI

**WORSEned**

**PERSIST > 5 days**
- WORSEned or RELAPSE

**Resolved or Improved (Grade 1)**
- Continue with ICPI

**Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible. Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota. WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.**

**Management Plan**
- Under guidance of neurology team
- Management escalation:
  - Consider IVIG or other immunosuppressive therapies
  - Treatment for specific disorders

**http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy**
Guideline 24. Pneumonitis Immune-Related Adverse Event (irAE)
Pulmonary irAEs have been observed following treatment they have occurred both after a single dose and after as many as 48 treatments. The frequency of pulmonary AEs may be greater with immunotherapy combination therapies than with monotherapy and more common in lung cancer than in melanoma. The majority of cases reported were Grade 1 or Grade 2 and presented with either asymptomatic radiographic changes (e.g. focal ground glass opacities, patchy infiltrates) or with symptoms of dyspnoea, cough, or fever. Subjects with reported Grade 3 or Grade 4 pulmonary AEs were noted to have more severe symptoms, more extensive radiographic findings, and hypoxia.

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
<th>Investigations</th>
<th>Treatment</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild (Grade 1)</strong></td>
<td>Clinically asymptomatic with Radiographic changes only (e.g. focal ground glass opacities, patchy infiltrates)</td>
<td>Sputum sample for MC&amp;S and PCP PCR Baseline bloods (FBC, U&amp;Es, LFTs, CRP, calcium) Chest X-ray - baseline for further assessments High resolution CT Scan (HR CT)</td>
<td></td>
<td>Monitor symptoms every 2-3 days and re-image if worsening Consider delay of ICPI</td>
</tr>
<tr>
<td><strong>Moderate (Grade 2)</strong></td>
<td>Mild to moderate new onset of symptoms limiting instrumental ADL (e.g. dyspnoea, cough, fever, chest pain)</td>
<td>Sputum sample for MC&amp;S Baseline bloods (FBC, U&amp;Es, LFTs, calcium, CRP) High resolution CT imaging (HR CT) Bronchoscopy +/- lavage</td>
<td>If no evidence of infection commence Prednisolone 0.5 - 1mg/kg/day (max. 60mg/day prednisolone) + PPI Consider antibiotics (ABX) If evidence of infection Hold ICPI Consider hospital admission Refer to a chest physician Monitor symptoms daily with clinical examination review if symptoms worsening (with repeat imaging)</td>
<td></td>
</tr>
<tr>
<td><strong>Severe/Life-Threatening (Grade 3+4)</strong></td>
<td>Severe new onset of symptoms limiting self-care ADL; or Hypoxia (new or worsening); or Acute Respiratory Distress Syndrome (ARDS)</td>
<td>Sputum sample for MC&amp;S Baseline bloods (FBC, U&amp;Es, LFTs, calcium, CRP) High resolution CT imaging (HR CT) Bronchoscopy if condition allows +/- Pulmonary function test</td>
<td>IV Methylprednisolone 2mg/kg/day + PPI Consider increasing to 4mg/kg/day if clinical improvement is unsatisfactory Consider empiric ABX and antifungal therapy</td>
<td>Discontinue ICPI Monitor symptoms daily with clinical examination, if symptoms worsening, repeat imaging is required Manage symptoms accordingly Consider the use of Infliximab if no improvement at 48 hrs. – discuss with chest physician</td>
</tr>
</tbody>
</table>

**Clinical Assessment & O2 SATS**
- Sputum sample for MC&S and PCP PCR
- Baseline bloods (FBC, U&Es, LFTs, calcium, CRP)
- Chest X-ray - baseline for further assessments
- High resolution CT Scan (HR CT)

**Assess response to treatment within 48 hours**

**Symptoms: Resolve or Improve to Mild**
See steroid tapering guidance – see guideline 27, P.36

**Persist WORSEN or RELAPSE**

**Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible.**
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

**Please see Guideline 27 on P.36 for advice regarding management of patients receiving high dose or long-term steroids**

**Continue with daily review, if no improvement within 72 hours; seek chest physician advice/review for further management**

http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy
Guideline 25. Renal Toxicities Immune-Related Adverse Event (irAE)

Elevated creatinine and biopsy confirmed tubulointerstitial nephritis and allergic nephritis have been infrequently observed following treatment with immunotherapy agents. The frequency of renal AEs may be greater with combination therapies than with monotherapy. Most cases were Grade 2 or Grade 3 and based on creatinine elevation. Patients with a history of RCC or prior nephrectomy do not appear to be at higher risk. Events were managed with corticosteroids and in all cases renal function partially or fully improved.

### Clinical Assessment

**Investigations:**
- Vital signs
- FBC, U&E, ALT, cortisol, TFTs and glucose
- Urinalysis:
  - Protein positive - urine sample protein creatinine ratio
  - Blood positive - urine sample to microbiology for casts
- If blood and protein in urinalysis send for both - protein creatinine ration and casts

**Treatment:**
- If clear urinalysis - institute adequate hydration, withhold nephrotoxins and repeat blood in 24 – 48 hours
- If positive urinalysis commence 1mg/kg/day oral prednisolone + PPI
- Actions:
  - Monitor creatinine every 48 hours
  - Exclude other causes
  - Review concomitant medication and stop nephrotoxic drugs
  - Prompt Referral to renal team for further advice - consider renal biopsy/US
- HOLD ICPI until adverse reaction resolves to Grade 1 or Grade 0 (or returns to baseline)

### Symptoms: Resolve or Improve to Mild

See steroid tapering guidance – see guideline 27, P.36

### Symptoms: Persist (≥ 5 days) or Worsen or Relapse

Review patient daily, if no improvement within 72 hours, seek nephrologist advice for further management

### Symptoms: Resolve or Improve to Mild

See steroid tapering guidance – see guideline 27, P.36

Guideline 26. Skin Toxicities Immune-Related Adverse Event

Dermatological irAEs common and although they are typically mild to moderate in severity, if left unrecognised or untreated, they can become life-threatening. These toxicities can be managed effectively in almost all patients by using established guidelines that stress vigilance and the use of corticosteroids and other immunosuppressive agents when necessary.

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2 (Moderate)</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
</table>
| Skin rash, affecting <10% Body Surface Area (BSA) with or without symptoms | Skin rash affecting 10% - 30% of BSA with or without symptoms | Skin rash affecting >30% of BSA or grade 2 with substantial symptoms | Skin sloughing >30% BSA with associated symptoms:  
- Generalised  
- Exfoliative  
- Ulcerative  
- Bullous dermatitis  
- Purpura |

Clinical Assessment:
- Exclude other causes e.g. virus, medication
- If substantial symptoms present – escalate to Grade 3

Investigations:
- Vital signs
- FBC, U&E, ALT, cortisol, TFTs and glucose
- Photograph rash
- Measure lesions

Treatment:
- Mild to moderate - Prednisolone 0.5 – 1mg/kg/day for 3 days then taper over 1-2 weeks + PPI
- Severe - i.v. Methylprednisolone 0.5 - 1mg/kg/day and convert to oral on response, taper over 2-4 weeks + PPI
- Anti-histamines
- Emollient with paraffin content

Actions:
- Withhold ICPI treatment
- Dermatology review - consider punch biopsy
- Monitor daily
- Consider admission to hospital if clinically indicated.

Symptoms: Resolve or Improve to grade 1-2 See steroid tapering guidance – see guideline 27, P.36

Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible. Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota. WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Symptoms: WORSEN, PERSIST (≥5 days), WORSEN or RELAPSE

Symptoms: Resolve or Improve to grade 1-2 See steroid tapering guidance – see guideline 27, P.36
**Guideline 27. Management of patients receiving high dose or long-term steroids for irAE’s**

Many patients will receive moderate- to high-dose steroid therapy for their immune-related toxicity for several weeks. Length of tapering is usually dictated by the severity of the irAE. Regular monitoring during tapering is strongly advised, as there is an increased risk of irAE recurrence. PPI cover should be maintained during tapering process.

