NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

EC145 in combination with pegylated liposomal doxorubicin hydrochloride for the treatment of folate receptor positive, platinum-resistant ovarian cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of EC145 within its licensed indication in combination with pegylated liposomal doxorubicin hydrochloride for the treatment of folate receptor positive, platinum-resistant ovarian cancer.

Background

Ovarian cancer is a common gynaecological cancer. In 2008, approximately 6,000 women were diagnosed with ovarian cancer in England and Wales and of these, 4,500 were in the advanced stage and their five-year survival rate was below 30%. In the same year, there were approximately 3800 deaths from ovarian cancer in England and Wales. The incidence of ovarian cancer increases with age (four out of five cases are diagnosed in women over 50 years) and is higher in women who have BRCA1 or BRCA2 gene mutations.

Ovarian cancer may be categorised according to the response to first-line platinum chemotherapy as follows: platinum-sensitive (disease responds to first-line platinum-based therapy but relapses after 12 months or more); partially platinum-sensitive (disease which responds to first-line platinum-based therapy but relapses between 6 and 12 months); platinum-resistant (disease which relapses within 6 months of completion of initial platinum-based chemotherapy) and platinum-refractory, that is, does not respond to initial platinum-based chemotherapy. Although a significant percentage of women with ovarian cancer respond to initial chemotherapy, between 55% and 75% of women whose tumours respond to first line therapy relapse within 2 years of completing treatment. The overall 5-year survival rate is less than 41%.

NICE Clinical Guideline No. 122 'The recognition and initial management of ovarian cancer' states that current management of ovarian cancer involves surgery to remove as much of the cancer as possible and chemotherapy. Increasingly chemotherapy is given before surgery. NICE Technology Appraisal No. 91 recommends the use of single-agent paclitaxel or pegylated liposomal doxorubicin hydrochloride (PLDH) to treat platinum-resistant ovarian cancer. It also recommends the use of topotecan when paclitaxel and PLDH are considered inappropriate.

The technology

EC145 (brand name unknown, Endocyte) is a folate-targeted chemotherapeutic conjugate, composed of a folate molecule plus a vinca alkaloid, which acts as a cytotoxic microtubule destabilising agent once absorbed by cells. EC145 targets and enters cancer cells via the folate vitamin receptor, which is over-expressed by many tumours. It is administered via intravenous infusion.

EC145 does not currently have a UK marketing authorisation. It is currently being studied in clinical trials in combination with PLDH compared with PLDH alone for the treatment of folate receptor positive, platinum-resistant ovarian cancer. Before receiving treatment, patients in the clinical trials received planar and single-photon emission computed tomography (SPECT) imaging with a folate-receptor targeted technetium-labelled imaging agent - EC20 - to identify those most likely to benefit from therapy with EC145. EC20 is currently being studied in clinical trials for the diagnosis of folate-receptor positive ovarian cancer.

Intervention(s)	EC145 in combination with pegylated liposomal doxorubicin hydrochloride
Population(s)	People with folate receptor positive, platinum-resistant ovarian cancer
Comparators	• Pegylated liposomal doxorubicin • Paclitaxel
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Costs of folate receptor diagnostic testing required for this treatment should be considered.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 222, April 2011. 'Trabectedin for the treatment of relapsed ovarian cancer.' Currently under review with TA 91. Earliest anticipated date of review publication February 2014. Technology Appraisal No. 91, May 2005. 'Topotecan, pegylated liposomal doxorubicin and paclitaxel for the treatment of advanced ovarian cancer' Currently under review with TA 222. Earliest anticipated date of review publication February 2014. Technology Appraisal No. 55, January 2003. 'Guidance on the use of paclitaxel in the treatment of ovarian cancer.' Transferred to the static guidance list. Suspended Technology Appraisal, 'Patupilone for the treatment of recurrent epithelial ovarian cancer.' Suspended Technology Appraisal, 'Gemcitabine for relapsed advanced ovarian cancer.' Proposed Technology Appraisal, 'Pazopanib for the treatment of epithelial ovarian, fallopian and peritoneal cancer.' Proposed Technology Appraisal, 'Paclitaxel encapsulated in XR-17 for the treatment of epithelial ovarian, fallopian or peritoneal cancer.' Related Guidelines: Clinical Guideline No. 122, April 2011, 'The recognition and initial management of ovarian cancer.'

Questions for consultation

Before treatment with EC145, diagnosis of folate-receptor positive disease is required using SPECT imaging.

- Is the EC20 test likely to be used as a diagnostic tool for other conditions, or only to diagnose folate-receptor positive ovarian cancer?

- Is the diagnosis of folate-positive disease with the EC20 test prior to treatment likely to be stipulated in the marketing authorisation for EC145, or are there other diagnostic tests which could also be used?

- Is SPECT imaging routinely available in UK clinical practice, or is the requirement for the use of the EC20 test prior to treatment with EC145 likely to lead to resource constraints?

Have the most appropriate comparators for EC145 for the treatment of platinum-resistant ovarian cancer been included in the scope?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which EC145 will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a ‘step-change’ in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

A Multiple Technology Appraisal (MTA) which includes the review of two published technology appraisals (TA91 and TA222) for the treatment of relapsed ovarian cancer is scheduled to begin in November 2012, with guidance anticipated in February 2014 ("Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for relapsed advanced ovarian cancer"). We welcome comments on the appropriateness of appraising this topic as part of the review or through the Single Technology Appraisal (STA) process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)