NICE and Herceptin

November 2005

The recent intervention by Secretary of State for Health Patricia Hewitt in the row over the use of the breast cancer drug Herceptin has once more raised questions about how decisions should be reached about the costs and benefits of new drugs and therapies in the NHS.

Herceptin

Herceptin (the brand name for the drug trastuzumab) is used in the treatment of breast cancer. It is only suitable for people with a particular form of breast cancer, who represent about 20 per cent of overall cases.

It was approved for use in the NHS in 2002, but only for patients with the advanced form of the disease, in other words, once the cancer had spread from the breast. This year, however, pressure has been building from patient groups, charities and the drug’s manufacturer Roche to extend the drug’s use to patients with early breast cancer, following some new results from three clinical trials. However, Herceptin is not yet licensed for use in early stage breast cancer, either in the UK or elsewhere in the world. Without a licence, it cannot be submitted for approval by the body that issues guidelines to the NHS on the clinical and cost effectiveness of therapies, the National Institute for Health and Clinical Excellence (NICE).

Health Secretary ‘fast tracks’ use of Herceptin

The Secretary of State has made clear her view that wider use of Herceptin should be approved for the NHS as a whole. In October, when it became clear that the application for a licence had not yet been made by the manufacturers, she ordered that the drug be ‘fast tracked’ by NICE as soon as an application had been made and that, in the meantime, women with breast cancer should be tested for their suitability for the drug. Although only clinicians and PCTs have the right to decide whether to use an unlicensed drug, Patricia Hewitt insisted that PCTs should consider funding the drug ‘because I believe it is the right thing to do’. Several PCTs have since offered to fund the drug. On 9 November, North Stoke Primary Care Trust reversed its earlier decision to refuse Herceptin to a patient with early stage breast cancer after the Secretary of State announced that she was ‘very concerned’ about their decision and called a meeting with their officials.

This intervention at ministerial level represents a substantial deviation from the procedures set up to recommend therapies for use in the NHS.

The standard process for new drug approval in the UK

Manufacturers first need to get a licence from either the European Medicines Agency (EMEA) or the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK. These agencies independently assess the safety and clinical effectiveness of drugs and other products.

The next level of approval, deciding whether a drug or treatment is appropriate for use in the NHS, is given by the National Institute for Health and Clinical Excellence (NICE). NICE was set up by the Labour government in 1999 as an independent source of advice on drugs and clinical best practice for the NHS. For drugs, NICE reviews the evidence on safety and clinical effectiveness, but goes further than the regulators, by assessing whether the drug in question represents value for money for the tax-funded NHS that has finite resources. Decisions are made by committees of individuals who are independent with no vested interests, either political or commercial.

Appraisals involve working with health care professionals, drug manufacturers and representatives of patients and the public. NICE also commissions independent assessments (usually from academic organisations) of the available evidence on both clinical and cost effectiveness and may commission additional work to, for example, model long-term effects of therapies. Those giving evidence to NICE are required to declare any interests, including charitable organisations. So, for example, the UK Breast Cancer Coalition is recorded in the official NICE minutes as having received funding from Roche in 2002, when charities were lobbying to get Herceptin approved the first time around.

NICE appraisals are seen as an important tool to deal with a problem that affects all health care systems in developed countries: how to prioritise the constantly increasing demand for new technologies from increasingly
well-informed networks of patient groups and clinicians. The downside is that the deliberations of the agency may delay the introduction of effective new medicines. The pressure on both clinicians and politicians is all the greater when those interventions are or may be life saving.

Nevertheless, the system does provide safeguards, which, in the case of Herceptin, the Secretary of State appears to have sidestepped. Initially it appears she was certain enough of the merits of a new technology to insist that NICE fast-track the drug. Now she has, in effect, pre-empted the eventual decision of NICE as well as of the EMEA/MHRA by putting pressure on providers to use an unlicensed drug.

**Issues raised by circumventing NICE**

The merits and demerits of the wider use of Herceptin are now being debated on the pages of medical journals and more widely in the press. There are three trials of the drug in existence, two in the United States and one international, all partly funded by the manufacturer Roche. The results from the studies were reported last month in the *New England Journal of Medicine*. Their editorial hailed as 'revolutionary' the potential of the drug to reduce significantly the recurrence of tumours in early stage breast cancer by at least 50 per cent.v

There are two caveats, both referred to in the research reports. First is the known risk of congestive heart failure, a risk serious enough to warrant a new warning by the US Food and Drug Administration, based on data from one of the studies. vi The warning contained advice to doctors on how to monitor the risk and under what circumstances they should modify the dosage or even stop using the drug altogether. The second caveat concerns the timescale: the dramatic reductions in tumour recurrence have been tracked over a relatively short period - 12 months - and the efficacy of the drug in the longer term remains unknown. Tumour recurrence is a short-term outcome measure but there is limited evidence about the drug’s contribution to long-term (five-year or longer) survival. Sceptics point to the uncertainty over long-term survival, particularly when compared to the known risk of heart failure.vii

An editorial in *The Lancet* has called for a more rational approach, with NICE to be given the time it needs to properly assess the clinical and cost effectiveness of the drug.viii

In summary, circumventing the standard process for new drug approval raises two important issues:

Fast-tracking might equate to more risk: NICE has been instructed to begin reviewing the evidence about Herceptin at the same time as the European drugs regulator, the EMEA, is doing so. In the past, NICE would begin the process only once the regulator had completed its deliberations, by which time more evidence about the safety and effectiveness of new drug would be available for scrutiny. More speed might equate to more risk.

Local decisions being undermined: The government has chosen to pre-empt the decision-making process in NICE and also to override decisions at local PCT level. As discussed above, the appraisal process at NICE has been designed to be independent. Once a drug or technology has been recommended by NICE, the NHS should then begin to implement it as best practice. NICE has no formal role to play in making sure that the drugs are actually used across the NHS (and there have been obvious failures to follow NICE advice), but NICE has signalled its intention to collect and disseminate information on whether the NHS is following its advice. For cancer, it has published audits on drugs, including Herceptin, undertaken by the National Audit Office, cancer charities and Roche.ix However, in instances where there is no guidance, or guidance is still being worked on, the decisions rest at local level: ‘NHS bodies should continue to use existing arrangements to access the publicly available evidence and to determine local policies for the managed entry of the new intervention’.x Despite its rhetoric on increasing local autonomy in the NHS in general, the government has clearly indicated that, in this case, the centre knows best.

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i DH press release Hewitt fast-tracks cancer drug to save 1000 lives DH press release 2005/0339 Wednesday 5th October 2005

ii Speech by Rt Hon Patricia Hewitt MP, Secretary of State for Health, 25th October 2005


iii BBC News, Tuesday 6th November

http://news.bbc.co.uk/1/hi/england/staffordshire/4419618.stm

iv New England Journal Of Medicine, Vol 353, 16, 1724-136 October 20, 2005 r

http://content.nejm.org/cgi/content/full/353/16/1734


vi http://www.commonground.ca/iss/0510171/cg171_cancerdrug.shtml


viii NICE http://www.nice.org.uk/page.aspx?o=17519 Minutes of the Technology Appraisals Committee Meeting held on 20th March 2001

ix http://www.nice.org.uk/page.aspx?o=implementation

x Department of Health HSC/1999/176

http://www.dh.gov.uk/PublicationsAndStatistics/LettersAndCirculars/HealthServiceCirculars/HealthServiceCircularsArticle/fs/en?CONTENT_ID=4004777&chk=x6f5Xo