



*National Institute for  
Clinical Excellence*

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Clinical Excellence**

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***Guidance on  
the use of  
trastuzumab  
for the  
treatment of  
advanced breast  
cancer***

## Technology Appraisal No. 34

Guidance on the use of trastuzumab for the treatment of advanced breast cancer.

**Issue date:** March 2002

**Review date:** April 2005

### Ordering Information

Copies of this guidance can be obtained from the NHS Response Line by telephoning 0870 1555 455 and quoting ref: N0064. A patient version of this document can be obtained by quoting ref: N0066.

A bi-lingual patient leaflet is also available, ref: N0067.

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### Distribution of Guidelines

This document has been circulated to the following:

- Health Authority Chief Executives in England and Wales
- NHS Trust Chief Executives in England and Wales
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- Local Health Group General Managers
- Medical and Nursing Directors in England and Wales
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### This guidance is written in the following context:

This guidance represents the view of the Institute which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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**Guidance on  
the use of  
trastuzumab  
for the  
treatment of  
advanced  
breast cancer**

**1. Guidance**

- 1.1 Trastuzumab in combination with paclitaxel (combination trastuzumab is currently only licensed for use with paclitaxel) is recommended as an option for people with tumours expressing human epidermal growth factor receptor 2 (HER2) scored at levels of 3+ who have not received chemotherapy for metastatic breast cancer and in whom anthracycline treatment is inappropriate.
- 1.2 Trastuzumab monotherapy is recommended as an option for people with tumours expressing HER2 scored at levels of 3+ who have received at least two chemotherapy regimens for metastatic breast cancer. Prior chemotherapy must have included at least an anthracycline and a taxane where these treatments are appropriate. It should also have included hormonal therapy in suitable oestrogen receptor positive patients.
- 1.3 HER2 levels should be scored using validated immunohistochemical techniques and in accordance with published guidelines. Laboratories offering tissue sample immunocytochemical or other predictive tests for therapy response should use validated standardised assay methods and participate in and demonstrate satisfactory performance in a recognised external quality assurance scheme.

This section (Section 1) constitutes the Institute's guidance on the use of trastuzumab for the treatment of advanced breast cancer. The remainder of the document is structured in the following way:

2 Clinical Need	8 Related Guidance
3 The Technology	9 Review of Guidance
4 Evidence	Appendix A: Appraisal Committee
5 Implications for the NHS	Appendix B: Sources of Evidence
6 Further Research	Appendix C: Information for Patients
7 Implementation	

A bi-lingual summary is available from our website at [www.nice.org.uk](http://www.nice.org.uk) or by telephoning 0870 1555 455 and quoting the reference number N0065.

Mae crynodeb ar gael yn Gymraeg ac yn Saesneg ar ein gwefan yn [www.nice.org.uk](http://www.nice.org.uk) neu drwy ffonio 0870 1555 455 gan ddyfynnu cyfeirnod N0065

## 2

### Clinical Need and Practice

- 2.1 Approximately 32,000 new cases of breast cancer were reported in England and Wales in 1996. In 1998, breast cancer caused over 11,000 deaths in England and Wales and was the leading cause of death in women aged 35 to 54 years.
- 2.2 Advanced and metastatic breast cancer (MBC) are defined by clinical staging based on the tumour, node and metastasis staging system (stage III denotes locally advanced disease and stage IV indicates metastatic breast cancer).
- 2.3 Between 16% and 20% of women initially presenting with breast cancer have advanced disease with distant metastases and around 50% of those presenting with early or localised breast cancer will eventually develop MBC.
- 2.4 Some breast tumours contain an amplification of the human epidermal growth factor receptor (HER2), which causes overexpression of the HER2 protein and is associated with a poorer prognosis. Approximately 15%-20% of people with MBC overexpress HER2 at the 3+ level, measured by immunohistochemical techniques. The average period of survival after diagnosis of MBC is 18-24 months, but this is reduced by up to 50% for patients overexpressing HER2.
- 2.5 First-line systemic therapy for advanced or metastatic breast cancer is chemotherapy for oestrogen receptor-negative patients (usually an anthracycline-containing regimen or sometimes a combination of cyclophosphamide, methotrexate and fluorouracil), and hormone manipulation therapy for oestrogen receptor-positive patients. However, the choice of therapy is influenced by the rate of progression and distribution of disease and by whether the drugs have already been administered as adjuvant therapies.
- 2.6 Current NICE guidance states that docetaxel and paclitaxel should be available for the treatment of advanced breast cancer where initial cytotoxic chemotherapy (including an anthracycline) has failed or is inappropriate.

