The Department of Health and the National Assembly for Wales have asked the National Institute for Clinical Excellence (NICE or the Institute) to conduct an appraisal of pegylated liposomal doxorubicin hydrochloride (Caelyx) for the second-line or subsequent treatment of advanced ovarian cancer and provide guidance on its use in the NHS in England and Wales. The Appraisal Committee has had its first meeting to consider both the evidence submitted and the views put forward by the representatives nominated for this appraisal by professional organisations and patient/carer and service user organisations. The Committee has developed preliminary recommendations on the use of pegylated liposomal doxorubicin hydrochloride.

This document has been prepared for consultation with the formal consultees. It summarises the evidence and views that have been considered and sets out the preliminary recommendations developed by the Committee. The Institute is now inviting comments from the formal consultees in the appraisal process (the consultees for this appraisal are listed on the NICE website, www.nice.org.uk).

Note that this document does not constitute the Institute's formal guidance on this technology. The recommendations made in Section 1 are preliminary and may change after consultation.

The process the Institute will follow after the consultation period is summarised below. For further details, see the Guide to the Technology Appraisal Process (this document is available on the Institute’s website, www.nice.org.uk).

- The Appraisal Committee will meet again to consider the original evidence and this Appraisal Consultation Document in the light of the views of the formal consultees.
- At that meeting, the Committee will also consider comments made on the document by people who are not formal consultees in the appraisal process.
- After considering feedback from the consultation process, the Committee will prepare the Final Appraisal Determination (FAD) and submit it to the Institute.
- Subject to any appeal by consultees, the FAD may be used as the basis for the Institute’s guidance on the use of the appraised technology in the NHS in England and Wales.

The key dates for this appraisal are:
Closing date for comments: 5 pm on Thursday 31 February 2002
Second Appraisal Committee meeting: Thursday 7 March 2002

Details of membership of the Appraisal Committee are given in Appendix A and a list of the sources of evidence used in the preparation of this document is given in Appendix B.
1 Appraisal Committee’s preliminary recommendations

1.1 Pegylated liposomal doxorubicin hydrochloride (PLDH) is recommended as one option for the second-line (or subsequent) treatment of women with advanced ovarian cancer that is initially resistant or refractory to first-line platinum-based combination therapy or has become resistant after successive courses of platinum-based combination therapy (see section 2.5).

1.2 It is recommended that PLDH treatment for advanced ovarian cancer is supervised by oncologists who specialise in the chemotherapy of ovarian cancer.

1.3 The use by oncologists of PLDH to treat advanced ovarian cancer should be accompanied by ongoing monitoring of its use, with careful documentation of indications for treatment, clinical outcomes and adverse effects.

1.4 PLDH is not recommended for patients with condition-related poor performance status (e.g. ECOG 3 or worse – defined in Appendix D) or sub-acute or established bowel obstruction, or for patients who have previously not responded to PLDH or another drug in the same class.

1.5 Treatment response should be monitored by appropriate tumour markers (e.g. CA-125) and/or appropriate radiological techniques. Patients with evidence of disease progression based on evidence from serological tests or radiological imaging should stop treatment. Deteriorating performance status should also prompt consideration of treatment withdrawal.
2 Clinical need and practice

2.1 Ovarian cancer has an incidence of 21.6 cases per 100,000 women per year in England and Wales, making it one of the more common cancers in women. Each year about 6000 cases are diagnosed.

2.2 The early stages of the disease are often asymptomatic. Most patients are therefore not diagnosed until they have advanced disease. This gives a relatively poor prognosis for the disease. The 5-year survival rate is only about 30%.

2.3 A number of potential prognostic factors which may influence survival and response have been suggested, including the amount of residual disease after 'debulking' surgery, the stage and grade/histology of the tumour, and performance status and age of the patient. Tumour markers (e.g. CA-125) are also potential prognostic indicators, correlating with disease progression. CA-125 along with abdominal CAT scanning is often used to assess both tumour load and response to therapy.