*Steroid tapering should only be considered when symptoms are improving.*

**Suggested oral steroid tapering:**

- Corticosteroid taper over at least 3-6 weeks
- Reduce prednisolone dose by 10mg every 3-7 days (as toxicity allows) until dose is 10mg/day.
- Once steroid dose is 10mg/day, reduce by 5mg every 5-7 days then stop.
- Patients will need regular blood test and symptom monitoring during tapering
- Ambulatory monitoring may be possible with regular telephone review and local blood testing

**Suggested intravenous steroid tapering:**

- Corticosteroid taper over at least 6 weeks
- Continue IV methylprednisolone 2mg/kg/day for a total of 3-5 days then switch to oral e.g. prednisolone max. 60mg/day.
- Methylprednisolone 1mg/kg/day x 3 days, then switch to oral e.g. prednisolone max. 60mg/day.

**Upon discharge:**

- Reduce prednisolone dose by 5 to 10mg every 7 days (as toxicity allows) until dose is 10mg/day.
- Patients will need regular blood test and symptom monitoring during tapering
- Ambulatory monitoring may be possible with regular telephone review and local blood testing

**CAUTION** - during and after the tapering process as the adrenal axis may be suppressed and there is a risk of iatrogenic hypoadrenalism– if symptoms occur follow adrenal crisis guidance – guideline 18 on P.27.

**Insomnia:**

This is the most common steroid-related side effect. Sleep hygiene counseling is important. Patients may require short-term use of 1st line treatment for insomnia e.g. zopiclone.

**Hyperglycaemia:**

A baseline HbA1c should be requested at steroid initiation and random afternoon blood sugar monitoring (BM) should be undertaken whilst on treatment. If new hyperglycemia is detected, Endocrinology advice should be sought (many patients will require short term insulin in this setting). Pre-existing diabetes may require escalation in oral hypoglycemic agents or insulin.

**Osteoporosis:**

Vitamin D and calcium levels should be taken at baseline and if low, replaced as appropriate. In patients on steroids for >3 months, or with pre-existing osteoporosis, a bisphosphonate should be considered e.g. weekly alendronic acid.

**Infection:**

In patients receiving the equivalent of prednisolone 25mg for ≥ 6 weeks we suggest PJC prophylaxis with co-trimoxazole (80/400mg Mon/Wed/Fri).

Prophylactic antifungals i.e. Fluconazole and monitoring of patients oropharynx.

If patients are on other immuno-modulatory agents e.g. Mycophenylate mofetil, consideration may be given to CMV prophylaxis with valgancyclovir, especially if CMV IgG negative and lymphopenic.
Guideline 28. ABDOMINAL ASCITES (Management Pathway)

Ascites is the accumulation of protein rich fluid in the peritoneal cavity and can be classed as an exudate or transudate. Ascites typically develops in the setting of recurrent and/or advanced cancer, the commonest sites being ovarian, breast and colo-rectal.

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed /neutropenic and at risk sepsis. If present, this should be managed according to guidelines.

Observations: Calculate NEWS score.

Investigations: FBC, U&E, LFT, Clotting screen; CXR, AXR, Abdominal USS

Signs and symptoms: abdominal pain and distension; dyspnoea; bulging flanks with dullness to percussion; nausea; vomiting; increased fatigue; dyspnoea; decreasing appetite.

Grade 1 (Green)
Asymptomatic; clinical or diagnostic observations only; intervention not indicated.

Grade 2 (Amber)
Symptomatic; medical intervention indicated

Grade 3 (Red)
Severe symptoms; invasive intervention indicated
Grade 4 (Red)
Life threatening consequences; urgent operative intervention indicated

• Check all blood results and act on abnormalities e.g. neutropenia or pancytopenia
• Arrange for elective admission for insertion of ascitic drain under USS control in accordance with local guidelines/practice
• Discuss with Acute Oncology team
• Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist

• Check all blood results and act on abnormalities e.g. neutropenia or pancytopenia
• Admit as an emergency and arrange for urgent drainage of ascites under USS control
• Plan further management in accordance with trust local guidelines depending upon differential diagnosis
• Discuss with the Acute Oncology team.

Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 29. CARCINOMATOUS LYMPHANGITIS (Management Pathway)
Carcinomatous lymphangitis refers to a diffuse infiltration and obstruction of the pulmonary parenchymal lymphatic channels. It is associated with many malignancies but 80% are adenocarcinomas, predominantly breast, but also lung, colon and stomach.

Clinical presentation:
Clinically patients present with:
• Increasing breathlessness
• May also have a progressive dry cough or haemoptysis.

Radiation pneumonitis/treatment related pulmonary fibrosis should be considered as can cause similar symptoms.

Diagnosis is based on clinical suspicion in a patient with metastatic cancer and appropriate symptoms. Chest X-rays can appear normal in 30-50% of cases, but characteristic changes include:
• Bronchovascular markings with irregular outlines
• Reticular-nodular shadowing
• Bilateral lower lobe changes

Other more general changes include:
• Hilar and mediastinal lymphadenopathy
• Pleural effusions.

High resolution CT Scanning is the investigation of choice if CXRs are equivocal or the clinical picture is not obvious.

Treatment:

• Corticosteroids (such as dexamethasone 4mg bd, with appropriate PPI cover and not be taken later than 2pm to avoid insomnia) may be beneficial to aid in the management of the associated dyspnoea.

• Discussion with the patient’s oncology team is warranted as to whether there are any systemic oncological treatments available, as treating the malignancy itself is the only long-term option.

• Unfortunately the prognosis of patients who develop carcinomatous lymphangitis is poor, with less than 50% surviving 3 months.

Consider urgent referral to the palliative care team for symptom management and advice.

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 30. CENTRAL VENOUS ACCESS DEVICES (CVAD) PROBLEM MANAGEMENT
RISKS AND COMPLICATIONS.

There are several risks and complications related to the insertion and maintenance of CVADs. These are briefly discussed below. If you have any concerns relating to any of the following problems please refer to your Local Management Guidelines or contact your Acute Oncology Team.

**Removal of the line is not always necessary; please seek appropriate advice from your Acute Oncology Team or the 24 hour oncology on call rota before removing a line.**

### Infection

**Localized infection:** Tunnel infections can occur in skin tunnelled CVADs, around the insertion site of PICCs or in the port pocket. These areas should be examined prior to access and/or daily by HCP or self-monitoring for any signs of redness, swelling or discharge, pain or tenderness at the exit site. (Absence of discharge does not rule out local infection because if a patient is neutropenic, pus may not be produced). If neutrophils are in normal range and the patient is well and apyrexial, localized infection can be treated with oral or intravenous antibiotics according to the clinical condition of the patient at that time. Lack of response to antibiotics should be acted upon quickly so that infection does not progress further.

**Luminal infection:** Often presents as pyrexia/shivers/rigor following catheter flushing. If untreated this can progress to sepsis. If a CVAD infection is suspected the patient should be admitted to hospital for blood cultures and intravenous antibiotics. This is a serious complication of CVADs and can be life threatening if the patient has recently received chemotherapy and is neutropenic.

*Any heath professional caring for a patient with a CVAD must be able to recognize the signs and symptoms of sepsis. First dose of antibiotics for patients with neutropenic sepsis should be delivered as per national directives within 1 hour of arrival to hospital to injection time.*

*Seek advice regarding line removal from the AO Team or Oncology on call rota.*

### Thrombosis

Thrombosis is the formation of a clot within a blood vessel. Signs and symptoms of thrombosis secondary to CVAD insertion include; pain in the arm, shoulder or chest, swelling, auxiliary blood vessel formation. Thrombosis should be managed according to locally agreed guidelines.

### Phlebitis

This is the inflammation of the intima of the vein and it can be mechanical or infective in origin. Mechanical phlebitis is most common in PICCs and can occur within 72 hours to a week of CVAD insertion. Signs and symptoms include pain, erythema, warmth, and a venous cord may be palpable. Mechanical phlebitis can be treated effectively with application of heat pads every 4-6 hours for 20 minutes at a time. Patients should also be offered analgesia as required. CVADs should not be removed without seeking appropriate advice from the AOS Team.

### Haematoma

This results from uncontrolled bleeding around the site of insertion. It is a hard and painful swelling with infiltrated blood. Hirudoid cream can be used to soothe and relieve bruising and haematoma: 5-15cm of cream applied over affected area up to 4 times daily and gently massaged into the skin. Firstly check if the patient is taking any anticoagulant therapy or aspirin. Also check platelet count and clotting.