## 3

### 3 The Technology

- 3.1 Trastuzumab is a recombinant humanised monoclonal antibody that specifically targets the HER2 protein. It is licensed for two indications for the treatment of MBC overexpressing HER2 at level 3+. Firstly, it is licensed in combination with paclitaxel for patients with MBC who have not received chemotherapy for metastatic disease and in whom an anthracycline is unsuitable. Secondly, it is licensed as a monotherapy for patients who have received at least two chemotherapy regimens for MBC; prior chemotherapy must have included at least an anthracycline and a taxane, unless these treatments are inappropriate; patients who are oestrogen receptor-positive must also have failed to respond to appropriate hormonal therapy.

- 3.2 Trastuzumab is administered intravenously. Following an initial loading dose of 4 mg per kg body weight, patients receive a weekly dose of 2 mg per kg body weight until disease progression. Side-effects associated with trastuzumab have been noted to include cardiotoxicity and infusion-related reactions.
- 3.3 The basic NHS price according to the British National Formulary (September 2001) for trastuzumab is £407 per 150 mg vial. For a typical patient, a 38-week course of combination therapy costs approximately £15,500 for trastuzumab and £9,600 for paclitaxel. The cost of a 12-week course of treatment with trastuzumab monotherapy is approximately £5,300.
- 3.4 There are costs of testing a woman's suitability for treatment and of monitoring in addition to the cost of administering treatment. HER2 levels must be assessed in patients who are potentially eligible for treatment with trastuzumab, and patients receiving trastuzumab should have left ventricular ejection fraction measured before and during treatment.

## 4

### Evidence

#### 4.1 Clinical effectiveness

##### **Combination therapy**

- 4.1.1 One randomised controlled trial (RCT) (n=469) of first-line trastuzumab combination therapy was available. All individuals had HER2 overexpression at least at level 2+. Patients who had not previously received anthracyclines were randomised to an anthracycline in combination with cyclophosphamide with or without trastuzumab. Patients who had previously received an anthracycline as adjuvant therapy (n=188) were randomised to paclitaxel (n=96) or paclitaxel plus trastuzumab (n=92). The primary endpoint was time to progression and the median duration of follow-up was 30 (range 30-51) months. Patients in all arms of the trial were given the option of receiving trastuzumab monotherapy at the time of disease progression, meaning that allocation to this further treatment was non-random.
- 4.1.2 When only the two relevant treatment arms involving paclitaxel were considered, there was no significant difference in overall survival between the group treated with trastuzumab plus paclitaxel and the group treated with paclitaxel alone (22 vs 18 months, p=0.17). However, the addition of trastuzumab resulted in longer median times to disease progression (7 vs 3 months, p<0.001), duration of response (11 vs 5 months, p<0.01) and time to treatment failure (6 vs 3 months, p<0.001). There was no statistically significant difference between the two treatments in terms of complete response (relative risk [RR] 3.65, 95% CI 0.89 to 15.22), but overall tumour response (RR 2.48, 95%

CI 1.49 to 4.12), disease progression (RR 0.38, 95% CI 0.27 to 0.53) and treatment failure (RR 0.46, 95% CI 0.33 to 0.63) favoured treatment with trastuzumab. For patients with HER2 3+, trastuzumab and paclitaxel was associated with a longer median survival than paclitaxel alone (25 vs 18 months, no p-value provided).

- 4.1.3 Quality of life, assessed using the pain and dyspnoea domains and the breast cancer module of the EORTC QLQ-C30 questionnaire, was higher in the group receiving trastuzumab plus chemotherapy than in the group receiving chemotherapy alone.
- 4.1.4 The most important adverse event seen in the trial was cardiac dysfunction, which occurred in 27% of the group given an anthracycline, cyclophosphamide and trastuzumab, 8% of the group given an anthracycline and cyclophosphamide alone, 13% of the group given paclitaxel and trastuzumab, and 1% of the group given paclitaxel alone. The cardiotoxicity was potentially severe, and in some cases life threatening, but the symptoms were reported generally to improve with standard medical management.
- 4.1.5 Although not originally observed during clinical trials, serious infusion-related reactions have been reported in 74 from a total of approximately 25,000 patients who received trastuzumab, with the reactions leading to the death of 15 patients. These reactions, which include anaphylaxis and severe dyspnoea, usually occur within 24 hours of the infusion, although delayed reactions have also been reported. Allergic or hypersensitivity reactions, haematological toxicity, hepatic and renal toxicity, diarrhoea and an increased risk of infections have also been noted.

