Adverse effects of anticancer medicines can lead to delays or cessation of treatment. Prompt management or prevention can lead to improved patient outcomes. Adverse effects are influenced by factors such as the drug regimen, stage of disease, and a patient’s co-morbidities and psychosocial status. The most common adverse effects of anticancer medicines are listed in this fact sheet.

The number of patients receiving oral anticancer therapy in an outpatient or community setting has increased in recent years. Oral anticancer medicines include cytotoxic agents, targeted therapies, hormonal therapies and immunomodulators.

Like parenteral chemotherapy, oral medicines cause adverse effects and are associated with an increased risk of medication errors; particularly if non-cancer specialists prescribe, dispense or administer and bypass the normal safeguards used for anticancer medicines.

Oral anticancer medicines can cause life-threatening adverse effects, such as neutropenic sepsis and diarrhoea. As such, it is important for patients and their carers to recognise the potential complications associated with their treatment, and the necessary actions to be taken. Community pharmacists play an important role in this education for patients.

Medical emergency:
Recognise when to immediately refer patients to the nearest emergency department:
- temperature of 38°C or higher
- shivers, sweats, chills or shakes
- flu-like symptoms
- shortness of breath
- chest pain or discomfort
- pain or tingling in arms
- uncontrolled vomiting or diarrhoea

Access to eviQ is free at eviQ.org.au
Working together to lessen the impact of cancer
Chemotherapy-induced nausea and vomiting (CINV)

Nausea and vomiting are the most common and distressing adverse effects of chemotherapy. If poorly managed, they can lead to non-compliance with treatment and metabolic imbalance with a decline in overall performance status.

Nausea and vomiting associated with anticancer medicines is generally classified according to three phases of onset: acute, delayed or anticipatory. Other categories include breakthrough and refractory. The choice of antiemetic is dependent on the emetic potential of the anticancer medicine prescribed. The emetic potential can be defined as high, moderate, low, minimal or no risk. The table below lists available antiemetic agents and recommended doses.

The recommended anti-emetics for each protocol are also listed on eviQ.

**Patient Education**

Educate patients to maintain fluid intake (e.g. electrolyte replacement with Gastrolyte®) and to report signs of dehydration including dizziness, reduced urine output and confusion.

To reduce feeling of nausea, suggest patients take antiemetic medications 30 to 60 minutes prior to meals and to avoid alcohol, fried food and foods with a strong smell. Peppermints, peppermint tea and ginger may help with nausea.

### Antiemetic drug classes and suggested doses

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Compound</th>
<th>High risk</th>
<th>Moderate risk</th>
<th>Low risk</th>
<th>Acute emesis</th>
<th>Delayed emesis</th>
<th>Oral dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>5HT3RA</td>
<td>Granisetron</td>
<td>Intravenously</td>
<td>3 mg</td>
<td>or</td>
<td>2 mg</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Ondansetron</td>
<td>or</td>
<td>8 mg</td>
<td>or</td>
<td>16 mg (in divided doses)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Palonosetron</td>
<td>or</td>
<td>0.25 mg</td>
<td>or</td>
<td>0.5 mg (fixed combination with netupitant)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neurokinin (NK1) receptor antagonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aprepitant</td>
</tr>
<tr>
<td>Fosaprepitant</td>
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<tr>
<td>Netupitant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Corticosteroids (dexamethasone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
</tr>
<tr>
<td>Delayed emesis</td>
</tr>
<tr>
<td>Low risk</td>
</tr>
<tr>
<td>Delayed emesis</td>
</tr>
</tbody>
</table>

### Recommended doses of dopamine receptor antagonists for the treatment of breakthrough or refractory CINV*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>0.5 mg to 2 mg orally/intravenously every 4 to 6 hours</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10 mg orally or intravenously three time a day (maximum of 30 mg/24 hours, up to 5 days)</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>10 mg orally or 12.5 mg intravenously every 6 hours</td>
</tr>
<tr>
<td>Promethazine</td>
<td>10 mg to 25 mg orally or 12.5 mg to 25 mg intravenously (central line only)1 every 4 to 6 hours</td>
</tr>
</tbody>
</table>

* the concomitant prescribing of any combination of prochlorperazine, promethazine, metoclopramide or haloperidol should be used with caution, as excessive dopamine blockade can increase the risk of extrapyramidal symptoms.

