NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA 116 Breast cancer - gemcitabine

This guidance was issued in January 2007.
The review date for this guidance is January 2010.

Recommendation

- A review of the guidance should be placed on the static list. That we consult on the proposal.

Consideration of options for recommendation:

Options	Comment
A review of the guidance should be planned into the appraisal work programme.	There is no new evidence which changes that previously considered by the Appraisal Committee and therefore it is not appropriate to plan a review into the appraisal work programme.
The decision to review the guidance should be deferred [to a specified date].	There is no new evidence and therefore this is not an option.
A review of the guidance should be combined with a review of a related technology and conducted at the scheduled time for the review of the related technology.	No relevant guidance review has been identified.
A review of the guidance should be combined with a new appraisal that has recently been referred to the Institute.	This is not an option, as there are no relevant topics that have recently been referred to the Institute.
A review of the guidance should be incorporated into an on-going clinical guideline.	No update to the guidance is needed as there is no new evidence.
A review of the guidance should be updated into an on-going clinical guideline.	No update to the guidance is needed as there is no new evidence.
A review of the guidance should be transferred to the 'static guidance list'.	**There is no new evidence and therefore the guidance should be transferred to the 'static list'.**

Original remit(s)

To assess the clinical and cost effectiveness of gemcitabine for advanced or metastatic breast cancer.

Current guidance

Gemcitabine in combination with paclitaxel, within its licensed indication, is recommended as an option for the treatment of metastatic breast cancer only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate.

Relevant Institute work

Published

TA30 Taxanes for the treatment of breast cancer. September 2001. This guidance has been updated replaced by CG81 Advanced breast cancer.

TA34 Trastuzumab for breast cancer. March 2002. Should be updated as part of work on the Institute's upcoming breast cancer guideline (GE decision February 2005).

TA54 Vinorelbine for the treatment of advanced breast cancer. December 2002. This guidance has been updated replaced by CG81 Advanced breast cancer.

TA62 Capecitabine for the treatment of locally advanced and metastatic breast cancer. May 2003, this guidance has been updated and replaced by CG81 Advanced breast cancer.

CG81 Advanced breast cancer. February 2009. Expected review date 2012.

CSGBC Improving outcomes in breast cancer. August 2002. Expected review date: TBC.

In progress

Technology Appraisal (STA) - Breast cancer (advanced and/or metastatic) - sunitinib (in combination with capecitabine). Expected date of publication October 2011.

Technology Appraisal (STA) - Breast cancer (advanced or metastatic) – lapatinib. Expected date of publication TBC.

Technology Appraisal (STA) - Breast cancer (first line treatment) - sunitinib (in combination with a taxane). Expected date of publication TBC.

Technology Appraisal (STA) - Bevacizumab in combination with non-taxane chemotherapy for the first line treatment of metastatic breast cancer. Expected date of publication TBC.

Technology Appraisal (MTA) - Breast cancer (metastatic hormone-receptor) - lapatinib and trastuzumab (with aromatase inhibitor). Expected date of publication May 2011.

Suspended

Technology Appraisal (MTA) - Breast cancer - intensity modulated radiotherapy.

Technology Appraisal (STA) - Breast cancer (advanced or metastatic) hormone-sensitive – lapatinib

Technology Appraisal (STA) - Breast cancer (locally advanced or metastatic) – ixabepilone.

Technology Appraisal (STA) - Breast cancer - bevacizumab (in combination with a taxane). Expected date of publication TBC.

In topic selection

[redacted]

[redacted]

[redacted]

Safety information

None

Details of new indications

None

Details of new products

None

On-going trials

A Randomized Phase III Trial of Gemcitabine and Docetaxel Versus Gemcitabine and Paclitaxel in Patients With Metastatic Breast	Primary Outcome Measures: Time to progression Secondary Outcome Measures:

Cancer: A Comparison of Different Schedules	Pharmacology toxicity and Quality of Life Overall survival Overall response rate Estimated Study Completion Date: July 2010

New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline(R) In-Process and Embase. References from 2007 onwards were reviewed. No new information was identified.

