



Guidelines for the Management of Chemotherapy and Systemic Anticancer Therapy Induced Toxicities Within Primary Care

**(Adult solid tumour oncology and
Adult haemato-oncology)**

“Quality and safety for every patient every time”

Document Control

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GUIDELINES FOR THE MANAGEMENT OF CHEMOTHERAPY AND SYSTEMIC ANTICANCER THERAPY INDUCED TOXICITIES WITHIN PRIMARY CARE

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GUIDELINES FOR THE MANAGEMENT OF CHEMOTHERAPY AND SYSTEMIC ANTICANCER THERAPY INDUCED TOXICITIES WITHIN PRIMARY CARE

Introduction

Traditional cytotoxic chemotherapy and the newer targeted systemic anticancer therapies **and Immunotherapies** are part of a number of treatment modalities used to manage patients with malignant disease. Although chemotherapy can be administered via a variety of routes, this document focuses on the potential side effects associated with systemic anticancer therapies (**SACT**) administered to adults, primarily via the intravenous, subcutaneous or oral route.

Patients who are receiving chemotherapy/ systemic therapies will have been given specific verbal and written information regarding the side effects associated with their individual treatment regimen. Patients will also have been advised of specific side effects that require urgent investigation / treatment e.g. neutropenia and they will have been provided with written contact details pertaining to their local 24-hour telephone information / advice line.

Best practice is for a letter to be sent to the patients GP within seven working days of the patient's treatment commencing. The letter will outline details of the patients ongoing treatment, including: details of drugs given and doses; supportive medications used; interventions required; response to treatment; details of modifications to the treatment plan including reasons for modification; results of investigations; details of information provided to the patient; follow up and or continuing care arrangements.

Although all patients within the Northern Cancer Alliance are provided with 24- hour contact numbers, it is acknowledged that patients may present to primary care with side effects associated with SACT. This document has been produced as a resource for Health Care Professionals (HCP) working in primary care to assist them in the management of mild to moderate SACT related side effects. Additional information and support is available to HCP's via the patient's Cancer Unit or Cancer Centre.

Effective communication between primary and secondary care is paramount in effectively managing side effects associated with SACT.

Healthcare professionals treating or providing advice on treatment to patients in primary care must ensure they are individually professionally accountable for the advice/ clinical decision they make and must act at all times in accordance with their own Professional Bodies code of practice and have read and understood the disclaimer below.

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Disclaimer

Whilst every care has been taken to ensure accuracy of the information, it is not intended to be a comprehensive guide to using these medicines. References have not been included as it is recognised that many of the recommendations are not based on clinical trial evidence but rather on clinical experience. The Northern Cancer Alliance cannot accept responsibility for any errors or omissions or for any consequences from application of information in this information and make no warranty, expressed or implicit with respect to the contents of guideline. Readers are advised to exercise clinical judgement as it is acknowledged that drug protocols are being continually revised and new side effects treatment strategies developed. For full information on the dosage, administration and possible adverse effects of the drugs listed we recommend that the manufacturer's data sheets (SPC) and patient information leaflets (PILS) be consulted at <http://www.medicines.org.uk/emc/> Please note: some drug doses, combinations or indications described in this document may be outside of the product licence

Immunotherapy

Immunotherapy treatments such as atezolizumab, Ipilimumab, Nivolumab and Pembrolizumab are immune check point inhibitors and are indicated for the treatment of a number of advanced cancers. Administration of these treatments can result in severe and fatal immune-mediated adverse reactions (irAEs) involving the gastrointestinal, endocrine, skin, liver, nervous, lung and other organ systems. Unless an alternate aetiology has been identified, signs and symptoms suggestive of irAEs must be considered inflammatory and Immunotherapy related.

Early diagnosis and appropriate management are essential to minimise life threatening complications and prevent low grade toxicities escalating to high grade toxicity. Systemic high dose corticosteroid with or without additional immunosuppressive therapy may be required for management of severe irAEs.

Please contact the local hospital acute oncology service or the on call oncology consultant for specialist advice regarding management if a patient on immunotherapy presents to primary care.

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ALOPECIA

Temporary alopecia is a frequently encountered side effect associated with chemotherapy and a number of chemotherapeutic agents can cause alopecia including cyclophosphamide, ifosfamide, doxorubicin (adriamycin), epirubicin, taxanes (paclitaxel and docetaxel), and etoposide. The incidence of alopecia increases when these drugs are used in higher doses or in combination with other chemotherapeutic drugs.

All patients who are receiving agents that may cause alopecia are provided with home care information pertaining to hair loss.

Hair usually begins to grow when treatment that induces alopecia is complete. HCP's may consider referral to the patient's haematology / oncology team if hair does not begin to return within 6 months following the completion of treatment.