### **Monotherapy**

- 4.1.6 No comparative RCTs of trastuzumab monotherapy (i.e. versus systemic therapy without trastuzumab) were available. Of the studies that were identified, two were case-series of trastuzumab (H0551g, n=46; H0649g, n=222) and one was a RCT of trastuzumab monotherapy, which was concerned with an unlicensed indication and was essentially a dose ranging study (H0650g, n=113). Women in H0650g received first-line monotherapy with trastuzumab, which is an unlicensed indication.
- 4.1.7 In H0649g, 4% of women experienced a complete response to treatment and 12% experienced a partial response. The overall response rate was 15%. Smaller proportions of women responded to treatment in study H0551g.

- 4.1.8 The median duration of survival in H0649g was 13 months for all women and 16 months in a sub-group analysis of women overexpressing HER2 at 3+ levels. In the manufacturer's submission, survival reported in H0649g was indirectly compared with survival reported in two RCTs of vinorelbine monotherapy. Both RCTs contained a treatment arm consisting of vinorelbine monotherapy as second-line or salvage therapy for MBC. In one of these RCTs, 91% of participants had received prior treatment with anthracyclines for advanced breast cancer. The median duration of survival for people receiving vinorelbine monotherapy was 8 months. The reported median duration of survival in the other study was 10 months. Participants in these two RCTs were not selected on the basis of their HER2 status, which may suggest that their prognosis was better than those in H0649g.
- 4.1.9 The manufacturer also submitted evidence from the Imperial Cancer Research Fund database at Guy's and St Thomas' Hospital NHS Trust on patients who had received third-line chemotherapy for MBC and who were not treated on the basis of their HER2 expression status. Analysis of these data showed that the median survival for these patients was 6.3 months.
- 4.1.10 Trastuzumab monotherapy appeared to have a relatively low toxicity level. For study H0649g, the common adverse events (occurring in approximately 40% of people) were infusion-related fever and/or chills that usually occurred only during the first infusion. The most clinically significant adverse event was cardiac dysfunction, which occurred in 10 people (5%). However, only 1% of participants in this study discontinued treatment because of treatment-related adverse events. In study H0551g toxicity was reported as minimal, although two patients died as a result of cardiac dysfunction. In study H0650g the adverse events recorded were mainly mild to moderate in nature and were mostly associated with the higher dose regimen; only one person experienced cardiac dysfunction.

## 4.2 Cost-effectiveness

### ***Combination therapy***

- 4.2.1 The manufacturer evaluated the cost-effectiveness of trastuzumab in combination with paclitaxel versus paclitaxel alone for patients with HER2 3+, based on results from the RCT. Estimates of direct medical and social care costs were included in the evaluation, including the costs of HER2 testing (£21 for a single test) and cardiac testing (£520-£640 for four tests).

4.2.2 The manufacturer estimated the incremental cost-effectiveness ratio to be £37,500 per Quality-Adjusted Life-Year (QALY) gained (and substantially less per life-year gained). This survival benefit used to estimate the QALY gain was based on a weighting of case-mix reflecting the selection of patients in the pivotal trial who, after the trial, crossed over to trastuzumab monotherapy. After extrapolating the trial results for this selection of patients, approximately 10 months mean survival advantage was imputed into the economic evaluation. A number of other sources, in particular two non-controlled studies that examined the use of taxane monotherapy as first-line treatment for metastatic breast cancer, suggest a survival advantage of combination therapy compatible, or even better, than this.

### **Monotherapy**

4.2.3 One economic evaluation of monotherapy comparing trastuzumab with vinorelbine monotherapy was available to the Committee. Direct information relating to clinical effectiveness was unavailable (as there were no RCTs of trastuzumab other than a dose ranging study). Health outcomes were expressed in terms of life years and QALY by extrapolating survival from non-controlled studies. Direct medical and social care costs were included in the evaluation. Information on clinical effectiveness was imputed from H0649g and an RCT of vinorelbine versus melphalan that contained patients who were at an earlier stage of the disease and who were not selected on the basis of HER2 expression status. Patients who received vinorelbine in the RCT survived for approximately a median of 8 months. The manufacturer referenced two other non-controlled studies in an attempt to validate this period of survival for patients receiving vinorelbine. One of these studies examined median survival in patients at a similar disease stage who received vinorelbine monotherapy; in this study, median survival was approximately 6 months.