2.4 Radiotherapy is usually of limited effectiveness and has side effects on organs within the abdominal cavity. First-line chemotherapy (given to over 75% patients with ovarian cancer) usually consists of paclitaxel and a platinum-based therapy (cisplatin or carboplatin). While most patients (70% to 80%) initially respond to such therapy, most responders eventually relapse (55% to 75% within 2 years). Responses can occur when first-line chemotherapy is repeated for a second and sometimes a third time, although they occur proportionately less frequently and do not last as long. (A complete response is usually defined as malignant disease undetectable for at least 4 weeks. A partial response is usually defined as at least a 50% reduction in tumour size for more than 4 weeks.)
2.5 On the basis of tumour-response to platinum-based therapy, ovarian cancer can be categorised as follows:

- more than 6 months' response: platinum-sensitive
- 0 to 6 months’ response: platinum-resistant
- no response: platinum-refractory.

2.6 Women whose condition is initially platinum-sensitive are more likely to respond to second and subsequent courses of platinum-based therapy and to subsequent therapies with other drugs. The two factors shown to be predictive of second and subsequent response to first-line therapy are the length of the progression-free interval after the previous dose(s) and the stage the cancer has reached. Current best practice for women who respond to platinum-based therapy is to give second and possibly subsequent courses of the same treatment. Nevertheless, second-line therapies may not only be palliative (in that they can alleviate symptoms), but may also prolong survival. At the same time, however, they are likely to be toxic.

2.7 Six drugs are licensed in the UK for therapy after the failure of platinum-based therapy: topotecan, hexamethylmelamine (altretamine), treosulfan, chlorambucil, paclitaxel and PLDH. Of these, paclitaxel (in combination with cisplatin or carboplatin) is now commonly used as first-line therapy. Etoposide and gemcitabine are used as second-line therapy although they are unlicensed for this indication. Drugs other than PLDH used in second-line and subsequent therapy have not been formally appraised for this guidance.

3 The technology

3.1 PLDH (Caelyx ®, manufactured by Schering-Plough) is a Stealth® liposomal formulation of doxorubicin hydrochloride. Doxorubicin is obtained from Streptomyces peucetius var. caesius and belongs to the class of drugs known as anthracyclines, a group of antibiotics that have potent antineoplastic activity. They intercalate with DNA, and so inhibit DNA synthesis. Furthermore, anthracyclines interact with cell membranes thereby altering their functions and generating hydrogen peroxide and hydroxy radicals, which are highly destructive to cells.
3.2 In the case of PLDH, doxorubicin is encapsulated in liposomes that have been pegylated – that is they have surface-bound methoxypolyethylene glycol. Pegylation protects the liposomes from detection by the body’s immune system, so increasing the time they remain in circulation in the blood. Encapsulating doxorubicin in pegylated liposomes enhances drug localisation and concentration in tumour tissues and so increases the efficacy of the drug and limits its toxicity. A relatively new drug, PLDH has been licensed for the treatment of AIDS-related Kaposi’s sarcoma since 1997 and in October 2001 received approval in the UK for use in the treatment of advanced ovarian cancer.

3.3 PLDH is administered intravenously at a dose of 50 mg per square metre of patient’s surface area (typically, about 90 mg in total), once every 4 weeks, for as long as the disease does not progress and the patient continues to tolerate the treatment. Administration should be immediately discontinued in patients who experience early symptoms or signs of infusion reaction. After appropriate premedications (antihistamine and/or short-acting corticosteroid) therapy can be restarted but at a slower rate. The dose of PLDH may also be reduced or delayed in patients with adverse events such as palmar–plantar erythrodysesthesia (PPE), stomatitis (ulceration of the mouth) and haematological toxicity. PPE is characterised by an intense, often painful, macular reddening that primarily involves the palms of the hands and soles of the feet. The skin changes may range from a painful desquamating dermatitis, with mild erythema and hyperaemia, to severe crusting, ulceration and epidermal necrosis. For full details of side effects and contraindications, please see the Summary of Product Characteristics.

3.4 The price for a 10-ml vial of PLDH is £411.30 and for a 25-ml vial it is £813.49 (British National Formulary 42, September 2001). The cost per course of therapy for a patient with a surface area of 1.7 square metres is £2850, and for a patient with a surface area of 1.9 square metres is £3270. The overall cost depends on the number of courses undertaken.
4 Evidence and interpretation

The Appraisal Committee considered evidence from a number of sources (see Appendix B).