Scalp cooling may be offered to oncology patients depending on the drugs used and patient preference. It is noted that scalp cooling should not routinely be offered to patients where there is a likelihood of metastatic disease in the cranium.

HAIR COLOUR CHANGES

Patients being treated with tyrosine kinase inhibitors (TKIs) such as pazopanib and sunitinib may experience hair colour changes and depigmentation of the skin and eyes. Patients receiving these treatments should be reassured that these adverse events are harmless and that hair dyes can be used provided they are mild and the scalp is monitored for reactions. Hair discoloration often reverses on discontinuation of treatment.

CONSTIPATION

The key to successfully managing constipation lies in assessment and accurately identifying the underlying cause. HCP's should be mindful of the patient's normal bowel habit and be aware of symptoms that could suggest an intestinal obstruction or spinal cord compression.

Several chemotherapy agents and supportive drugs may be associated with constipation including vinca alkaloids (vincristine, vinblastine and vinorelbine), cisplatin and etoposide. Note patients receiving vinca alkaloids need to be assessed for paralytic ileus which would present with constipation and absence of bowel sounds, ultra sound may be indicated. This is a medical emergency due to the risk of perforation. Antiemetics such as ondansetron, and granisetron, which are given intravenously or orally prior to chemotherapy and following chemotherapy, can also cause constipation.

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All patients who are receiving agents / drugs that may result in constipation are provided with home care information including:-

- Maintaining adequate fluid intake - 2 litres of fluid per day.
- Maintaining a healthy, high fibre diet (unless contraindicated e.g. patients with or at risk of developing bowel obstruction) - approximately five portions of fruit and vegetables and one portion of cereal per day.
- Gentle exercise.

If this information proves to be inadequate, patients are advised to try medications that can be purchased over the counter e.g. Senna. Patients are encouraged to seek medical advice if over the counter medication's fail to resolve the problem within 48 hours. The following pharmacy only medications may be useful (stool stimulants / softening agents): -

- Macrogols (Movicol): 1 to 3 sachets daily in divided doses (Patients with impaired cardiovascular function should not take more than 2 sachets).
- Docusate Sodium – 100mg BD or 10mls at night.

Occasionally constipation can become severe and the patient may require suppositories or an enema. These should only be administered following advice from the patient's oncology / haematology team.

DIARRHOEA

Several chemotherapy agents may be associated with diarrhoea, including 5-fluorouracil (5FU), methotrexate, oral capecitabine and irinotecan* (* See page 6). Diarrhoea can lead to dehydration, metabolic disturbances, infection and malnutrition and can be life threatening. The relative risk of diarrhoea relates to the chemotherapy agent/s being administered, dose, and tumour site and regime e.g. concurrent radiotherapy

All patients who are receiving agents that may result in diarrhoea are provided with home care instructions including

- Maintaining fluid intake - 2 litres of fluid per day.
- Maintaining a healthy, low residue diet.

Note: If a patient presents with symptoms consistent with neutropenic sepsis they should be treated as a medical emergency.

Haematology patients

If this advice proves to be inadequate or diarrhoea persists / is severe, patients are advised to contact their haematology team to exclude infection.

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Solid tumour patients

If a patient experiences diarrhoea they are advised to try medications that can be purchased over the counter e.g.

- Loperamide - 4mg initially and then 2mg after each loose stool (maximum 16mg daily)
- Electrolyte replacement e.g. Dioralyte sachets

Patients are instructed to contact the 24-hour contact number if over the counter medication's fail to resolve the problem within 48 hours.

The following prescription only medication may be useful:

- Codeine Phosphate - 30 mg 4 times a day

N.B. Fluorouracil (5FU) continual intravenous infusions should not be discontinued without discussions with the patient's medical team.

DIARRHOEA associated with Irinotecan

All patients who are receiving irinotecan are provided with supportive medication and home care information should they develop diarrhoea at home.

If diarrhoea commences within 24 hours of chemotherapy being administered it is likely to be a cholinergic reaction. Symptoms of a cholinergic reaction may include

- sweating
- hyper salivation
- visual disturbances
- abdominal cramps
- watery eyes
- hypotension

If a patient develops any of these symptoms within the first 24 hours then they are instructed to contact the 24-hour contact number.

If diarrhoea occurs after 24 hours patients are instructed to follow the information and advice that they have been given by the hospital, i.e.

- Loperamide 4mg after the first loose stool and then 2mg every 2hrs for 12hrs after the last liquid stool
- If diarrhoea persists for more than 24hrs, despite following the Loperamide schedule identified above then the patient and/or HCP must contact the 24-hour contact number.

N.B. Emergency admission is indicated when diarrhoea persists for 48 hours.

