Helping cancer patients in the community

Cancer patients are spending more time out of hospital and in the community. Steve Williamson describes cancer services in the UK and looks at how community pharmacists can support those undergoing treatment

There are around 1.8 million people with cancer at any one time in the UK and it can be estimated that at least half of these are being treated with chemo- or radiotherapy. Last month, the Department of Health published "Improving outcomes: a cancer strategy".[1] This builds on previous publications recognising the need for increased focus on early detection and prevention of cancer and long-term follow up for those living with the disease.

The impact of more effective treatments means management of some cancers is now similar to long-term conditions. For example, patients receiving oral imatinib for chronic myeloid leukaemia have a 95 per cent five-year survival rate[2] and can continue treatment for many years.

The most common cancers in the UK are breast, lung, colorectal and prostate. Breast cancer has the best prognosis, with an 80 per cent five-year survival rate, and lung cancer has the poorest prognosis, with an average five-year survival of just 7 per cent. Only 25 per cent of patients survive one year so early diagnosis of lung cancer is critical and community pharmacists can play an important role (see Resources).

Patients with suspected cancer must be diagnosed within 31 days of referral or presentation (either by their GP or following acute hospital admission) and must have their first treatment within 31 days of diagnosis. This 62-day timescale forms part of DoH cancer wait targets. After diagnosis, treatment is planned by specialists at a multidisciplinary team ("MDT") meeting.

Role of the pharmacist

Specialist oncology pharmacists work as part of the secondary care team, managing cancer patients alongside oncologists, haematologists, oncology nurses, physiotherapists, counsellors and others. These pharmacists are responsible for ensuring safe delivery of chemotherapy services, pharmaceutical care of patients and advising on choice of therapy. The British Oncology Pharmacy Association has produced standards and competencies for pharmacist verification of prescriptions for anticancer medicines.[3,4]

Non-specialist pharmacists, including community pharmacists, might not be directly involved in the supply of cancer medicines, but patients taking these medicines may access community pharmacy for advice on products to manage side effects and, potentially, to supplement their treatment.

Traditionally, cancer therapies have been managed by secondary care specialists but as care improves and patients survive longer there will be more room for primary care involvement. For example, recent years have seen growth in oral cancer medicines, which means more patients are treated with medicines that can be taken at home. These medicines have the potential to be dispensed from community pharmacies (see **Special feature**, pp144–5).

Cancer treatments

Cancer treatments comprise surgery, traditional chemotherapy or targeted therapies, radiotherapy and hormonal therapy. Choice depends on cancer type but surgery is often combined with radiotherapy or chemotherapy, or both — chemotherapy alone is rarely curative. Some patients will receive all four treatments.

There are two branches to solid tumour oncology: clinical oncology and medical oncology. Both types of oncologist give systemic anticancer therapies (SACTs) to patients but only clinical oncologists administer radiotherapy. Haematologists or haemato-oncologists prescribe SACTs for blood, lymph and bone marrow cancers. SACTs are used for patients with localised or metastatic malignancy, as well as for patients whose cancer has, potentially, been cured by surgery but for whom further adjuvant systemic therapy improves their prognosis.

Chemotherapy Although drug development is moving towards biologically targeted therapies, chemotherapy currently remains the backbone of cancer treatment.

Some cytotoxic drugs destroy cells, including those not actively dividing, at all stages of the cell cycle (cycle specific). Others only affect cells at specific parts of the cycle (phase specific). Because cancer drugs act through a complex interaction with the cellular biology of tumours, it is important to consider the impact of scheduling and duration of treatment. At any one time cells in a tumour will be at various stages of the cell cycle and if a phase-specific agent were administered only a fraction of the cancer cells would be susceptible. Consequently, cytotoxic medicines are given in different combinations and in cycles of three to four weeks. A course of chemotherapy will involve a number of cycles, which might be fixed or which might be given until disease progression, that is, until they stop being effective. Cancer cells can develop resistance to cytotoxic drugs through a variety of mechanisms so patients who respond well to first-line chemotherapy can relapse and different drugs will be needed. →

