SW Gynaecological Cancer Treatment Guidelines 2005
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A Introduction

The SWCIS Gynaecological Tumour Panel consists of a multidisciplinary team of experts involved in the management of gynaecological malignancies. In 1997, prospective data collection of the management of gynaecological cancer was commenced with longitudinal follow-up. This is co-ordinated by SWCIS using a one page minimum data-set for each gynaecological cancer site and is intended to establish current patterns of care and facilitate development of services in the region.

The Calman Hine Report published in May 1995 proposed a network of cancer units and cancer centres for the diagnosis and treatment of cancer in the UK. The Royal College of Obstetricians and Gynaecologists in association with the British Gynaecological Cancer Society have endorsed this report.

Since the publication of this report and the COG guidelines\(^1\) (1999), gynaecological cancer services have been re-organised and new guidelines have been developed in the South West of England. The effect of these changes on patient treatment and outcomes must be investigated by prospective data collection and audit as established by the SWCIS registration process.

Frequently, patients are given choices regarding their treatment according to their individual circumstances. In addition, debate and controversy surround the whole of clinical practice and this should be shared with patients. Entry into trials to solve these dilemmas should be encouraged. The purpose of these guidelines is not to be prescriptive but to act as a guide to clinicians in order to establish minimum standards of management.

Clearly guidelines cannot cover all connotations of the breadth of gynaecological cancers and some patient individualisation will be appropriate, but dramatic deviations from the guidelines should be documented for audit purposes. We aspire to common standards of patient management, thorough data collection and clinical audit in order to measure outcomes and drive improvements in the service.

The guidelines will be reviewed on an annual basis to reflect the outcomes of new trials and changing treatment options.

\(^1\) Improving outcomes in gynaecological cancers NHS Exec 1999 Catalogue Number 16149
Fig 1: Flow diagram for management of epithelial ovarian cancer

**Presentation**
- WHO status
- Breast exam
- CT/CXR
- US colonoscopy (if indicated)
- CA125
- CEA
- αFP
- βHCG
- LDH if <40 yrs
- Pelvic mass/ascites
- Diagnosed at laparotomy

**Evaluation (all suspected ovarian carcinomas should be referred to a Cancer Centre)**
- Fertility sparing staging, unilateral salpingo-oophorectomy, inspect/biopsy other ovary, washings, omental bx, sample enlarged nodes. Consider appendectomy, random peritoneal bx
- Simple Hyst, BSO, omentectomy, washings, appendectomy, peritoneal biopsies as required. Bx enlarged nodes. Bowel resection if achieves optimal debulking or obstruction imminent. Aim for zero residuum but accept <2cm based on clinical judgement
- CT/CXR chest/abdomen platinum based chemotherapy X 3
- CT/CXR chest/abdomen platinum based chemotherapy X 6

**Primary Treatment**
- IAG1
- >IAG1
- platinum based chemotherapy x 6
- Observe
- Palliative care 2nd line chemo
- Re-evaluate
- PR/CR
- PD
- Fit
- Unfit

**Adjuvant Treatment**
- Local Follow up & individualised treatment for relapse
- Consider laparotomy or DXT for local resistant relapse

**Followup**
B Guidelines for the management of epithelial ovarian carcinoma

1 Background

Epithelial ovarian cancer is the commonest gynaecological cancer in the developed world and has an annual incidence of 5000 women each year in the United Kingdom and is the most important cause of gynaecological cancer related mortality in the western world. It is insidious in onset and difficult to diagnose as it frequently presents with non-specific symptoms like bloating and abdominal discomfort. Owing to the paucity of symptoms and their insidious onset, most women present with advanced disease and 5 year survival rates are approximately 30% (1).

2 Diagnosis (ICD code is C56X)

The suspicion of ovarian cancer is based upon clinical signs, USS/CT imaging, CA125 and cytology of ascites when present. A diagnosis may be reached by FNA cytology or biopsy. The diagnosis is then confirmed with laparotomy and histology.

3 Referral guidelines

The Royal College of Obstetricians and Gynaecologists (RCOG) have published a Clinical Guideline on the Management of Ovarian Cysts in Postmenopausal Women(2). A risk of malignancy index (RMI) can be calculated for patients using a combination of Ca125 and scan features of the ovarian cyst. The RMI score obtained can be used to triage women for management in Gynaecological Cancer Units and Centres.

Calculating the risk of malignancy index (RMI); these are modifications of the original RMI using modified scores

\[ RMI = U \times M \times CA125 \]

- \( U = 0 \) (for ultrasound score of 0); \( U = 1 \) (for ultrasound score of 1); \( U = 3 \) (for ultrasound score of 2–5)

Ultrasound scans are scored one point for each of the following characteristics: multilocular cyst; evidence of solid areas; evidence of metastases; presence of ascites; bilateral lesions.

- \( M = 3 \) for all postmenopausal women dealt with by this guideline

CA125 is serum CA125 measurement in u/ml

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2 Reproduced from Guideline No. 34, Ovarian Cysts in Postmenopausal Women, October 2003, with the permission of the Royal College of Obstetricians and Gynaecologists.
Guidance 1  All suspected cases of ovarian cancer will be referred to the lead gynaecological oncology clinician(s).

In accordance with the RCOG guidelines on referral patterns postmenopausal women in the low risk group can be managed by general gynaecologists, those in the intermediate group in a cancer unit, high risk patients should be treated in a cancer centre.

Guidance 2  Women with ovarian cancer should have a family cancer history recorded and high risk women should be referred to a cancer genetics service.

4  Surgery

The standard treatment is surgical debulking of tumour followed by platinum based chemotherapy. Participation in clinical trials evaluating the role of primary chemotherapy and interval debulking surgery (IBS) is recommended where possible. Outside clinical trials, the patient should be offered standard treatment unless there is a clear indication to deviate from the guidelines.

4.1  Preoperative investigations

Guidance 3  All patients should be assessed pre-operatively by a Consultant/appropriately trained and supervised senior SpR.

Preoperatively all patients should be investigated with serum Ca125 and CEA levels, a chest x-ray, an abdomino-pelvic ultrasound, CT abdomen and pelvis may be considered for assessing operability. All patients should have fitness assessed with FBC, U&Es, LFTs, group and save or cross-match. In addition all patients should have preoperative nutritional assessment.

Guidance 4  All patients should have an adequate bowel history elicited and patients with suspected bowel involvement should be assessed for the likelihood of bowel surgery and bowel preparation offered if necessary.

All candidates for bowel surgery should be assessed preoperatively by a Stoma therapist.
4.2 Operative procedures

All patients should have a midline incision. The largest diameter of the presenting tumour and the largest diameter of post surgical residuum must be recorded.

Guidance 5 Young women with suspected Stage 1A disease will be eligible for conservative surgery comprising salpingo-oophorectomy, inspection +/- biopsy of the other ovary, representative omental biopsy, peritoneal washings, sub-diaphragmatic scrapes, inspection of the whole peritoneal cavity, selective biopsy of palpable pelvic or para-aortic nodes. All other women will have the above plus pelvic clearance and debulking to zero residuum where possible.

Bowel resection or urinary cystectomy will be reserved for patients in which obstruction is imminent or the surgeon believes that these procedures are necessary to debulk to deposits less than 2 cm residuum. If ovarian cancer is found at laparotomy by a surgeon other than the lead gynaecological oncology clinician(s) and optimal debulking is not considered possible: either the abdomen should not be closed before the lead gynaecological oncology clinician(s) has been called to assess the resectability of the disease or a representative biopsy should be taken and the patient referred to the Oncology Team for re-laparotomy or chemotherapy and interval debulking as appropriate.

Guidance 6 In low risk patients it is considered good practice to take an omental biopsy and peritoneal washings in all women with an adnexal mass with a low index of suspicion of cancer who are managed conservatively.

There is very low morbidity associated with an omental biopsy this but will give important information about staging if the histology shows an unexpected cancer.

5 Chemotherapy following surgery

Standard treatment is platinum based chemotherapy. The results of ICON3 indicate that single agent carboplatin is as effective as paclitaxel plus carboplatin. All patients with stage IC-IV should be considered for chemotherapy. Patients with stage Ia/b with adverse features i.e. clear cell or grade 3 histology should also be considered for chemotherapy (ICON1). Paclitaxel in combination with a platinum-based compound or platinum -based therapy alone (cisplatin or carboplatin) should be offered (4-6). The choice of treatment should be made after the patient has discussed the potential risks and benefits (6).

Guidance 7 Paclitaxel and carboplatin is the de facto gold standard regimen.
Regimes used are Paclitaxel 175 mg/m$^2$ (3hr) + carboplatin AUC 6 or AUC(EDTA) 5 for 6 cycles every 3 weeks. Alternatively Carboplatin can be used at dose of AUC 5-6 for 6 cycles every 3-4 weeks.

6 Treatment of recurrent disease

6.1 Second Line Treatment

Treatment following relapse is palliative in intent. In patients who are platinum sensitive ie relapse > 6 months platinum can be repeated. In patients who are platinum resistant ie relapse < 6 months - options include chemotherapy or radiotherapy and supportive care.

Examples of chemotherapy regimens are:
- Topotecan (NICE guidance 28) 1.4mg/m2 D1-5 every 3 weeks,
- Paclitaxel 175 mg/m2 (3hr) every 3 weeks if not given first line,
- Pegylated liposomal doxorubicin 50 mg/m2 D 1 q 3weeks $^{(7)}$,
- Oral Etoposide 50 mg bd x 7-10 days every 3 weeks,
- Weekly Cisplatin 50-70 mg/m2 x 6 plus oral Etoposide 50 mg po daily $^{(8)}$,
- Altretamine 260 mg/m2 /day in 4 divided doses x 14 days, repeated q 4 weeks for up 1 year or until PD or toxicity $^{(9)}$.

6.2 Third Line Treatment

May be considered for patients with performance status 0-2 and disease-free interval of several months. The choice of chemotherapy regimen depends on toxicity and patient choice. Tamoxifen 40mg daily may have some effect.
Summarised below are chemotherapy protocols for ovarian cancer

1. SINGLE AGENT CARBOPLATIN

   DOSE CARBOPLATIN = AUC 6(GFR+25) mg in 500 ml 5% dextrose over 1 hr
   FREQUENCY: 3 – 4 WEEKS

2. PACLITAXEL + CARBOPLATIN

   PACLITAXEL 175 mg/m² over 3 h
   CARBOPLATIN AUC 6 (AUC EDTA 5) over 1 hr
   FREQUENCY: 3 WEEKS

3. PACLITAXEL

   PACLITAXEL 175 mg/m² over 3 hr
   FREQUENCY: 3 WEEKS

4. TOPOTECAN

   TOPOTECAN 1.5 mg/m² IVI D 1-5
   FREQUENCY: 3 WEEKS

5. LIPOSOMAL DOXORUBICIN

   CAELYX 50 mg/m² IVI
   FREQUENCY: 3 WEEKS

6. CAP

   CYCLOPHOSPHAMIDE 500 mg/m²
   DOXORUBICIN 50 mg/m²
   CISPLATIN 50 mg/m²
   FREQUENCY: 3 WEEKS

7. CISPLATIN + PACLITAXEL

   PACLITAXEL 175 mg/m²
   CISPLATIN 50-75 m/m²
   FREQUENCY: 3 WEEKS

8. ORAL ETOPOSIDE

   ETOPOSIDE 50 mg po bd x 7-10 days
   FREQUENCY: 3 WEEKS
Guidance 8  Patients for chemotherapy following relapse should be considered for appropriate clinical trials.

7  Interval debulking surgery

Primary surgery may not be appropriate where patients are not medically fit for surgery, there are radiological signs of widespread low volume tumour not amenable to surgical debulking or there are radiological signs of widespread large volume disease not amenable to surgical debulking. This means bulky abdominal disease involving the upper gut, liver or peritoneal surface. Bulky disease which appears to be primarily omental should be resectable. In addition patients where the diagnosis of ovarian cancer is uncertain eg advanced GI cancer, CEA and Ca19-9 may be helpful in the diagnosis.

7.1 Clinical evidence

Non-randomised studies (3, 11-14) have shown that neoadjuvant chemotherapy does not appear to adversely affect survival. Optimal cytoreduction can be achieved at interval debulking surgery with lower morbidity in those patients responding to chemotherapy. One randomised control trial (15) suggested that secondary cytoreductive surgery in chemosensitive patients may improve survival compared to those treated conventionally with surgery-chemotherapy.

In these patients the diagnosis needs to be established if possible by FNA or biopsy (may require laparoscopy). Platinum based chemotherapy can then be commenced for probable ovarian or peritoneal cancer. For non-gynaecological cancer appropriate chemotherapy is instituted as per local guidelines. This would mean avoiding morbidity/mortality from major surgery and minimising delay in starting chemotherapy. Where interval debulking surgery is considered, surgery is likely to be less radical.

Guidance 9  Primary chemotherapy can be considered where primary surgery is not thought likely to result in optimum debulking with a view to repeating CT halfway through planned chemotherapy for ovarian/peritoneal cancer to assess suitability for interval debulking.