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EXTRAVASATION

Extravasation is defined as the misdirection of intravenous medication from the vein into the surrounding tissue. Morbidity from extravasation may range from temporary local pain or inflammation to extensive tissue necrosis with loss of motor and sensory function in the affected extremity. The severity of tissue injury depends on the type of drug, dose, concentration, physiochemical characteristics, site of extravasation and duration of soft tissue exposure.

Extravasations can occur when using any type of intravenous access device e.g. peripheral cannula, central line, and implanted port and signs of a potential extravasation may include

- Redness
- Swelling
- Pain or burning sensation
- Superficial skin loss
- Tissue necrosis

Patients and / or HCP's should contact the 24-hour advice line immediately if an extravasation is suspected as the patient may require immediate medical or plastic surgery review to minimize tissue damage, ulceration and necrosis and damage to underlying structures such as tendons and nerves.

FATIGUE

Cancer-related fatigue can affect over three quarters of patients undergoing chemotherapy. All patients who are receiving chemotherapy are provided with home care information including:

- Gentle exercise
- Energy conservation techniques
- Adequate nutritional intake

HCP's may wish to explore contributing factors that can exacerbate fatigue including:

- Anaemia
- Inadequate nutritional intake
- Disturbed sleep patterns
- Anxiety & depression
- Inadequate social support
- Disease process
- Co-morbidities e.g. dyspnoea, pain, infection

Appropriate investigation and / or referral to the appropriate HCP may minimise the impact of contributing factors on the patient's experience of fatigue.

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MOUTH PROBLEMS (Mucositis / Stomatitis)

The mouth and digestive tract are lined by mucous membranes containing rapidly dividing cells that are more sensitive to the effects of chemotherapy. A patient may therefore present, during or after chemotherapy or radiotherapy with mouth problems. Although these problems may be related to the patient's cancer, they are more often related to their treatment. Several chemotherapy agents may be associated with mouth problems including 5-fluorouracil (5FU), methotrexate, cytarabine, bleomycin, etoposide, mitomycin c, mitoxantrone, doxorubicin (adriamycin), taxanes and vinca alkaloids.

Three to ten days following chemotherapy, patients may experience a sore sensation or inflammation known as mucositis, followed by ulcers. Oral mucositis, which occurs in varying degrees, is recognized as a frequent; dose limiting potential serious complication of chemotherapy and prevention is better than cure. When ulceration develops, treatment is generally of a supportive nature until the cells regenerate, which takes approximately seven to fourteen days. This can cause pain and difficulties in maintaining adequate nutrition however mouth care can reduce these adverse effects. All patients who are receiving chemotherapy are provided with home care information including:

- Maintenance of good oral hygiene rinsing the mouth frequently and effective brushing of the teeth with a soft brush 2–3 times daily.
- Altered taste – sharp, highly flavoured foods or foods of varying temperatures can occasionally reduce this problem.
- Dry mouth - avoid foods that are very hot, cold, spicy or acidic although some people gain relief from sucking fresh or tinned pineapple chunks in their own juice.

The key to successfully managing oral mucositis lies in assessment and accurately identifying and managing the underlying problem. Patients and HCP's should be aware of symptoms that could suggest neutropenic sepsis and manage these patients appropriately.

RED / PAINFUL MOUTH

Patients are advised to inspect their mouth and providing there are no signs of oral candida, ulceration or infection they can try medications that can be purchased over the counter .e.g. Difflam (benzylamine hydrochloride 0.15% w/v).mouthwash for pain relief.

Patients are encouraged to seek medical advice if over the counter medications fail to resolve the problem within 48 hours, as stronger medication may be required.

Note: Patients and HCP's should also be mindful that systemic analgesics could mask signs of febrile neutropenia.

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MOUTH ULCERS

Mouth ulcers can be associated with neutropenia and an urgent full blood count should be acquired, especially for patients with a haematological malignancy. For those patients who experience problems with mouth ulcers then the following medication may be useful:

- Chlorhexidine gluconate 0.2% w/v mouthwash (Corsodyl) – rinse mouth with 10 ml for about 1 minute twice daily. Leave an interval of at least 30 minutes between using mouthwash and toothpaste.
- Benzylamine hydrochloride 0.15% w/v mouthwash (Difflam) - rinse or gargle, using 15 ml (diluted with water if stinging occurs) every 1½–3 hours as required, usually for not more than 7 days.
- Sucralfate suspension 1g/5ml - 1g (5ml), three times a day.
- Aciclovir 400mg five times daily should be considered if there is a clinical suspicion of herpes simplex infection. (Usually for 5 days or longer if healing is incomplete)

Topical pain relieving agents may be useful:

- Carmellose gelatine paste (Gelclair) – 1 sachet mixed with 40ml of water, 3 times a day.
- Carmellose Sodium (Orabase) – apply a thin layer of the protective paste when necessary after meals.