4.2.4 The estimated incremental cost-effectiveness ratio was approximately £7,500 per life-year gained if trastuzumab was used instead of vinorelbine, when it was assumed that the additional survival attributable to trastuzumab monotherapy was 8 months. The manufacturers also provided a cost per QALY of approximately £19,000 by assuming that the 8 months of additional survival was equivalent to 2.6 quality-adjusted months.

## 4.3 Considerations

### *Combination therapy*

- 4.3.1 The Appraisal Committee considered that a survival gain of approximately 10 months used in the economic evaluation was likely to be an underestimate of the true survival gain attributable to combination therapy given that patients in the non-controlled studies of taxane monotherapy were not HER2 selected. The Appraisal Committee also concluded that the utility weights used to adjust survival for changes in quality of life were low.
- 4.3.2 Based on these factors, the Appraisal Committee believed that trastuzumab combination therapy was likely to be lower than the estimate of £37,500 per QALY gained provided by the manufacturer.
- 4.3.3 The Appraisal Committee also noted that improvements in survival of this magnitude due to therapeutic intervention have rarely been recorded in women with metastatic breast cancer.

### *Monotherapy*

- 4.3.4 The evidence for the effectiveness of trastuzumab monotherapy was limited to two case-series and one RCT, which was concerned with an unlicensed indication and was essentially a dose ranging study. The report for the first case-series (H0551g) did not state the line of therapy being assessed or the length of follow-up. The second case-series (H0649g), which was relatively well reported, suggested that in terms of response rate trastuzumab monotherapy was an effective treatment in patients with MBC and HER2 overexpression at levels 3+.
- 4.3.5 Although the Appraisal Committee had some reservations about the quality and robustness of the economic evaluation for trastuzumab monotherapy, as survival was not based on results from controlled studies, it was believed that these misgivings would not increase the ratio sufficiently to suggest that it is not cost-effective.

## 5

### Implications for the NHS

- 5.1 Patients who receive treatment with trastuzumab should be monitored for the possibility of cardiotoxicity.
- 5.2 The manufacturer estimated the gross impact of providing trastuzumab plus paclitaxel instead of paclitaxel alone and trastuzumab monotherapy to be approximately £17 million per annum. This estimate is based on the following assumptions: HER2 status is assessed in 20,000 patients with

metastatic disease at a cost of £21 per test; 1600 patients receive monotherapy at a cost of £5,300 per person; 450 patients receive combination therapy costing an additional £15,500 to provide trastuzumab and paclitaxel instead of paclitaxel alone; each person receives four cardiac tests at a cost of £580 for each set of four tests. (Overall calculation:  $[20,000 \times £21] + [1,600 \times £5,300] + [450 \times £15,500] + [1,600 \times £580]$ ).

## 6

### Further Research

- 6.1 Information linking side-effects associated with treatments with quality of life would enhance the comprehensiveness of future economic evaluations of treatments for advanced breast cancer.

## 7

### Implementation

- 7.1 Clinicians with responsibility for treating women with breast cancer should review their current practice in the light of the guidance set out in Section 1.
- 7.2 Local clinical guidelines and protocols for the management of women with breast cancer should be reviewed in the light of this guidance.
- 7.3 It is likely that the rate of HER2 testing will increase as a result of this guidance. The suitability of current service provision for HER2 testing should be reviewed in the light of the guidance set out in section 1.3.
- 7.4 Prospective clinical audit programmes should record the proportion of treatments adhering to this guidance. Such programmes are likely to be more effective in improving patient care when they form part of the organisation's formal clinical governance arrangements and where they are linked to specific post-graduate activities.

## 8

### Related Guidance

- 8.1 The Institute issued guidance in September 2001 on the use of taxanes for the treatment of breast cancer:

National Institute for Clinical Excellence (2001) Guidance on the use of taxanes for the treatment of breast cancer: *NICE Technology Appraisal Guidance* No. 30. London: National Institute for Clinical Excellence. Available from: [www.nice.org.uk](http://www.nice.org.uk)

- 8.2 Guidance in progress and anticipated publication dates:

Guidance on the use of vinorelbine for breast cancer (July 2002)

Service Guidance for the NHS in England and Wales Improving Outcomes in Breast Cancer (July 2002)

Guidance on the use of capecitabine for breast cancer (March 2003)

## 9

### Review of Guidance

Identification and management of genetic risk in familial breast cancer (publication date to be confirmed)

- 9.1 This advice will be reviewed in the light of new evidence in April 2005, or earlier should significant new data become available.