8  Follow-Up

8.1 Clinical trials

Patients in clinical trials should adhere to the appropriate trial protocol.
8.3 Patients off trials

There is no evidence or consensus to guide follow-up protocols. Reliable data on follow-up is confined to trials with a conservatively managed control arm such as Portec in endometrial cancer which advocated intensive surveillance. The aim of follow-up is to identify and treat recurrence, to identify and treat treatment related physical and psychological sequelae, to provide reassurance and to collect survival data. Recurrence of most gynaecological cancers is most likely in the first 2-3 years after primary treatment.

A standard intensive surveillance protocol would comprise 3 monthly clinical review for 2 years followed by 6 monthly review until 5 years before discharge. CA125 and imaging should not be routinely offered. This should be the maximum offered. Less intensive surveillance may be offered according to local protocols.

Low risk borderline tumours ie those without microinvasion, those without non-invasive implants in other tissues and those with completely excised lesions can be discharged at 1 year.

All patients should be told about symptoms associated with recurrence and should have a clear pathway of rapid access to the team between follow-up intervals to avoid delay while a patient waits for the next appointment (16).

9 References

2. RCOG Guideline No 34. Ovarian Cysts in postmenopausal women, October 2003
5. NICE Technology Appraisal Guidance No. 91 Ovarian cancer (advanced) - paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan (review) R May 2005
6. NICE Technology Appraisal Guidance No. 55 Ovarian cancer - paclitaxel (review) R Jan 2003
7. NICE Technology Appraisal Guidance No. 45 now replaced by No 91
12. Surwit E et al., Int J Gynecol Cancer 1996, 6:356-361
Fig 2: Flow diagram for management of cervical cancer

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Evaluation</th>
<th>Primary Treatment</th>
<th>Adjuvant Treatment</th>
<th>Followup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IA1 Colposcopy (Loop/cone)</td>
<td>WHO status Path review @Centre MDT</td>
<td>simple hysterectomy (patient choice or other gynae symptoms)</td>
<td>observe</td>
<td>10 annual smears</td>
</tr>
<tr>
<td>Stage IA2 Colposcopy (Loop/cone)</td>
<td>WHO status Path review @Centre MDT</td>
<td>repeat cone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IB1 EUA, biopsy</td>
<td>WHO status CXR/CT MRI pelvis Centre MDT review</td>
<td>radical hymt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IB2</td>
<td>WHO status CT/CXR chest/abdo MRI pelvis Centre MDT review</td>
<td>radical trachelectomy individualised to patient needs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage II to IV</td>
<td></td>
<td>open radical hymt</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For lesions <2cm CT/MRI node neg:
- CT/MRI node pos **consider** lap nodes
- unfit
- unfit, no extrapelvic disease
- fit, extrapelvic disease

For lesions >2cm <4cm CT/MRI node neg:
- CT/MRI node pos
- unfit
- unfit, no extrapelvic disease
- fit, extrapelvic disease

For lesions >4cm CT/MRI node pos:
- open radical hymt
- unfit
- unfit, no extrapelvic disease
- fit, extrapelvic disease

For adverse features (adenoca, LVI, poorly diff):
- fit
- extrapelvic disease
- unfit
- unfit, no extrapelvic disease

For WHO status CXR/CT MRI pelvis Centre MDT review:
- fit
- extrapelvic disease
- unfit
- unfit, no extrapelvic disease
C Guidelines for the management of cervical carcinoma

1 Evaluation

1.1 Staging guideline

The FIGO staging system is based on clinical assessment at EUA, cystoscopy, the initial diagnostic biopsy, limited imaging with Chest Radiograph and IVP. This remains even in the scanning era, as the majority of cervix cancer cases in the world are in developing countries. Clinical stage I FIGO cases who undergo operation and who subsequently have positive pelvic nodes discovered remain clinical FIGO stage I, but pathology stage III.

1.2 Staging technique

All patients will have FIGO Staging performed by a Consultant/appropriately trained and supervised senior SpR.

The extent of staging is dependent on the stage of disease and requires an adequate unequivocal histological diagnosis of malignancy.

In those patients undergoing assessment for radical therapy, additional radiological staging should comprise MRI scan of the pelvis. CT scan of the chest, abdomen and pelvis should be performed for those patients at increased risk of distant metastases \(^{(1)}\).

Formal examination under anaesthesia, cystoscopy and sigmoidoscopy will be reserved for cases of clinical doubt or stage 1B2 or greater.

All cases should be discussed at the gynaecological cancer multidisciplinary team meeting.

A clinical and radiological stage should be agreed and recorded at the multidisciplinary team meeting.
### 1.3 Staging classification - cervix

<table>
<thead>
<tr>
<th>Stage</th>
<th>UICC</th>
<th>FIGO</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td></td>
<td></td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td></td>
<td></td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>Tis</td>
<td></td>
<td></td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>I</td>
<td></td>
<td>Cervical carcinoma confined to uterus (extension to corpus should be disregarded)</td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td></td>
<td>Invasive carcinoma diagnosed only by microscopy. All macroscopically visible lesions—even with superficial invasion—are T1b/IB. Stromal invasion with a maximal depth of 5 mm measured from the base of the epithelium and a horizontal spread of 7 mm or less. Vascular space involvement, venous or lymphatic, does not affect classification</td>
</tr>
<tr>
<td>T1a1</td>
<td>IA1</td>
<td></td>
<td>Measured stromal invasion 3 mm or less in depth and 7 mm or less in horizontal spread</td>
</tr>
<tr>
<td>T1a2</td>
<td>IA2</td>
<td></td>
<td>Measured stromal invasion more than 3 mm and not more than 5 mm with a horizontal spread 7 mm or less</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td></td>
<td>Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a2/IA2</td>
</tr>
<tr>
<td>T1b1</td>
<td>IB1</td>
<td></td>
<td>Clinically visible lesion 4 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1b2</td>
<td>IB2</td>
<td></td>
<td>Clinically visible lesion more than 4 cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td></td>
<td>Cervical carcinoma invades beyond uterus but not to pelvic wall or to the lower third of the vagina</td>
</tr>
<tr>
<td>T2a</td>
<td>IIA</td>
<td></td>
<td>Tumour without parametrical involvement</td>
</tr>
<tr>
<td>T2b</td>
<td>IIB</td>
<td></td>
<td>Tumour with parametrical involvement</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td></td>
<td>Tumour extends to the pelvic wall and/or involves the lower third of the vagina, and/or causes hydronephrosis or nonfunctioning kidney</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td></td>
<td>Tumour involves lower third of the vagina, no extension to pelvic wall</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td></td>
<td>Tumour extends to pelvic wall and/or causes hydronephrosis or nonfunctioning kidney</td>
</tr>
<tr>
<td>T4</td>
<td>IVA</td>
<td></td>
<td>Tumour invades mucosa of the bladder or rectum, and/or extends beyond true pelvis (Bullous edema is not sufficient to classify a tumour as T4)</td>
</tr>
<tr>
<td>M1</td>
<td>IVB</td>
<td></td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>
2 Treatment early stage disease

2.1 FIGO Stage Ia1
If margins are negative, invasion is less than 3mm and no lymphovascular invasion is found, then options are:

1. If fertility is desired – close surveillance protocol
2. If fertility is not an issue; consider with the patient the options of vaginal hysterectomy or total abdominal hysterectomy and node-sampling.

If margins are positive for invasion, or >3mm depth or lymphovascular invasion, then continue the appropriate work-up pathway for radical therapy.

Guidance 1 FIGO stage Ia1 disease will be managed by cone biopsy or simple hysterectomy as required.

2.2 FIGO Stage Ia2
Stage Ia2 disease should be reviewed by the oncology team and individualised to simple or radical surgery as appropriate. Adverse histological factors such as depth of invasion, high grade and presence of lymphovascular space invasion should be taken into account in deciding radicality of treatment.

If fertility is desired, the patient must make an informed decision with a clear understanding of the risk of recurrence.

Guidance 2 The minimum extent of cervical surgery should then comprise generous cone biopsy but with consideration to extraperitoneal or laparoscopic pelvic lymph node dissection. Where there is any doubt as to the extent of the lesion or completeness of excision radical hysterectomy should be employed.

Predictions of the risk are shown below (2):

<table>
<thead>
<tr>
<th>Depth of invasion or stage</th>
<th>Risk of involved nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3mm deep cT1a1/FIGO Ia1</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>3-5mm (cT1a2/FIGO Ia2)</td>
<td>4%</td>
</tr>
<tr>
<td>stage cT1b/FIGO Ib</td>
<td>16%</td>
</tr>
</tbody>
</table>

If fertility is required in patients with stage 1A2 / IB1 disease, radical trachelectomy should only be performed by experienced radical vaginal surgeons and must be entered into the national database. It is recommended that the criteria used by the London group should be applied.

Pelvic node dissection will comprise complete pelvic and common iliac node dissection with each being examined separately histologically.
2.3 FIGO Stage IB1, 2A

Radical hysterectomy and pelvic lymphadenectomy can be considered as primary therapy in the following situations:
- Depth of invasion more than 3 mm
- Lesion less than 4 cm in diameter
- Absence of a highly aggressive histology
- Absence of extensive lymphovascular invasion
- Contraindications to primary radiation therapy such as prior radiotherapy,
  TB,
  syphilis,
  PID not responding to conservative therapy with antibiotics,
  previous pelvic abscess,
  Crohn’s disease,
  ulcerative or ischaemic colitis,
  severe diverticular disease,
  large uterine fibroids or undiagnosed adnexal masses
- Suitable surgical and anaesthetic risk

Para-aortic node sampling is indicated if there is a clinical suspicion of node involvement to plan extent of radiotherapy fields.

The place of oophorectomy at the time of radical surgery should be discussed on an individual basis with the patient.

Outcome is similar for patients treated surgically or with primary chemoradiotherapy but with differing side effect profile. This should be discussed with the patient prior to decision regarding modality of treatment. Morbidity is significantly increased in those patients receiving dual treatment and such eventuality should be discussed at the preoperative MDT (multidisciplinary team) planning session.

Guidance 3 Stage IB1 and selected IIA carcinomas will be managed by radical hysterectomy and lymph node dissection in those patients fit to undergo extended surgery.

3 Adjuvant therapy

All tumours will be reviewed histologically by the Gynaecological Pathologist at the MDT meeting.

Patients with more than 2 positive pelvic nodes or with positive resection margins will be offered adjuvant pelvic radiotherapy. In patients with fewer than 2 positive nodes with other adverse features (such as large volume nodal deposits or extranodal extension by tumour) adjuvant radiotherapy should be considered.
Adjuvant therapy may be offered in the absence of nodal metastases when adverse prognostic factors are present such as extensive lymphovascular invasion, high grade or aggressive cell type \(^4\). Adjuvant chemoradiotherapy may be recommended after assessment of the side effect profile \(^5\). Patients with histologically proven para-aortic node disease may be considered for extended field radiotherapy with or without chemotherapy \(^6\).

**Guidance 4** CT or MRI will be used to plan adjuvant therapy.

### 3.1 FIGO Stage IB2

Review of the literature supports concurrent chemoradiotherapy as the primary treatment of choice in the tumours > 4cm in size compared with surgery or radiotherapy alone \(^7\)-\(^10\).

For exophytic tumours or those patients with contraindications to XRT, radical hysterectomy should be undertaken.

**Guidance 5** Standard treatment is concurrent chemoradiotherapy (see below).

### 4 Locally advanced cancer

#### 4.1 FIGO Stage 2B – IVA

The mainstay of primary therapy is radiotherapy or concurrent chemoradiotherapy depending on fitness.

Selected cases of usually younger women with equivocal or early IIB disease may exceptionally be considered for surgery when there is no radiological evidence of lymphadenopathy.

#### 4.2 Radiotherapy/Chemoradiotherapy

Chemoradiotherapy using weekly cisplatin should be considered for patients with adequate renal function.

MRI of pelvis should be used for planning radiotherapy.

The regimen of radiotherapy is designed to deliver a minimum dose of 75 Gy to the primary tumour using a combination of external beam and intracavity radiotherapy. It is assumed that the pelvic sidewall receives 20% of the point A dose during intracavity irradiation.
Uninvolved lymph nodes are treated prophylactically in all but stage IA. They should receive a minimum dose of 50 Gy (45Gy external beam plus 5-6 Gy intracavity) for low risk (<4 cm) disease and 55 Gy (50 Gy external beam plus 5-6 Gy intracavity) for high risk (>4 cm) tumours.

Disease extending beyond the cervix and/or involving the pelvic lymph nodes should receive a minimum dose of 60 Gy.

Rectal doses should not exceed 60-65 Gy.

Total doses given above are based on conventional radium intracavity treatments using a dose rate of about 0.5 Gy/hr. For the medium dose rate Selectron (>1.5Gy/hr) there is a 10% reduction in the dose. For high dose rate Selectron (1.5 Gy/minute) the dose is reduced by 40-45%.