DRY MOUTH

Dry mouth (xerostomia) may be caused by drugs with antimuscarinic (anticholinergic) side-effects (e.g. antispasmodics, tricyclic antidepressants, and some antipsychotics), by irradiation of the head and neck region or by damage to or disease of the salivary glands. Patients with a persistently dry mouth may develop a burning or scalded sensation and have poor oral hygiene. A dry mouth has been cited as the third most intense and distressing side effect of chemotherapy.

All patients who are receiving chemotherapy are provided with home care information including frequent sips of cool drinks, sucking pieces of ice, eating fresh fruits, fruit sweets, or sugar free chewing gum. The following prescription only medication may be useful:

- Artificial saliva products e.g. Glandosane spray onto oral and pharyngeal mucosa as required
- Pilocarpine - 5 mg 3 times daily (with or immediately after meals) has been found to reduce oral dryness and increase salivary flow in patients receiving head and neck radiotherapy.

Note: Emergency admission is indicated if a patient is unable to maintain oral intake of food and liquid

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ORAL CANDIDIASIS

If oral candidosis (thrush) is present the following prescription only medication may be useful:

- Nystatin suspension – 100,000 units (1ml) every 6 hours. The suspension should be kept in contact with the affected areas as long as possible.
- Fluconazole - 50mgs daily for 7 days (occasionally a higher dose may be required e.g. 100mg twice daily for 14 days).

Potentially immunocompromised patients may need systemic treatments such as intravenous fluconazole or other antifungal agents.

Admit the patient to hospital if there is widespread and invasive infection (such as oesophageal candidiasis, characterized by difficulty or pain on swallowing, and retrosternal pain), or there is evidence of invasive candidiasis or systemic illness (candidaemia).

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NAUSEA & VOMITING

In the 1990's nausea and or vomiting was often cited by patients as the most distressing side effect of chemotherapy but this has improved with the advent of 5-HT₃ antagonists (in combination with corticosteroids) and NK-1 receptor antagonists. Uncontrolled nausea and vomiting can however lead to delays in therapy and dose reduction both of which can have negative impacts on tumour response rates.

Although some cytotoxic drugs may cause severe and often delayed nausea and vomiting, not all cytotoxic drugs are emetogenic. All patients who are receiving potentially emetogenic chemotherapy regimes are given intravenous antiemetic prior to the administration of their chemotherapy and supplied with a discharge script containing oral antiemetic. The key to successfully managing this problem lies in accurately assessing the patients nausea and vomiting, being aware of symptoms that could suggest an alternative cause for the patient's nausea and vomiting and modify their treatment accordingly. HCP's should also check that patients are taking their discharge medications as prescribed.

Northern Cancer Alliance Network Chemotherapy Group has produced an Antiemetic policy, of which a summary is provided below. The full policy is available at

<http://www.necn.nhs.uk/wp-content/uploads/2018/03/NESCN-Antiemetic-Guidelines-for-CINV-v2.5-March-18.pdf>

Note. HCP's should be mindful of the patient's hydration and if patients are dehydrated or unable to maintain adequate fluid intake (2 litres / day) then emergency admission is indicated.

Minimal risk emetogenic chemotherapy (<10%)

Some chemotherapy drugs do not usually cause nausea and vomiting in the majority of patients for example Vinca-alkaloids, bleomycin, fludarabine and oral etoposide; therefore no antiemetics are routinely required

Low emetogenic chemotherapy (10 – 30%)

some chemotherapy causes mild emesis for example fluorouracil (5fu), methotrexate, temozolamide, topotecan etoposide (iv), mitoxantrone and taxanes.

Moderately emetogenic chemotherapy (30 – 90%)

some chemotherapy drugs are moderately emetogenic, including irinotecan, cyclophosphamide, ifosfamide, carboplatin, oxaliplatin and doxorubicin (adriamycin).

Highly emetogenic chemotherapy (>90%)

chemotherapy agents that can cause severe emesis include cisplatin, cyclophosphamide (at high doses) and dacarbazine.