A search of the American Society of Clinical Oncology's website identified a presentation at the 2007 Breast Cancer Symposium of final results for a Phase III study of gemcitabine plus paclitaxel compared with paclitaxel alone in patients with unresectable, locally recurrent, or metastatic breast cancer ('JHQG trial' NCT00006459). These results, presented in abstract form only, appear to confirm the benefit in favour of gemcitabine plus paclitaxel (hazard ratio 0.82, 95% C.I 0.67 to 1.00) with an overall survival advantage of 18.6 months (range 16.6 to 20.7) on the gemcitabine plus paclitaxel arm compared with 15.8 months (range 14.4 to 17.4) on the paclitaxel monotherapy arm.

Implementation

A submission from Implementation is attached at the end of this paper.

Equality and diversity issues

No additional equality and diversity issues have been identified.

Appraisals comment:

The manufacturer's submission for TA116 included the comparators, docetaxel monotherapy, docetaxel in combination with capecitabine and paclitaxel monotherapy. The Committee subsequently restricted the positive recommendation for gemcitabine in combination with paclitaxel to situations where docetaxel monotherapy or combination therapy were considered appropriate. The current treatment recommendations for people with metastatic breast cancer in the Advanced Breast Cancer Clinical Guideline (CG81) recommend anthracyclines as a first line treatment option unless contra-indicated. In the event of contra-indication or disease progression, the guideline recommends the use of single agent docetaxel followed by vinorelbine or capecitabine. The guideline further indicates that combination therapy (for example docetaxel in combination with capecitabine and under TA116 gemcitabine in combination with paclitaxel) may be considered for patients for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity. The recommendations in the clinical guideline do not include a recommendation

for paclitaxel monotherapy suggesting that the guidance in TA116 may not be a material restriction to the NHS.

The Appraisal Committee's decision to reject the manufacturer's assertion that gemcitabine in combination with paclitaxel offered a cost-effective alternative to paclitaxel monotherapy concerned the uncertainty around the overall survival estimate for paclitaxel monotherapy reported at the time as interim results from the JHQG trial. In particular, the 95% confidence interval for the hazard ratio for median overall survival included 1.00. Final results (subsequently presented in abstract form) do not differ from those presented to the Committee in the original appraisal. Therefore the completion of this clinical trial does not suggest a review is required. Further evidence of ongoing or completed relevant trials has not been identified during the search described above. The trial identified in the systematic search reported above compares different gemcitabine combination therapy schedules. As such it would not resolve or confirm the uncertainty associated with the clinical effectiveness of gemcitabine combination therapy with paclitaxel over paclitaxel monotherapy.

Although gemcitabine has become generic, there has been no change to the published list price of the technology since the appraisal. In addition the published list prices of the comparator technologies have not changed. Therefore, taking into account the recommendations in the NICE clinical guideline, the evidence base and the pricing of the technologies, there is no reason to suggest a review of this guidance is necessary.

Summary

No reasons that would require a reconsideration of the recommendations have been identified. Current guidance TA116 recommends gemcitabine only within certain circumstances and there is no change to the evidence underpinning that recommendation. The recommendations of TA116 have recently been incorporated in Clinical Guideline 81.

GE paper sign off: Helen Chung, Associate Director, 3 February 2010

Contributors to this paper:

Information Specialist: Hasina Fernandes
Technical Lead: Joanne Fielding
Technical Adviser: Zoe Garrett
Implementation Analyst: Mariam Bibi
Project Manager: Adeola Matiluko

Technology appraisal 112: Gemcitabine for the treatment of metastatic breast cancer

1. National Hospital Prescribing Data

1.1 Data showing trends in prescribing costs and volume are presented below. Unfortunately this data does not link to diagnosis so needs to be treated cautiously in relation to the specific recommendations of the guidance. Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Figure 1. Trend in cost of prescribing gemcitabine in hospitals in England