Para-aortic nodes are not normally treated but may be included if involved. Dose greater than 45 Gy is seldom tolerated.

After radical hysterectomy and lymph node dissection, the pelvis will not usually tolerate more than 50 Gy with external beam radiotherapy. The indications for post-op radiotherapy are findings of >2 involved lymph nodes or positive resection margins.

To optimise dosimetry and avoid overdose in the pelvis from combined treatment, radiotherapy to the pelvis is given with external beam therapy first followed by intracavity therapy.

The regimens of radiotherapy follow (Table 1) and state the corrected dose rate for MDR and HDR. Using intra-uterine tube and ovoids, the maximum rectal dose (MR) is about two thirds of Point A dose.

To optimise outcome after radiotherapy, unscheduled gaps or prolongation of the total course of treatment should be avoided if possible. The overall treatment time for external beam and intracavity radiotherapy should not exceed 7 weeks.

The Hb should be maintained above 12 g/dl throughout radiotherapy.

*Table 1: External beam and brachytherapy doses according to FIGO stage*

<table>
<thead>
<tr>
<th>STAGE</th>
<th>EXTERNAL</th>
<th>CAESIUM</th>
<th>SELECTRON</th>
<th>SELECTRON</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>LDR</td>
<td>MDR</td>
<td>HDR</td>
</tr>
<tr>
<td>IB(&lt;4cm)</td>
<td>45Gy/25/5W</td>
<td>30Gy</td>
<td>27Gy</td>
<td>16.5/3/8 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(MR 20Gy)</td>
<td>(MR 18Gy)</td>
<td>MR 11Gy/3/8</td>
</tr>
<tr>
<td>IB(&gt;4cm)</td>
<td>50Gy/25-28/5 ½W</td>
<td>25Gy</td>
<td>22.5Gy</td>
<td>14Gy/2/8 days</td>
</tr>
<tr>
<td>II,IIIB,IVA*</td>
<td></td>
<td>(MR 15Gy)</td>
<td>(MR 13.5)</td>
<td>MR9.3Gy/2/8</td>
</tr>
<tr>
<td>IIIA</td>
<td>50Gy/25-28/5 ½W</td>
<td>15Gy at 0.5cm (MR 15Gy)</td>
<td>13.5Gy at 0.5cm (MR 13.5Gy)</td>
<td>8Gy at 0.5cm/2/8 days</td>
</tr>
</tbody>
</table>

MR=maximum rectal dose
* +5GY /3/3d pelvic sidewall boost if required.
4.3 External beam radiotherapy techniques

1. Treatment volume for extended pelvis
MRI should be used for planning radiotherapy to ensure adequate margins around known tumour. The minimum margins for the treatment volume are outlined below:

**Anterior / posterior margins**
- Top border: L4/5 interspace; shield top corners if possible
- Lower border: bottom of obturator foraminae or introitus for tumour in lower third vagina
- Lateral borders: 1.0-1.5 cm lateral to bony pelvis or nodes

**Lateral margins**
- Anterior border: mid symphysis pubis
- Posterior border: lower S2 or S2/3 junction

2. Treatment volume for true pelvis

**Anterior / posterior margins**
- Top border: mid SI joints
- Lower border: bottom of obturator foraminae
- Lateral borders: 1.0-1.5 cm lateral to bony pelvis or nodes

**Lateral margins**
- Anterior border: mid symphysis pubis
- Posterior border: lower S2 or S2/3 junction
3. Treatment volume for pelvic sidewall boosts
After intracavity treatment use opposed A/P fields.

<table>
<thead>
<tr>
<th>Border</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial border</td>
<td>composite 70 Gy isodose line at its most lateral point</td>
</tr>
<tr>
<td>Lower border</td>
<td>bottom of obturator foramina</td>
</tr>
<tr>
<td>Upper border</td>
<td>mid SI joints</td>
</tr>
<tr>
<td>Lateral border</td>
<td>1.0-1.5 cm lateral to bony pelvis or nodes</td>
</tr>
</tbody>
</table>

4. Treatment volume for para-aortic fields
Use opposed A/P fields

<table>
<thead>
<tr>
<th>Border</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper border</td>
<td>top of L1</td>
</tr>
<tr>
<td>Lower border</td>
<td>bottom of L4 (gap to extended pelvis field)</td>
</tr>
</tbody>
</table>

4.4 Chemoradiotherapy

For patients with suitable performance status and adequate renal function, chemoradiotherapy with weekly cis-platin 40mg/m² (maximum dose 70 mg) over 5 weeks is given during external beam radiotherapy.

5. Palliative chemotherapy

Chemotherapy has a limited role in palliation. It may be considered in selected patients with adequate renal function and performance status. The choice of chemotherapy regimen needs to be carefully considered to minimise toxicity. Single agent cisplatin 75mg/m² is recommended over combination cisplatin regimens. Combination chemotherapy produces more responses but does not significantly extend life compared with single agents.

6. Recurrent disease

Pelvic recurrence should receive pelvic XRT +/- chemotherapy if this has not been given.

Central pelvic recurrence following previous radiotherapy should be considered for exenteration in appropriate patients after exclusion of other metastases.

Multisite or extrapelvic recurrence should be considered for palliative chemotherapy if symptomatic as above.
7 Follow-up

7.1 Clinical trials

Patients in clinical trials should adhere to the appropriate trial protocol.

7.2 Patients off trials

There is no evidence or consensus to guide follow-up protocols. Reliable data on follow-up is confined to trials with a conservatively managed control arm such as Portec in endometrial cancer which advocated intensive surveillance. The aim of follow-up is to identify and treat recurrence, to identify and treat treatment related physical and psychological sequelae, to provide reassurance and to collect survival data. Recurrence of most gynaecological cancers is most likely in the first 2-3 years after primary treatment.

7.3 Follow-up of stage 1a1 and low risk stage 1a2 disease

The minimum surveillance of patients whose primary tumour was managed by cone biopsy only is cytological surveillance in line with the National Cervical Screening Programme ie annual cervical cytology for 5 years. The minimum surveillance of patients whose primary tumour was managed by simple hysterectomy is cytological surveillance in line with the National Cervical Screening Programme ie 2 vault smears 6 and 12 months after surgery.

7.4 Follow-up of high risk Stage 1a2 to Stage 4 disease.

A standard intensive surveillance protocol would comprise 3 monthly clinical review for 2 years followed by 6 monthly review until 5 years before discharge. There is no evidence that vault cytology is helpful. This should be the maximum offered. Less intensive surveillance may be offered according to local protocols.

All patients should be told about symptoms associated with recurrence and should have a clear pathway of rapid access to the team between follow-up intervals to avoid delay while a patient waits for the next appointment (11).
8 References

Fig 3: Flow diagram for management of endometrial cancer

**Presentation**
- Clinically confined to uterus (Stage I)
- Cervical extension (Stage II)
- Advanced Disease

**Evaluation**
- WHO status TVS EUA Endo. biopsy
- Path review at MDT (Unit/Centre)
- CT/CXR
- MRI

**Primary Treatment**
- Simple hyst, BSO, washings
- DXT + brachytherapy
- Surgery
- Chemotherapy

**Adjuvant Treatment**
- DXT consider brachytherapy
- Palliative care / hormone therapy

**Followup**
- nil (Follow up in Unit)
- None
- DXT
D Guidelines for the management of endometrial carcinoma

1 Background

1.1 Introduction

Endometrial Cancer is the second commonest gynaecological cancer in England and Wales with 3000 new cases per year. The overall 5 year survival is 70%\(^{(1)}\) which is disappointing considering 75% of patients present with early (stage I) disease. Preparation for this guideline included an electronic database search of PubMed and the Cochrane Library. Large numbers of RCTs are lacking in the treatment of endometrial cancer. Evidence is classified following the NHS Executive classification system - section H.

1.2 Aetiology

The main risk factor associated with endometrial cancer is unopposed oestrogens. These can be: endogenous eg 1 Anovulation and nulliparity eg PCOS; eg 2 Obesity, because in postmenopausal women the major source of unopposed oestrogen is the conversion of androstenedione to oestrone in adipose tissue.

Or exogenous eg Unopposed oestrogen HRT which increases the risk of endometrial cancer by a factor of 7-10.

Guidance 1 Unopposed oestrogen should not be prescribed to women with an intact uterus. (B)

Women taking tamoxifen are also at risk due to its oestrogen agonist effects and this risk increases with duration of use. Abnormal bleeding on tamoxifen should be investigated. Ultrasound can be misleading in assessment of women on tamoxifen and outpatient (pipelle) sampling can be inadequate.

Guidance 2 Abnormal bleeding in tamoxifen users should be investigated, ideally using out-patient hysteroscopy. Conversion to an aromatase inhibitor should be considered by the breast Clinical Oncologist. (B)

Women with a family or previous history of breast or colon cancer are at increased risk. Women from an HNPCC family are at up to a 30% age related risk.
Guidance 3  Women with endometrial cancer should have a family cancer history recorded and high risk women should be referred to a cancer genetics service. (B)

2  **Presentation**

2.1  Referral pathway

For the GP

Guidance 4  If endometrial cancer is suspected the patient should be referred to the cancer unit/centre using the Trust's 2 week wait system\(^{(2)}\). (C)

For non-oncological consultants

Guidance 5  Trusts should have a robust 2 week wait system and an efficient system for diagnosis and triage of cases. Confirmed cases should be referred to the lead cancer gynaecologist at the next gynaecological oncology clinic. (C)

Differential diagnosis includes cervix cancers with superior spread to the endometrium from the endocervix or isthmus and locally advanced vaginal, bladder and rectal cancers. Adencarcinomas of the cervix and endometrium may be differentiated by immunostaining.

Over 90% of endometrial carcinomas present with irregular or postmenopausal vaginal bleeding. However only 20% of patients with postmenopausal bleeding will have a malignant origin for their bleeding of which over 50% will be due to endometrial carcinoma. The older the woman the higher the chances are that the bleeding is due to tumour. A small proportion will present with an offensive vaginal discharge due to a draining pyometra. It may also be a chance finding at operation for apparent benign disease.

The endometrial biopsy should be reviewed at the gynaecology MDT to confirm the diagnosis and assess histological subtype prior to a treatment plan being formulated. If a sarcoma is suspected, further opinion may be required from the special sarcoma MDT prior to proceeding.

Guidance 6  Gynaecology MDTs should ensure that pathways for collaboration with their local sarcoma MDT are in place.

3  **Evaluation and staging**

The association of endometrial cancer with advanced age, heart disease, diabetes and obesity means that high rates of comorbidity are expected in this
patient population. For this reason patients may not be fit for standard protocols and may require individualised treatments.

Primary assessment in all cases is with transvaginal ultrasound (TVS)\(^3\). This has a negative predictive value approaching 100% for the exclusion of endometrial cancer, but sensitivity depends on the cut-off used for normal endometrial thickness (usually no more than 4mm). All postmenopausal patients with an endometrial thickness >4mm or persistent bleeding despite a normal endometrial thickness should have an endometrial biopsy. (NHS Executive, 1999). The value of endometrial thickness in perimenopausal bleeding is questionable as the range of thickness is so variable. If the endometrium is difficult to identify then hysteroscopy should also be considered.

**Guidance 7** TVS is an important primary screening tool in patients with posmenopausal bleeding. A cut off of 4mm is recommended. (B)

Various sampling devices are available to obtain an endometrial biopsy. Randomised trials have shown the Pipelle and Vabra aspirators to give equal diagnostic accuracy although the Pipelle causes less discomfort. Both perform as well as D&C in diagnostic accuracy. (B)

**Guidance 8** Outpatient endometrial sampling is a useful quick test to be used in conjunction with TVS if the endometrial thickness is >4mm.

Outpatient hysteroscopy is an important addition to the assessment of abnormal uterine bleeding. There have been no randomised trials to study its effectiveness compared to other methods. In one study 95% of all pathological conditions were detected by hysteroscopy \(^4\).

**Guidance 9** Hysteroscopy should be used in patients with an endometrial thickness greater than 4mm if readily available. (B)

Pelvic examination may help to detect any extra-uterine disease.

### 3.1 Staging guideline

The FIGO staging system is based on a mixture of clinical assessment and pathological findings. It may differ with each sub-stage. The UICC-TNM stage system makes a clear distinction between clinical and pathological stage. It also incorporates lymph and vascular channel invasion stages. These features have significant prognostic implications in endometrial cancer \(^5\). The UICC-TNM stage also incorporates residual stage classifications (R0, R1 & R2) which describe the extent of primary surgical excision.

For this reason, SWCIS recommends that the UICC-2003 TNM system is used for endometrial cancer (Table 2). As clinicians are more familiar with the FIGO system it is likely that both will be used in transition.
3.2  Staging technique

Guidance 10  A chest X-ray is essential for staging. (C)

An MRI scan will help identify the site and size of the primary tumour, any evident myometrial invasion, the presence of occult cervical involvement and possibly the presence of lymph node metastases\(^{(6)}\) (B). There is no evidence for the routine use of MRI in G1/G2 disease. For G3 disease or where cervical involvement is suspected, MRI or CT should be considered because the role of lymphadenectomy and radical hysterectomy respectively should be discussed with the patient (C). The ASTEC trial will clarify the role of lymphadenectomy in due course.

