NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA 055 Guidance on the use of paclitaxel (first line only) in the treatment of ovarian cancer.

This guidance was issued in January 2003 and reviewed in December 2005. The decision was made to review the appraisal again on publication of the ICON5 trial results, which were published in March 2009.

TA 055 originally covered all lines of treatment. The use of paclitaxel in second-line or subsequent treatment of advanced ovarian cancer was updated separately (alongside pegylated liposomal doxorubicin and topotecan) and TA 091 was published in May 2005. This replaced recommendations 1.3, 1.4 and 1.5 from TA 055.

Recommendation

- A review of the guidance should be transferred to the static guidance list.

Consideration of options for recommendation:

Options	**Comment**
A review of the guidance should be planned into the appraisal work programme.	No new evidence has been identified that would change the guidance on the use of paclitaxel for first line treatment of ovarian cancer.
The decision to review the guidance should be deferred [to a specified date].	There are relevant trials in progress however its unlikely that an update to the current guidance would result in any change to the existing recommendations
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 technologies.
A review of the guidance should be combined with a new appraisal that has recently been referred to the Institute.	No relevant technologies.
A review of the guidance should be incorporated into an on-going clinical guideline.	No new information to warrant being incorporated into a review.
A review of the guidance should be updated into an on-going clinical guideline.	Updating the guidance is not appropriate within the ongoing clinical guideline on ovarian cancer, as the topic does not match the prioritisations set for the guideline.
A review of the guidance should be transferred to the 'static guidance list'.	If the results of ICON 7 produce evidence likely to have a material effect on the last guidance issued then the guidance can be transferred back to the active list for further appraisal.

Original remit(s)

No remit – originally a 1st wave topic (TA 003).

Current guidance

1.1 It is recommended that paclitaxel in combination with a platinum based compound or platinum-based therapy alone (cisplatin or carboplatin) are offered as alternatives for first-line chemotherapy (usually following surgery) in the treatment of ovarian cancer.

1.2 The choice of treatment for first-line chemotherapy for ovarian cancer should be made after discussion between the responsible clinician and the patient about the risks and benefits of the options available. In choosing between treatment with a platinum-based compound alone or paclitaxel in combination with a platinum-based compound, this discussion should cover the side-effect profiles of the alternative therapies, the stage of the woman's disease, the extent of surgical treatment of the tumour, and disease-related performance status.

[Other recommendations are still in the published guidance but are now superseded by TA091 Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer.]

Relevant Institute work

TA91 Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer (Review of Technology Appraisal Guidance 28, 45 and 55). Due for review in November 2009.

Recognition and initial management of ovarian cancer. Clinical Guideline in progress, publication June 2011. [17th wave]

On-going trials

NCT00660842 A Quality of Life Study Comparing Weekly Versus Every 3 Week Chemotherapy in Patients With Ovarian Cancer (MITO-7) National Cancer Institute, Naples	Phase III Recruiting Estimated completion: November 2010
NCT00483782 Carboplatin and Paclitaxel With or Without Bevacizumab in Treating Patients With Newly Diagnosed Ovarian Epithelial Cancer, Fallopian Tube Cancer, or Primary Peritoneal Cavity Cancer (ICON 7) National Cancer Institute (NCI), Medical Research Council	Phase III Recruiting Estimated completion: 2012
NCT00108745 Paclitaxel or Polyglutamate Paclitaxel or Observation in Treating Patients With Stage III or Stage IV Ovarian Epithelial or Peritoneal Cancer National Cancer Institute (NCI), Gynecologic Oncology Group	Phase III Recruiting Completion date: Not stated
NCT00262847 Carboplatin and Paclitaxel With or Without Bevacizumab in Treating Patients With Stage III or Stage IV Ovarian Epithelial, Primary Peritoneal Cancer, or Fallopian Tube Cancer National Cancer Institute (NCI), Gynecologic Oncology Group	Phase III Suspended Completion date: Not stated
NCT00075712 Timing of Surgery and Chemotherapy in Treating Patients With Newly Diagnosed Advanced Ovarian Epithelial, Fallopian Tube, or Primary Peritoneal Cavity Cancer	Recruiting Phase III Completion date:

National Cancer Institute (NCI) Royal College of Obstetricians and Gynaecologists	Not stated

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 2005 onwards were reviewed.

Implementation

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

Equality and diversity issues

No equality and diversity issues have been identified

Appraisals comment

There has been one completed trial (ICON 5) that evaluated the adding one of three cytotoxic drugs (gemcitabine, PLDH or topotecan) to carboplatin and paclitaxel compared with carboplatin and paclitaxel alone. The trial assessed overall survival and progression free survival of patients with advanced ovarian cancer. The study showed that a third cytotoxic agent provided no additional benefit in overall survival and progression free survival.