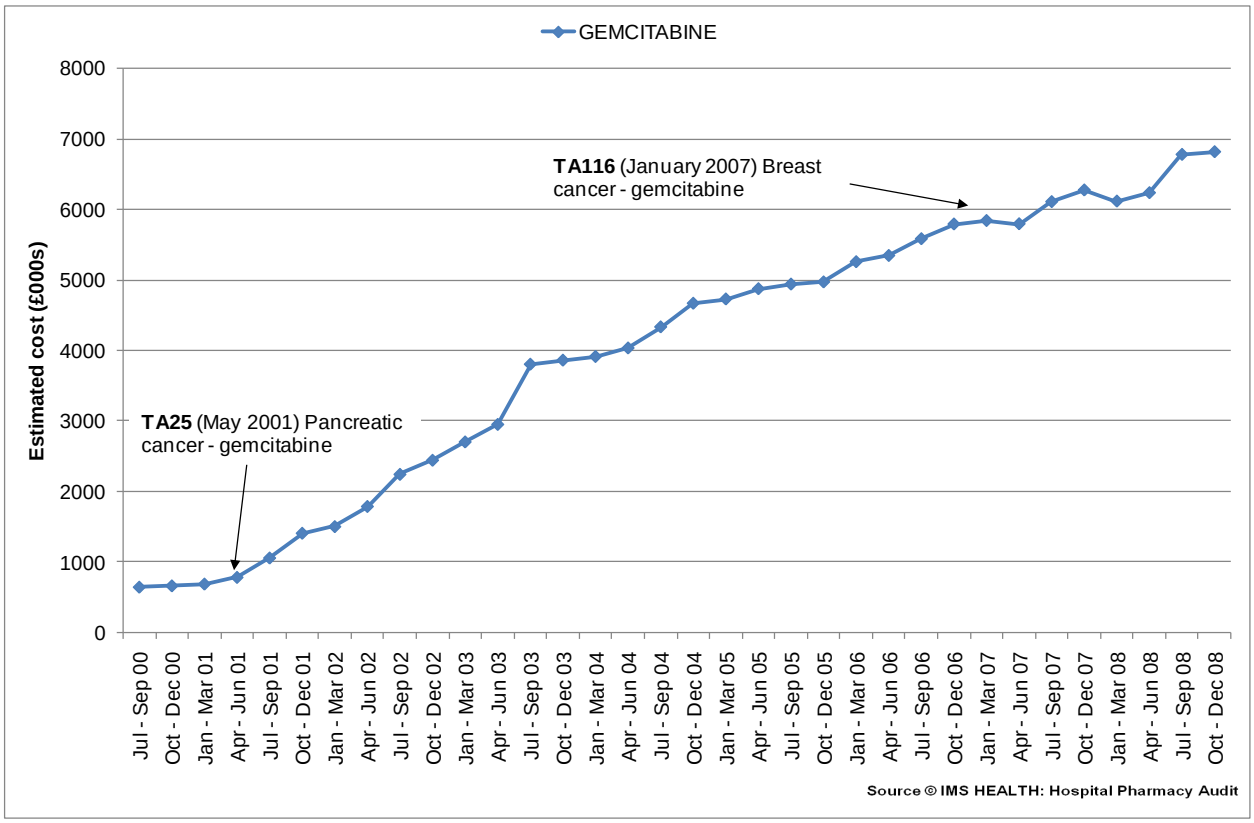
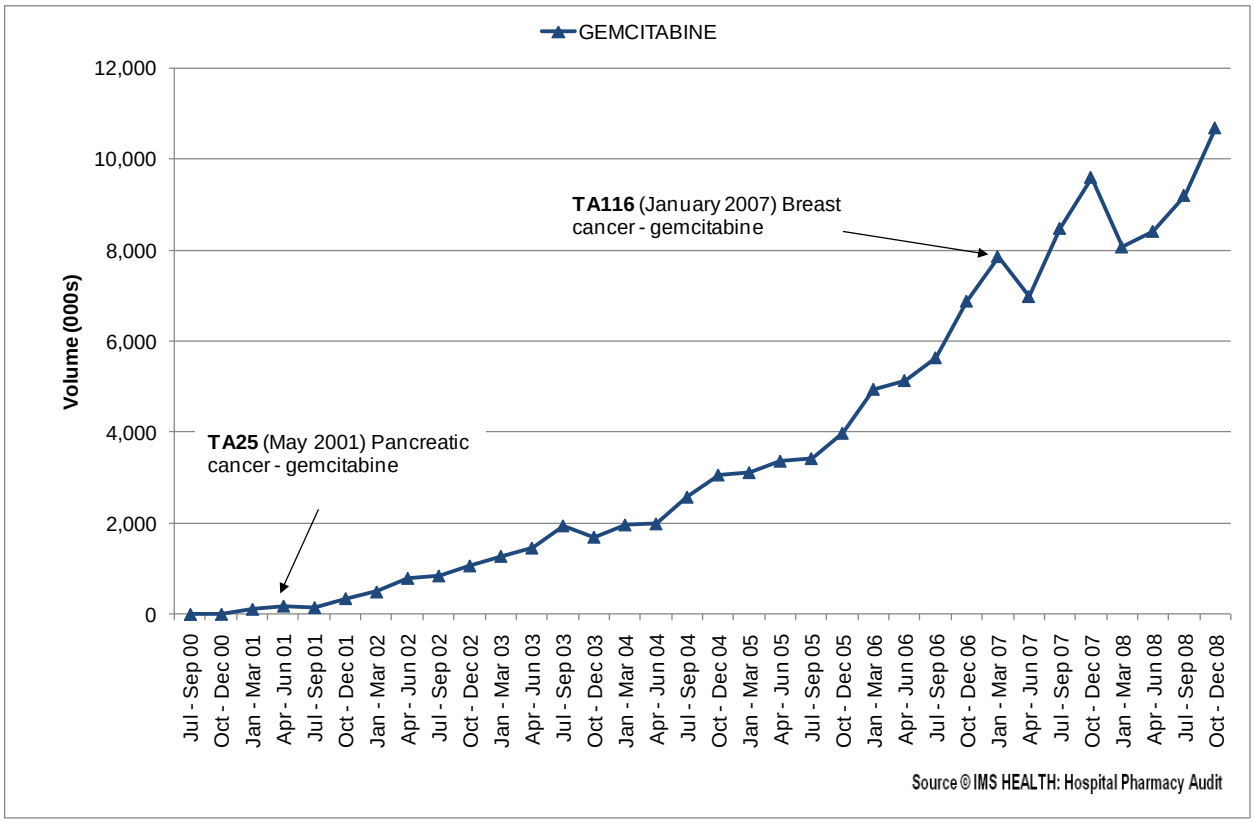