### Catheter Migration

Although secured in place, the catheter tip can migrate from its desired position just above the right atrium. This can be due to the patient being very active, or the catheter not being secured properly or in the case of skin tunnelled catheters poor granulation may result in the Dacron cuff slipping. The sign is that the length of the catheter outside the body gets longer. It is important to always check the length before any manipulation of the catheter. If the Dacron cuff is visible or the length of the PICC is greater outside the body, chest x-ray will be required to confirm the position of the catheter tip. Symptoms of catheter migration can include pain in the neck and a rushing sound in the ear during flushing. Management will depend on tip position but may require removal of device.
Guideline 30 continued. CENTRAL VENOUS ACCESS DEVICES (CVAD) PROBLEM MANAGEMENT RISKS AND COMPLICATIONS.

Air Embolus
This is a very rare complication. Methods to reduce the risk of air embolus should be used when inserting, accessing or removing a CVAD. Only health professionals trained and competent to do so should be inserting, accessing or removing. Local policies should be adhered to. If a patient suddenly becomes acutely short of breathe and distressed, air embolism should be suspected. Check the CVAD for any obvious damage and clamp above if any are apparent. Lay the patient in left lateral Trendelenburg position and call for urgent medical assistance.

Catheter Damage
If it is an open-ended catheter that is split above the clamp, use an atraumatic clamp (or clamps covered in gauze) above the damaged area. Apply an occlusive dressing over the split area. Consider repairing the CVAD if appropriate or it may require removal.

Accidental Removal
Arrangements then need to be made for replacement of the CVAD. Inspect the catheter to ensure that it is intact if in doubt then X-ray confirmation is required.

Unable to aspirate blood
Patency of CVADs should be established prior to administration of any drug or solution (RCN 2010). This is to ensure that any risk of extravasation is minimized. Occlusion can be termed complete, partial or withdrawal occlusion.

Complete occlusion can be due to a clot or drug precipitation within the line or a fibrin sheath completely enveloping the device. It results in an inability to either withdraw blood or infuse liquids.

Partial occlusion can be due to a small blood clot within the catheter or an external obstruction, for example a twist or a kink in the catheter. It results in difficulty withdrawing blood.

Withdrawal occlusion can result from a fibrin tail or malposition of the tip of the catheter and results with inability to withdraw blood but fluids can be administered with ease.

Fibrin sheaths can form as quickly as 24 hours following insertion, fluids can be administered but aspiration of blood is impossible as the fibrin acts as a valve (Amesur 2007).

Consider cathetergram when diagnosing the reason for catheter blockage.

Unblocking Central Venous Catheters
Thrombolytics such as urokinase are used to re-establish patency of CVADs obstructed with intraluminal or extra luminal thrombus or fibrin sheath. This agent breaks down fibrin. Thrombolytics should be prescribed by the medical staff and administered by staff that have been trained to do so, only after other reasons for catheter obstruction have been ruled out.

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 31. Cerebral/or CNS oedema and/or cerebral space occupying lesion. (Management Pathway)

Cerebral space occupying lesion – may be primary disease site or metastatic deposits.

Acute cerebral /other CNS oedema – may be disease related e.g. developing around an intrinsic lesion within the brain tissue e.g. a tumour or an abscess or treatment related in the patient who is receiving radiotherapy

**Identify:** Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of bone marrow transplant. These patients may be myelosuppressed/ neutropenic and at risk of sepsis. If present, this should be managed according to guidelines.

**Observations:** Calculate NEWS score.

**Investigations:** Urgent FBC, U&E, CT scan of head (If CT negative and strong suspicion of brain lesion, due to clinical presentation, consider MRI brain).

**Full Clinical / neurological assessment:** Signs and symptoms may include new onset of seizures, headache, visual disturbance, nausea and/or vomiting, cognitive dysfunction, confusion, disorientation and/or memory loss, motor dysfunction, symptoms of stroke.

**Questions:**
- Cancer diagnosis/primary disease/ known metastatic disease
- Currently receiving or have recently completed SACT treatment
- Currently receiving or have recently completed radiotherapy treatment
- Are the presenting symptoms new
- Are there any co-existing conditions such as epilepsy, hypertension or medication that may account for the patients’ symptoms?

**NOTE:** If there is no history of previous malignancy please see MUO/CUP guideline 38 on P49

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**Grade 1 (Green)**

- Fully functional status (i.e. able to work) with minor neurologic findings, no medication needed
- Patients should be discussed with either the Acute Oncology Team or on call oncologist as they may require specialist review and management planning prior to discharge.
- Advise to contact the 24 hour advice line if symptoms worsen or persist

**Grade 2 (Amber)**

- Neurologic findings present are sufficient to require home care, nursing assistance may be required. Medications including steroids/anti-seizure agents may be required.
- Commence dexamethasone
  - 8-16mg oral OD (IV if required) with PPI cover
  - Anti-epileptic medication if having convulsions.
  - Admit for monitoring and care.
- Patients should be discharged until the Acute Oncology Team has reviewed them.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist

**Grade 3 (Red)**

- Neurologic findings requiring hospitalisation for initial management
- Dexamethasone 16mg oral OD (IV if required) with PPI cover
- Anti-epileptic medication if having convulsions.
- Admit for monitoring, on going assessment and management in accordance with local trust guidelines.
- Early critical care management/advice if deterioration.
- **Note:** need for caution in patients with no previous known malignancy and lymphoma suspected steroids might cause rapid resolution of the tumour, which may make histological diagnosis very difficult. If possible, steroids should be avoided before biopsy if lymphoma suspected. This should also be considered in patients presenting with MSCC

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**Referral to the Acute Oncology Team is recommended for all patients, immediate advice is available from the Acute Oncology on call rota.**

Patients with no known malignancy will require neurosurgical referral

Patients with known primary disease presenting with metastatic disease require referral to the Brain and CNS MDT.

Patients on active anti-cancer treatment will require oncological review prior to further treatment.

Consider palliative care referral in patients with poor performance status, advanced disease, for symptom control advice.
Guideline 32. EXTRAVASATION (Management Pathway)

This is the accidental administration of drugs into the extra vascular tissue instead of into the vein. If the drug extravasated is a vesicant, the damage to the surrounding tissue can be extensive and tissue necrosis can occur.

Extravasation may be linked to peripheral cannulation or a Central Venous Access Device (CVAD).

**SUSPECT PERIPHERAL EXTRAVASATION IF:**

a) Patient complains of burning or stinging pain at or around cannula site
b) There is evidence of swelling, induration, and leakage at site
c) There is resistance on plunger of syringe or absence of free flow of infusion
d) There is no blood return (if found in isolation via a peripheral cannula this should not be regarded as an indication of a non-patent vein).

**Action:**

- If extravasation occurs during peripheral administration of SACT; Act immediately according to your local extravasation guidelines.
- If a patient presents as an emergency following previous peripheral administration of SACT; Act immediately - Extravasation of a vesicant drug should be treated as an emergency. If it is discovered the local Acute Oncology Team should be contacted, if out of hours use the Acute Oncology on call rota contact. The local extravasation policy should be followed, and recommended antidotes should be administered appropriately.

Although administration of drugs via CVADs carry less risk of extravasation than peripheral administration, if it does occur the damage is likely to be larger and more severe than with peripheral administration. This is because the event is not likely to be noticed immediately and delays to the treatment of extravasation result in damage limitation rather than cure.

**SUSPECT CVAD EXTRAVASATION IF:**

**Signs and symptoms include:**

- The patient complains of pain around the insertion, along the tunnel or over the port area
- There is evidence of redness and swelling around the insertion, along the tunnel or over the port area
- There is visible leaking of the drug via the skin tunnel or around the exit site.

*Extravasation of a vesicant drug should be treated as a medical emergency.*

If it is discovered the local Acute Oncology Team should be contacted, if out of hours use the 24 hour telephone on call contact. The local extravasation policy should be followed, and recommended antidotes should be administered appropriately.

**IMMEDIATE ACTION FOR ALL DRUG CATEGORIES IF CVAD EXTRAVASATION IS SUSPECTED.**

If the patient is receiving an active infusion STOP the infusion immediately

- Leave the central venous catheter in place.
- Attempt to aspirate as much drug as possible with a new syringe.
- For ports, aspirate then remove needle
- Inform a senior member of the Acute Oncology Team
- Organise X-ray of line or cathetergram

For vesicant extravasations or large volumes of irritant drugs refer to plastic surgeon as soon as possible after detection.
Guideline 33. HYPERCALCAEMIA OF MALIGNANCY  (Management Pathway)
Definition: A disorder characterized by laboratory test results that indicate an elevation in the concentration of calcium (corrected for albumin) in blood. Corrected calcium $>3.4$ mmol/L requires URGENT treatment.