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Summary – Standard Anti emetic Cover (NESCNC Guidance March 18)

Chemotherapy Induced Nausea and Vomiting (CINV) Anti-emetic Guidelines

Summary – Standard Antiemetic Cover

Minimal Emetic Risk: 2-Chlorodeoxyadenosine, bevacizumab, bleomycin, busulfan, cetuximab, fludarabine, rituximab, vinblastine, vincristine, vinorelbine			
No antiemetic should be administered routinely before or after chemotherapy. However, normally supply metoclopramide as a rescue measure with first cycle			
Low Emetic Risk: fluorouracil, bortezomib, cabazitaxel, cytarabine <1000 mg/m ² , docetaxel, doxorubicin HCL liposome injection, etoposide, gemcitabine, methotrexate, mitomycin, mitoxantrone, paclitaxel, panitumumab, pemetrexed, temsirolimus, topotecan, trastuzumab			
	Agent	Dose on day of Chemotherapy	Dose(s) on Subsequent Days
Corticosteroid	Dexamethasone	8mg oral or IV	No standard medication required. However, normally supply metoclopramide as a rescue measure with first cycle
Moderate Emetic Risk: azacitidine, alemtuzumab, bendamustine, carboplatin <AUC ₄ , clofarabine, cyclophosphamide<1500 mg/m ² , cytarabine>1000 mg/m ² , daunorubicin, doxorubicin, epirubicin, idarubicin, ifosfamide, irinotecan, oxaliplatin			
5-HT ₃ Receptor Antagonist	Ondansetron	8mg oral twice daily OR 8mg IV**	Ondansetron 8mg oral Twice Daily for 2 to 3 days Metoclopramide 10mg oral Twice Daily (for patients under 60kg) OR Three Times Daily (patients over 60kg) for 3 to 5 days when required
	Palonosetron	0.5mg oral OR 0.25mg IV	Metoclopramide 10mg oral Twice Daily (for patients under 60kg) OR Three Times Daily (patients over 60kg) for 3 to 5 days when required
Corticosteroid	Dexamethasone	8mg oral or IV	4mg to 8mg oral for 2 to 3 days
High Emetic Risk: carboplatin ≥ AUC ₄ *, carmustine, cisplatin, cyclophosphamide>1500 mg/m ² , dacarbazine, dactinomycin, streptozocin, and combined anthracycline and cyclophosphamide regimens: All patients should be offered a three-drug combination of an NK1 receptor antagonist, a 5-HT ₃ receptor antagonist, and dexamethasone. The NK1 antagonist and 5-HT ₃ receptor antagonist may be given as a combination product			
	Agent	Dose on day of Chemotherapy	Dose(s) on Subsequent Days
NK1 Antagonist	Aprepitant	125mg oral	80mg oral; days 2 and 3
	Fosaprepitant	150mg IV	Day 1 only
5-HT ₃ Receptor Antagonist	Ondansetron	8mg oral twice daily OR 8mg IV**	Ondansetron 8mg oral Twice Daily for 2 to 3 days Metoclopramide 10mg oral Twice Daily (for patients under 60kg) OR Three Times Daily (patients over 60kg) for 3 to 5 days when required
	Palonosetron	0.5mg oral OR 0.25mg IV	Metoclopramide 10mg oral Twice Daily (for patients under 60kg) OR Three Times Daily (patients over 60kg) for 3 to 5 days when required
Combined NK ₁ antagonist and 5-HT ₃ receptor antagonist	Netupitant-palonosetron	300mg netupitant / 0.5mg palonosetron oral	Metoclopramide 10mg oral Twice Daily (for patients under 60kg) OR Three Times Daily (patients over 60kg) for 3 to 5 days when required
Corticosteroid	Dexamethasone	8 mg oral or IV (can increase to 12mg if needed)	4mg to 8mg oral for 2 to 3 days
*3 drug combination for carbo >AUC₄ if not adequately controlled with 2 drug regimen/ patient risk factors			
**Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.			

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REFRACTORY NAUSEA AND VOMITING

Although patients who are receiving agents that cause mild, moderate or severe emesis will routinely receive discharge medication with supporting advice, if nausea or vomiting persists, despite the patient taking their prescribed antiemetics, then the patient should be considered to have refractory Nausea and Vomiting

In this circumstance it is important to exclude other causes of nausea and vomiting many of which will / can commonly present in cancer patients:

- Constipation
- Bowel Obstruction
- Anxiety
- Metabolic Abnormalities (eg Renal Failure)
- Hyper-calcaemia
- Peptic Ulcer Disease
- Radiotherapy
- Raised Intra Cranial Pressure

Treatment

An additional anti-emetic should be added from a different therapeutic class. If necessary medication should be given rectally or parenterally to regain control.

If any medication was previously being given on a 'when required' basis this should be switched to a regular dosing schedule.

The use of multiple drugs may be necessary, and scheduling of treatment to avoid troughs of drug levels may be necessary.

Closely monitor hydration and electrolytes and correct any abnormalities if they present.

The following prescription only medication may be useful:

- Cyclizine – as 50 mg either orally or intramuscular injection (IM) up to 3 times daily.

Note: HCP's should contact the patient's oncology team for advice if nausea and vomiting persists.