4.1 Clinical effectiveness

4.1.1 The evidence considered by the Committee included the Assessment Report, submissions by consultees, and views put forward at the meeting by clinical experts and representatives of patient/carer organisations.

4.1.2 The review carried out by the Assessment Group found results from only one Phase III study, a randomised controlled trial which involved 474 patients and compared PLDH with topotecan as a second-line treatment for advanced ovarian cancer. In this study, PLDH performed at least as well as topotecan in almost all outcomes, but not statistically significantly better in any. For example, the response rate was 19.7% for PLDH and 17.0% for topotecan (relative risk = 0.87, 95% confidence interval 0.59 to 1.26). The median time to progression was 16.1 weeks for PLDH and 17.0 weeks for topotecan (hazard ratio = 1.18, 95% confidence interval 0.97 to 1.42). Only for the platinum-sensitive subgroup of patients did survival and time to progression reach statistical significance in favour of PLDH in a post-hoc comparison.

4.1.3 PLDH has a different adverse effects profile from topotecan. In the Phase III clinical study, 49% of all patients treated with PLDH developed PPE (23% with grades 3 and 4 severity) and about 40% of patients developed stomatitis. These adverse events may cause great discomfort, but are not life-threatening. In contrast, the adverse effects of topotecan centre on haematological problems, which may be fatal. In the Phase III study, haematological adverse events were much more frequent among patients treated with topotecan than among those treated with PLDH. Patients receiving topotecan require frequent monitoring for haematological effects and many need blood transfusions.
4.1.4 A second Phase III study, to compare PLDH with paclitaxel, was stopped when paclitaxel received approval as a first-line therapy and no results have been reported.

4.1.5 Six Phase II studies of PLDH as a second-line therapy have been conducted, involving a total of 336 women. In these studies, 36 women out of 293 (12%) had a response, of whom 3 (1%) had a complete response. Median response duration (based on very small numbers of patients) ranged from 18 to 41 weeks.

4.2 Cost effectiveness

4.2.1 There are three analyses of PLDH against topotecan as a second-line therapy for advanced ovarian cancer, two of which are related. One of the related analyses was commissioned by the manufacturer of PLDH, and the other was in the manufacturer's submission to NICE. An independent analysis was carried out during preparation of the Assessment Report.

4.2.2 The two related analyses argue that since in a clinical trial PLDH performed as well as topotecan on all outcomes, it can be assumed that the two drugs have the same clinical effects, and so a cost-minimisation analysis can be undertaken. It is argued that since PLDH has a better adverse effects profile, is cheaper, and has the same effectiveness, it is to be preferred to topotecan. These two analyses showed that the cost per person for treatment with PLDH was about £10,000, and for treatment with topotecan it was about £12,100 or £12,600. The difference in favour of PLDH was statistically significant. These costs included the costs of treating adverse events.

4.2.3 The third analysis, for the Assessment Report, showed that the overall cost of PLDH was lower than that of topotecan by an average of £2600 per person, and that PLDH was no less effective than topotecan.

4.3 Consideration of the evidence

4.3.1 In summary, a Phase III clinical study has indicated that the clinical effectiveness of PLDH is similar to that of topotecan as a second-line treatment for patients with advanced ovarian cancer. The two drugs have
different side-effect profiles, with a lower frequency of haematological side
effects among patients treated with PLDH, but a high incidence of PPE. Since
the group of women who respond to PLDH overlaps only partially with the
group responding to topotecan, and since the side effects of the two drugs are
quite different, the two drugs are not interchangeable.

4.3.2 PLDH is simpler to administer than topotecan. Less staff time is required for
administration, and the risks of infection and administrative errors are
lessened.

4.3.3 Bearing in mind all costs, PLDH is somewhat cheaper than topotecan.
Considering together clinical and cost effectiveness, ease of administration
and side-effect profile, PLDH will therefore be the drug of choice for many, but
not all, patients with advanced ovarian cancer for whom first-line
chemotherapy has failed.