Figure 2. Trend in volume of prescribing gemcitabine in hospitals in England



2. External literature (ERNIE database results)

2.1 The Information Centre for Health and Social Care (2008) Hospital Prescribing, 2007: England

http://www.ic.nhs.uk/webfiles/publications/Primary%20Care/Prescriptions/hospre08/Hospital_prescribing_2008_report2.pdf

Data showing the use gemcitabine for the treatment of metastatic breast cancer in primary care, in hospitals and those prescribed in hospitals, but dispensed in the community.

Cost (£000s)	Primary care	% growth primary	FP10HP*	% growth	Hospital	% growth hospital	Total	% growth total
Gemcitabine	-	-	-	-	25,800.9	7.5	25,800.9	7.5

*FP10HP = prescriptions written in hospitals but dispensed in the community

The data shows that all prescribing for gemcitabine is carried out in a hospital setting.

2.2 Richard M (2009) "Uptake of NICE approved cancer drugs 2007/2008" Department of Health: London

An analysis of prescribing data across cancer networks showed a 17% increase in prescribing of gemcitabine from 2005 to 2007/08.

Variations in usage between cancer networks were wider for some NICE approved drugs than others. There was a 1% reduction in variation from 2005 to 2007/08 across networks for gemcitabine. (NB data is not linked to diagnosis).

An additional literature search was carried out by information services using the following databases:

- Cinahl (EBSCO Host)
- Embase (Ovid)
- HMIC (Search 2)
- Medline (Ovid)
- Medline in Process (Ovid)

The search found no results that linked directly to the uptake of this piece of guidance.