Complete Summary

GUIDELINE TITLE

Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 46 p. (Technology appraisal; no. 91).

GUIDELINE STATUS

This is the current release of the guideline.

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SCOPE

DISEASE/CONDITION(S)

Ovarian cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology

INTENDED USERS

Advanced Practice Nurses
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To examine the clinical effectiveness and cost-effectiveness of intravenous formulations of topotecan monotherapy, pegylated liposomal doxorubicin hydorocholoride (PLDH) monotherapy, and paclitaxel used alone or in combination with a platinum-based compound for the second-line or subsequent treatment of advanced ovarian cancer

TARGET POPULATION

Women with relapsed advanced ovarian cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Paclitaxel
2. Pegylated liposomal doxorubicin hydrochloride (PLDH)
3. Topotecan

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Overall survival
    - Progression-free survival
    - Response (including complete and partial response)
    - Quality of life
    - Adverse effects of treatment
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology

considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Centre for Reviews and Dissemination, University of York (See the "Companion Documents" field.)

Search Strategy

Seventeen databases were searched for randomised controlled trials and systematic reviews for the clinical effectiveness of pegylated liposomal doxorubicin hydrochloride (PLDH), topotecan and paclitaxel and economic evaluations of the cost effectiveness of PLDH, topotecan and paclitaxel.

Inclusion/Exclusion Criteria

Two reviewers independently screened all titles and/or abstracts including economic evaluations. The full manuscript of any study judged to be relevant by either reviewer was obtained and assessed for inclusion or exclusion. Disagreements were resolved through discussion. For the assessment of clinical effectiveness, randomised controlled trials (RCTs) that compared topotecan monotherapy, PLDH monotherapy or paclitaxel administered alone or in combination with a platinum based compound with any other comparator including usual supportive care were included. For the assessment of cost-effectiveness, a broader range of studies was considered.

NUMBER OF SOURCE DOCUMENTS

A total of 2,542 titles and abstracts were screened for inclusion in the review of clinical and cost-effectiveness; 194 studies were ordered as full papers and assessed in detail. Nine randomised controlled trials (RCTs) were identified.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Centre for Reviews and Dissemination, University of York (See the "Companion Documents" field.)

Data Extraction and Quality Assessment

Data from included studies were extracted by one reviewer and independently checked for accuracy by a second reviewer. Individual studies were assessed for quality by one reviewer and independently checked by a second for accuracy.

Methods of Analysis/Synthesis

The results of the data extraction and quality assessment of the randomised controlled trials (RCTs) were presented in structured tables and as a narrative summary. For the cost-effectiveness section of the report, details of each identified published economic evaluation, together with a critical appraisal of its quality, were presented in structured tables.

Handling the Company Submissions

All the clinical effectiveness data included in the three company submissions were assessed. Where this met the inclusion criteria it was included in the clinical effectiveness review. All economic evaluations (including accompanying models) included in the company submissions were assessed and a detailed assessment of the assumptions underlying the submitted analyses were undertaken. A new model was developed to assess the costs of the alternative treatments, the differential mean survival duration and the impact of health-related quality of life. Monte-Carlo simulation was used to reflect uncertainty in the cost-effectiveness results.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can

comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The Assessment Group identified three published economic evaluations that compared two or more of the technologies under review. In addition, three manufacturers each submitted an economic analysis, and the Assessment Group developed its own economic model.

See Section 4.2 of the original guideline document for a detailed discussion of the cost-effectiveness analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note: This guidance applies only to paclitaxel, pegylated liposomal doxorubicin hydrochloride (PLDH) and topotecan.

For the purposes of this guidance, the following definitions are used:

- platinum-sensitive ovarian cancer: disease that responds to first-line platinum-based therapy but relapses 12 months or more after completion of initial platinum-based chemotherapy
- partially platinum-sensitive ovarian cancer: disease that responds to first-line platinum-based therapy but relapses between 6 and 12 months after completion of initial platinum-based chemotherapy
- platinum-resistant ovarian cancer: disease that relapses within 6 months of completion of initial platinum-based chemotherapy
- platinum-refractory ovarian cancer: disease that does not respond to initial platinum-based chemotherapy.

- Paclitaxel in combination with a platinum-based compound (carboplatin or cisplatin) is recommended as an option for the second-line (or subsequent) treatment of women with platinum-sensitive or partially platinum-sensitive advanced ovarian cancer, except in women who are allergic to platinum-based compounds.
- Single-agent paclitaxel is recommended as an option for the second-line (or subsequent) treatment of women with platinum-refractory or platinum-resistant advanced ovarian cancer, and for women who are allergic to platinum-based compounds.
- PLDH is recommended as an option for the second-line (or subsequent) treatment of women with partially platinum-sensitive, platinum-resistant or platinum-refractory advanced ovarian cancer, and for women who are allergic to platinum-based compounds.