5 Proposed recommendations for further research

5.1 Evidence for the clinical and cost effectiveness of PLDH depends almost
terribly on a single randomised control trial that was sponsored by the
manufacturer of the drug. The review team in its Assessment Report has
indicated that there would be value in acquiring more information about this
drug.

5.2 PLDH is one of a number of drugs currently in use or being developed for
treatment of advanced ovarian cancer when first-line therapy has failed.
Research is required into PLDH as a second-line or subsequent therapy,
either singly or in combination with other drugs. The comparators should
include those second-line treatments with a significant response rate in
platinum-refractory or platinum-resistant patients and best supportive care (in
the case of the use of PLDH as last-line therapy). Data sufficient to allow cost-
effectiveness analyses should be collected.

5.3 Research is required into the identification of those tumours that are likely to
respond to PLDH, in order to increase response rates in the treated group
and thus make the drug more cost-effective. These studies should include the
molecular pathological characteristics of tumours that may favour the use of PLDH as opposed to that of other drugs.

6 Preliminary views on the resource impact for the NHS

This section outlines the Appraisal Committee’s preliminary assessment concerning the likely impact on NHS resources if the guidance in Section 1 were to be implemented. When guidance is issued, this section is intended to assist NHS planners and managers in its implementation. Therefore the Institute particularly welcomes comments and information from those who would be involved in the implementation of the guidance so that this section can be made as helpful and robust as possible.

6.1 It is assumed that about 2000 women per year would be eligible for treatment with either PLDH or topotecan or both (in sequence, not at the same time). However, it is likely that, having been treated with one of these drugs, only about 500 women per year would be suited for treatment with the other. Assuming that currently 2000 patients a year in England and Wales are being treated with topotecan at an overall cost of £12,500 per patient, current total costs are estimated to be £25 million per year.

6.2 If this situation were to continue on the introduction of PLDH, and if 500 of these women were subsequently treated with PLDH at an overall cost of £10,000 per patient, the additional cost would be £5 million per year.

6.3 However, if all 2000 patients were first treated with PLDH, and 500 of these were subsequently treated with topotecan, the total cost would be £26.25 million per year – an additional cost of £1.25 million per year over the current situation.

6.4 If, when given a first choice of PLDH or topotecan, half of all eligible women were to choose PLDH, then the increase in costs would be mid-way between those of the first two cases, that is, £3.1 million per year.

6.5 These figures refer to different scenarios in the steady state. The first-year increase may be slightly above that of the steady-state increase, because
many current patients would already have taken topotecan. None of the above figures take into account that the addition of PLDH to the list of available drugs would reduce the usage of later line chemotherapeutic agents other than topotecan.

7 Proposals for implementation and audit

This section presents proposals for implementation and audit based on the preliminary recommendations for guidance in Section 1. Technical details for criteria for audit are presented in Appendix C.

7.1 Clinicians with responsibility for treating women with advanced ovarian cancer should review their current practice in line with the guidance set out in Section 1.

7.2 Local clinical guidelines, protocols or care pathways on the care of women with ovarian cancer should incorporate the guidance set out in Section 1.

7.3 To measure compliance locally with the guidance, the following criteria should be used.

- PLDH is one option for the second-line (or subsequent) treatment of a woman who has advanced ovarian cancer that is initially resistant or refractory to first-line platinum-based combination therapy or has become resistant after successive courses of platinum-based combination therapy.

- PLDH is not used in women with condition-related poor performance status, sub-acute or established bowel obstruction or who have previously not responded to PLDH or another drug in the same class.

- Treatment response is monitored by appropriate tumour markers and/or appropriate radiological techniques.

- Consideration for treatment to be stopped occurs when there is disease progression, based on evidence from serological tests or radiological imaging or when the woman has deteriorating performance status.
• The indications for treatment by PLDH, and the clinical outcomes and the adverse effects of women on PLDH are documented completely and accurately.

• The use of PLDH in the treatment for advanced ovarian cancer is supervised by an oncologist who specialises in the chemotherapy of ovarian cancer.