Questions:
- Is there a cancer diagnosis/primary disease?
- Are they taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Have they previously suffered from hypercalcaemia?
- Are they taking any other medication? (Stop any calcium supplements).

Investigations:
- ECG - look for shortened QT interval or other conduction abnormalities
- Bloods - Calcium adjusted for albumin, Phosphate, PTH, Vitamin D, Urea and electrolytes

Examination:
- Assess for symptoms of hypercalcaemia and duration
- Fluid balance status

Signs /symptoms:
- Polyuria and thirst
- Anorexia
- Nausea/Vomiting
- Constipation
- Abdominal pain
- Fatigue / Lethargy
- Mood disturbance
- Cognitive dysfunction
- Confusion
- Seizures
- Renal impairment
- Pancreatitis
- Peptic ulceration
- Muscle weakness
- Band keratopathy
- Hypertension
- Cardiomyopathy
- Shortened QT interval
- Dysrhythmias
- Coma

Grade 1 (Green)
Corrected serum calcium of $>ULN - 2.9$ mmol/l (ULN = upper limit of normal)
Check FBC, ESR, U&E, LFT, TFT, PTH, cortisol, vitamin D & myeloma screen, start IVI & seek advice from endocrinologist – consider new cancer. Review need for any drugs, which may affect renal blood, e.g. NSAIDs, diuretics, ACEIs, ARBs

Grade 2 (Amber)
Corrected serum calcium $>2.9 - 3.0$ mmol/l
Often asymptomatic and does not usually require urgent correction

Grade 3 (Red)
Corrected serum calcium $>3.0 - 3.4$ mmol/l
May be well tolerated if risen slowly, but may be symptomatic and prompt treatment is usually indicated.

Grade 4 (Red)
Corrected serum calcium $>3.4$ mmol/l
Requires urgent correction due to the risk of dysrhythmia and coma.

Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

http://www.endocrineconnections.com/content/5/5/G9.full
Guideline 34. **HYPOMAGNESAEMIA** (Management Pathway)

A disorder characterised by laboratory test results that indicate a low concentration of magnesium in the blood. Many cancer drugs can lead to hypomagnesaemia for example cisplatin, carboplatin, liposomal doxorubicin, cabozantanib, cetuximab, and panitumumab. Other drugs commonly used in cancer patients, e.g. diuretics, gentamicin and other aminoglycoside antibiotics, can cause or contribute to low magnesium. Patients with severe treatment related diarrhoea are also at risk. Normal magnesium range = 0.70 – 0.99 mmol/L (Values will be lab assay specific)

**Hypomagnesaemia** is often detected on blood tests when the patient is being assessed for other reasons therefore most patients are asymptomatic as the levels are only mildly depressed (> 0.50mmol/L). When serum magnesium levels drop more significantly (< 0.50mmol/L) most patients have non-specific symptoms but they may then go on to develop:
- Cardiac or muscle related symptoms such as weakness, cramping, tachycardia / palpitations.
- Neurological complaints can be that of vertigo, ataxia, depression, and in severe cases seizures or altered mental state.

**Investigation:** ECG and consider continuous cardiac monitoring. Check potassium levels.

**Note:** review antiemetics and PPI’s as there may be contraindications in patients with low magnesium

**Examination Findings**

**Neuromuscular Irritability:** Hyperactive deep tendon reflexes; muscular fibrillation; +ve Trousseau (facial nerve hypersensitivity) & Chvostek (metacarpal hyper flexion) signs; dysarthria or dysphagia secondary to oesophageal dysmotility.

**CNS Hyper sensitivity:** Irritability and combativeness; disorientation; psychosis; ataxia, vertigo, nystagmus & seizures

**Cardiac findings (ECG):** Paroxysmal atrial and ventricular dysrhythmias; repolarisation alternans

**Grade 1 (Green)**

< LLN - 0.5 mmol/L

- These patients are typically asymptomatic.
- Consider oral Magnesium replacement to avoid a fall to critical levels: Magnaspartate, Mag Glycerophosphate (discuss with pharmacy).
- Encourage Mg rich diet e.g. spinach, pumpkin seeds, avocado, almonds, figs, swiss chard.

**Grade 2 (Amber)**

< 0.4- 0.5 mmol/L

- Consider oral Magnesium replacement to avoid a fall to critical levels: Magnaspartate, Mag Glycerophosphate (discuss with pharmacy).
- Check bloods in 24- 48 hours.
- Correct any other electrolyte imbalance as necessary.
- Encourage Mg rich diet e.g. spinach, pumpkin seeds, avocado, almonds. figs, swiss chard.

**Grade 3 (Red)**

< 0.3 – 0.4 mmol/L

- Admit for administration of Magnesium Sulfate by intravenous infusion.
- Correct any other electrolyte imbalance as necessary
- Consider continuous cardiac monitoring
- Encourage Mg rich diet e.g. spinach, pumpkin seeds, avocado, almonds. figs, swiss chard.

**Grade 4 (Red)**

< 0.3 mmol/L

- Life threatening consequences
- Admit for administration of Magnesium Sulfate by intravenous infusion.
- In severe cases such as cardiac arrhythmias Magnesium Sulfate can be given as a bolus but under HDU / ITU supervision.
- Consider continuous cardiac monitoring

[https://bnf.nice.org.uk/drug/magnesium-sulfate.html#indicationsAndDoses](https://bnf.nice.org.uk/drug/magnesium-sulfate.html#indicationsAndDoses)

Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 35. (2 page guideline) **Hyponatraemia Management Pathway**

**Hyponatraemia** can be defined as serum sodium <135 mmol/L. The clinical significance of hyponatraemia depends on its severity, its speed of onset and its underlying cause. Severe hyponatraemia can be life threatening.

### Initial Assessment

**Observations:** Calculate NEWS score. Fluid balance.

**Investigations:** FBC, U&E. Serum Osmality, Glucose, Cortisol, Thyroid Function, LFT. Urine osmolality and Na+

**Symptoms:**

1. **Severe**
   - Vomiting
   - Cardiorespiratory arrest
   - Seizures
   - Reduced consciousness
   - Coma - GCS<8

2. **Moderately severe**
   - Nausea without vomiting
   - Confusion
   - Headache

3. **Mild or absent symptoms**
   - • Vomiting
   - • Nausea without vomiting
   - • Cardiorespiratory arrest
   - • Seizures
   - • Reduced consciousness
   - • Coma - GCS<8

The clinical significance of hyponatraemia depends on its:

- Severity
- Speed of onset
- Underlying cause
- Range and degree disease and of co-morbidities.

Management decisions should be based on presenting clinical symptoms rather than the degree of hyponatraemia.

N.B. Severe symptoms are unlikely with serum sodium >130 mmol/L and alternative causes of neurological dysfunction should be considered in this context.

The decision to treat with hypertonic fluid and supervision of treatment should be the responsibility of a senior clinician with appropriate training and skill.

The aim is to achieve a 5mmol/l rise in serum Na+ within the first hour, reducing immediate danger from cerebral oedema while minimising the risk of over-rapid correction and osmotic demyelination.

### STEP 1. Patients with severe symptoms require immediate management, irrespective of cause

- **Within 1st Hour**
  - IV infusion 150 mls of 3% hypertonic saline or equivalent
  - Over 20 mins in close monitoring environment
- **Check Na+**
  - IV infusion 150 mls of 3% hypertonic saline or equivalent
  - Over 20 mins whilst waiting result
- **Repeat twice or until 5mmol/l increase in Na+**

Follow up management after 5mmol/l rise in Na+
- Stop infusion hypertonic saline
- Keep IV line open with minimal volume 0.9% saline
- Start diagnosis - specific management
- Limit increase in Na+ to 10mmol in first 24h
- Limit increase Na+ to additional 8mmol/l every 24h thereafter until Na+ 130mmol/l
- Check Na+ 6h, 12h and daily until stable

### STEP 2 recommended approach if no improvement following 5mmol/l rise in Na+ in the first hour

- IV infusion 150 mls of 3% hypertonic saline or equivalent
  - Over 20 mins in close monitoring environment
  - Aim additional 1mmol/l increase in Na+
- **Indications for stopping infusion**
  - Symptom improvement
  - Na+ increases >10mmol/l in total or 130mmol/l (which ever is first)
- Explore other causes of symptoms and refer to endocrinology for further advice and guidance.