Guidance 11  The value of MRI in planning treatment is unproven and should not be used as a routine investigation.

<table>
<thead>
<tr>
<th>Table 2: Staging classification endometrial cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary tumour stage</strong></td>
</tr>
<tr>
<td><strong>UICC</strong></td>
</tr>
<tr>
<td>TX</td>
</tr>
<tr>
<td>T0</td>
</tr>
<tr>
<td>Tis</td>
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<tr>
<td>T1</td>
</tr>
<tr>
<td>T1a</td>
</tr>
<tr>
<td>T1b</td>
</tr>
<tr>
<td>T1c</td>
</tr>
<tr>
<td>T2</td>
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<td>T2a</td>
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<td>T2b</td>
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<td>T3</td>
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<tr>
<td>T3a</td>
</tr>
<tr>
<td>T3b</td>
</tr>
<tr>
<td>T3c</td>
</tr>
<tr>
<td>T4</td>
</tr>
<tr>
<td>M1</td>
</tr>
<tr>
<td>R</td>
</tr>
</tbody>
</table>
4 Primary treatment

4.1 Carcinoma in situ and early invasive cancer; stage Tis – T1/FIGO stage 0-I (G1/G2)

Seventy-five percent of patients with endometrial cancer have suspected stage 1 disease at presentation and 25%-60% of patients with apparent stage Tis will have invasive cancer on final assessment of the uterine histology. If medically operable the surgical procedure should include peritoneal washings, total hysterectomy and bilateral salpingo-oophorectomy. During surgery the abdominal organs including the diaphragm, liver, omentum and pelvic and abdominal peritoneal surfaces should be carefully inspected (B). Until the value of MRI is established, retrospectively established Stage 1C G1/G2 disease will continue to be treated by simple hysterectomy bilateral salpingo-oophorectomy and washings. The literature is divided about the prognostic value of positive peritoneal washings and there is no evidence for altered management based on washings (7) (B). It is however part of staging and has no morbidity.

**Guidance 12** The minimum surgical treatment of endometrial cancer is total hysterectomy bilateral salpingo-oophorectomy and peritoneal washings.

4.2 Stage 1 G3 disease

The role of lymphadenectomy in addition to hysterectomy, BSO and washings remains in equipoise pending ASTEC. Patients should be counselled about the issue and a patient centred decision made. (B)

The risk of positive nodes in endometrial cancer increases with histological grade and depth of myometrial invasion. In a surgicopathological study, 10% of 621 women with stage 1 disease were found to have pelvic lymph node metastases. The frequency of positive nodes was highest in those with grade 3 (poorly differentiated) tumours and in those with deep myometrial invasion (7). Some gynaecological oncologists contend that low grade and non-invasive endometrial cancers do not justify routine lymphadenectomy as the incidence of node metastases is so low. Several studies have attempted to address the question of whether lymphadenectomy might be beneficial to overall survival. There are no data from prospective RCTs. All the studies published to date have been retrospective and conflicting. Four of them showed no evidence of benefit on survival (8,9) but 2 studies did show a possible beneficial role of a lymphadenectomy on survival (10,11).

**Guidance 13** There is no evidence that lymphadenectomy improves survival in patients with low to moderate risk endometrial cancer. The evidence that survival is improved in high risk disease is
inadequate. Patients should be informed that the evidence for lymphadenectomy is weak and it should therefore only be offered as part of a randomised controlled trial (ASTEC) or through informed choice after non-directional counselling.

4.3 Laparoscopic surgery

Laparoscopic surgery in gynaecological oncology is an expanding treatment option but there have been concerns regarding tumour spillage under high CO2 pressures, port site metastases and the comorbidity of many patients with endometrial cancer. Eltabbakh concluded that the survival of women with early stage endometrial cancer is not worsened by laparoscopy. However, this was a retrospective review and longer follow-up is needed. A randomised trial of laparoscopic versus open surgery demonstrated that LAVH for endometrial cancer is associated with a lower peri-operative morbidity compared to the conventional abdominal approach. This study does not allow detection of any differences in recurrence or overall survival.

Guidance 14 Laparoscopic surgery is the treatment of choice and should be offered to suitable women with endometrial cancer if the surgeon possesses the necessary surgical skills.

4.4 Adjuvant post-operative radiotherapy

FIGO Stage I
Patients with stage I endometrial cancer thought to be at a higher risk of relapse generally receive post-operative radiotherapy to the pelvis although there is no evidence to show any significant improvement in survival.

Treatment protocols have been developed empirically based on local experience and reported series of patients. An early randomised trial by Aalders et al in 1980 showed that the addition of external beam radiotherapy to intracavitary treatment reduced relapse in the pelvis from 6.9% to 1.9%. There was no difference in survival.

The GOG study has also shown that external beam radiotherapy improved pelvic control. The pelvic relapse rate was 1.6% compared with the control group of 8.5%. Patients with stage IB,C and IIA and papillary serous or clear cell pathology were excluded.

More recently, the PORTEC trial in the Netherlands studied the value of post-operative radiotherapy in medium risk stage I patients. This was defined as grade I/stage IC; grade 2/stage IB,C and grade 3/stage IB. All patients received intracavitary treatment. The addition of external beam therapy to the pelvis improved the rate of recurrence in the pelvis from 14% to 4%. Patients under the age of 60 did much better than the older patients. It was argued that adjuvant radiotherapy could be delayed to salvage relapse as survival was
similar in the 2 groups of patients. It is important to note that patients with grade 3/stage IC were excluded.

For high risk patients, many centres have used both external beam therapy and vault radiotherapy for post-operative treatment. Surgical pathological studies have indicated that the risk of metastases is increased if the tumour is poorly differentiated and if there is marked myometrial invasion. Lymphadenectomy is not generally performed in the UK and the use of adjuvant radiotherapy has been based on the presence of high risk features.

ASTEC trial is addressing the value of external beam radiotherapy for high risk features following conventional surgery and also after conventional surgery and lymphadenectomy. High risk is one or more of the following: grade 3, stage IC, papillary serous or clear cell type or positive peritoneal cytology irrespective of histopathology. Centres are asked to state in advance whether they will give vault radiotherapy to all patients or only those randomised to external beam therapy.

PORTEC 2 is identifying high risk patients as grade 1,2/ stage IC and age 60 or older; grade 3/stage IB and age 60 or older; grade 1,2/stage IIA any age and grade 3/stage IIA.

A recent informal questionnaire of radiotherapy centres in the UK by the British Institute of Radiology has shown there is no universal agreement on the definition of no risk, intermediate risk and high risk. Also there is no agreement on the use of intracavitary radiotherapy alone, external beam therapy alone or a combination of the two.

This guideline attempts to rationalise practise in the Southwest region until the results of ASTEC and PORTEC 2 are available.

Guidance 15 There is no evidence that routine adjuvant post-operative radiotherapy for grade 1 or 2 and stage IA/IB improves survival. Patients may either be treated with radiotherapy on relapse or be considered for post-operative vault radiotherapy.

Guidance 16 Women with grade 3, stage IC or positive peritoneal washings (stage IIIA) should be considered for external beam therapy and vault treatment to improve local control as the risk of local relapse can be as high as 50%.

4.5 FIGO stage II disease

Patients fit for surgery with tumour involving the cervix on clinical assessment or MRI should be offered radical hysterectomy and pelvic lymphadenectomy.
Patients not fit for radical surgery with stage II disease may be treated with simple hysterectomy and post-operative radiotherapy. In patients not fit for surgery may be treated with radical radiotherapy.

Radiotherapy should be considered following surgery where the pathology shows cervical involvement.

Relative contra-indications for pelvic radiotherapy include previous radiotherapy and chronic bladder or bowel disease such as colitis, severe diverticulitis and pelvic abscess.

**Guidance 17** Women with stage II endometrial cancer should be considered for radical hysterectomy and pelvic lymphadenectomy with post-operative radiotherapy for positive lymph nodes (as for cervical cancer).

### 4.6 FIGO stage III/IVdisease

Surgery may be curative in cases of early serosal involvement or limited spread to the vagina. Post-operative radiotherapy to the pelvis should also be given.

Treatment for clinically obvious stage III disease needs to be individualised but cytoreductive surgery with omentectomy if involved may be an option (C).

Palliative surgery including bowel or urinary diversion maybe appropriate is stage IV disease although radiotherapy and/or platinum based chemotherapy may also offer useful palliation (C).

### 5 Adjuvant treatment

#### 5.1 Radiotherapy regimens

The regimen of radiotherapy is in the table below:

*Table 3: External beam and brachytherapy doses according to FIGO stage*

<table>
<thead>
<tr>
<th>Stage Post TAH/BSO</th>
<th>External RT</th>
<th>Caesium LDR</th>
<th>Selectron MDR</th>
<th>MicroSelectron HDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>G3, IABC GI,2, IC AnyG, II, IIIA</td>
<td>45Gy/25/5w</td>
<td>15Gy at 0.5cm</td>
<td>13.5Gy at 0.5cm</td>
<td>8Gy/2/4 - 8days</td>
</tr>
<tr>
<td>Inoperable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I,II,IIIA</td>
<td>45Gy/25/5w</td>
<td>15Gy to serosa</td>
<td>13.3Gy to serosa</td>
<td>8gy/2/4 - 8days to serosa</td>
</tr>
</tbody>
</table>

The corrected dose for MDR and HDR are stated.
For inoperable tumours, radical radiotherapy maybe appropriate. CT/MRI is required for Brach therapy dosimetry to determine the thickness of the uterine wall.

Vault radiotherapy may be considered in selected low risk tumours.

5.2 Adjuvant hormone therapy

A number of non-randomised studies in the 1970s and 1980s suggested that adjuvant progestogens may be of benefit in reducing recurrence rates and therefore overall survival but they were of variable quality with variable doses and heterogeneous patient characteristics.

The most recent report concerns an RCT of oral MPA for 3 years versus control in a high-risk group of patients treated in the COSA-NZ-UK trial. No statistically significant differences were noted between the 2 groups when analysed on an “intention to treat” basis \(^{(18)}\).

The meta-analysis of Martin-Hirsch et al and the recent Cochrane Review of Progestogen Therapy for Endometrial Cancer also failed to demonstrate that adjuvant progestogen therapy has a significant beneficial effect on the survival of patients with endometrial cancer \(^{(19,20)}\) \(A\).

**Guidance 18** There is no evidence for a role of adjuvant progestogens in the primary management of endometrial cancer

5.3 Adjuvant chemotherapy

There is no role for adjuvant chemotherapy following surgery.

However, papillary serous tumours behave more like ovarian cancer and maybe considered for adjuvant platinum based chemotherapy after surgery. \(C\)

**Guidance 19** Platinum based chemotherapy may be considered for patients with papillary serous carcinomas in view of their pattern of spread and poor prognosis.
6 Palliative therapy in advanced or recurrent disease

6.1 Radiotherapy regimens

Palliative radiotherapy is useful for controlling symptoms such as bleeding and pain.

6.2 Hormone therapy

There is general agreement that progestogens can be useful as palliative treatment for recurrent disease, however response rates are low with an 8% complete and 6% partial response rate. The median survival is 10 months\(^{(21)}\).

6.3 Chemotherapy

The response rate for progestagens for advanced and recurrent cancer is dismal. The response rate for platinum based chemotherapy is over 50%. Palliative chemotherapy maybe helpful in selected patients who are able to tolerate treatment for relief of symptoms (C).

Guidance 20 Platinum based chemotherapy maybe considered for selected patients with advanced or recurrent tumours for palliation.

7 Follow-up

7.1 Clinical trials

Patients in clinical trials should adhere to the appropriate trial protocol.

7.2 Patients off trials

There is no evidence or consensus to guide follow – up protocols. Reliable data on follow-up is confined to trials with a conservatively managed control arm such as Portec in endometrial cancer which advocated intensive surveillance. The aim of follow-up is to identify and treat recurrence, to identify and treat treatment related physical and psychological sequelae, to provide reassurance and to collect survival data. Recurrence of most gynaecological cancers is most likely in the first 2-3 years after primary treatment.

A standard intensive surveillance protocol would comprise 3 monthly clinical review for 2 years followed by 6 monthly review until 5 years before discharge. There is no evidence that vault cytology is helpful. This should be the maximum offered. Less intensive follow-up of low risk women treated by surgery alone may be offered according to local protocols.
7.2.1 Uterine Sarcomas

A minority of patients with uterine sarcomas will present with salvageable isolated pulmonary metastases. An annual chest X-ray should be performed for 5 years.

All patients should be told about symptoms associated with recurrence and should have a clear pathway of rapid access to the team between follow-up intervals to avoid delay while a patient waits for the next appointment (22).