- Topotecan is recommended as an option for second-line (or subsequent) treatment only for those women with platinum-refractory or platinum-resistant advanced ovarian cancer, or those who are allergic to platinum-based compounds, for whom PLDH and single-agent paclitaxel are considered inappropriate.
- Within these recommendations, the choice of treatment for second-line (or subsequent) chemotherapy should be made after discussion between the responsible clinician and the patient about the risks and benefits of the options.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of paclitaxel, pegylated liposomal doxorubicin hydrochloride (PLDH) and topotecan in women with relapsed advanced ovarian cancer, to increase response to treatment, survival and quality of life

POTENTIAL HARMS

Topotecan

- Adverse effects include dose-limiting myelosuppression (a decrease in the ability of bone marrow to produce blood cells), gastro-intestinal effects, asthenia (lack of strength or energy), alopecia (hair loss) and anorexia (loss of appetite).
- The Summary of Product Characteristics states that patients with poor performance status have a lower response rate and an increased incidence of complications such as fever and infection. In addition (based on clinical experience), those with extensive abdominal tumour deposits leading to bowel obstruction are less likely to benefit from treatment.

Paclitaxel

Adverse effects include severe hypersensitivity reactions (routine premedication with a corticosteroid, an antihistamine and a histamine H2-receptor antagonist is recommended to prevent this), myelosuppression, peripheral neuropathy, cardiac conduction defects with arrhythmias, alopecia, muscle and joint pain, nausea and vomiting.

Pegylated Liposomal Doxorubicin Hydrochloride (PLDH)

- The principal treatment-related adverse effects are palmar-plantar erythrodysesthesia (PPE [intense, often painful reddening of the hands and feet]) and stomatitis (ulceration of the mouth). The Summary of Product Characteristics recommends that all people receiving PLDH routinely undergo frequent electrocardiogram monitoring.
- Based on clinical experience, patients with poor performance status tend to have a lower response rate, while those with extensive abdominal tumour deposits leading to bowel obstruction are less likely to benefit from treatment.

For full details of side effects and contraindications, see the 'Summary of product characteristics'.

CONTRAINDICATIONS

CONTRAINDICATIONS

Topotecan

Contraindications include pregnancy and breastfeeding, a history of severe hypersensitivity to the drug, and severe bone-marrow depression before the first course of treatment. The Summary of Product Characteristics states that topotecan is not recommended in people with severe renal or hepatic impairment.

Pegylated Liposomal Doxorubicin Hydrochloride (PLDH)

Contraindications include breastfeeding and a history of hypersensitivity to the drug.

Paclitaxel

Contraindications include pregnancy and breastfeeding, severe hypersensitivity the drug and baseline neutrophils < 1500/mm^3.

For full details of side effects and contraindications, see the 'Summary of product characteristics'.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

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

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- Clinicians who care for women with ovarian cancer should review their current practice and policies to take account of the guidance (see the "Major Recommendations" field).
- Local guidelines, protocols or care pathways that refer to the care of women with advanced ovarian cancer should incorporate the guidance.
- To measure compliance locally with the guidance, the following criteria could be used. Further details on suggestions for audit are presented in Appendix C of the original guideline document.
    - A woman with advanced ovarian cancer that is platinum-sensitive or partially platinum-sensitive is offered paclitaxel in combination with a platinum-based compound as second-line (or subsequent) treatment option, unless she is allergic to platinum-based compounds.
    - A woman with advanced ovarian cancer that is platinum-refractory or platinum-resistant or a woman who is allergic to platinum-based compounds is offered single-agent paclitaxel as a second-line (or subsequent) treatment option.
    - A woman with advanced ovarian cancer that is partially platinum-sensitive, platinum-refractory or platinum-resistant or a woman who is allergic to platinum-based compounds is offered pegylated liposomal doxorubicin hydrochloride (PLDH) as a second-line (or subsequent) treatment option.
    - A woman with advanced ovarian cancer that is platinum-refractory or platinum-resistant, or a woman who is allergic to platinum-based compounds, and for whom PLDH and single-agent paclitaxel are considered inappropriate, is offered topotecan as a second-line (or subsequent) treatment option.
    - The responsible clinician and the woman discuss the risks and benefits of the options available before the choice of treatment for second-line (or subsequent) chemotherapy is made.
- Local clinical audits on the management of ovarian cancer also could include measurement of compliance with accepted clinical guidelines or protocols or with the measures for the treatment of ovarian cancer that are suggested in Guidance on commissioning cancer services: Improving outcomes in gynaecological cancers.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 46 p. (Technology appraisal; no. 91).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 May

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer (review). Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 4 p. (Technology appraisal 91). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

- Topotecan, pegylated liposomal doxorubicin hydrochloride and paclitaxel for second-line or subsequent treatment of advanced ovarian cancer. Assessment report. Centre for Reviews and Dissemination, University of York. 2004 Sep. 411 p. Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N0872. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan as chemotherapy drugs for the second-line (and subsequent) treatment of advanced ovarian cancer. Understanding NICE guidance -- information for people with advanced ovarian cancer, their families and carers, and the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 7 p. (Technology appraisal 91).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the Department of Health Publications Order Line 0870 1555 455. ref: N0873. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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