### Differential diagnosis of hyponatraemia following emergency treatment

Measurement of urine osmolality and urine Na+ concentration is central to defining the aetiology of hyponatraemia. Please see following page (P46) for further guidance.

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible. Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

http://www.endocrineconnections.com/content/5/5/G4/F3.expansion.html
Guideline 35 continued. **Hyponatraemia**  
Differential diagnosis  
Hyponatraemia can be defined as serum sodium <135 mmol/L. The clinical significance of hyponatraemia depends on its severity, its speed of onset and its underlying cause. Severe hyponatraemia can be life threatening.

**Differential diagnosis of hyponatraemia following emergency treatment**

- **Hyponatraemia**
  - **Urine osmolality**
    - <100 mOsm/kg
      - **Primary polydipsia**, inappropriate *iv.* fluid intake
      - Low solute intake
    - >100 mOsm/kg
      - **Urine Na+**
        - <30 mmol/l
          - Heart failure
          - Portal hypertension
          - Nephrotic syndrome
          - Hypoalbuminaemia
          - Third space loss
          - GI loss
          - Previous diuretic use
        - >30 mmol/l
          - SIADH
          - AVP-like drugs
          - NSAID
          - Salt wasting
          - Vomiting
          - Hypoadrenalism
          - Cerebral salt wasting
      - *Taking diuretics or ACEI*
      - Consider all other causes

Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

**WITHHOLD!** SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 36. MALIGNANT PERICARDIAL EFFUSION (Management Pathway)

An accumulation of fluid within the pericardial sac leading to an effusion can be a presenting symptom in acute oncology patients. Two thirds of cancer patients have subclinical pericardial effusions with no overt cardiovascular signs or symptoms. 50% of cases initially present with symptoms of cardiac tamponade. Symptoms are often attributed to underlying cancers and are often a pre-terminal event; however, prompt diagnosis and management can achieve significant palliation.

Causes

Most malignant pericardial effusions result from direct malignant involvement with the pericardium. Other, rarer causes of effusions in cancer patients include radiation-induced pericarditis or chemotherapy-induced pericarditis associated with agents such as doxorubicin or cyclophosphamide.

Clinical Findings

- Dyspnoea (majority), fatigue, or asthenia may be the initial symptoms.

Other common symptoms include:
- Cough
- Chest pain
- Orthopnoea

On examination, findings include:
- Elevated JVP
- Tachycardia
- Hypotension
- Pulsus paradoxus (an abnormally large decrease in pulse and systolic blood pressure (>20mmHg) with inspiration)
- Kussmaul's sign (increased distension of jugular veins with inspiration)

Diagnosis:

- Chest X-ray may show a widened cardiac shadow
- Echocardiography shows the size of the effusion and haemodynamic consequence
- ECG to investigate small ECG complexes

Questions:

- Cancer diagnosis/primary disease
- Cardinal questions related to breathlessness

Differential diagnosis would include chest infection, pulmonary embolism (PE), disease progression (i.e. consolidation / pleural effusion); ascending aortic aneurysm (due to indwelling intravascular catheter)

Grade 1 (Green)
Small effusion with no haemodynamic consequence

- Enquire regarding signs of sepsis/productive cough - escalate to Grade 3 Red as appropriate
- Discuss with the Acute Oncology team prior to discharge for ambulatory management.
- Early referral to cardiology for management advice
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen

Grade 2 (Amber)
Moderate effusion with no or minimal haemodynamic consequence and good left ventricular function

- Admit patient for on-going assessment, monitoring and symptom management
- Withhold anticoagulation
- Consider immediate therapeutic drainage if cardio-vascular compromise.
- Treatment is best managed with urgent referral to cardiology or cardiothoracic surgical teams – contact SpR on call.
- Inform Acute Oncology Team
- All treatment options should be balanced against the patient’s symptoms, overall performance status, level of disease and predicted benefits.

Grade 3 (Red)
Effusion with haemodynamic consequence

Grade 4 (Red)
Cardiac tamponade - life-threatening consequences; urgent intervention required

Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 37. MALIGNANT PLEURAL EFFUSION (Management Pathway)

Contact the respiratory team and inform the acute oncology team

Proven malignant pleural effusion

- NO
  - Observe unless drain advised for other reasons

Symptomatic?

- YES
  - Long life expectancy and limited systemic disease
    - NO
      - Systemic therapy likely to lead to rapid resolution
        - NO
          - Follow local pathway for insertion of intercostal tube and drainage.
        - YES
          - Urgent oncology referral for possible SACT
    - YES
      - Consider referral to thoracic surgeons for thoracoscopic drainage / pleuradesis / PleurX or other indwelling catheter

- NO
  - Systemic therapy likely to lead to rapid resolution

NOTE: There may be an ambulatory service available locally for the management of stable patients requiring drainage of pleural effusion – contact the respiratory or acute oncology team for advice.

Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible. Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota. WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 38. Malignancy of Unknown Origin (MUO) Cancer of Unknown Primary (CUP) (Management Pathway)
The aim of this pathway is to enable early identification of patients that would benefit from anti-cancer treatment and to prevent unnecessary investigations in those patients who are unfit for treatment or do not wish to proceed with treatment.
https://www.nice.org.uk/Guidance/CG104

Initial Assessment
Observations: Calculate NEWS score.
History: Full history including rate of change of symptoms. Assess and record current performance status and co-morbidities.
Assess/establish patients understanding and wishes with regards to investigation and treatment pathway.
Examination: Complete clinical examination (including a breast, PR, PV, testicular and skin examination)
Laboratory Investigations:
- All patients: FBC, U&E, LFT, Creatinine, Calcium, LDH, CRP.
- Men with midline disease /brain metastases: Serum αFP and βhCG
- Women with pelvic or peritoneal disease: CA125
- Men with bone metastases: PSA
- Patients with liver only disease: αFP
- Consider myeloma screen - for bone lesion seen on scan with no obvious primary – immunoglobulins/electrophoresis, serum free light chains and urine for bence jones protein
- If FBC is abnormal – request blood film which may demonstrate a haematological malignancy such as lymphoma/leukaemia or suggest the possibility of bone marrow metastases
- Urinalysis for blood
- Patients with altered bowel habit: consider CEA

Note: other tumour markers are generally not useful in diagnosis
Imaging:
- CT thorax, abdomen and pelvis is the staging investigation of choice in most circumstances
- Other investigations (including endoscopies) only as indicated by signs and symptoms

Further management:
- Discuss with the Acute Oncology Team
- If clinical, radiological and pathological findings suggest a specific cancer primary refer to relevant MDT (please see guidance below)
- Otherwise refer to unknown primary MDT and/ or Acute Oncology Team (consider local protocol).
- Please ensure patient is informed of results and plan for onward referral – some patients may be managed as outpatients if the appropriate infrastructure is in place
- Early referral to palliative care for advice on symptom management and continuing care should be considered where appropriate

Patterns of disease requiring URGENT specific action:
- Spinal cord compression – urgent admission and referral to acute oncology team and/or spinal cord co-ordinator
- Men with midline disease – urgent referral to oncology (? germ cell)
- Superior Vena Cava Obstruction - urgent referral to lung MDT for consideration of stent
- Suspected lymphoma, myeloma, plasmacytoma – urgent referral to haematology

Patterns of disease requiring specific action:
- Men with bone metastases and elevated PSA – referral to urology MDT
- Women with axillary nodes – referral to breast surgeons/ MDT
- Women with peritoneal disease – referral to gynaecology /MDT, unless histology suggests non gynaecology origin
- Solitary liver lesion – requires referral to hepatobiliary MDT
- Neck nodes – requires referral to head and neck or neck nodes clinic as appropriate locally
- Isolated brain metastasis – requires referral to neurology MDT

Always make sure that the Acute Oncology Team are informed of patients’ assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology on call rota.
Guideline 39. PNEUMONITIS - Radiation or chemotherapy induced (Management Pathway)
Definition: A disorder characterized by inflammation focally or diffusely affecting the lung parenchyma