7 References

Fig 4: Flow diagram for management of squamous vulva carcinoma

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Evaluation</th>
<th>Primary Treatment</th>
<th>Adjuvant Treatment</th>
<th>Followup</th>
</tr>
</thead>
<tbody>
<tr>
<td>diagnostic biopsy</td>
<td>verrucous</td>
<td>Independent Path review @Centre MDT</td>
<td></td>
<td>observe</td>
</tr>
<tr>
<td>excise small lesions</td>
<td>confirmed</td>
<td></td>
<td>wide excision</td>
<td>observe</td>
</tr>
<tr>
<td>wedge large lesions</td>
<td>confirmed</td>
<td></td>
<td>lateral</td>
<td>contrastateral node dissection</td>
</tr>
<tr>
<td>WHO status</td>
<td>upstage</td>
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<td>RWE UGND</td>
<td>DXT</td>
</tr>
<tr>
<td>IA Path review @Centre MDT</td>
<td>Stage IB/2</td>
<td></td>
<td>RWE BGND</td>
<td>palliative care</td>
</tr>
<tr>
<td>IB and above: Path &amp; Clinical review at Centre MDT WHO status</td>
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<td>radical surgery</td>
<td>chemoradiation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>node negative (CT)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Node negative (FNA/bx)</td>
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36
E Guidelines for the management of vulval cancer

As informed by the RCOG working party report 2005 (see contributors Appendix 3) and reviewed by O McNally at Musgrove Park Hospital for SWCIS June 2005. Evidence is classified following the NHS Executive classification system - section H.

1 Summary of recommendations

1.1 Indication for referral

Guidance 1
Vulval cancer frequently presents with a lump. In a woman who presents with an unexplained vulval lump referral should be urgent. (C) NICE guidelines July 2004.

Guidance 2
Vulval cancer can also present with vulval bleeding, pruritus, pain and ulceration. In women with these symptoms it is reasonable to use a period of ‘treat, watch and wait’ as a method of management but this should include the offer of active follow-up until these symptoms resolve or a diagnosis is confirmed. If symptoms persist referral should be routine. (C) NICE guidelines July 2004.

1.2 Management

Guidance 3
Women with high grade VIN, VIN with high grade multicentric disease, VIN in the immunosuppressed, Paget disease and melanoma in situ should be followed-up by either specialist multidisciplinary vulva clinics or gynaecological oncologists (C).

Guidance 4
Vulval cancer should be managed in Gynaecological Cancer Centres by multidisciplinary teams (B/C).

Guidance 5
The patient should be seen within two weeks of referral and definitive treatment commenced no later than 4 weeks following diagnosis.

Guidance 6
Radical treatment should not be undertaken without prior biopsy confirmation of malignancy (C).

**1.3 Surgery**

**Guidance 7**  
Wide radical local excision of the primary tumour with a minimum margin of 1 cm of disease free tissue is often sufficient $^{(1,2)}$ (B).

**Guidance 8**  
Groin node dissection should be omitted in stage 1a squamous cancers $^{(3)}$, verrucous tumours and basal cell carcinomas (B).

**Guidance 9**  
Surgery is the cornerstone of therapy for the groin nodes in women with vulval cancer. Individual patients not fit enough to withstand surgery can be treated with primary radiotherapy (A/B). Cochrane review van der Velden, J; Ansink, A

**Guidance 10**  
Groin node surgery can often be undertaken through separate incisions (triple incision technique) to reduce morbidity. The incidence of skin bridge recurrence in early stage disease is very low $^{(4)}$ (B).

**Guidance 11**  
In lateral tumours$^{3}$ only an ipsilateral groin node dissection need initially be performed $^{(5)}$ (B). Contralateral lymphadenectomy may be required if ipsilateral nodes are positive.

**Guidance 12**  
Superficial groin node dissection alone should not be performed as it is associated with a higher risk of groin node recurrence $^{(5)}$ (B).

**Guidance 13**  
Preservation of the long saphenous vein may reduce both groin wound and subsequent lower limb problems $^{(6)}$ (C).

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3 A lateralized lesion is defined as one in which wide excision (at least 1 cm beyond the visible tumour edge) would not impinge upon a midline structure (Clitoris, Urethra, Vagina, Perineal body, Anus) Statement of the EORTC Vulva Group
2 Background

Increased understanding and multi-disciplinary care have led to enormous progress in the management of this disease with a shift from ultra radical surgery, and therefore significant morbidity, to individualisation of more conservative surgery with high rates of success. Modern therapy also recognises the sexual function of the vulva.

2.1 Incidence, prognosis & mortality

Vulval cancer is rare and represents 5% of gynaecological cancers. In the year 2000 there were 996 cases in the UK giving a crude incidence rate of 1.7/100,000 females and it was ranked as the 20th most common cancer in women (25th overall) (Office for National Statistics http://www.statistics.gov.uk).

The overall 5 year survival is 62%. The five-year survival in cases with no lymph node involvement is in excess of 80%. This falls to less than 50% if the inguinal nodes are involved and 10-15% if the iliac or other pelvic nodes are involved. A multifactorial analysis of risk factors in squamous vulval cancer demonstrated that nodal status and primary lesion diameter, when considered together, were the only variables associated with prognosis(6) (B).

The most recent mortality figures (2002) recorded 364 deaths for all age groups, giving a death rate of 1.2/100,000 women ranking it the 19th most common cause of cancer death in women (23rd overall).

2.2 Predisposing factors

There are recognised risks of developing cancer with lichen sclerosus (4-7%) (7) (B), VIN and multifocal disease (5-90%) (8)(C) (9)(B), Paget disease (10) (C) and melanoma, in situ (11,12) (C). Lichen sclerosus is relatively common and it is not practical to keep all such women on follow-up once their symptoms are controlled. It is recommended however that when discharged to primary care written advice is given to both the patient and her GP warning that any persistent ulceration or new growth should prompt an urgent referral back to the appropriate specialist (13).

High grade VIN, VIN with high grade multicentric disease, VIN in the immunosuppressed, Paget disease and melanoma in situ probably pose higher risks for progression and as such should be followed-up by either gynaecological oncologists or in specialist multidisciplinary vulva clinics.
Two types of vulvar SCC have been established by epidemiologic, virologic and clinicopathologic studies. One type is seen mainly in younger patients who smoke and appears to be HPV related as VIN is commonly also found while the second is more commonly seen in elderly patients, apparently unrelated to smoking and HPV infection, with concurrent VIN being uncommon. Until recently, this division was based largely on HPV status, but at a molecular level the number of alterations occurring in vulvar carcinogenesis appears to determine the HPV status of the final invasive lesion with early loss of heterozygosity being observed early on in HPV-negative cancers. Such changes have also been found in the corresponding high grade VIN lesions and PCR techniques have demonstrated HPV presence in all types of epithelial changes synchronous with carcinoma of the vulva.

The lifetime progression rate of VIN is thought to be 3 to 5% \(^{14}\).

Chronic pruritus is often an antecedent. Chronic tissue damage as a result of itching and scratching has been implicated in the development of the more common keratinizing, HPV-negative SCCs observed in the older group of women. More recently this theory has been reconciled by the itch-scratch-lichen sclerosis hypothesis, with lichen sclerosis providing the possible link between the itch, scratch and invasive disease not seen to occur in other irritating dermatoses. The relationship between squamous hyperplasia of the vulval and cancer remains controversial.

### 2.3 Clinical presentation

This presents usually as a visible lesion with ninety per cent of women at presentation having a visible tumour on clinical examination (C) (NICE). Ulceration, bleeding and palpable thickening are very suggestive of cancer. There is often a history of longstanding itch related to a concurrent dermatosis. Occasional groin metastasis giving rise to a palpable lump may be the first presentation.

The vulval lesion is usually raised and may be ulcerated, leukoplakic or warty in appearance. Warty carcinomas of the vulva, increasing in incidence, account for 20% of cases and may initially be wrongly diagnosed as condylomata acuminate.

Most SCCs occur on the labia majora, but the labia minora, clitoris, and perineum may be the primary site of disease, 5% are multifocal.
3 Pathology

3.1 Macroscopic
Ninety per cent of women at presentation have a visible tumour on clinical examination (C) NICE guidelines 2004

3.2 Microscopic
Ninety per cent of all vulval cancers are squamous cell carcinomas with melanomas, Paget disease, Bartholin gland tumours, adenocarcinomas and basal cell carcinomas accounting for most of the remaining tumours. The histology is, however, important as it represents a variable in determining the likelihood of lymph node involvement. The presence of infiltrative growth patterns, compared with a pushing pattern, is associated with a higher local recurrence rate. Lymphovascular space involvement (LVSI) is also associated with an increased local recurrence rate (B). LVSI has not been associated with an increased risk of groin node metastasis. Both LVSI and infiltrative growth patterns are markers of poor prognosis, but these factors do not indicate the need for adjuvant treatment. Research is required to establish the influence of these factors on the outcome of this disease.

3.3 Spread
Vulval cancer spreads by direct extension to adjacent structures, embolisation to the inguinal and femoral nodes (the regional lymph nodes) or by haematogenous spread. Overall, about 30% of operable patients have nodal spread.

3.4 Staging
Vulval cancer is staged surgico-pathologically using the International Federation of Gynaecology and Obstetrics (FIGO) staging system last updated in 2000 (Appendix 2)

4 Screening
There is no screening procedure for vulval cancer. Patients with carcinoma of the vulva are at an increased risk of developing other genital cancers, particularly cervical cancer. Similarly, patients with invasive intraepithelial disease of the cervix are at an increased risk of developing invasive and intraepithelial vulval and vaginal neoplasia (7).
5 **Referral pathways**

Vulval cancer should be managed in Gynaecological Cancer Centres by Multidisciplinary Teams with specialist nursing expertise. This concept is based upon:

- Strong support for centralised referral from a National Survey of Scottish Gynaecologists \(^{(15)}\) (C).
- Indication of more varied practice and worse outcomes from a population based survey conducted in the West Midlands \(^{(16)}\) (B).
- More favourable outcomes in centres as opposed to peripheral units as documented in a hospital based study in Holland \(^{(17)}\) (C). (This study may be biased because of age differences in the two populations).

5.1 **Primary care**

*Referral indication*

The commonest presenting symptoms of vulval cancer include pruritus, discomfort or pain, a visible or palpable lesion, ulceration, bleeding dysuria and vaginal discharge \(^{(18,19)}\).

In a woman who presents with an unexplained vulval lump referral should be urgent \((C)\) NICE guidelines July 2004.

In women with vulval bleeding, pruritus, pain and ulceration it is reasonable to use a period of ‘treat, watch and wait’ as a method of management but this should include the offer of active follow-up until these symptoms resolve or a diagnosis is confirmed. If symptoms persist referral should be routine \((C)\) NICE guidelines July 2004.

The patient should be referred to a local unit lead for gynaecological oncology or to the nearest Gynaecological Cancer Centre.

5.2 **Gynaecological cancer unit**

The patient should be seen within two weeks of referral.

For small suspicious lesions patients should be referred to the gynaecological cancer centre either after a small biopsy that leaves the lesion identifiable or no biopsy at all. The site and size of the lesion are important variables in treatment planning and if the lesion has been removed prior to referral it might arguably compromise definitive treatment. Ideally, all lesions should be photographed.

Referral should include sending all relevant histopathological material to the specialist gynaecological pathologist in the gynaecological cancer centre.
5.3 Gynaecological cancer centre
All new cases of vulval cancer should be discussed at the Cancer Centre Multidisciplinary Team Meeting. It is also important to identify psychosexual issues prior to treatment (20).

The patient should be seen within two weeks of referral.

Results of previous investigations should be available at the visit.

The patient should be informed of the diagnosis and counselled as to the proposed management options and plan which may include surgery, and/or radiotherapy (with or without concurrent chemotherapy).

The appointment should allow for adequate time to counsel and support the patient and if at all possible the patient should be introduced to the Clinical Nurse Specialist in Gynaecological Oncology.

The patient's general practitioner should be informed of the diagnosis and management plan within two working days of the clinic visit.

Some patients will require an examination under anaesthesia. Such an examination is best performed in the cancer centre or by the gynaecological oncologist who will be responsible for her care. For large cancers of the vulva it is ideal to have both the gynaecological oncologist and clinical oncologist perform a joint assessment. If a surgical approach is not an option the patient should be managed by the clinical oncologist with a specific interest in gynaecological malignancy and should expect to receive an appointment within two weeks.

Surgical treatment should commence within four weeks of diagnosis. In exceptional circumstances a longer interval may be acceptable, particularly if complex planning is required or significant co-morbidities need to be controlled.

Radiotherapy treatment should commence within four weeks of the decision to treat by radiotherapy although in exceptional circumstances a longer interval may be acceptable.

6 Diagnosis & investigations

6.1 Examination
When evaluating a vulval lesion the size and location should be documented. Care should be taken to assess any involvement of the vagina, urethra, base of bladder or anus. With large tumours one should palpate whether the
tumour is infiltrating deep to the pubic and ischial bone. Because of the pain often associated with large tumours, the examination may have to be performed under general anaesthesia. The presence or absence of groin lymphadenopathy should also be noted.