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**Please read:**
- Prevention of chemotherapy-induced nausea and vomiting (CINV)

**Patient information:**
- Nausea and vomiting during cancer treatment
Oral Mucositis

Patients may present with mild redness or sores in the mouth which can quickly progress to painful ulceration in a short timeframe. Patients receiving combination anticancer medicines and radiation are at a higher risk of mucositis.

Signs and symptoms include:
- pain
- erythema of the buccal mucosa or soft palate
- burning sensation in the mouth, with or without eating/drinking
- dysphagia (difficulty in swallowing) secondary to ulcers
- altered saliva
- altered taste
- oral bleeding
- infection ± dental caries and disease.

Patient Education
- Advise the patient to report symptoms such as pain, difficulty swallowing, oral thrush or mouth ulcers as the mouth is a common source of infection.
- If these symptoms are associated with fever, the patient should seek immediate medical attention, at the hospital, for neutropenic sepsis.
- To avoid oral mucositis recommend self-care measures including basic oral care, maintaining adequate fluid intake, adding sauces to moisten meals and smoking cessation strategies.

Neutropenic sepsis

Neutropenic sepsis is a life-threatening toxicity and should be managed as a MEDICAL EMERGENCY.

Anticancer medicines can interfere with the production of white blood cells, red bloods cells and platelets. Haematological toxicities, including neutropenia, thrombocytopenia and anaemia, are common adverse effects of anticancer treatment.

Neutropenia can sometimes occur without any symptoms, but is associated with an increased risk of infections. Community pharmacists should suspect neutropenic sepsis in patients having cancer treatment who become unwell or develop a fever. Neutropenic patients may not present with the classic signs of infection and may deteriorate very rapidly.

Please read:
- Immediate management of neutropenic fever

Patient information:
- Infection during cancer treatment

In immunocompromised, such as cancer patients, oral candidosis requires specialist management, and patients should be referred to their treating team.

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Diarrhoea

Hypovolaemic shock and death has been known to occur following anticancer-induced diarrhoea.

Diarrhoea is potentially associated with ALL anticancer medicines, including oral agents. It is important to know that with some medicines such as irinotecan, which is given intravenously, diarrhoea can be a life-threatening complication of treatment. Immediate management is crucial, so it is important to know the medicines your patient has received.

The following medicines require specific management and referral to a treating hospital for further management:

• **Irinotecan**: Used in the treatment of colorectal cancer, this can cause life-threatening diarrhoea that requires urgent specific treatment.

• **Immunotherapy: especially Ipilimumab**: Used in the treatment of metastatic melanoma, requires specialist management by a health professional experienced in its use.

**Patient Education**

Advise patients taking oral anticancer medicines to STOP taking their medication and seek medical attention if they develop diarrhoea that does not settle with loperamide (Gastrostop®, Imodium®, Diareze®).

If diarrhoea is associated with irinotecan or ipilimumab use, refer immediately to a hospital for further management.

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**Constipation**

Constipation in the cancer patient may be a symptom of an organic condition, a complication of systemic disease, or an adverse effect of anticancer treatment. Some anticancer medicines (e.g. vinca alkaloids), immunomodulators (e.g. thalidomide [Thalomid®]), supportive therapies (e.g. 5HT3 receptor antagonists for CINV such as ondansetron, granisetron) and opioid analgesics for pain relief, may also be associated with constipation.

**Patient Education**

Advise the patient to initiate a bowel management plan as advised by their treating team (i.e. after 3 days without a bowel movement). This may include a stimulant laxative (bisacodyl or senna), stool softener (docusate) ± osmotic laxative (Movicol®), increasing fluid intake and increasing physical activity. Referral from their doctor to a dietitian may also be considered.

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**Peripheral neuropathy**

Peripheral neuropathy is a common complication of several classes of anticancer medicines, including taxanes, platinum-based compounds, vinca alkaloids, and some medicines that are used to treat multiple myeloma. e.g. thalidomide and its analogues.