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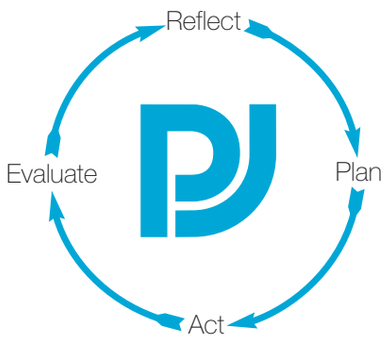

REFLECT

1 How is cancer treatment toxicity assessed?
2 What treatment options are available for common side effects of cancer therapy?
3 What advice can be given to cancer patients with regards to nutritional supplements or herbal products?

Before reading on, think about how this article may help you to do your job better.

Targeted therapies Most current research of cancer medicines is focused on developing drugs directed toward specific pathways involved in tumour growth and progression. As understanding of tumour biology increases, more selective drugs, targeting cellular changes specific to cancer cells, are being developed. It is expected that these will be less harmful to normal cells and, consequently, cause fewer side effects than conventional chemotherapy.

Targeted cancer therapies interfere with cancer cell proliferation and spread in different ways. Many focus on proteins that are involved in the cell signal transduction pathway. This complex communication system governs basic cellular functions and activities, such as division, movement, how a cell responds to specific external stimuli and even cell death. By blocking signals that regulate cell division, targeted therapies can help stop disease progression. Other targeted therapies can cause cancer cell death directly, by inducing apoptosis, or indirectly by stimulating the immune system to recognise and destroy cancer cells.

Most targeted therapies are either small molecules or monoclonal antibodies. Small molecule drugs (eg, imatinib) diffuse into cells and act on intracellular targets. Monoclonal antibodies (eg, trastuzumab) have a large molecular weight so cannot penetrate the cell plasma membrane and are directed at extracellular targets.

Radiotherapy Radiotherapy involves targeted exposure of tumour cells to radiation administered as photons (ie, X-rays, gamma rays) to kill tumour cells by damaging DNA.

Treatment toxicity

Cytotoxic agents are classed as high risk medicines because of their many potentially harmful side effects and the decision to use chemotherapy depends on the balance between toxicity and benefit. Because these drugs attack all cells undergoing rapid cell division, toxic effects are most obvious in bone marrow, mucous membranes and hair.

One advantage of targeted therapies is that they generally do not cause cumulative bone marrow toxicity. That is not to say these therapies do not have significant toxicities — patients on the epidermal growth factor receptor (EGFR) inhibitors (eg, erlotinib, gefitinib, cetuximab) are still prone to diarrhoea and skin reactions — but the mechanisms involved are different. Chemotherapy toxicities can generally be divided into haematological and non-haematological types.

Like chemotherapy, radiotherapy produces adverse effects in normal tissues. Side effects are either acute, subacute or late. Acute effects are common, rarely serious, and usually self-limiting. They tend to occur in skin or mucosal surfaces (eg, oropharynx, oesophagus, intestines, bladder) and are due to radiation-induced cell death. Subacute toxicities occur two weeks to six months after treatment (eg, radiation pneumonitis) and late effects (eg, fibrosis or long-term organ damage) occur six months or more after treatment.

Steve Williamson will be available to answer questions online on the topic of this article until 21 February 2011

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Bone marrow suppression The bone marrow stem cell population continually produces cells that mature and differentiate into erythrocytes, some white blood cells (granulocytes or leukocytes) or platelets. Neutropenia (defined by the neutrophil count, not the total white cell count) is the direct effect of chemotherapy on the bone marrow. The degree depends on drug, schedule and dose. It usually occurs seven to 10 days following a cycle of chemotherapy. Platelet count can also drop but thrombocytopenia is less common than neutropenia. Anaemia (erythrocyte count) induced by chemotherapy requires a blood transfusion — it is not appropriate to treat with iron supplements. A fall in the erythrocyte count would not be seen for six to eight weeks after administration.