Andrew Dillon  
Chief Executive  
March 2002

## APPENDIX A

### Appraisal Committee Members

The Appraisal Committee is a statutory committee whose members sit for 3 years. Two meetings are held per month and the majority of members attend one or the other. Declared interests may also exclude a member from individual technology appraisals. The Committee are supplemented by technology specific experts as indicated in Appendix B.

**Professor R. L. Akehurst**  
Dean, School of Health Related  
Research  
Sheffield University

**Professor David Barnett  
(Chairman)**  
Professor of Clinical Pharmacology  
University of Leicester

**Professor Sir Colin Berry**  
Professor of Morbid Anatomy  
St Bartholomew's and Royal London  
School of Medicine

**Dr Sheila Bird**  
MRC Biostatistics Unit,  
Cambridge

**Professor Martin Buxton**  
Director of Health Economics Research  
Group  
Brunel University

**Dr Karl Claxton**  
Lecturer in Economics  
University of York

**Professor Sarah Cowley**  
Professor of Community Practice  
Development  
Kings College, London

**Professor Nicky Cullum**  
Reader in Health Studies  
Department of Health Sciences  
University of York

**Mr Chris Evennett**  
Chief Executive  
Mid-Hampshire Primary Care Group

**Professor Terry Feest**  
Clinical Director and Consultant  
Nephrologist  
Richard Bright Renal Unit and  
Chairman of the UK Renal Registry

**Ms Jean Gaffin**  
Formerly Executive Director  
National Council for Hospice and  
Specialist Palliative Care Service

**Mrs Sue Gallagher**  
Chief Executive  
Merton, Sutton and Wandsworth  
Health Authority

**Dr Trevor Gibbs**  
Head, Global Clinical Safety &  
Pharmacovigilance  
GlaxoSmithKline

**Mr John Goulston**  
Director of Finance  
The Royal Free Hampstead NHS Trust

**Professor Philip Home**  
Professor of Diabetes Medicine  
University of Newcastle

**Dr Terry John**  
General Practitioner  
The Firs, London

**Dr Diane Ketley**  
Research into Practice Programme  
Leader  
NHS Modernisation Agency

**Dr Mayur Lakhani**  
General Practitioner, Highgate Surgery,  
Leicester and  
Lecturer, University of Leicester

**Mr M Mughal**  
Consultant Surgeon  
Chorley and South Ribble NHS Trust

**Mr James Partridge**  
Chief Executive  
Changing Faces

**Professor Philip Routledge**  
Professor of Clinical Pharmacology  
University of Wales

**Professor Andrew Stevens  
(Vice Chairman)**  
Professor of Public Health  
University of Birmingham

**Dr Cathryn Thomas**  
General Practitioner  
Senior Lecturer  
Department of Primary Care and  
General Practice  
University of Birmingham

## APPENDIX B

### Sources of Evidence

The following documentation and opinion was made available to the Appraisals Committee:

a. **Assessment Report:**

- Prepared by The NHS Centre for Reviews and Dissemination (*A rapid and systematic review of the clinical effectiveness and cost-effectiveness of trastuzumab and vinorelbine for breast cancer*, February 2001)
- Prepared by The NHS Centre for Reviews and Dissemination (*A rapid and systematic review of the clinical effectiveness and cost-effectiveness of trastuzumab for breast cancer*, October 2001)

b. **Manufacturer/sponsor submissions:**

- Roche

c. **Professional/specialist group submissions from:**

- British Psychosocial Oncology Society
- Imperial Cancer Research Fund
- MRC Clinical Trials Unit
- National Cancer Research Institute
- Royal College of General Practitioners
- Royal College of Pathologists
- Royal College of Physicians

d. **Patient group submissions from:**

- Breakthrough Breast Cancer, CancerBACUP and the UK Breast Cancer Coalition joint submission
- Breast Cancer Care
- Macmillan Cancer Relief

e. **Other group submissions from:**

- Department of Health
- National Assembly for Wales

f. **External expert and patient advocate submissions from:**

- Professor Robert Coleman, Professor of Medical Oncology, Cancer Research Centre, Weston Park Hospital, University of Sheffield
- Bernie Gardiner, Information Nurse Specialist, Breast Cancer Care
- Margaret King, Vice Chair, UK Breast Cancer Coalition

## APPENDIX C

### Guidance on the use of trastuzumab for the treatment of advanced breast cancer Patient information

The patient information in this appendix has been designed to support the production of your own information leaflets. You can download it from our website at [www.nice.org.uk](http://www.nice.org.uk) where it is available in English and Welsh. If you would like printed copies of the leaflets please ring the NHS Response Line on 0870 1555 455 and quote reference no N0066 for the English patient leaflet and N0067 for the bi-lingual patient leaflet.

