



Position statement on safe practice and the pharmaceutical care of patients receiving oral anticancer chemotherapy January 2004

Background ⁽ⁱ⁾ :

Anti-cancer chemotherapy is one of the rare fields of therapeutics in which, with the exception of haematology, most treatment has historically been given intravenously. Until recently very few of the available drugs were suitable for oral administration, thus most treatment has hence been administered only by specialist staff. In the last two years several new oral anti-cancer agents have become commercially available and many more are in the development pipeline. Roche estimated that in 2002 alone over 4000 patients were treated with capecitabine and by 2005 it is likely that tens of thousands of outpatients will be receiving oral anti-cancer treatment of some kind.

Oral anti-cancer treatment may offer advantages to patients and to the NHS. It does not necessitate admission or *direct* supervision and places a lesser burden on pharmacy and nursing staff in overstretched chemotherapy reconstitution and day units. For pharmacy, although there may be a considerable reduction in the workload of the chemotherapy reconstitution unit, a very significant burden may be shifted to dispensaries and to less specialised staff. To manage this transition safely & efficiently thorough planning will be needed. Treating patients with oral drugs challenges the traditional approach to anti-cancer treatment, particularly the use of potent anti-cancer chemotherapy drugs, which have a narrow therapeutic index. Home-based treatment may continue for weeks at a time without direct professional intervention or supervision. The significance of and reasons for intermittent, pulsed, treatment may be hard for some patients to grasp yet misinterpretation carries the risk of serious harm. Education of primary care professionals and patients about the use and potential for misuse of oral chemotherapy will be critical to patient safety⁽ⁱⁱ⁾

Compliance with treatment is relatively easy to achieve when professionals administer treatment personally. When the responsibility for administration is shifted to the patient, safe and effective treatment requires concordance rather than, simply, compliance. Cancer patients are often thought of as well motivated to comply with their treatment instructions. In a study of patients with lymphoma, Lee et al⁽ⁱⁱⁱ⁾ found 100% overall compliance for oral medicines. In a study of breast cancer patients however, Lebovitz et al^(iv) found that only 43% took their oral cyclophosphamide as prescribed and some exceeded the prescribed dose. Experience with capecitabine has shown the importance of ensuring that patients recognise side-effects so that treatment can be modified accordingly⁽ⁱⁱ⁾

Definitions

For the purposes of this document the term "oral anticancer drugs" is used to refer to all drugs with direct anti-tumour activity, orally administered to cancer patients, including

Drugs such as bexarotene, busulphan, capecitabine, chlorambucil, cyclophosphamide, estramustine, fludarabine, hydroxyurea, idarubicin, melphalan, methotrexate, procarbazine, tegafur/uracil, tioguanide. Oral vinorelbine is likely to be licensed in 2004.

Partially targeted treatments such as imatinib and gefitinib

Other drugs such as thalidomide

Pulsed, intermittent treatments where oral administration replaces parenteral administration in cyclical regimens; chronic maintenance therapies.

It does *not* include hormonal or anti-hormonal agents.

- *It would be inappropriate for BOPA to make firm recommendations about non-oncology practice. We recognise, however, that many cytotoxic agents and other potentially hazardous drugs are*

used in other specialities. We urge oncology pharmacists to draw these guidelines to the attention of relevant colleagues and to encourage them to apply the principles to their own areas of practice

Principles of Safe Practice

The principles of the chemotherapy standards in the Manual of Cancer Standards (or the equivalent for Wales & Scotland) should always be applied

All cancer patients receiving active anti-cancer treatment should be under the care of specialist oncology/haematology staff.

Trust chemotherapy policies and procedures must explicitly encompass oral as well as parenteral chemotherapy

All anticancer drugs, whether conventional or non-conventional cytotoxics, should be regarded as potentially hazardous, regardless of the intended route of administration. Formal risk assessment should be applied to determine for each drug the level of risk posed and hence the risk reduction and management strategy needed.

The prescribing and dispensing of oral chemotherapy should be carried out and monitored to the same standards as those for parenteral chemotherapy.

Responsibility for administration of oral drugs ultimately lies with the patient (or a relative or carer) but it is the responsibility of all members of the multidisciplinary oncology/haematology team to ensure as far as practically possible they are adequately prepared for this.

Effective communication between primary and secondary care and with patients is pivotal to safe and effective treatment

Other than in exceptional and clearly defined and mutually agreed circumstances, prescribing and dispensing should remain the sole responsibility of the hospital-based oncologist/haematologist and pharmacy respectively.

Prescribing

Prescribers should have expert guidance and support at the point of prescribing

All anticancer drugs should be prescribed only in the context of written protocols

The treatment plan should be documented in the notes and should include criteria for modifying and stopping treatment.

Electronic systems, or prescription proformas or templates, similar to those for parenteral chemotherapy should be used

Prescriptions must state clearly for each course of treatment, the dose, frequency of administration, intended start date, duration of treatment and, where relevant, the intended stop date.

For drugs for which a variety of schedules are in common use it is especially important that the intended schedule is unambiguously specified on every prescription. (Capecitabine, for example, may be given 2 weeks on treatment & 1 week off, 3 weeks on and 1 week off, 2 weeks on and 2 weeks off or continuously).

All intended deviations from protocol, such as dose modifications, should be clearly identified as such

Dispensing & labeling

Prescriptions must be screened by authorised pharmacists before dispensing

All pharmacy staff who are or could be involved with dispensing oral anticancer drugs must have access to full copies of all the relevant protocols

All dispensary staff must have ready access to specialist oncology pharmacy advice

The information available to dispensary staff must address the management of toxicity, the criteria for mid-course dose adjustments or stopping treatment, and identify in what circumstances and with which drugs continuous rather than intermittent treatment may be used.

This applies to all treatment, both in and outwith the context of Clinical Trials

Dispensary staff should work to detailed operating procedures analogous to those used for dispensing parenteral chemotherapy

The format and detail of dosing instruction should be standardised and approved by an appropriate senior pharmacist. Label directions must be clear and unambiguous and include where relevant, the intended period of treatment, start and stop dates (for short term or intermittent treatment) and an appropriate indication of the need for safe handling.

Whilst it is *essential* that all patients receive a manufacturer's PIL with their oral chemotherapy

drugs the use of unbroken patient packs may also pose risks to patients if they are then given more tablets than are needed for the intended course of treatment. The decision on whether or not to issue whole packs should therefore be based on a documented local risk assessment. Manufacturers' PILs may be supplemented with locally developed information. Consideration must be given to the management of patients with swallowing difficulties. Avoid breaking/crushing tablets or opening capsules whenever possible : Queries should be directed to the local pharmacy medicines information service : the advice of an oncology or technical services pharmacist must be sought. Use of a suspension or solution is preferred and a suitable preparation should be obtained from an NHS hospital pharmacy or commercial compounding/manufacturing facility with appropriate safe-handling facilities.

Patient Education & Information

Before every treatment cycle, all patients should be seen by a specialist pharmacist or nurse. The pharmacist/technician handing the drugs to the patient (or relative or carer) must ensure that they fully understand

- how and when to take their medicines. Some patients may find it particularly hard to remember the idea of repeated short courses of treatment with 'gaps' between them.
- what to do in the event of missing one or more doses
- what to do in case of vomiting after taking a dose
- likely adverse effects and what to do about them
- the need for and how to obtain further supplies
- the role their GP is expected to play in their treatment
- principles of safe handling, storage and disposal
- that if used, medicine spoons or measures should be used once only and then disposed of safely.

As much of this information as possible should first be given at the pre-treatment visit and reinforced on subsequent visits.

This responsibility should be confined to staff who have received training specifically for the role. When drugs are handed to the patient by non-pharmacy staff this should be the responsibility of a specialist nurse trained to the same standard.

Patients' access to advice and support when at home

Patients should be provided with details of appropriate and readily accessible 24-hour points of contact with medical, nursing and pharmacy staff to which they can direct queries.

General risk management

Prescribing and dispensing arrangements and procedures should take into account the

- risk of wastage due to the possible need for interruption of treatment, dose modifications, inappropriate storage, loss of medicines by a patient
- risk to others, especially young children, if the medicine is not safely stored in the home

Trusts should also consider the implications of the changes in activity type on their contract income. This will further depend on whether treatment consists of single agent oral therapy or an oral & i.v. combination regimen.

Audit

All aspects of practice should be subject to regular audit

References :

(i) Adapted from O'Neill VJ, Twelve CJ. (2002) Oral cancer treatment : developments in chemotherapy and beyond. Br J Cancer, 87: 933-937

(ii) Cassidy J, Twelves C, Cameron D, Steward W, O'Byrne K, Joddrell D, Banken L, Goggin T, Jones D, Roos B, Bush E, Weidekamm E, Reigner B (1999) Bioequivalence of two tablet formulations of capecitabine and exploration of age, gender, body surface area and creatinine clearance as factors influencing systemic

exposure in cancer patients. *Cancer Chemother. Pharmacol*, 44: (6) 453-460

(iii) Lee CR, Nicholson PW, Souhami RL, Deshmukh AA. (1992). Patient compliance with oral chemotherapy as assessed by a novel electronic technique. *J Clin Oncol*, 10: (6) 1007-1013

(iv) Lebovits AH, Strainn JJ, Schleifer SJ. (1990) Patient non-compliance with self-administered chemotherapy. *Cancer*, 65: 17-22