It is essential to perform a full blood count before administering chemotherapy. A low neutrophil count is often the limiting factor with regard to patients receiving their chemotherapy on time. The levels at which treatments are delayed may vary from regimen to regimen and even from prescriber to prescriber but, in general, treatment should not proceed if the values are as follows:

- White cell count $<3\times10^9$ cells/L
- Absolute neutrophil count $<1.5\times10^9$ cells/L
- Platelet count $<100\times10^9$ cells/L

It is important to counsel patients on the risk of bone marrow suppression and the care needed to minimise infection risk. For example, in Northumbria Healthcare NHS Foundation Trust patients are advised to:

- Wash their hands before eating or preparing food and after handling animals, fresh flowers or pot plants
- Wash and peel all fruit and vegetables
- Avoid unpasteurised milk and cheese, and raw or undercooked eggs and meat
- Avoid contact with anyone who has an obvious infection and with people who have been in contact with chickenpox
- Avoid animal faeces and changing nappies of recently vaccinated children

Vaccination against influenza is a good idea but patients should discuss this with their doctor, in order to time vaccination optimally in relation to their cancer treatment.

Patients are warned that if they develop a febrile illness or feel unwell with symptoms of infection, they require an immediate full blood count, checked either by their GP, hospital emergency care or chemotherapy ward. Patients presenting with the following symptoms in the community should be referred:

- A raised temperature (>38C)
- Shivering or shaking
- Sore throat, cough or shortness of breath
- Cystitis
- Rash, bruising or bleeding with no apparent cause

Non haematological toxicities Assessment of non-haematological toxicities follows the US National Institutes for Health (National Cancer Institute) Common Toxicity Guidelines.[5] These are based on grading toxicity from 0 to 4 (0=no toxicity, 4=severe). One of the key items is the patient's performance status ("PS"), which is used to ensure patients are fit enough to continue treatment. Patients who are "PS 0" (able to carry our normal activity) or "PS1" (restricted in physical activity but ambulant and able to carry out light work) are usually deemed fit to proceed with treatment. Caution is needed in patients who are "PS2" and above. PS2 means the patient is up and about more than 50 per cent of waking hours, capable of all self-care but unable to work. PS3 indicates a patient capable of limited self-care and up and about less than 50 per cent of waking hours, and PS4 means the patient is bed- or chair-ridden.

A summary of how other features (eg, fatigue, infection, nausea) are assessed in clinical practice can be accessed on *PJ Online*.

Dealing with side effects

Patients receiving anticancer treatments are highly likely to experience side effects and it is vital that they are provided with supportive care to help them cope. Cancer patients are likely to have a hand-held record, which contains details of their treatment and blood tests. Sometimes these records also contain charts for patients to self-assess their side effects, as well as information on avoiding infections and things to tell their doctor, and pharmacists can reinforce this advice.

National standards for ensuring quality and safe chemotherapy services require a 24-hour helpline to be available, but the current provision of this service across the UK is variable.

Fatigue Fatigue can be one of the most distressing side effects of both anticancer therapy and cancer. Patients often have low energy levels and become easily exhausted. Some patients believe they have to keep busy but they should be encouraged to reduce their daily activities and to build in extra time to

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rest. Light exercise may help people to feel better. Patients should also try to eat well, but this might be difficult (see below). Other tips that pharmacists can give patients with fatigue are listed in Panel 1. Most people get back to their normal energy levels between six months and a year after their chemotherapy ends.