ANTICIPATORY EMESIS

Although HCP's should contact the patient's oncology team for advice regarding anticipatory emesis, the following prescription only medication may be useful and should be given up 24 hours before, or on the morning of, the patient's anticipated treatment day.

- Lorazepam – 1 to 2mg twice daily

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BONE MARROW SUPPRESSION

Neutropenia is defined by the neutrophil count, not the total white cell count. Platelet count can also drop, though thrombocytopenia is less common than neutropenia. A fall in the red blood cell count would not be seen for 6 to 8 weeks after administration, HCP's should be aware that an anaemia (low red blood count) induced by chemotherapy will require a blood transfusion and is not appropriate to treat with iron supplementation. It is essential to perform a full blood count (FBC) before administering chemotherapy. A low neutrophil count is often the limiting factor with regard to patients being able to receive their chemotherapy on time. The levels at which treatments are delayed may vary from regimen to regimen and even from prescriber to prescriber. In general treatment does not proceed if the values are less than shown below:

Example of commonly used blood count limits

Platelets	100 x 10 ⁹ cells/L
White Cell Count	3 x 10 ⁹ cells/L
Absolute Neutrophil Count*	1.5 x 10 ⁹ cells/L

Note: Patients must be warned that if they develop a febrile illness or are feeling unwell with symptoms of infection, they require immediately, a full blood count and neutrophil count checked either by their GP, Hospital Emergency Care ward or chemotherapy unit.

NEUTROPENIC SEPSIS

Neutropenic sepsis is one of the most serious and life-threatening complications associated with systemic chemotherapy. If neutropenic sepsis is suspected then the patient should be treated as an acute medical emergency requiring immediate referral to the patient's haematology / oncology team.

THROMBOCYTOPENIA

Most chemotherapy agents can induce thrombocytopenia. A low platelet count can result in bleeding from the nose, gums, urinary tract, gastrointestinal tract and into the skin (petechiae).

All patients who are receiving agents that may induce thrombocytopenia are provided with home care instructions including the need to:

- Avoid intramuscular or subcutaneous injections.
- Avoid medications that can interfere with platelet function e.g. Aspirin, Ibuprofen and other NSAID's.
- Contact the 24-hour contact number if they develop signs of thrombocytopenia and / or bleeding.

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BLADDER / URINARY TOXICITY

Two chemotherapy agents, cyclophosphamide and ifosfamide can irritate the bladder and ureter leading to haemorrhagic cystitis. In patients who are receiving ifosfamide and high dose cyclophosphamide, the risk is minimised by routinely administering intravenous (or oral) Mesna and hydration.

All patients who are receiving agents that may induce haemorrhagic cystitis are provided with home care information including:

- Maintaining adequate fluid intake - 2 litres of fluid per day.
- Monitoring urine output (volume, appearance and unusual sensations).
- Contact the 24-hour contact number if they develop haematuria, pain or discomfort on micturition or reduced urine output.

CARDIOMYOPATHY AND ARRHYTHMIAS

Several chemotherapy agents can cause cardiotoxicity. The most commonly used cardiotoxic agents are the anthracyclines, e.g. doxorubicin, epirubicin and paclitaxel. The monoclonal antibodies Trastuzumab (Herceptin) and bevacizumab (Avastin) capecitabine and 5-fluorouracil, the latter is often given as a continuous infusion can also be cardiotoxic.

The relative risk of cardiotoxicity increases:

- In individuals with associated risk factors
- With escalating doses
- Previous exposure to cardiotoxic agents
- Previous chemotherapy in childhood

Capecitabine and 5-fluorouracil have been known to cause angina due to coronary artery spasm. Should this occur the treatment must be stopped and the patient referred urgently to the acute Trust

All patients who are receiving potentially cardiotoxic agents will have been assessed by their haematologist / oncologist and appropriate cardiac assessment and monitoring instigated if clinically indicated.

Cardiomyopathy has four clinical presentations:

- Acute toxicity presents as transient cardiac arrhythmias or pericardial effusion within days of receiving the drug and this is very uncommon.
- Sub-acute cardiac toxicity is also uncommon, appearing up to 30 months after the drug is used resulting in increasing tachycardia and fatigue and eventually signs of heart failure with low cardiac output.

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- Chronic cardiac toxicity can occur with repeated exposure to a drug. It is related to the cumulative dose of the drug, which increases with prolonged treatment.
- Late presentation of cardiomyopathy usually occurs 5 or more years after completion of treatment and leads to cardiac failure.

EYE PROBLEMS

Occasionally some chemotherapy agents, such as cyclophosphamide, fluorouracil (5FU), methotrexate and doxorubicin can cause gritty, watery or dry eyes. The key to successfully managing eye problems lies in assessment and accurately identifying and managing the underlying problem. Providing there are no signs of local or systemic infection, patients with dry or gritty eyes are advised to try medications that can be purchased over the counter e.g.