There are a number of ongoing trials that are not complete. ICON 7 is a randomised phase III trial that is studying carboplatin, paclitaxel and bevacizumab compared with carboplatin and paclitaxel in people with newly diagnosed ovarian cancer. This study finished recruiting participants in February 2009. This estimated study reporting dates are 2010 for progression-free survival results and 2011 - 2012 for overall survival results.

MITO-7 is a phase III trial evaluating the effect of giving standard first line chemotherapy (carboplatin and paclitaxel) in lower doses once a week rather than high dose once every 3 weeks. The study will analyse the effect of this smaller more frequent dosage on quality of life, side effects and efficacy of chemotherapy. This estimated study completion date is November 2010.

Another phase III trial that is studying how well giving chemotherapy before and after surgery works and compares it to giving chemotherapy after surgery alone in treating patients with newly diagnosed advanced ovarian epithelial, fallopian tube, or primary peritoneal cavity cancer.

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Summary

In view of the results of the completed trial (ICON 5) it is unlikely that an update to the current guidance would result in any change to the existing recommendations. It is unnecessary to conduct a review at this time. It is also unlikely that the findings of the ongoing studies would result in any change to the existing recommendations. Therefore, it would seem appropriate to transfer the guidance to the static list and should any new evidence surface that would have a material effect on the last guidance issued then the guidance can be transferred back to the active list for further appraisal.

GE paper sign off:
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27 July 2009

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NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

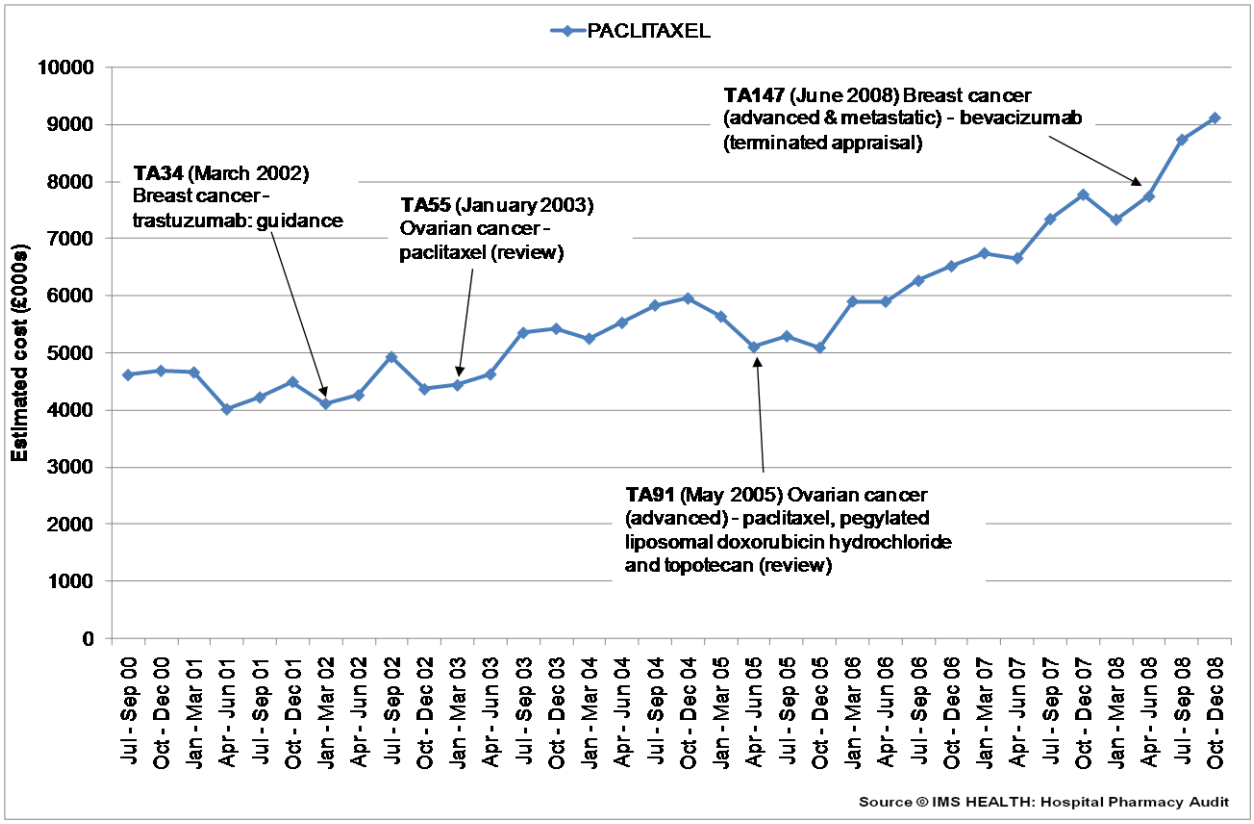
IMPLEMENTATION DIRECTORATE

Guidance Executive Review

Technology appraisal 55: Guidance on paclitaxel for the treatment of ovarian cancer.