6.2 Investigations
All cases should have the diagnosis based upon a representative biopsy of the tumour that should include the area of epithelium where there is a transition of normal to malignant tissue (see section on pathology specimens). Diagnostic biopsies should be of a sufficient size (greater than 1mm to allow differentiation between superficially invasive and frankly invasive tumours) and orientated to allow quality pathological interpretation. Biopsies should be referred to a pathologist with a specialist interest in gynaecological pathology.

There may be exceptions to these rules. If, for instance an elderly woman with major medical problems and a severely symptomatic lesion presented, a small punch biopsy under local anaesthetic could provide adequate diagnostic information to allow planning of definitive therapy. In certain situations where the clinical diagnosis is apparent and the patient very symptomatic, ie heavy bleeding and or pain, definitive surgery to the vulval lesion may be performed but biopsy with frozen section is recommended prior to proceeding with any radical procedure.

After confirming the diagnosis, the objectives of further investigations are to determine the extent of the disease and suitability for treatment.

The following investigations are suggested for the majority of patients although one must accept that in a predominantly elderly population this cannot be considered either complete or proscriptive, as each case must be fully assessed according to individual need:
- Full blood count (Pre-treatment assessment)
- Biochemical profile (Pre-treatment assessment, abnormal liver function might suggest metastatic disease)
- Chest X-ray (Pre-operative assessment, exclude metastases)
- ECG (Pre-operative assessment)
- Cervical smear if no recent normal cervical smear.
- Locally available imaging to assess for concurrent pelvic pathology and retroperitoneal nodes (21-25).
- Fine needle aspiration of any clinically suspicious nodes or other metastases where the result will alter management (ie may elect for radiation therapy).
7 Treatment of primary disease

The treatment of vulval cancer is primarily by surgery. This has become more individualised and conservative although the need for adequate resection margins (1cm) and groin node dissection remain important basic principles. The impetus for more conservative approaches stems from the well recognised psychosexual sequelae \[^{26,27}\](C). Reconstructive surgery has a role in the management of these cancers. Radiotherapy is used in the adjuvant setting and with or without chemotherapy and surgery in advanced disease.

Management may vary considerably from quite simple to very complex. Each case should be considered on its merits and an agreed plan of management devised by the gynaecological cancer team. Factors such as tumour size, location, medical fitness and the wishes of the patient will all influence management. The management of the nodes and the primary tumour should be considered on their own merits. Tumours should be staged using the FIGO or TNM classifications. FIGO staging is surgical-pathological and not clinical.

It should be emphasised that these patients are often elderly and have significant co-morbidity. As such they require access to skilled anaesthetic services including an epidural service, high dependency and or critical care. A key component of patient management is skilled nursing care. All of these services should be available in a Cancer Centre.

7.1 Surgery

7.1.1 Early stage disease

Depth of invasion
Lesions less than 2 cm diameter and confined to the vulva or perineum with stromal invasion less than or equal to 1.0 mm (FIGO Stage la) can be managed by wide local excision only without groin node dissection. This is because the risk of lymph node metastases is negligible \[^{2}\].

Dissection of the groin nodes should be performed when the depth of invasion is greater than 1 mm (Stage 1b or worse) or the maximum diameter of the tumour is greater than 2 cm (Stage 2 or worse) \[^{3}\](B). This surgery can often be undertaken through separate incisions (triple incision technique) to reduce morbidity. The incidence of skin bridge recurrence in early stage disease is very low \[^{4}\](B).

Surgery to the primary tumour should be radical enough to remove the tumour with adequate margins. The incidence of vulval recurrence has been shown to be related to the measured disease free surgical margin as measured in the
fixed histopathological specimen. Given the reduction and contraction of tissues following excision and fixation this equates to at least a 10mm margin of the fresh surgical specimen. The risk of recurrence increases as the disease free margins decrease ($\geq 8$ mm 0%; 8-4.8 mm 8%; <4.8 mm 54%) \(^{(1,2)}\) (B). Therefore wide radical local excision with a minimum margin of 1 cm of disease free tissue should be sufficient.

Excision of atypical skin (Lichen sclerosus or VIN) affecting the remainder of the vulva should be considered as these areas might contain separate foci of invasion. Removal of any lichen sclerosus or VIN skin should not be to the same depth as that for invasive disease unless occult invasion is suspected. A pre-operative vulvoscopy may help in the planning of surgery.

When the surgical margins are found to be less than 1cm it may be appropriate to perform a further local resection though evidence is lacking that this will result in a reduction in local recurrence. There is not enough evidence to recommend adjuvant local therapy routinely in patients with close surgical margins.

**Lateral vulval tumours**

Extensive crossover of lymphatic channels of the vulva may result in nodal involvement of the contralateral groins in addition to the ipsilateral groin nodes. Therefore bilateral groin node dissection is usually required. However in lateral tumours \(A \text{ lateralised lesion for the purposes of this document and agreed by consensus is defined as one in which wide excision, at least 1 cm beyond the visible tumour edge, would not impinge upon a midline structure}\) only an ipsilateral groin node dissection need initially be performed \(^{(5)}\)(B). If the ipsilateral nodes are subsequently shown to be positive for cancer, the contralateral nodes should also be excised or irradiated as the nodes are more likely to be positive in this scenario.

**Groin node dissection**

Appropriate groin node dissection is the single most important factor in decreasing mortality from vulval cancer. However, groin node dissection should be omitted if the patient has stage 1a disease as the incidence of lymph node metastases is negligible \(^{(3)}\)(B). It is recommended that the superficial inguinal nodes as well as the deep femoral nodes be removed. Superficial inguinal node dissection alone is associated with a higher risk of groin node recurrence \(^{(5)}\)(B). Preservation of the long saphenous vein is reported to reduce both groin wound and subsequent lower limb problems \(^{(6)}\)(C). Following inguinofemoral lymphadenectomy, sartorius muscle transposition may be of benefit in preventing subsequent femoral vessel damage particularly in those patients who are thin and in those in whom adjuvant groin radiation therapy is anticipated\(^{(28)}\). Dye studies and lymphoscintigraphy may be of value in the detection of sentinel nodes \(^{(29-31)}\).
7.1.2 Advanced vulval cancer

Surgery to the primary lesion
Resection of advanced disease involves careful pre-operative planning and if reconstruction is required, this should be planned jointly with a plastic surgeon. The size and location of the tumour will influence the surgical approach. Wide radical local excision with a minimum of 1 cm disease free margin may be used however, some tumours will require a radical vulvectomy. If these surgical approaches risk sphincter damage, leading to urinary or faecal incontinence, treatment by radiotherapy should be considered either with curative intent or to reduce tumour volume to permit less destructive surgery. Two studies have suggested that preoperative radiation in advanced vulval cancer reduced the need to perform defunctioning stomas (32-33) (B). It should be noted however that in this post radiation setting, surgery can be more complicated and there is increased morbidity. Reconstructive surgical techniques should be employed to enable primary surgical closure and reduce morbidity due to scarring. It should be stressed that the published experience of post radiation surgery is limited and should not be undertaken lightly. Ano-vulvectomy might still be considered as an option in selected cases. This is an area where further research is vital.

Management of the groin nodes
Groin node dissection should be undertaken when there are clinically suspicious groin nodes present. In cases with large primary lesions and clinically suspicious nodes, a radical vulvectomy with 'en bloc' groin node dissection may be warranted (B). In cases with fixed or ulcerated groin nodes surgery and or radiotherapy should be considered. There are no data suggesting the superiority of one over the other although if surgery is used, it is likely that post-operative radiation will also be required. Pathological assessment of these nodes should be undertaken prior to radiotherapy preferably by fine needle aspiration cytology in order to maximise the chances of maintaining skin integrity and minimising the risk of wound problems.

Multimodality treatment is increasingly used in the management of advanced vulval cancer to allow for sphincter preserving surgery and as an alternative to surgery for histologically proven involved groin lymph nodes. Surgery following groin radiation may however be associated with increased morbidity both in the groin and in the lower limb. Overall, surgery should still be considered the cornerstone of therapy for the groin nodes (34).
7.1.3 Surgical management of non squamous vulval cancer

Carcinoma of the Bartholin gland
This is a rare vulval cancer. Histologically it is usually a squamous carcinoma or adenocarcinoma. The current evidence base is insufficient to suggest different management from squamous tumours. The lesions are often deep seated or likely to be associated with metastatic disease. The close proximity to the anal sphincter may necessitate partial resection with reconstruction and this may necessitate a defunctioning temporary colostomy (35,36) (C). Any perimenopausal woman with a persisting Bartholin abscess or cyst should be suspected of having a possible carcinoma and appropriate biopsies and histological review undertaken.

Basal cell carcinoma and verrucous carcinoma
These squamous variants are rarely associated with lymph node metastases and can be managed by wide local excision. Basal cell carcinomas are also amenable to treatment by radiotherapy, which should be the preferred treatment if resection would compromise function (ie sphincter damage).

Malignant melanomas
This group of tumours have not been shown to benefit from block dissection of the groin. Wide local excision is preferred. Relapse in this subgroup is high and closely correlates with the depth of invasion. On the vulva (which includes mucosal surfaces) Breslow’s classification (37) is more appropriate than Clarke’s levels. As yet there are no new strategies to minimise the risk of relapse in melanomas (38) (B).

7.1.4 Post-operative care

Morbidity related to surgery
The primary objectives of less radical surgery are to reduce morbidity whilst maintaining high cure rates for early vulval cancers. The complications associated with vulval and inguinal surgery are:

- Wound breakdown
- Wound infection
- Deep vein thrombosis and pulmonary embolism
- Pressure sores
- Introital stenosis
- Urinary incontinence
- Rectocele
- Faecal incontinence
- Inguinal lymphocyst
- Lymphoedema
- Hernias
- Psychosexual
7.2 Radiotherapy & chemotherapy
The clinical oncologist supervising treatment should have specific expertise in the management of gynaecological malignancies. He or she should manage integrated treatment plans involving radiotherapy with or without concurrent chemotherapy \(^{(39)}\).

7.2.1 Adjuvant radiotherapy
The factors influencing the need for adjuvant radiotherapy are:

**Surgical margins**
There is not enough evidence to recommend adjuvant local therapy routinely in patients with close surgical margins. Adjuvant treatment for positive margins has an improved survival compared to observation alone \(^{(40)}\).

**Groin node positivity**
Adjuvant radiotherapy should be considered when two or more lymph nodes are involved with microscopic metastatic disease or there is complete replacement and or extra capsular spread in any node \(^{(41),(A),(41,42),(B)}\). There is no evidence to show whether adjuvant radiotherapy should be given to both sides or to the involved side only. Treatment should be to the groins and the pelvic nodes.

7.2.2 Primary treatment
Radiotherapy with or without chemotherapy is increasingly used in the management of advanced vulval cancer. Pre-operative radiotherapy may allow for sphincter preserving surgery. Radiotherapy may also be of use in place of surgery for histologically proven involved groin lymph nodes. It is unknown whether post radiation groin node removal is advantageous in terms of outcome.

7.2.3 Treatment Schedules
The majority of schedules are based upon those developed by the Toronto Group \(^{(44),(C)}\). Fraction size is important with 1.7 Gy being close to tolerance although it is recognised that some centres may use slightly larger fractions (1.8 Gy). Doses will have to be reduced for radical treatment if fractions greater than 1.7 Gy are employed.

Radical treatment will usually require that a prophylactic dose (45-50 Gy) be delivered to the primary and nodal sites and the tumour then be boosted by a second phase of treatment by electrons, conformal radiotherapy or
brachytherapy to a total dose of 65 Gy. The total prescribed dose is determined by the clinical context.

A recent Cochrane review suggests that there is no evidence that prophylactic groin irradiation should be used in preference to surgery \(^\text{(34)}\).

With regard to the use of concurrent chemotherapy and radiation therapy, there are no randomised clinical trials. Retrospective analyses of several small trials have suggested some improvement in local control in regimens employing cisplatinum and 5-fluorouracil, Mitomycin C and 5-fluorouracil and 5-fluorouracil alone.

**Adjuvant in intent** There is no macroscopic disease. The total dose is 45-50 Gy with no concurrent 5 Fluorouracil (5FU).

**Planned pre-operative irradiation** Maximum dose 55 Gy with or without concurrent chemotherapy.

**Definitive radical radiotherapy** Maximum dose 65 Gy with concurrent chemotherapy.

8 Treatment of recurrent disease

Recurrence rates for invasive squamous cell carcinoma range from 15 to 33%. In a review of the literature the vulva was found to be the most common site of recurrence (69.5%) with the groin nodes affected in 24.3%, the pelvis in 15.6% and distant metastases in 18.5% \(^\text{(45)}\) \(^\text{(C)}\). Survival following regional relapse is poor and thus all attempts to prevent it must be made at the time of primary treatment. Skin bridge recurrence has been reported to be more likely to occur in patients with positive lymph nodes \(^\text{(46)}\) \(^\text{(C)}\). If the nodes are known or suspected to be positive at the time of primary treatment an en-bloc dissection should be performed to remove the tissue between the vulva and involved nodes.