- Hypromellose 0.3% eye drops, which may need to be instilled frequently e.g. hourly, for adequate relief.

Patients are encouraged to seek medical advice if over the counter medication's fail to resolve the problem within 48 hours.

FERTILITY / FAMILY PLANNING

Some chemotherapy agents, such as ifosfamide, high dose cyclophosphamide, doxorubicin (adriamycin), epirubicin and etoposide can cause temporary or permanent infertility. All patients who are receiving agents that can reduce fertility will have been assessed by their oncologist and appropriate interventions or strategies instigated e.g. sperm storage, ovarian preservation.

Although fertility may begin to return when treatment is complete, patients and HCP are advised to maintain ongoing communications with the oncology team regarding issues pertaining to contraception and family planning.

As chemotherapy can adversely influence foetal development, patients are provided with contraceptive advice during treatment and women of a childbearing age are advised to contact the 24-hour contact number if their period is late and they think they may be pregnant.

Female patients who experience problems associated with entering an early menopause as a result of chemotherapy are advised to contact their haematology / oncology team for advice.

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HEARING PROBLEMS

Occasionally some chemotherapy agents, such as cisplatin and to a lesser degree, carboplatin and oxaliplatin, can cause hearing problems. This usually presents as tinnitus in the first instance and progresses to hearing loss, especially at higher tones.

All patients who are receiving agents that can cause hearing problems will have been assessed by their oncologist and appropriate assessment and monitoring of hearing instigated e.g. audiograms.

All patients who are receiving agents that may cause hearing problems are provided with home care information including:

- Contact the 24-hour contact number if they develop tinnitus or problems with their hearing.

HYPOMAGNESAEMIA

Hypomagnesaemia can occur in patients who receive additional hydration and have increased diuresis within their chemotherapy regime e.g. cisplatin. It can also occur in patients who have diarrhoea and / or vomiting. HCP's may wish to explore potential signs of hypomagnesaemia and inform the patient's haematology / oncology team as required. Symptoms may include:

- Muscle fatigue
- Weakness
- Skin flushing
- Hypotension
- Thirst
- Nausea
- Drowsiness
- Cardiac arrhythmias
- Fitting

GUIDELINES FOR THE MANAGEMENT OF CHEMOTHERAPY AND SYSTEMIC ANTICANCER THERAPY INDUCED TOXICITIES WITHIN PRIMARY CARE

MUSCULOSKELETAL PAIN

Occasionally some chemotherapy agents such as taxanes (paclitaxel and docetaxel) and vincristine can cause musculoskeletal pain. The key to successfully managing musculoskeletal pain lies in accurate assessment, identifying the underlying cause as pain can signify infection or disease relapse. HCP's may consider referral to the patient's haematology / oncology team if symptoms persist / worsen.

All patients who are receiving agents which may cause joint pains are provided with home care information including:

- Local and systemic remedies that can be purchased over the counter e.g. mild oral or topical analgesics. Advice should be sought from the chemotherapy unit/centre regarding suitable analgesia for particular patients. **Caution with NSAID's and use of regular paracetamol, until underlying cause identified.**
- Inform their haematology / oncology team at their next visit of any musculoskeletal pain.

HCP's should be mindful that systemic analgesics could mask signs of febrile neutropenia.

PALMAR-PLANTAR ERTHRODYSAESTHESIA (PPE) HAND-FOOT SYNDROME

Some cancer patients receiving chemotherapy can experience a drug reaction characterised by redness and tenderness of the palms of the hands and soles of the feet. This is called Palmar plantar erthrodysaesthesia (PPE) or hand-foot syndrome. Other signs and symptoms can include a tingling sensation and swelling or small blisters and breaks in the skin. This can also occur in other parts of the body, including the armpits and groin surface. It can also be seen in pressure areas, for example, where tight fitting underwear presses against the skin. In some patients this syndrome can be so severe that it may impair the use of their hands or feet.

PPE is usually associated with patients who are receiving fluorouracil (5FU), oral capecitabine, liposomal doxorubicin (caelyx / myocet) and tyrosine kinase inhibitors (TKI) such as Sunitinib, Pazopanib and Axitinib. All patients who are receiving agents that may induce PPE are provided with home care information including:

- Topical application of emollient, e.g. Aqueous Cream or E45.
- Contact the 24-hour contact number if they develop redness, tenderness, tingling, swelling or small blisters / breaks in the skin of their hands and soles of the feet.