1. National Hospital Prescribing Data

Data showing trends in prescribing costs 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.



2. External literature

2.1 The Information Centre for Health and Social Care (2008) Hospital Prescribing, 2007: England
http://www.ic.nhs.uk/statistics-and-data-collections/primary-care/prescriptions/hospital-prescribing-2007:-england

Data showing the use of paclitaxel.

Cost (£000s)	Primary care	% growth primary	FP10HP*	% growth	Hospital	% growth hospital	Total	% growth total
Paclitaxel	**0.0**	**-**	**0.0**	**-**	**28,460.0**	**15.9**	**28,460.0**	**15.9**

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

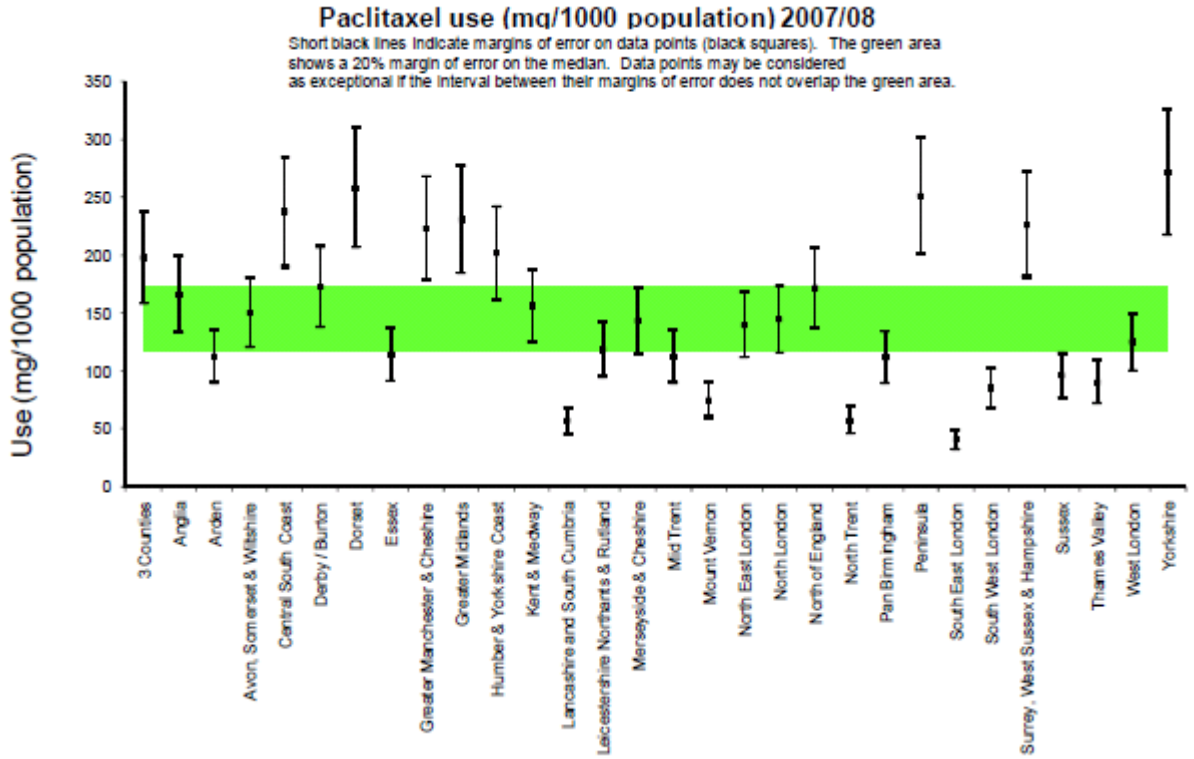
The data shows that all prescribing for paclitaxel is carried out in a hospital setting. Unfortunately this data does not link to diagnosis so needs to be treated cautiously in relation to the specific recommendations of the guidance.

2.2 Richard M (2009) "Uptake of NICE approved cancer drugs: Report of Review undertaken by the National Cancer Director" Department of Health: London

The 2009 report shows: (i) Overall usage of 13 of the 14 NICE drugs has increased (median 73%, range 4% to 291%) (ii) Usage has decreased for only one NICE drug - fludarabine (-18%). This is likely to be due to other drugs being used in preference, for example rituximab.

Variations in usage between cancer networks were wider for some NICE approved drugs than others. The variation in usage for paclitaxel for the half year equivalent for 2007/2008 was 3.2, an increase in variation of 4% since 2005.

The following chart shows regional variation in prescribing of paclitaxel:



2.3 A literature search was carried out 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.