#### What is NICE Guidance?

The National Institute for Clinical Excellence (NICE) is a part of the NHS. It produces guidance for both the NHS and patients on medicines, medical equipment, diagnostic tests and clinical and surgical procedures and under what circumstances they should be used.

When the Institute evaluates these things, it is called an appraisal. Each appraisal involves the manufacturers of the drug or device, the professional organisations and the groups who represent patients and their carers.

NICE was asked to look at the available evidence on trastuzumab (the brand name for this drug is Herceptin) and provide guidance that would help the NHS in England and Wales decide where they should be used in the treatment of advanced breast cancer.

#### What is advanced breast cancer?

Cancer is a disease of the body's cells. Normally, all cells divide and reproduce themselves in an orderly and controlled manner. In cancer, the cells multiply without proper control and grow into a lump (which is called a tumour).

Approximately 32,000 new cases of breast cancer were reported in England and Wales in 1996. In 1998, breast cancer caused over 11,000 deaths in England and Wales and was the leading cause of death in women aged 35 to 54 years.

Between 16 and 20 women out of every 100 diagnosed with breast cancer have a disease which has spread to other parts of the body. Around half of the women who are diagnosed with localised breast cancer will eventually develop metastatic cancer. It is called metastatic breast cancer if the cancer cells have spread to other parts of the body.

Some breast cancer involves a naturally produced protein in the body (called the epidermal growth factor). This protein attaches itself to another protein called HER2, which is found on the surface of the breast cancer cell. When combined they stimulate the cancer cells to multiply.

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**How is breast cancer treated?**

The type of treatment given to cancer patients depends on many factors. These include:

- the type of cancer,
- where in the body it started,
- what the cancer cells look like under the microscope,
- how far they have spread, if at all
- the general health of the patient

Patients are often given chemotherapy. Chemotherapy is the use of anti-cancer drugs to destroy cancer cells and usually involves a drug called anthracycline. However, the choice of treatment is influenced by how quickly the disease is developing, how far it has spread and by whether the drugs have been used previously.

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**What is trastuzumab (Herceptin)?**

Trastuzumab is a drug that specifically targets the HER2 protein. It attaches itself to the HER2 protein and prevents the protein that encourages cancer cell growth from reaching the cancer cell.

It can be used on its own or in combination with another drug called paclitaxel.

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**What has NICE recommended?**

NICE has recommended that trastuzumab (Herceptin) is recommended in certain circumstances for women with breast cancer:

- Trastuzumab (Herceptin) in combination with paclitaxel is recommended as an option for women with breast cancer who have not had chemotherapy for their metastatic breast cancer and for whom anthracycline treatment is not appropriate. However these women will also have had a test that shows their level of HER2 protein is measured as 3+.
- Trastuzumab by itself is recommended for women with tumours with HER2 at levels of 3+ who have had at least two chemotherapy treatments for metastatic breast cancer. Previous chemotherapy must have included at least an anthracycline drug and a taxane drug where these treatments are appropriate. It should also have included hormonal therapy in patients sensitive to oestrogen.

HER2 levels should be measured using validated techniques and in accordance with published guidelines. NICE have recommended that laboratories offering these tests should participate in and demonstrate satisfactory performance in a recognised external quality assurance scheme.

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**What should I do?**

If you or someone you care for has advanced breast cancer then you should discuss this guidance with your doctor or consultant.

  

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**Will NICE review its guidance?**

Yes. The guidance will be reviewed in April 2005.

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**Further Information**

Further information on NICE and the full guidance issued to the NHS is available on the NICE website ([www.nice.org.uk](http://www.nice.org.uk)).

The guidance can also be requested from the NHS Response Line on 0870 1555 455, quoting reference N0064.

If you have access to the internet and would like to find out more about advanced breast cancer, visit the NHS Direct website at [www.nhsdirect.nhs.uk](http://www.nhsdirect.nhs.uk).