Nausea and vomiting The action of cytotoxic drugs on the replicating cells in the lining of the gastrointestinal tract (particularly those located in the small intestine) results in the stimulation of the vagus nerve, which causes the release of various gastrointestinal hormones. These include 5-hydroxy-tryptamine, which stimulates $5HT_3$ receptors in the upper and lower small intestine, leading to nausea and vomiting. Cytotoxic drugs also directly stimulate receptors in the chemoreceptor trigger zone and higher cerebral centres in the central nervous system. Chemotherapy-induced nausea and vomiting is classed as acute (occurring within 36 hours), delayed (beyond 36 hours) or anticipatory (before treatment).

Risk of nausea and vomiting varies with different drugs, doses and regimens, and among individuals. Effective control depends on a step-wise approach depending on the emetogenicity of the chemotherapy. Vomiting, although distressing, is more easily controlled, especially if newer anti-emetics are used in combination. Nausea is more difficult to control and can be extremely unpleasant.

Anti-emetics routinely given are $5HT_3$ receptor antagonists: granisetron or ondansetron. Although these agents have some pharmacological differences in $5HT_3$ receptor affinity, selectivity and metabolism, such minor variations have not resulted in clinically significant differences. Other antiemetics used include domperidone, metoclopramide and dexamethasone.

Two new drugs launched in the past few years, palonosetron and aprepitant, are increasingly considered for resistant cases. Aprepitant acts on neurokinase-1 receptors to block the actions of substance P, which has been implicated in delayed nausea and vomiting. Palonosetron is a $5HT_3$ antagonist that has different receptor specificity from other $5HT_3$ antagonists and is also more effective in delayed nausea and vomiting. European guidelines for chemotherapy induced nausea and vomiting are available[6] but local protocols will vary slightly depending on availability of these new agents.

Diarrhoea Diarrhoea is a common side effect of fluoropyrimidines and EGFR targeted therapies. The usual approach for grade 1 symptoms (increase of >4 stools per day over baseline) is to treat with loperamide (4mg initially, then 2mg after each loose stool, to a maximum of 16mg in 24hrs). Many patients are given an advance supply to use as needed.

Patients receiving agents that can cause diarrhoea are instructed to drink at least 2L of fluid a day. Those with diarrhoea should be advised on electrolyte replacement (eg, Dioralyte). Patients should be advised to seek medical attention if loperamide fails to resolve the problem within 48 hours. Codeine phosphate (30mg *qds*) may be prescribed.

In grade 2 diarrhoea there is an increase of four to six stools per day over baseline and intravenous fluids are required.

Irinotecan can cause a severe early onset diarrhoea, which is part of a cholinergic reaction to the drug and is associated with sweating, hypersalivation, visual disturbances and abdominal cramps.

Constipation Other drugs (eg, ondansetron and vinca alkaloids) can cause constipation, which can lead to pain, discomfort and increased nausea. A high fluid intake is essential during chemotherapy. Treatment of constipation using osmotic or stimulant laxatives has been found to be most effective. In Northumbria, we have found macrogols effective (eg, Movicol oral powder, one to three sachets daily until problem resolves). Alternatively, we prescribe docusate sodium capsules or oral solution (100mg or 10ml *bd*).

Oral mucositis Inflammation of mucous membrane in the mouth is another common manifestation of gastrointestinal toxicity. Initial symptoms include pain, tingling, dry mouth and loss of taste. These can progress to frank ulceration, which can affect the lips, tongue, palate and gums, reaching a peak after around seven days. Frequency and severity are related to the dose and schedule administration of the drug.

All patients receiving cytotoxic drugs can develop mucositis although some drug groups (eg, antimetabolites such as 5-fluorouracil and methotrexate) carry a higher risk than others. Patients having radiotherapy to treat head and neck malignancies are more susceptible to mouth problems and painful oesophagitis.

Good mouth care and oral hygiene is important to prevent and reduce mucositis. Soft toothbrushes are recommended and patients are encouraged to use a mouthwash. In general, no mouthwash has been proven superior for chemotherapy patients; frequent mouthwashing is considered more important than product choice. Any dentures should be cleaned morning and evening. Very hot or cold fluids should be avoided. Lip balm will help keep lips moist.

Pharmacists counselling patients with a sore mouth should be able to recognise severity of symptoms. A grade 1 sore mouth (erythema of the mucosa, minimal symptoms, normal diet) can be treated with a simple saline mouthwash or chlorhexidine gluconate 0.2 per cent (alcohol free formulations may reduce sting).

For more severe oral mucositis benzydamine mouthwash (Difflam; diluted with a little water if it stings) can be recommended first-line. Soluble analgesics (eg, aspirin, paracetamol, co-codamol) used as mouthwash are a second-line option, as is lidocaine 1 per cent gel (applied *qds*).

Patients receiving intensive regimens may be prescribed antiviral and antifungal prophylaxis. Oral candida has a distinctive appearance, often presenting with creamy white raised lesions, so it is always worth examining the patient's mouth, but this presentation can be hidden by erythema. Confirmed oral candida may require systemic antifungal treatment (eg, fluconazole).

Some US-based patient forums talk about "magic mouthwash". These are specials formulations containing ingredients such as local anaesthetics, antihistamines, corticosteroids and antibiotics, but are not used in the UK.

Those who are unable to eat or drink as normal can be advised to moisten the mouth every two hours with mouthwash (or a foam mouth care swab dipped in mouthwash).

There are a number of products that people with dry mouth might wish to try, including artificial saliva products (eg, Biotene Oralbalance gel, Glandosane spray, Salivix pastilles), but tips for this symptom also include choosing moist foods, trying to drink

PANEL 1: ADVICE FOR PATIENTS WITH FATIGUE*

- Plan ahead where possible, to avoid having to rush and the associated stress. For example, write a shopping list and go when the shops are quiet. Prioritise your tasks so the most important are done first.
- Put chairs around your home so you can easily stop and rest when needed.
- Wear clothes that are easy to put on and remove (eg, loose-fitting, few buttons).
- Keep a stock of nutritious snacks and drinks so you can have something easily whenever you feel like eating.
- Do things that you enjoy (it will take your mind off cancer and make you feel more relaxed).
- Keep a fatigue diary of how you are feeling and how your energy levels change. This will help you gauge if you are more or less tired than before and which activities make you feel better or worse.
- Do not be afraid to ask for help.

* Adapted from Cancer Research UK

PANEL 2: TAKE CARE WITH SUPPLEMENTS

- Patients keen to supplement their diet can take a good-quality, one-a-day multivitamins and minerals pill. They should not exceed the stated dose.
- Evidence suggests that antioxidants (eg, co-enzyme Q10, selenium, vitamins A, C and E) might reduce the activity of drugs generating free radicals (eg, alkylating agents and doxorubicin) and radiotherapy. Until more is known, patients should avoid such supplements, especially at high doses, during therapy.
- There is evidence to suggest that echinacea interacts with treatment for Hodgkin's disease, leukaemia, myeloma or lymphoma.
- Evidence suggests that St John's wort may reduce the effect of chemotherapy and increase radiotherapy side effects.
- There is evidence to suggest that patients with breast or endometrial cancer could suffer adverse interactions with black cohosh, red clover or wild yam.
- Mistletoe is not proven to be a safe and effective cancer treatment. Patients should be advised to assure themselves that products are supported with evidence.

at least 1.5L of fluid a day and sucking ice chips. Pharmacists could consider if any concurrent medicines are contributing.

Sensory neuropathy Some agents (eg, thalidomide, taxanes, platinum and vinca alkaloids) can cause peripheral neuropathy. There is no specific treatment but patients should be advised to contact the hospital team if they develop pins and needles, numbness, tingling or pain in their extremities or difficulty in fine motor skills, or if they begin to stumble when walking. These side effects usually begin to disappear when treatment is completed (or terminated) but can persist.

Skin toxicity Skin toxicity can be a problem with fluoropyrimidines, in particular with capecitabine (Xeloda), where patients suffer "hand foot syndrome". This is characterised by red swelling and blistering of the palms (with splitting of the ends of the fingers) and soles of the feet, which can make normal use of the hands and walking difficult.

EGFR inhibitors also cause skin toxicity in the form of a distinctive pustular, papular rash that usually involves the face, head and upper torso. This can be painful and dramatic.

Patients on either of these treatments should be encouraged to use moisturisers and barrier creams to keep their skin well hydrated. Anecdotally, patients with EGFR skin rash have benefitted from using colloidal oatmeal based products, such as Aveeno, and a product called Udderly Smooth. More severe cases are treated with steroids and tetracycline antibiotics.

Alopecia Alopecia due to suppression of the hair follicles is often seen during cytotoxic therapy. Hair loss normally becomes apparent three to five weeks after starting treatment. The process is reversible and hair will grow after treatment but its colour and texture may change. Wearing a cold cap (a specially designed cap that reduces blood flow to the scalp) before, during and after chemotherapy can reduce the risk or severity of hair loss. However, cold capping is not appropriate for tumours that commonly metastasise to the scalp (eg, lymphomas).

Other advice

Loss of appetite and weight loss can be a concern. Many cytotoxics alter the taste of food (eg, platinum drugs cause a metallic aftertaste) and radiotherapy on the mouth can also change taste, leading to loss of appetite. Sore mouth problems and nausea and vomiting can also contribute. Patients should be encouraged to maintain a high calorie, healthy balanced diet.

Those avoiding foods that taste strange can be advised to try them again every few weeks because taste may return to normal. If all foods seem to taste the same, strong flavours are recommended (eg, adding herbs, garlic, lemon juice and spices [although those with sore mouth should avoid spicy foods] and marinating).

Cancer patients and their carers might also seek advice on complementary products. There is little evidence to support the use of complementary medicines, such as herbal supplements, to treat cancer but patients are often keen to take something they believe will help. General advice should be to exercise caution over taking these products while receiving anticancer medicines. The Royal College of Radiologists Faculty of Clinical Oncology has issued advice to doctors on herbal and nutritional supplements and their interactions with cancer treatment.[7] Useful points are listed in Panel 2.

Pharmacists have an important role in supporting patients receiving anticancer medicines. Part of this challenge is knowing where to access appropriate information on anticancer medicines. The British National Formulary is not the best source of drug information about cancer treatments — most chemotherapy regimens are given as combinations of drugs with doses often different from those quoted (see Resources).

With the continual growth in numbers of cancer patients and recent management targets pharmacists in all sectors will be expected to contribute to the care of cancer patients and give expert advice on their medicines.

Signposting

- The Macmillan Cancer Support and Cancer Research UK websites (www.macmillan.org.uk and www.cancerhelp.org.uk) contain a lot of useful information for patients and carers.
- Macmillan Cancer Support also operates a support line (0808 808 0000), which is open Monday to Friday 9am to 8pm.

Further reading/resources

- Pazzur R (editor). Cancer management: a multidisciplinary approach medical, surgical & radiation oncology. 12th edition. Available via www.cancernetwork.com.
- Williamson S, Polwart C. The oral anticancer medicine handbook. North of England Cancer Network 2009.
- The Royal Pharmaceutical Society has a guidance pack to help pharmacists in the early diagnosis of lung cancer. This can be accessed at www.rpharms.com.

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PRACTICE POINTS

Reading is only one way to undertake CPD and the regulator will expect to see various approaches in a pharmacist's CPD portfolio.

1 Does your area have a 24-hour helpline for chemotherapy patients? Find out.
2 Discuss with a colleague, the questions you would ask a patient undergoing chemotherapy to assess their well-being.
3. Identify your local oncology pharmacist (all trusts treating cancer are required to have a pharmacist trained in oncology) who will be able to advise on cancer treatments and options for managing side effects.

Consider making this activity one of your nine CPD entries this year.