Signs and symptoms of radiation or chemotherapy induced pneumonitis
Clinical pneumonitis, or inflammation of the lung(s), can often display non-specific signs. These can include:
- Mild hypoxia
- Pleural rub/effusion
- Fine crepitations – widespread if drug induced, localised if following focal radiation
- Low grade fever
- The development of acute or sub acute dyspnoea, which after history and examination does not reveal pneumonia, tumour recurrence, or any other specific aetiology
- In addition to dyspnoea, there may be a new or worsening cough
Clinical radiation pneumonitis may develop in 20% of lung carcinoma patients:
- The median time to onset of symptoms is 3 weeks after radiation therapy (but may be up to 3 months)

Initial Assessment:
- Clinical evaluation, history, physical examination and review of observations
- Chest X-ray
- Calculation of Wells score
- CT (high resolution and CTPA) to exclude cancer progression and pulmonary embolus

Grade 1 (Green)
No new symptoms

Grade 2 (Amber)
Dyspnoea/symptoms on exertion
Mild or moderate symptoms, manageable on an outpatient basis
High dose steroids
- e.g. prednisolone 50mg od.
- With PPI cover
Specialist advice needed for on-going steroid dosing

Grade 3 (Red)
Dyspnoea /symptoms at normal levels of activity
Severe symptoms requiring hospitalisation
- Review by chest physician
Treat with high dose steroids:
- Intravenous – methylprednisolone 1-2mg/kg od with PPI cover
- Oral - prednisolone 50mg od with PPI cover
- Inhaled

Grade 4 (Red)
Dyspnoea/symptoms at rest or requiring ventilatory support
Monitor closely as Urgent intervention may be indicated
(e.g. tracheotomy or intubation)

Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
Guideline 40. SUPERIOR VENA CAVA OBSTRUCTION (SVCO) (Management Pathway)

SVCO is an obstructive emergency that may occur as the result of progression of a malignancy or may be the diagnostic symptom. SVCO is caused by external pressure, thrombus or direct tumour invasion causing obstruction of the superior vena cava and occurs in 3-8% of patients with cancer.

Questions:
- Cancer diagnosis/primary disease
- Cardinal questions related to breathlessness
- Differential diagnosis would include Chest infection, pulmonary embolism (PE), disease progression (i.e. consolidation / pleural effusion); ascending aortic aneurysm (due to indwelling intravascular catheter)

Signs and symptoms:
- Dyspnoea
- Headaches
- Chest pain
- Stridor due to laryngeal oedema
- Dilated anterior chest wall veins
- Swelling of face and neck
- Non-pulsatile JVP
- Confusion
- Coma

Investigations: CTPA to define tumour extent, site of occlusion or stenosis and extent of any thrombus. SVCO can be an incidental finding on CT.

Seek advice from the Acute Oncology and/or the Respiratory team as soon as possible to guide investigations and management.

Grade 1 (Green)
Oedema in head or neck
Vascular distension, cyanosis; plethora

Grade 2 (Amber)
Oedema in head or neck with functional impairment (mild dysphagia, cough, visual disturbances)

Grade 3 (Red)
Mild or moderate cerebral oedema (headache, dizziness) or mild/moderate laryngeal oedema or diminished cardiac reserve (syncope after bending)

Grade 4 (Red)
Significant cerebral oedema (confusion) or significant laryngeal oedema (stridor) or significant haemodynamic compromise

• Enquire regarding signs of sepsis/productive cough - escalate to Grade 3 Red as appropriate
• Consider steroid therapy to manage symptoms of oedema and prevent deterioration
• Enquire if history of underlying chest complaints e.g. asthma, COPD – advise patients around usual management of exacerbations advise to discuss with GP or other associated health professional managing this condition.
• Discuss with the Acute Oncology team – arrange urgent oncology and/or respiratory review
• Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist

• Admit for further assessment and on-going management
• Monitor for evidence of:
  - Desaturation
  - Infection
  - SACT/chemotherapy toxicities
  - Haemodynamic compromise
• Address life threatening symptoms e.g. stridor
• Treatment initially aimed at symptom management
• Commence high dose steroids + PPI – if not contraindicated
• Seek Urgent Advice from the Acute Oncology and/or the Respiratory team to guide investigations and management.

Manage in accordance with trust local guidelines depending upon differential diagnosis and clinical status. Further management may include:
- Stent insertion – performance status
- Chemotherapy – performance status
- Radiotherapy – any contraindications e.g. previous radiotherapy to chest. Inability to lie flat.
- If thrombus is present consider anticoagulation if no contraindications

Inform the Acute Oncology Team of the patients’ assessment and/or admission as soon as possible. Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.
### Glossary

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<tr>
<td><strong>anti-TPO Ab</strong></td>
<td><strong>Antithyroid Peroxidase Antibody</strong></td>
<td><strong>Anti-Xa l</strong></td>
<td><strong>Anti–factor Xa assay</strong></td>
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<td><strong>APTT</strong></td>
<td><strong>Activated Partial Thromboplastin Time</strong></td>
<td><strong>ARDS</strong></td>
<td><strong>Acute Respiratory Distress Syndrome</strong></td>
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<tr>
<td><strong>AST</strong></td>
<td><strong>Aspartate aminotransferase</strong></td>
<td><strong>BRAF</strong></td>
<td><strong>BRAF is a human gene that encodes a protein called B-Raf.</strong></td>
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<td><strong>BSA</strong></td>
<td><strong>Body surface area</strong></td>
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<td><strong>CEA</strong></td>
<td><strong>Carcinoembryonic antigen</strong></td>
<td><strong>CDT screen</strong></td>
<td><strong>Connective Tissue Disease</strong></td>
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<td><strong>CLL</strong></td>
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<td><strong>Cytomegalovirus</strong></td>
<td><strong>COPD</strong></td>
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<td><strong>C-Reactive Protein Test</strong></td>
<td><strong>C&amp;S</strong></td>
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<td><strong>Computed tomography pulmonary angiography</strong></td>
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<td><strong>Central Venous Access Device</strong></td>
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<td><strong>CXR</strong></td>
<td><strong>Chest X-ray</strong></td>
<td><strong>DIC</strong></td>
<td><strong>Disseminated intravascular coagulation</strong></td>
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<td><strong>DNACPR</strong></td>
<td><strong>Do Not Attempt Cardiopulmonary Resuscitation</strong></td>
<td><strong>DPD deficiency</strong></td>
<td><strong>Dihydropyrimidine dehydrogenase deficiency</strong></td>
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<td><strong>Deep vein thrombosis</strong></td>
<td><strong>EBV</strong></td>
<td><strong>Epstein–Barr virus</strong></td>
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<td><strong>Free Thyroxine 3</strong></td>
<td><strong>FSH</strong></td>
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<td><strong>gGT</strong></td>
<td><strong>Gamma-glutamyl transferase</strong></td>
<td><strong>GCSF</strong></td>
<td><strong>Granulocyte-colony stimulating factor</strong></td>
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<td><strong>IGF-1</strong></td>
<td><strong>Insulin-like growth factor</strong></td>
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<td><strong>International normalised ratio</strong></td>
<td><strong>irAE</strong></td>
<td><strong>Immune-Related Adverse Event</strong></td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<td>Intensive therapy unit</td>
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<td>JVP</td>
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<td>LDH</td>
<td>Lactate dehydrogenase enzyme</td>
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<td>LH</td>
<td>Luteinizing hormone</td>
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<td>LLN</td>
<td>Lower limit of normal</td>
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<td>LMWH</td>
<td>Low molecular weight heparin</td>
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<tr>
<td>MRA</td>
<td>Metastatic spinal cord compression</td>
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<td>MTOR inhibitors</td>
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<td>Non-steroidal Anti-inflammatatory Drugs</td>
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<td>PE</td>
<td>Pulmonary embolism</td>
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<td>Pneumocystis Jiroveci Pneumonia</td>
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<td>Palmar-plantar erythrodysesthesia</td>
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<td>PPI</td>
<td>Proton pump inhibitor</td>
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<td>PR</td>
<td>Per rectum</td>
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<td>PSA</td>
<td>Prostate-specific antigen</td>
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<td>SACT</td>
<td>Systemic Anti-Cancer Therapy</td>
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<tr>
<td>SALT</td>
<td>Speech and language therapy</td>
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<tr>
<td>SOB</td>
<td>Shortness of breath</td>
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<tr>
<td>SVCO</td>
<td>Superior vena cava obstruction</td>
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<tr>
<td>TKI</td>
<td>Tyrosine kinase inhibitor</td>
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<td>Thyroid stimulating hormone</td>
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<td>Urea and Electrolytes</td>
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<td>Upper limit of normal</td>
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<td>Venous thromboembolism</td>
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### Project leads:

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<thead>
<tr>
<th>Name</th>
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<tbody>
<tr>
<td>Dr. Ruth Board</td>
<td>Consultant Medical Oncologist and Lead Cancer Clinician</td>
<td>Royal Preston Hospital</td>
</tr>
<tr>
<td>Philippa Jones</td>
<td>Macmillan Acute Oncology Nurse Advisor</td>
<td>Wolverhampton NHS Trust</td>
</tr>
<tr>
<td>Joanne Upton</td>
<td>Chemotherapy Lead Nurse and Skin Cancer Advanced Nurse Practitioner</td>
<td>The Clatterbridge Cancer Centre</td>
</tr>
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</table>

### Development group (alphabetical order)

<table>
<thead>
<tr>
<th>Name</th>
<th>Position and Title</th>
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</thead>
<tbody>
<tr>
<td>Nicky Adams</td>
<td>Macmillan Acute Oncology Nurse Consultant</td>
<td>Walsall Healthcare NHS Trust</td>
</tr>
<tr>
<td>Dr Clare Barlow</td>
<td>Consultant Medical Oncologist</td>
<td>Taunton and Somerset NHS Trust</td>
</tr>
<tr>
<td>Lisa Barrott</td>
<td>Cancer Matron and Acute Oncology Nurse Lead</td>
<td>Royal Sussex County Hospital</td>
</tr>
<tr>
<td>Dr. Tim Cooksley</td>
<td>Acute Physician</td>
<td>Christie Hospital NHS Foundation Trust</td>
</tr>
<tr>
<td>Alison Hodge</td>
<td>Advanced Nurse Practitioner Acute Oncology &amp; CAU</td>
<td>The Royal Marsden NHS Foundation Trust</td>
</tr>
<tr>
<td>Dr. James Larkin</td>
<td>Consultant Oncologist</td>
<td>The Royal Marsden</td>
</tr>
<tr>
<td>Dr. Anna Olsson-Brown</td>
<td>Medical Oncology Registrar</td>
<td>The Clatterbridge Cancer Centre NHS Foundation Trust</td>
</tr>
<tr>
<td>Dr Clare Philiskirk</td>
<td>SpR Acute Internal Medicine</td>
<td>Sandwell and West Birmingham NHS Hospital trust</td>
</tr>
<tr>
<td>Dr Lavinia Spain</td>
<td>Medical Oncology Fellow</td>
<td>The Royal Marsden NHS Foundation Trust</td>
</tr>
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</table>

### Consultation and specialist opinion group (alphabetical order)

<table>
<thead>
<tr>
<th>Name</th>
<th>Position and Title</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Dr. CG Antoniades</td>
<td>Reader &amp; Honorary Consultant Hepatologist</td>
<td>Division of Digestive Diseases, Imperial College London &amp; Liver Intensive Care, King’s College London</td>
</tr>
<tr>
<td>Dr. Craig Barrington</td>
<td>Clinical Oncology Registrar</td>
<td>South West Wales Cancer Centre</td>
</tr>
<tr>
<td>Dr. Oliver Brain</td>
<td>Consultant Gastroenterologist</td>
<td>John Radcliffe Hospital, Oxford</td>
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<tr>
<td>Dr. Juliet Brock</td>
<td>Clinical Oncology Consultant</td>
<td>Sussex Cancer Centre</td>
</tr>
<tr>
<td>Dr. Sarb Clare</td>
<td>Consultant in Acute Medicine</td>
<td>Sandwell and West Birmingham NHS Hospital Trust</td>
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<tr>
<td>Dr. Sinead Clarke</td>
<td>Macmillan GP and CCG Lead.</td>
<td>Cheshire CCG</td>
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<tr>
<td>Dr. Peter Correa</td>
<td>Consultant Clinical Oncologist</td>
<td>University Hospitals Coventry &amp; Warwickshire</td>
</tr>
<tr>
<td>Dr. Pippa Corrie</td>
<td>Consultant and Associate Lecturer in Medical Oncology.</td>
<td>Cambridge University Hospitals NHS Foundation Trust</td>
</tr>
<tr>
<td>Dr. Antonia Creak</td>
<td>Consultant Clinical Oncologist. Clinical lead for CUP and Acute Oncology</td>
<td>Sussex Cancer Centre</td>
</tr>
<tr>
<td>Name</td>
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<td>Organization</td>
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<tr>
<td>Dr D Durai</td>
<td>Consultant Gastroenterologist</td>
<td>University Hospital of Wales</td>
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<tr>
<td>Dr. Jackie Dominey</td>
<td>GP Clinical Lead End of Life</td>
<td>Solihull CCG</td>
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<td>Dr. Ricky Frazer</td>
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<tr>
<td>Dr. Andreas Hiersche</td>
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<td>BSUH</td>
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<tr>
<td>Dr. Claire Higham</td>
<td>Consultant Endocrinologist</td>
<td>Christie Hospital NHS Foundation Trust</td>
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<tr>
<td>Dr. Chris Jenkins</td>
<td>Consultant Haematologist</td>
<td>Aneurin Bevan University Health board</td>
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<tr>
<td>Dr. Andrew Lansdown</td>
<td>Consultant Endocrinologist</td>
<td>Cardiff and Vale University Health Board</td>
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<tr>
<td>Dr. Ashling Lillis</td>
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<tr>
<td>Dr. Anna Lock</td>
<td>Palliative Care Consultant</td>
<td>SWBH</td>
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<tr>
<td>Professor Paul Lorigan</td>
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<tr>
<td>Dr. Ciara Lyons</td>
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<td>Northern Ireland Cancer Centre</td>
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<tr>
<td>Dr. Ernie Marshall</td>
<td>Consultant Oncologist Clinical Director of Chemotherapy</td>
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<td>Dr. Claire Mitchell</td>
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<tr>
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<td>Dr. Tom Newsom-Davis</td>
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<tr>
<td>Dr. Jenny Pascoe</td>
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<td>University Hospitals Birmingham</td>
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<tr>
<td>Dr Mridula Rajwani</td>
<td>Chief Registrar in Ambulatory Medicine</td>
<td>Oxford</td>
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<tr>
<td>Dr Paula Scullin</td>
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<tr>
<td>Dr. Raj Sinha</td>
<td>Speciality Doctor in Medical Oncology</td>
<td>Sussex Cancer Network</td>
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<tr>
<td>Dr Susannah Stanway</td>
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<tr>
<td>Dr. Andrew Stewart</td>
<td>Cons Haematologist</td>
<td>University Hospital of the North Midlands</td>
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<tr>
<td>Dr. Joanna Stokoe</td>
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<td>Sussex Cancer Centre</td>
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<tr>
<td>Dr Natalie Walker</td>
<td>Consultant Physician</td>
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<tr>
<td>Dr Sarah Williams</td>
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<td>University Hospitals Birmingham</td>
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<tr>
<td>Dr. Matthew Winter</td>
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<td>Sheffield</td>
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<td>Dr. Alison Young</td>
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<td>Leeds Teaching Hospital</td>
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<tr>
<td>Dr Nadia Yousaf</td>
<td>Consultant Medical Oncologist (Lung/AOS)</td>
<td>Royal Marsden</td>
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<tr>
<td>Caroline Adcock</td>
<td>Acute Oncology CNS</td>
<td>The Shrewsbury and Telford NHS Hospitals Trust</td>
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<tr>
<td>Melanie Bowling</td>
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<td>Burton Hospital Trust</td>
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<tr>
<td>Sharon Budd</td>
<td>Trauma Nurse</td>
<td>Royal Derby Hospital</td>
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<tr>
<td>Helene Buijs</td>
<td>Macmillan Senior Acute Oncology CNS</td>
<td>Northwick Park Hospital</td>
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<tr>
<td>Amanda Callister</td>
<td>Senior Chemotherapy Nurse</td>
<td>St. James’s Hospital, Leeds</td>
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<tr>
<td>Leigh Collins</td>
<td>Advanced Nurse Practitioner</td>
<td>University Hospital Bristol</td>
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<td>Clare de Marco Masetti</td>
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<td>Bolton Foundation Trust</td>
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<tr>
<td>Liz Gifford</td>
<td>Clinical Nurse Specialist Skin Cancer</td>
<td>University Hospitals Southampton</td>
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<tr>
<td>Val Harris</td>
<td>Melanoma CNS</td>
<td>Velindre Cancer Centre</td>
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<tr>
<td>Caroline Harnett</td>
<td>Lead Acute Oncology and CUP Clinical Nurse Specialist</td>
<td>Torbay and South Devon NHS Foundation Trust</td>
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<td>Jackie Hodgetts</td>
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<td>Rachel Powell</td>
<td>Oncology CNS</td>
<td>Heart of England NHS Foundation Trust</td>
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<td>Rosie Roberts</td>
<td>Chemotherapy Specialist Nurse</td>
<td>Velindre Cancer Centre / Wales Cancer Network</td>
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<td>Caroline Thomas</td>
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<tr>
<td>Jenni Thomas</td>
<td>Acute Oncology/Chemotherapy Sister</td>
<td>Sandwell and West Birmingham Hospitals.</td>
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<tr>
<td>Joan Thomas</td>
<td>Nurse Unit manager</td>
<td>Peninsula Health, Australia</td>
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<td>Sarah Tucker</td>
<td>Acute Oncology Clinical Nurse Specialist</td>
<td>University College Hospital</td>
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<tr>
<td>Emily (Hui- Ying) Wang</td>
<td>Macmillan Acute Oncology and CUP Clinical Nurse Specialist</td>
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<tr>
<td>Tracy Wild</td>
<td>The Pennine Acute Hospitals NHS Trust</td>
<td>Macmillan Acute Oncology Nurse</td>
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<td>Sonja Watson</td>
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<td>Royal Sussex County Hospital</td>
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<tr>
<td>Anita Young</td>
<td>Macmillan AOS CNS</td>
<td>ULHT</td>
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<tr>
<td>Dharmisha Chauhan</td>
<td>Sarcoma, Melanoma and Skin Specialist Pharmacist</td>
<td>The Royal Marsden NHS Foundation Trust</td>
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<tr>
<td>Rhiannon Walters-Davies</td>
<td>Medicines at Home Manager</td>
<td>Velindre Cancer Centre</td>
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</tbody>
</table>
Edna Young  Lay Representative  National Chemotherapy Board
Conor Fitzpatrick  Therapy Radiographer  The Christie Hospital
Raxa Ford  Senior Lead Review Radiographer  BSUH
Alfred So  Medical Student  University of Manchester.