8.1 Treatment

Treatment and outcome depend on the site and extent of the recurrence \(^\text{(45)}\). Wide excision of the local recurrence can result in a 5-year survival rate of 56% when the inguinal nodes are negative \(^\text{(47)}\). If excision would impair sphincter function irradiation should be considered as the first choice. If irradiation has already been given to maximum dose, then excision should be considered. Such cases require careful joint planning with clinical oncologists and plastic and reconstructive surgeons experienced in the treatment of vulval disease.

Groin recurrence has a much poorer prognosis and is difficult to manage. In patients who have not been treated previously with groin irradiation then
radiotherapy (with or without additional surgery) would be the preferred option. The options are much more limited in those who have already been irradiated and palliation, which may include surgery, should be considered. In women who have had both surgery and radiotherapy to the groins, the palliative care team should become involved soon after the confirmation of groin recurrence. There is no standard chemotherapy or other systemic treatment effective in patients with metastatic disease. Such patients should be considered for clinical trials.

9 Follow-up

9.1 Hospital review
As patients who relapse locally have a good chance of cure and/or prolonged remission with prompt re-treatment, the patient should be followed-up in an environment where trained personnel are available to recognise the earliest signs or symptoms of recurrence and the morbidity of treatment. Patients should be followed annually. Long term review is still recommended as these patients remain at an increased risk of developing carcinomas elsewhere in the genital tract and pelvis. Follow-up intervals are currently arbitrary but the following schedule is suggested:
3 monthly for 2 years
6 monthly until 5 years
Annually

All patients should be told about symptoms associated with recurrence and should have a clear pathway of rapid access to the team between follow-up intervals to avoid delay while a patient waits for the next appointment (48).

9.2 Community care
Patients who have received successful curative therapy will require little community care. Those undergoing palliative or non-curative treatment who may be symptomatic and expectant of relapse should receive regular support and surveillance from the general practitioner and community nursing services. Pain control should be monitored regularly. Careful hygiene and dressing of fungating lesions will require very close nursing supervision.
10 Appendix 1: Staging

When compared with the surgical staging of vulvar cancer, the percentage error in clinical staging increases from 18% for Stage I disease to 44% for Stage IV disease. Therefore the revised FIGO staging system below is now used.

Revised FIGO staging (1995)

<table>
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<th>Stage</th>
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<th>Clinical/pathological findings</th>
</tr>
</thead>
<tbody>
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<td>0</td>
<td>Tis</td>
<td>Carcinoma in situ, intraepithelial carcinoma</td>
</tr>
<tr>
<td>IA</td>
<td>T1N0M0</td>
<td>Tumour confined to the vulva or perineum ( \leq 2\text{cm} ), negative nodes, stromal invasion of ( &lt;1\text{mm} )</td>
</tr>
<tr>
<td>IB</td>
<td>T2N0M0</td>
<td>Tumour 2cm or less confined to the vulva or perineum, stromal invasion ( &gt;1\text{mm} ), negative nodes</td>
</tr>
<tr>
<td>II</td>
<td>T2N0M0</td>
<td>Tumour confined to the vulva and/or perineum, ( &gt;2\text{cm} ), negative nodes</td>
</tr>
<tr>
<td>III</td>
<td>T3N0M0</td>
<td>Tumour or any size with:</td>
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<tr>
<td></td>
<td>T3N1M0</td>
<td>(1) adjacent spread to lower urethra or anus,</td>
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<td></td>
<td>T1N1M0</td>
<td>(2) unilateral regional lymph node metastasis</td>
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<td>T2N1M0</td>
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</tr>
<tr>
<td>IVA</td>
<td>T1N2M0</td>
<td>Tumour of any size with invading any of the following:</td>
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<tr>
<td>IVB</td>
<td>T2N2M0</td>
<td>Upper urethra, bladder mucosa, rectal mucosa, pelvic bone or bilateral lymph node metastasis.</td>
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<tr>
<td></td>
<td>T3N2M0</td>
<td>Any distant metastasis including pelvic lymph nodes</td>
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<td></td>
<td>T4 any N M0</td>
<td></td>
</tr>
</tbody>
</table>

TNM

<table>
<thead>
<tr>
<th>T: Primary Tumour</th>
<th>N: Regional Lymph Nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 Tumour confined to vulva, ( \leq 2\text{cm} )</td>
<td>N0 No lymph node metastasis</td>
</tr>
<tr>
<td>T2 Tumour confined to vulva, ( &gt;2\text{cm} )</td>
<td>N1 Unilateral regional lymph node metastasis</td>
</tr>
<tr>
<td>T3 Tumour involves any of the following: lower urethra, vagina or anus</td>
<td>N2 Bilateral regional lymph node metastasis</td>
</tr>
<tr>
<td>T4 Tumour involves any of the following: bladder mucosa, rectal mucosa, upper urethra or pubic bone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M: Distant Metastases</td>
</tr>
<tr>
<td></td>
<td>M0 No distant metastasis</td>
</tr>
<tr>
<td></td>
<td>M1 Distant metastasis including pelvic lymph nodes</td>
</tr>
</tbody>
</table>
11 Appendix 2: Nursing Considerations

A patient diagnosed with cancer can expect contact with a variety of professionals, and others, in hospital, at home or in a hospice. This includes cancer nurses, palliative care nurses, and community nurses as well as other members of the multidisciplinary team\(^{(1)}\). It is self evident then that at the level of the Cancer Centre where the more complex and rarer cancers are treated, appropriately educated specialist nursing staff should manage nursing care. This should include cancer nurse specialists with expertise and experience in the management of patients who have undergone major surgery and radiotherapy with associated change in functional ability, altered body image and altered appearance.

**Access to support and information**

Within a multidisciplinary team, the Clinical Nurse Specialist, (CNS), is in a key position to be able to address the often complex and sensitive issues identified and experienced by the patient\(^{(2)}\). Similarly the successful development of medical and nursing partnerships enables women with gynaecological cancers to gain proper access to essential expert knowledge and information and thereby to make informed decisions\(^{(3)}\). The use of clear and accurate written literature should also be promoted. Access to self-help and support groups such as V.A.C.O., (Vulval Awareness Campaign Organisation), may also be of significant benefit allowing women to share experiences and seek support from other women diagnosed and treated for the same condition.

**Client group**

Whilst a significant proportion of patients diagnosed with vulval cancer are over the age of 60, in recent years there has been an increase in the percentage of younger women, who are also diagnosed with vulval malignancies. Therefore consideration should be given to the diversity of the client group and their respective individual needs, (physical, psychological, social, spiritual, emotional), dependent on age and circumstances.

**Altered body image / psychosexual effect**

Vulval cancer management leaves obvious residual effects, and disfigurement and dysfunction will be a part of these women’s lives\(^{(3)}\). Access to specialist trained psychosexual counsellors and clinical nurse specialists should be available, and both patients and partners should be made aware of the potential consequences of treatment during initial consultations prior to therapy, (surgery and / or radiotherapy), with reinforcement thereafter\(^{(4)}\). Research indicates that a high proportion of women who have undergone major gynaecological surgery, (cervix or vulva), would have liked to have had
more information on the after-effects of the operation, including physical, sexual and emotional aspects\(^{(5)}\).

**Lymphoedema Management**
Treatments for vulval cancer frequently involve surgical removal of the inguinofemoral lymph nodes causing an interruption in the lymphatic pathway. Additionally radiotherapy treatment can cause further damage and fibrosis to the lymphatic system\(^{(6,7)}\). The incidence and impact of lower limb lymphoedema have not been studied widely. One study found that 13 out of 16 women were symptomatic within a six-week period following groin node dissection for vulval cancer\(^{(8)}\). Other studies suggest that up to 69% of women can be affected\(^{(9,10)}\).

The nursing considerations for women who have undergone treatment for vulval cancer include:

- Informing women pre-discharge of the possible risks of developing lower limb lymphoedema.
- Educating women on preventative measures that include a meticulous skin regime, advice on appropriate exercise and movement and the importance of maintaining a healthy body mass index.
- Ensuring that women are aware of early signs and symptoms associated with the condition.
- Raising awareness of how to access specialist lymphoedema management for the condition, should it occur.

All patients who develop lower limb lymphoedema should have access to the four cornerstones of lymphoedema care\(^{(12)}\):

- Skin care to maintain a good tissue condition and reduce the risk of infection.
- External compression in the form of elastic compression garments that help reduce new lymph formation and encourages lymph drainage by improving the efficiency of muscle pump.
- A programme of exercise and movement to promote lymph drainage without over exertion.
- Simple lymphatic drainage, a method of lymph drainage that can be carried out by the patient or carer and involves a series of simple hand movements.

The aims of this regime are to rehabilitate the cancer patient, to reduce any disability as far as possible, to help the patient achieve an independent lifestyle, and to give the patient the skills to manage their own condition.
**Tissue Viability**

Factors affecting normal tissue viability include surgical intervention, radiation effect and malignant fungating wounds when disease is advanced or recurred. Most surgical wounds are categorised as acute wounds, healing without complication in an expected time frame\(^{(12)}\). In vulval cancer however, this is often not the case as siting of wounds and pressure associated with lymphatic damage can and does lead to wound breakdown and infection, irrespective of all attempts made to minimise it. Therefore specific wound assessment should highlight the characteristics and nature of the wound\(^{(13)}\). These include: location, size of the wound, presence of slough and/or necrotic tissue, amount and nature of exudate being produced by the wound, whether odour is associated with the lesion, nature and type of pain directly attributed to the wound, the current state of the skin adjacent to the wound, and the effect on patients daily living.

Considerations for wound management include structured tissue viability assessment, incorporating regular review by a Tissue Viability Specialist Nurse, clinical photography, dietician input and nutritional supplementation, effective use of appropriate dressings and responsible antibiotic therapy as and when infection is accurately identified. The psychological impact of delayed wound healing for the patient must also be recognised and addressed to minimise the risk of longer term psychological effects such as depression, social isolation and loss of role in society. Caring for a patient with a fungating lesion when cancer progresses or recurs can offer many challenges. Therefore it is important to ensure that patients’ individual needs and wishes are addressed to promote optimum quality of life for people with malignant wounds\(^{(14)}\).

**Palliative Care**

Advanced disease presents specific problems associated with the original diagnosis. These include: fungating vulval or groin wounds as previously mentioned, progressive lymphoedema, uncontrollable bleeding, malodour, urinary and bowel complications, and pain. Close collaboration with primary care and palliative care teams to support the patient and their carers during this phase of the cancer experience is an essential element of the ongoing service provision of the specialist Cancer Centre team.

**Nursing Research**

There is still very little evidence-based research on which to base clear guidance and protocols of care for women diagnosed with vulval cancer, and
those who undergo subsequent treatment and care to cure, control or even palliate the disease. With the continued evolution of the National Forum of Gynaecological Oncology Nurses in the United Kingdom, and the appointment of a Research Co-ordinator to the national committee, consideration should be given to the development and promotion of national multi-centre based studies into the key aspects of nursing needs of women with vulval cancer.

References for Nursing considerations

Appendix 3: RCOG working party report 2005 Contributors

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McMillan Lead Cancer Nurse
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13 References


F Guidelines for the management of vaginal carcinoma

1 Staging

<table>
<thead>
<tr>
<th>TNM</th>
<th>Vagina</th>
<th>FIGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Vaginal wall</td>
<td>I</td>
</tr>
<tr>
<td>T2</td>
<td>Paravaginal tissue</td>
<td>II</td>
</tr>
<tr>
<td>T3</td>
<td>Extends to pelvic wall</td>
<td>III</td>
</tr>
<tr>
<td>T4</td>
<td>Mucosa of bladder/rectum, beyond pelvis</td>
<td>IVA</td>
</tr>
<tr>
<td>N1</td>
<td>Regional</td>
<td>-</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
<td>IVB</td>
</tr>
</tbody>
</table>

2 Management

All patients should be discussed through the gynaecology MDT. This is a rare tumour and treatment needs to be individualised.

Radiotherapy is the mainstay for treatment of cancer of the vagina.

3 Investigations

Prior to radiotherapy or chemotherapy all patients must have a tissue diagnosis.

Patients should have a staging CT scan of the abdomen and pelvis and a chest x-ray or CT chest prior to radiotherapy or chemotherapy.