GUIDELINES FOR THE MANAGEMENT OF CHEMOTHERAPY AND SYSTEMIC ANTICANCER THERAPY INDUCED TOXICITIES WITHIN PRIMARY CARE

PERIPHERAL NEUROPATHY

Occasionally some chemotherapy agents, such as thalidomide, taxanes (paclitaxel and docetaxel), platinum agents (carboplatin, cisplatin or oxaliplatin), and vinca alkaloids (vincristine, vinblastine and vinorelbine) can cause peripheral neuropathy.

All patients who are receiving agents that may induce peripheral neuropathy are provided with home care information including:

- Contact the 24-hour contact number if they develop pins & needles, numbness, tingling / pain in their extremities, difficulty in fine motor skills or begin to stumble when walking.

As these side effects usually begin to disappear when treatment is terminated or completed, HCP may consider referral to the patient's haematology / oncology team if symptoms persist for several months.

PULMONARY PNEUMONITIS / FIBROSIS

Acute or late onset pulmonary pneumonitis / fibrosis can occur in patients who receive bleomycin, methotrexate or a stem cell transplant.

Non-infectious pneumonitis is a class effect of rapamycin derivatives and can occur in patients who receive everolimus.

All patients who are receiving potentially pulmonary toxic agents will have been assessed by their oncologist and appropriate assessment and monitoring of lung function instigated. The risk will also be minimised by through the regular assessment of respiratory function.

HCP's may wish to explore potential signs of pulmonary toxicity including:

- dry non-productive cough
- fever
- dyspnoea,
- hypoxia
- infiltrate on chest

HCP's should contact the patient's haematology / oncology team for advice when symptoms are of a progressive nature however **an acute episode or exacerbation of breathlessness (with or without chest pain) should be treated as an emergency irrespective of the site of the patient's tumour or treatment.**

GUIDELINES FOR THE MANAGEMENT OF CHEMOTHERAPY AND SYSTEMIC ANTICANCER THERAPY INDUCED TOXICITIES WITHIN PRIMARY CARE

RENAL TOXICITY

Many cytotoxic drugs are excreted via the urinary system and three chemotherapy agents, cisplatin, carboplatin and high dose methotrexate can cause renal toxicity.

All patients who are receiving potentially renal toxic agents will have been assessed by their haematologist / oncologist and appropriate assessment and monitoring of renal function instigated e.g. glomerular filtration rate (GFR), urea & serum creatinine. The risk may also be minimised through the routine administration of intravenous hydration.

All patients who are receiving agents that can cause renal toxicity are provided with home care information including:

- Maintaining adequate fluid intake - 2 litres of fluid per day.

EGFR INHIBITOR INDUCED RASH

One advantage of targeted therapies is that unlike traditional chemotherapy they generally do not cause cumulative bone marrow toxicity and other cell damage related side effects of cytotoxics. That is not to say targeted therapies do not have significant toxicities, but they are slightly different, e.g. the EGFR inhibitors (erlotinib, gefitinib, cetuximab) toxicity profile is different from traditional chemotherapy with patients prone to diarrhoea and severe skin reactions.

Rash induced by erlotinib, gefitinib, cetuximab has a distinctive pustular/ papular appearance and usually involves the face, head and upper torso.

- Patients on these drugs are encouraged to use moisturisers and barrier creams to keep their skin well hydrated.
- Patients with EGFR skin rash have benefitted from using colloidal oatmeal based product, such as Aveeno, or a product called Udderly Smooth. Note the clinical evidence for use of these products is limited. See <http://www.aveeno.co.uk/> and <http://www.udderlysmooth.co.uk/>
- Severe cases of EGFR induced rash are treated with steroids (both topical and systemic) and tetracycline antibiotics.
- Can also consider adding in antihistamines e.g. chlorphenamine/ hydroxyzine and painkillers, paracetamol/ ibuprofen if itching and or painful.

Note: Topical retinoids and other acne medications (eg benzyl peroxide) are NOT recommended since rash is not acne. Their skin drying effects may exacerbate rash.

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HYPERTENSION

All drugs that block the vascular endothelial growth factor (VEGF) pathway are associated with hypertension. It is seen with bevacizumab, sorafenib, pazopanib, axitinib and sunitinib. Patients receiving these treatments should be monitored for hypertension and treated as needed with standard anti-hypertensive therapy.

THYROID DYSFUNCTION

Thyroid dysfunction has been observed with TKI such as Axitinib, Pazopanib and Sunitinib. Laboratory measurement of thyroid function will be performed at baseline by secondary care and monitored during treatment. Patients receiving these treatments should be observed for signs and symptoms of thyroid dysfunction and if hypothyroidism develops patients should be managed as per standard medical practice.

RESOURCES (Further Reading)

Macmillan Cancer Support – Cancer Information
www.macmillan.org.uk/cancerinformation

Cancer Research UK – Cancer Information
<http://www.cancerhelp.org.uk/>