These medicines cause inflammation, injury or degeneration of the peripheral nerve fibre(s), resulting in sensory, motor or cranial nerve dysfunction. Most treatment-related peripheral neuropathy is transient; however, some medicines can cause permanent dysfunction. As such, it is important that patients know the symptoms of this side effect and report them, as a treatment dose modification may be required.

Patients with peripheral neuropathy need to consider their safety due to a lack of sensation, and having less strength or muscle control.

**Patient Education**

• Educate patients on self care strategies, including wearing gloves and warm socks in cold weather, shielding fingers when cutting foods and adjusting water temperatures to avoid burns.
• Ensure the patient is aware to report any signs or symptoms of peripheral neuropathy and seek medical attention for any injuries sustained.
• Recommend patients avoid driving if symptoms become severe.

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**Please read:**

• Treatment induced diarrhoea

**Patient information:**

• Diarrhoea during cancer treatment

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**Please read:**

• Peripheral neuropathy supporting document
Managing common adverse effects of anticancer medicines

Dermatological toxicity

Acneiform (papulopustular) rash

Most patients taking oral medicines that target the Epidermal Growth Factor Receptor (EGFR) e.g. erlotinib, gefitinib and lapatinib, develop a rash on the face and upper body. It usually occurs within the first few weeks of taking these medications.

The rash occurs as a result of direct EGFR inhibition, and not as an allergic reaction to therapy and may correlate positively with response and survival. It is generally confined to the seborrheic areas including the face, scalp, shoulders and upper trunk. Patients report redness or a warm sensation like sunburn before the rash begins. After several days, tender pimples and pus bumps appear, and the surrounding skin feels slightly tender. Rashes tend to be mild to moderate.

Treatment may include prophylactic or early therapy with a tetracycline antibiotic (e.g. doxycycline 100mg twice daily) and hydrocortisone 1% cream to affected areas, and/or referral to a dermatologist.

Patient Education

Advising on the application of an alcohol-free emollient cream, avoiding sun exposure, wearing loose-fitting cotton clothing and avoiding the counter acne preparations as they may exacerbate the rash.

Hand Foot Syndrome (HFS) and Hand Foot Skin Reaction (HFSR)

Also known as Palmar Plantar Erythrodysaesthesia (PPE) is a common adverse effect associated with some anticancer medicines, including the oral agent capecitabine.

This syndrome is characterised by the gradual onset of bilateral symmetric reactions (redness, swelling and pain) over the palms of the hands and/or soles of the feet. It usually develops six weeks after medicine initiation. It occurs when medicines used to treat the cancer affect the growth of skin cells or capillaries (small blood vessels) in the hands and feet. Once the medicine is out of the blood vessels, it damages the surrounding tissues. A similar reaction, hand foot skin reaction, occurs with a number of targeted oral agents e.g. pazopanib, dabrafenib, sorafenib and sunitinib. These lesions tend to be more localised and hyperkeratotic.

Management of both HFS and HFSR include topical application of an emollient containing urea 10%. Some patients may require treatment interruption, dose reduction and referral to a dermatologist.

Patient Education

Advising on the avoidance of hands and feet to heat, unnecessary vigorous exercise, tight-fitting shoes, sun exposure, contact with detergents, topical anaesthetic containing creams and activities that cause friction and rubbing of the skin surfaces (clapping, typing, playing musical instruments, etc.).

Fatigue

Fatigue is a common side effect of cancer therapy.

Fatigue is a feeling of excessive tiredness or exhaustion for most or all of the time, typically not relieved by rest or sleep. It can present within days to weeks of starting therapy but can also be cumulative and can become severe and may require a dose reduction.

It is important to note that haemoglobin levels below 90 g/L are often accompanied by fatigue, and improvements in energy are measurable with anaemia correction to within normal haemoglobin levels. Blood transfusions are usually considered if a patient has fatigue related to anaemia.

Fatigue should be managed by educating patients:

• about fatigue
• to maintain an adequate nutrition and hydration status
• about the importance of relaxation/meditation
• to perform gentle exercise, as able
• to manage their day to include rest breaks and possibly reduce number of activities while receiving treatment
• to prioritise activities, thereby completing the most important tasks of the day when the patient may have energy.

Please read:

• Hand foot syndrome (HFS) - Palmar plantar erythrodysaesthesia (PPE) associated with chemotherapeutic agents

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