Organisations
Greater Manchester Cancer  GMCA Greater Manchester Combined Authority

Aknowledgements

The UKONS Board and project leads wish to thank:

- The development group of the original set of guidelines V.1
- The Clatterbridge Cancer Centre NHS Foundation Trust and The Royal Marsden NHS Foundation Trust for sharing their original Immune-Related Adverse Event (irAE) management guidelines which have been used to develop guidelines within this document
- The development group, specialist advisors and consultation group members for helping throughout the project.
## Oncology/Haematology Advice Line

### Triage Tool, Version 2 (November 2016)

#### Appendix 1. UKONS 24 Hour Triage Tool – Assessment Poster also available at [http://ukons.org/index.php/reports/P12](http://ukons.org/index.php/reports/P12)

### Toxicity/Symptom

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<td>Chills</td>
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<td>5</td>
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<td>Fatigue</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
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<tr>
<td>Anorexia</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
</tr>
</tbody>
</table>

#### Assessment Poster

- **UKONS 24 Hour Triage Tool**
- Available at [http://ukons.org/index.php/reports/P12](http://ukons.org/index.php/reports/P12)

#### CAUTION

- Please note patients who are receiving or have received IMMUNOTHERAPY may experience treatment-related problems at any time during treatment or up to 12 months afterwards. If you are unsure about the patient’s regimen, be cautious and follow triage symptom assessment.

#### Preventive Measures of breath

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
<th>Score 4</th>
<th>Score 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No change or exchange for normal</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

- **Performance Status**
- Is there a recent change in performance status?

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score 1</th>
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</tr>
</tbody>
</table>

#### Discharge

- How many days has this occurred for?
- How many times in a 24 hour period is there any abdominal pain or distension?
- Is there any blood in the stool or urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score 1</th>
<th>Score 2</th>
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</tbody>
</table>

#### Concrenption

- How long has the patient been pain-free?
- Is there any blood in the stool or urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score 1</th>
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</table>

#### Urology

- Are you passing urine normally? Is there a new problem or is this normal for you?
- Are there any changes in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score 1</th>
<th>Score 2</th>
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</tbody>
</table>

#### Fever

- Does the patient have a fever? Is it a new problem or is this normal for you?
- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

<table>
<thead>
<tr>
<th>Symptom</th>
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#### Infection

- Has the patient taken any antibiotics? Is it a new problem or is this normal for you?
- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

<table>
<thead>
<tr>
<th>Symptom</th>
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#### Nausea

- How many days has this occurred for?
- How many times in a 24 hour period is there any abdominal pain or distension?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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#### Vomiting

- What is the patient’s local status?
- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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<thead>
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#### Oral Cavity

- How many days has this occurred for?
- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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<thead>
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<th>Symptom</th>
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#### Anorexia

- How many days has this occurred for?
- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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#### Pain

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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#### Neurological/Motor

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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<th>Symptom</th>
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#### Confusion/Neurological Disturbance

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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#### Fatigue

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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#### Rash

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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#### Swelling

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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#### Ocular/eye problems

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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<tr>
<th>Symptom</th>
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#### Ocular/eye problems

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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#### Palmar Plantar Erythema

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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#### Exacerbation

- Is there any change in the urine?
- Has the patient taken any medication?
- Are the patient’s output and intake normal?

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</table>
**HOSPITAL NAME / DEPT:**

**UKONS 24 HOUR TRIAGE LOG SHEET**

<table>
<thead>
<tr>
<th>Patient Details</th>
<th>Patient History</th>
<th>Enquiry Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
<td>Diagnosis:</td>
<td>Date:</td>
</tr>
<tr>
<td>Hospital no:</td>
<td>Male ☐ Female ☐</td>
<td>Time:</td>
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<tr>
<td>DOB:</td>
<td>Consultant:</td>
<td>Who is calling?</td>
</tr>
<tr>
<td>Tel no:</td>
<td>Has the caller</td>
<td>Contact no:</td>
</tr>
<tr>
<td></td>
<td>contacted the</td>
<td></td>
</tr>
<tr>
<td></td>
<td>advice line</td>
<td>Drop in ☐ No ☐</td>
</tr>
<tr>
<td></td>
<td>previously</td>
<td></td>
</tr>
</tbody>
</table>

**Reason for call**
*(in patients own words)*

**Is the patient on active treatment?** SACT ☐ Immunotherapy ☐ Radiotherapy ☐ Other ☐ Supportive ☐ No ☐

**State regimen: ___________________________** Are they part of a clinical trial Yes ☐ No ☐

**When did the patient last receive treatment?** 1-7 days ☐ 8-14 days ☐ 15-28 days ☐ Over 4 weeks ☐

**What is the patient’s temperature? [ ] °C (Please note that hypothermia is a significant indicator of sepsis)**

**Has the patient taken any anti-pyretic medication in the previous 4-6 hours?** Yes ☐ No ☐

**Does the patient have a central line?** Yes ☐ No ☐ Infusional pump in situ Yes ☐ No ☐

**CAUTION! Please note patients who are receiving or have received IMMUNOTHERAPY may present with treatment related problems at anytime during treatment or up to 12 months afterwards. If you are unsure about the patient’s regimen, be cautious and follow triage symptom assessment.**

<table>
<thead>
<tr>
<th>Advise</th>
<th>24 hour follow up</th>
<th>Assess</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Significant medical history**

**Current medication**

**Action Taken**

**Attending for assessment, receiving team contacted Yes ☐ No ☐**

**Triage practitioner**

Signature: ___________________________ Print: ___________________________ Designation: ___________________________ Date / /

**Follow Up Action Taken:**

Consultants team contacted Yes ☐ No ☐ Date / /

Signature: ___________________________ Print: ___________________________ Designation: ___________________________ Date / / Time: