High Technology Drugs for Cancer
The Decision Process for Adding to a Formulary

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The management of drugs used in the treatment of cancer is receiving increased attention because of the recent acceleration in the pace of new drug development. Biotechnology products used primarily for the treatment of cancer patients, such as aldesleukin (interleukin-2), filgrastim (granulocyte colony-stimulating factor; rG-CSF) and sargramostim (granulocyte-macrophage colony-stimulating factor; rGM-CSF), have already reached the marketplace. Antisense oligodeoxynucleotides currently being studied may enable manipulation of individual nucleic acid sequences (oncogenes) that encode proteins active in the malignant process (Beardsley 1992; Heikkila et al. 1987; Szczylfik et al. 1991). Limited trials of genetically modified cells for treatment of breast and ovarian cancer, melanoma and brain cancer are pending as well (Erickson 1992).

Although high technology drugs are often equated with the products of biotechnology (Herfindal 1989), other new pharmaceutical technologies are also being used to produce innovative drugs and dosage forms for cancer therapy. Nanoparticles, microcapsules, microspheres, liposomes and polyethylene glycol covalent linkages represent new microcarrier systems that selectively deliver drug molecules to malignant tissue or reduce toxicity in normal tissue (Gupta 1990; Ho et al. 1986; Ranade 1989).

High technology drugs are very expensive to develop and produce. Extensive preclinical and clinical testing are necessary before approval for marketing. As new molecular targets emerge, and as the rate of new drug introductions increases, individuals, institutions and governments will have to decide whether the benefits of these therapies merit their costs. This necessitates a structured, disciplined approach to drug evaluation, formulary selection and drug use monitoring. Incorporation of pharmacoeconomic evaluation into the drug selection process for high technology cancer drugs will undoubtedly form an important part of this process.

Although some data have been generated on the pharmacoeconomics of biotechnology drugs (Jones-Grizzle & Bootman 1992), there are limited data concerning the pharmacoeconomics of other high technology drugs for cancer. In this article we review the approaches used to evaluate and select cancer drugs for inclusion in the formulary, based on a survey of English language literature since 1984.

1. The Formulary System

The concept of drug formularies can be traced back several centuries (Franke et al. 1964; Pearce & Begg 1992). The formulary concept has expanded beyond institutions to include managed healthcare groups (Kreling & Mucha 1992) and government-sponsored drug programmes (Greer 1992).

1.1 Traditional Formulary Systems

Formularies have served traditionally as a compiled listing of pharmaceuticals that ‘reflect the current clinical judgement of the medical staff’
Traditional approaches to formulary decision making focus on the concept of technical efficiency (using the least costly inputs to achieve the desired outcome). Agents that produce the desired therapeutic effect, possess an acceptable tolerability profile, and have the lowest cost are selected for inclusion. Physicians are encouraged to use these agents, but rarely are prevented from using non-formulary drugs.

The original intention of the formulary system was to improve prescribing and to minimise drug therapy costs. However, there is limited evidence supporting the success of traditional formularies in achieving these goals (Green 1986). A recent survey in the US found that over 70% of the formularies consisted of a simple approved drug list, without defined processes to promote optimal drug use (Rascati 1992). More aggressive formulary strategies have been recommended to realise improved prescribing and control of drug costs (Abramowitz & Fletcher 1986).

1.2 Contemporary Formulary Systems

The contemporary formulary is an active system intended to improve the quality and cost effectiveness of drug therapy. Compared with a traditional formulary system, it places greater emphasis on the economic efficiency of different drugs and goes beyond drug selection to include drug use management strategies (Abramowitz & Fletcher 1986; Herfindal 1989). This shift in focus is driven by the reality that no society can afford to allow unrestricted use of each of the high technology drugs that becomes available. Pharmacoeconomic analyses, as well as ethical and legal considerations, should play an important role in contemporary formulary decision making.

There is evidence that lower drug expenditures accrue in hospitals that use contemporary formulary strategies versus traditional formulary systems (Hazlet & Hu 1992). However, the impact of these strategies on the quality of pharmacotherapy is still debated. The contemporary approach to formulary management includes therapeutic and economic evaluation of products, development of criteria for drug use, retrospective and prospective monitoring, and promotion of rational drug use.

2. Steps in the Formulary Process

The decision-making process for adding a drug to the formulary depends on the drug use management system (traditional or contemporary) that is in place. The following steps are typical of those used by facilities that have opted for a more active approach.

2.1 Pharmacological and Clinical Evaluation

To request that a new drug be added to the formulary, the prescriber submits a detailed clinical justification for drug use to the pharmacy and therapeutics (P & T) committee (American Society of Hospital Pharmacists 1991). The evaluation of submissions received for high technology drugs may go beyond the knowledge base of P & T committee members. Some institutions use subcommittees to evaluate the clinical efficacy and role of new drugs (Seltzer et al. 1992). Drawing on clinicians who have expertise in the relevant specialty, the subcommittee evaluates the available data and arrives at a consensus concerning the appropriate clinical role of the product.

At this point in the process, only the clinical decisions concerning the use of the drug are addressed. Economic and ethical dilemmas associated with the use of the drug should be set aside for later consideration. A useful decision model that separates the technical and ethical components of biomedical decisions has been published (Holmes 1979).

The application of clinical decision analysis (CDA) to this step in the process may expand in the future. While the theory underpinning CDA is beyond the scope of this article (Weinstein & Feinberg 1980), the application of the process in the context of cancer treatment deserves consideration. CDA provides a systematic approach to decision making, despite the fact that some information may be unobtainable (Crane et al. 1991). In cancer therapy, especially with new high technology