7.4 Local clinical audits on the management of ovarian cancer also could include measurement of compliance with accepted clinical guidelines or protocols.

8 Related guidance


9 Proposed date for review of guidance

The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider any new evidence on the technology, in the form of an updated assessment report, and decide whether the technology should be referred to the Appraisal Committee for review.

9.1 This technology will be reviewed, together with topotecan, in March 2003.

Professor David Barnett
Chairman, Appraisal Committee
January 2002
Appendix A. Appraisal Committee members

NOTE The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members appears below. The Appraisal Committee meets twice a month other than in December, when there are no meetings. The Committee membership is split into two branches, with the chairman, vice-chairman and a number of other members attending meetings of both branches. Each branch considers its own list of technologies and topics are not moved between the branches.

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

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declaration of interests, are posted on the NICE website.

Dr Jane Adam
Radiologist, St. George’s Hospital, London

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

Dr Sunil Angris
General Practitioner, Waterhouses Medical Practice

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 Carol Black  
Consultant Physician, Royal Free Hospital & UCL, London

Professor John Brazier  
Health Economist, University of Sheffield

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

Professor Bruce Campbell  
Consultant Surgeon, Royal Devon & Exeter Hospital

Professor Mike Campbell  
Statistician, Institute of General Practice & Primary Care, Sheffield

Dr Karl Claxton  
Health Economist, University of York

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

Dr Nicky Cullum  
Reader in Health Studies, University of York

Professor Jack Dowie  
Health Economist, London School of Hygiene & Tropical Medicine, London

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

Dr Paul Ewings  
Statistician, Taunton & Somerset NHS Trust

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

Sally Gooch
Director of Nursing, Mid-Essex Hospital Services Trust

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

Professor Trisha Greenhalgh
Professor of Primary Health Care, University College London

Liz Heyer
Chief Executive, Barnet & Chase Farm Hospitals 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

Ruth Lesirge
Patient Representative; Director, Mental Health Foundation
Dr George Levvy
Patient Representative; Chief Executive, Motor Neurone Disease Association

Dr Gill Morgan
CEO, North & East Devon Health Authority

Professor Miranda Mugford
Health Economist, University of East Anglia

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

Mr James Partridge
Chief Executive, Changing Faces

Siân Richards
General Manager, Cardiff Local Health Group

Professor Philip Routledge
Professor of Clinical Pharmacology, University of Wales

Dr Rhiannon Rowsell
Pharmaceutical Physician, AstraZeneca UK Ltd

Dr Stephen Saltissi
Consultant Cardiologist, Royal Liverpool University Hospital

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

Professor Ray Tallis
Consultant Physician, Hope Hospital, Salford

Dr Cathryn Thomas
General Practitioner, and Senior Lecturer, Department of Primary Care and General Practice, University of Birmingham
Professor Mary Watkins
Head of Institute of Health Studies, University of Plymouth

Dr Norman Waugh
Public Health Consultant, University of Southampton
Appendix B. Sources of evidence considered by the Committee

The following documents were made available to the Committee in their first discussion of the appraisal of the use of pegylated liposomal doxorubicin hydrochloride (Caelyx®).

• **Overview** prepared by the NICE Appraisal Team

• **Evaluation report** consisting of
  - **Assessment report** prepared by the NHS Centre for Reviews and Dissemination, Centre for Health Economics, University of York (A rapid and systematic review of the clinical effectiveness and cost effectiveness of pegylated liposomal doxorubicin hydrochloride (Caelyx® UK, Doxil® USA) for ovarian cancer, 21st November 2001)

  - **Comments on the assessment report** received from:
    - Calderdale & Kirklees Health Authority
    - Royal Pharmaceutical Society
    - Royal College of Physicians
    - Royal College of Obstetricians & Gynaecologists
    - Royal College of Pathologists
    - Schering-Plough Ltd

- **Professional/Specialist Group submissions** from:
  - Calderdale and Kirklees Health Authority
  - Gateshead and South Tyneside Health Authority
  - National Cancer Research Institute (formally UKCCCR)
  - Royal College of Physicians

- **Patient Group submissions** from:
  - Overcome and CancerBACUP (joint submission)

- **Manufacturer/Sponsor submissions** from:
  - Schering-Plough Ltd

- **Expert submissions** from:
  - Dr Malcolm Adams, Consultant Clinical Oncologist, Velindre Hospital
  - Dr Chris Poole, Macmillan Senior Lecturer in Medical Oncology, City Hospital, Birmingham
  - Catriona Moore, Policy & Public Affairs Manager, CancerBACUP
Appendix C. Detail on criteria for audit of the use of PLDH in the treatment of women with advanced ovarian cancer

Possible objectives for an audit

An audit on the appropriateness and effectiveness of use of PLDH could be carried out to ensure that:

- PLDH is used only as indicated for women with advanced ovarian cancer
- Response to PLDH treatment is monitored appropriately and is continued only as long as it provides benefit
- PLDH treatment is supervised by an appropriate oncologist
- The indications, clinical outcomes and adverse effects of women on PLDH are documented completely and accurately.

Patients to be included in an audit and time period for selection

All women treated for advanced ovarian cancer over a reasonable time period, say, the past year. Alternatively, an audit could be constructed to identify women treated with PLDH to ensure that the treatment was monitored, supervised and documented effectively
Measures to be used as a basis for an audit

The measures that can be used in an audit of the appropriateness and effectiveness of use of PLDH for women with advanced ovarian cancer are as follows.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Standard</th>
<th>Exception(s)</th>
<th>Definition of Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Patient is offered PLDH in any of the following circumstances:</td>
<td>100% of patients covered by 1a and 1b</td>
<td>B. Woman has condition-specific poor performance status</td>
<td>Platinum-resistant = patient’s cancer has responded to platinum-based therapy for 0–6 months</td>
</tr>
<tr>
<td>a. Patient’s cancer is initially resistant or refractory to first-line platinum-based combination therapy</td>
<td></td>
<td>C. Woman has sub-acute or established bowel obstruction</td>
<td>Platinum-refractory = patient’s cancer has not responded to platinum-based therapy</td>
</tr>
<tr>
<td>b. Patient’s cancer has become resistant after successive courses of platinum-based combination therapy</td>
<td></td>
<td>D. Woman has had previous failed exposure to PLDH or to another drug in the same class</td>
<td>Responded = malignant disease is not detectable for at least 4 weeks or tumour size is reduced by at least 50% for more than 4 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Poor performance status = ECOG 3 or worse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Drug in same class as PLDH = topotecan, hexamethylmelamine (altretamine), treosulfan, chlorambucil or paclitaxel</td>
</tr>
<tr>
<td></td>
<td>Treatment response is monitored</td>
<td>100% of women receiving PLDH</td>
<td>None</td>
</tr>
<tr>
<td>---</td>
<td>---------------------------------</td>
<td>-------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>3.</td>
<td>Treatment is stopped when any of the following occur:</td>
<td>100% of women with 3a or 3b</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>a. Disease progression</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Deteriorating performance status</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 4. | The following are documented for each woman receiving PLDH | 100% of women on PLDH | None | Clinical outcomes = nature and length of response of the cancer
Clinicians should agree locally on adverse effects to be documented for audit purposes |
|   | a. Indications for the therapy | | | |
|   | b. Clinical outcomes | | | |
|   | c. Adverse effects | | | |
| 5. | PLDH treatment is supervised by an oncologist specialising in the chemotherapy of ovarian cancer | 100% of women receiving PLDH | None | An understanding of what constitutes supervision should be agreed within cancer networks |
Calculation of compliance with the measures

Compliance with each measure described in the table is calculated as follows:

\[
\frac{\text{Number of women whose care is consistent with the Criterion plus number of women who meet an Exception listed}}{\text{Number of women to whom the Measure applies}} \times 100
\]

Clinicians should review the findings of measurement, identify if practice can be improved, agree on a plan to achieve any desired improvement and repeat the measurement of actual practice to confirm that the desired improvement is being achieved.
# Appendix D. ECOG Performance Status

## ECOG PERFORMANCE STATUS*

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
</table>