4 Treatment

4.1 Stage O (VAIN)

Surgical excision

4.2 Stage I/II

Small, superficial (<5mm) and CIS
Surgery, intracavity radiotherapy or interstitial radiotherapy alone

**Upper 2/3 tumours**
Lymphatic drainage is to pelvic nodes and treatment is similar to carcinoma of the cervix.
- Phase I - external beam radiotherapy to pelvis (45Gy/25# - 50.4Gy/28#)
- Phase II – total dose 70-75 Gy
  - intra-cavity radiotherapy intra-uterine tube and ovoids to vault
  - or
  - if below vault - interstitial implant or dobbie
  - or
  - conformal plan

**Lower 1/3 tumours**
Lymphatic drainage is to inguino-femoral nodes and treatment is similar to carcinoma of the vulva.
- External beam radiotherapy to primary and lower pelvic and inguinal nodes (45GY / 25#)
- Interstitial implant or electrons to total 60-65 Gy

**Concomitant chemotherapy**
Should be considered in good performance status patients (see cervix and vulva guidelines).

### 4.2 Stage III/IVa
Radical radiotherapy as above or palliative radiotherapy (eg. 30Gy/10#)

### 4.3 Stage IVb
Consider palliative chemotherapy

*Authors: Dr Vicky McFarlane and Dr Sandra Tinkler  Date: 31.05.05*
5 Follow-up

5.1 Clinical Trials

Patients in clinical trials should adhere to the appropriate trial protocol.

5.2 Patients off trials

There is no evidence or consensus to guide follow-up protocols. Reliable data on follow-up is confined to trials with a conservatively managed control arm such as Portec in endometrial cancer which advocated intensive surveillance. The aim of follow-up is to identify and treat recurrence, to identify and treat treatment related physical and psychological sequelae, to provide reassurance and to collect survival data. Recurrence of most gynaecological cancers is most likely in the first 2-3 years after primary treatment.

A standard intensive surveillance protocol would comprise 3 monthly clinical review for 2 years followed by 6 monthly review until 5 years before discharge. There is no evidence that vaginal cytology is helpful. This should be the maximum offered. Less intensive surveillance may be offered according to local protocols.

All patients should be told about symptoms associated with recurrence and should have a clear pathway of rapid access to the team between follow-up intervals to avoid delay while a patient waits for the next appointment.
G Guidelines for the management of rare cancers

1 Definition

This group of tumours includes neoplasms that are rare by nature of the site in which they develop and those of an uncommon or unusual histological type that arise at a similar site to other common cancers. Since SWCIS has protocols for the diagnosis and management of all of the common gynaecological cancers, a pragmatic and practical way to identify (and define) rare cancers is simply to incorporate all neoplasms where no agreed management protocols exist.

2 Management

Where specialist centres exist for the treatment of specific rare tumours (e.g., pseudomyxoma peritonei, melanomas and sarcomas) referral to these centres is recommended. By definition there is likely to be little reliable evidence to support decision making in rare cancers. The literature comprises mainly case reports or case series from single institutions, and as such, is open to bias (especially selection bias) and must be regarded as unreliable. An internal assessment by the editors of the Textbook of Uncommon Cancer (John Wiley and Sons, Chichester) showed that only 10% of the book contained material directly relevant to clinical decisions and that nearly all of this was unreliable. Despite this it is important that there is a process for examining the clinical information that is available and making decisions that are based on what is known.

2.1 Searching for information about management

If the tumour is really very rare, reference texts and standard online review sources such as Cancer.gov or OncoLink may yield little information of value, and it may be necessary to seek primary papers about the condition. The following resources are recommended:

1. PubMed – this provides access to more than 12 million MEDLINE citations, life science journals, and links to many sites providing full text articles. Alternatively a MedLine search of the world's medical literature is advised and even then, MedLine may yield less information than for most cancers, and reliance may have to be placed on case reports and case series rather than extensive clinical studies. Original papers and disease-specific web sites may be searched by using a web search engine such as Google. The problem of
alternative spellings and multiple names for the same condition should be borne in mind.

2. Another approach is to look at websites devoted to rare diseases, a few of which are concerned with rare cancers, but none, at the moment, incorporates rare gynaecological cancer in general. There are also many websites for specific rare cancers, some of which have been designed for and are sometimes produced by patients. The Rare Cancer Alliance appears to be the creation of a single dedicated patient, Sharon Lane and has extensive original content.

3. A number of organizations cover all rare diseases, not just cancer, and these include the National Organization for Rare Disorders (NORD) whose definition of "rare" is rather broad and includes some of the more common cancers. The database is searchable from the NORD Web Page. The NIH Office of Rare Diseases is part of the US National Institutes of Health. Like NORD, this covers many of the commoner cancers in addition to those which are rare, and the rare disease list links to useful information from several databases for each disease. A contact telephone number for more personalized help is available. OrphaNet is a large French international multilingual rare disease resource. The quality and usefulness of the information varies considerably depending on the disease. Rare Cancer Mailing List (rare-cancer.org) is an e-mail discussion group specifically for patients who have rare cancers. Patients can sign up using the rare-cancer on-line sign-up form on the Association of Cancer Online Resources (ACOR) website.

2.2 Making treatment decisions based on the evidence

Review of the available data should include assessing the security of the diagnosis. Some rare cancers require confirmation by using special techniques such as immunohistochemistry or identification of chromosomal translocations. Ensure that these have been done and that the results conform to the reported pattern. If necessary request the opinion of a pathologist with special expertise in the diagnosis of this rare cancer. If such a pathologist cannot be identified locally one can often be identified through on-line searches of pathology reports on rare tumours of the type in question.

Staging should be carried out before making decisions on therapy. Reports in the literature should provide a guide as to the choice of the staging procedure and the extent of the staging process.

It is likely that there will be inadequate data on the treatment of the rare cancer. This data should be presented at an MDT and at least two consultants experienced in the appropriate treatment modalities should discuss and decide upon the therapeutic approach to be presented to the patient. Information that is used to inform these decisions should be filed in the patient's medical records for future reference and to aid colleagues.

Patients need to be told about the rarity of their condition and be offered help and support in finding out more about their cancer.
H Glossary of Terms

abdo abdomen
adenoca adenocarcinoma
αFP α fetoprotein is a serum marker that is elevated in yolk sac (endodermal sinus) tumours, a high proportion of other germ cell tumours and hepatocellular carcinomas
BGND bilateral groin node dissection
βhCG the β subunit of human chorionic gonadotropin is elevated in tumours with trophoblastic elements such as choriocarcinoma and germ cell tumours with trophoblastic components
BPLND Bilateral Pelvic Lymph Node Dissection
BSO bilateral salpingo-oophorectomy
Bx biopsy
Ca125 cancer antigen (no 125) serum marker that is expressed by carcinomas of Mullerian origin but levels also increase in association with peritoneal irritation
CEA carcino-embryonic antigen is a serum marker for adenocarcinomas of the gastrointestinal tract (including pancreas)
chemo chemotherapy
CR complete response
CT computerised tomographic scan
CXR Chest X-Ray
DXT radical pelvic radiotherapy
EUA examination under anaesthesia
exam examination
FBC full blood count
FIGO International Federation of Gynecology and Obstetrics staging system
FNA fine needle aspiration
G grade
gyn gynaecological
hCG human chorionic gonadotrophin
hyst hysterectomy
lap laparoscopic
LDH  lactate dehydrogenase
LFT  liver function tests
LVI  lymphatic/vascular channel involvement
MDT  Multi Disciplinary Team
MRI  magnetic resonance imaging
neg  negative
Path  histology review
pos  positive
PR  partial response
radical hyst  radical hysterectomy: removal of uterus, ovaries, fallopian tubes, cervix and related lymph nodes
RCOG  Royal College of Gynaecologists
RWE  radical wide excision (>8mm histological clearance)
simple hyst  simple hysterectomy: removal of uterus and cervix
TVS  transvaginal scan
U&E  urea and electrolytes
UGND  unilateral groin node dissection
US  ultrasound scan
WHO  World Health Organisation
*WHO status Performance status to be taken into account in the planning of treatment*
yrs  years

*WHO status codes
0 - Able to carry out all normal activity without restriction
1 - Restricted in physically strenuous activity but able to walk and do light work
2 - Able to walk and capable of all self care but unable to carry out any work. Up and about more than 50% of waking hours
3 - Capable of only limited self care, confined to bed or chair more than 50% of waking hours
4 - Completely disabled. Cannot carry on any self care. Totally confined to bed or chair
5 - Not recorded
I  Classification of evidence

To ensure that the statements made are evidence based, the current literature was reviewed and critically appraised. The reliability and quality of the evidence given has been graded following the NHS Executive classification system as follows:

Grade A: Based on randomised controlled trials (RCTs)
Grade B: Based on other robust experimental or good observational studies
Grade C: More limited evidence but the advice relies on expert opinion and has endorsement of respected authorities.
MACROSCOPIC FEATURES

Nature of specimen:

<table>
<thead>
<tr>
<th>Ovaries</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimensions …… x …… x …… mm</td>
<td>Tumour involvement:</td>
<td>Yes □ No □</td>
</tr>
<tr>
<td>Capsule:</td>
<td>Intact □</td>
<td>Breached by tumour □</td>
</tr>
<tr>
<td>Macroscopic surface involvement:</td>
<td>Yes □ No □</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimensions …… x …… x …… mm</td>
<td>Tumour involvement:</td>
<td>Yes □ No □</td>
</tr>
<tr>
<td>Capsule:</td>
<td>Intact □</td>
<td>Breached by tumour □</td>
</tr>
<tr>
<td>Macroscopic surface involvement:</td>
<td>Yes □ No □</td>
<td></td>
</tr>
</tbody>
</table>

Fallopian tubes

Right: Normal □ Abnormal □ Comment ………………………………………

Left: Normal □ Abnormal □ Comment ………………………………………

Uterus and cervix: Normal □ Abnormal □ Comment ………………………………………

Omentum:

- Biopsy □ Omentectomy □ Normal □ Abnormal □

Comment …………………………………………………………………………………………………………

Size of largest tumour nodule (if appropriate) …………………

Peritoneal biopsies: Not received □ Normal □ Abnormal □

Comment…………………………………………………………………………………………………………

MICROSCOPIC FEATURES – OVARIRES

Right

Tumour nature: benign □ borderline □ malignant/invasive □

Tumour type:

- Serous □ Mucinous □ Endometrioid □
- Clear cell □ Transitional □
- Mixed epithelial type □ (tick all that apply) Malignant mixed Mullerian tumour □
- Other □ ……………………………………………………………………………………………

Microinvasion (for borderline tumours): Not present □ Present □

Differentiation (if appropriate): Well/Grade 1 □ Moderate/Grade 2 □ Poor/Grade 3 □

Microscopic involvement of ovarian surface: Yes □ No □
**Tumour nature:**
- benign □
- borderline □
- malignant/invasive □

**Tumour type:**
- Serous □
- Mucinous □
- Endometrioid □
- Clear cell □
- Transitional □
- Mixed epithelial type □ (tick all that apply)
- Malignant mixed Mullerian tumour □
- Other □ …………………………………………………………………………………

**Microinvasion (for borderline tumours):** Not present □
- Present □

**Differentiation (if appropriate):**
- Well/Grade 1 □
- Moderate/Grade 2 □
- Poor/Grade 3 □

**Microscopic involvement of ovarian surface:**
- Yes □
- No □

**MICROSCOPIC FEATURES – OTHER TISSUES**

**Fallopian tubes:**
- Right: Not involved □
- Involved □
- Left: Not involved □
- Involved □

**Endometrium:**
- Normal □
- Abnormal □
- Comment ……………………………

**Myometrium:**
- Normal □
- Abnormal □
- Comment ……………………………

**Uterine serosa:**
- Not involved □
- Borderline changes (non-invasive implants) □
- Invasive carcinoma □

**Omentum:**
- Not involved □
- Borderline changes (non-invasive implants) □
- Invasive carcinoma □

**Peritoneal biopsies (if received):**
- Site(s) ………………………………………………………………………
- Not involved □
- Borderline changes (non-invasive implants) □
- Invasive carcinoma □

**Peritoneal washings (if received):**
- Not involved □
- Involved □

**Appendix (if received):**
- Not involved □
- Involved □
- Comment ……………..……

**Lymph nodes (if received):**
- Site(s) …………….Total number.........Number involved…… (see Notes)
- Extranodal spread: Yes □
- No □

**Comments/additional information:**
………………………………………………………………….………………………………………………
………………………………………………………………….………………………………………………
………………………………………………………………….………………………………………………

**Pathological FIGO stage:**………………………………………………………………………………

**Signature…………………………..………..Date……./..…../..…………..SNOMED codes ………/………...**
National Minimum Dataset modified for SWCIS
Cervical Biopsy Histopathology Report

Surname .....................................  Forenames ..................................  Date of birth ...............
Hospital ..........................................  Hospital No .................................. NHS No .........................
Date of request ..................................  Date of reporting............................. Report No.........................
Pathologist ............................................................  Surgeon ...........................................................

MACROSCOPY
Wedge □  Cone □  Loop □  biopsy of cervix measuring ……mm x …… mm and …… mm deep
The cervix was divided into ……… blocks labelled     A – …………………
(A) separate fragment(s) labelled ……………. was (were) also received.

MICROSCOPY
Wart virus (HPV) infection   Absent □  Koilocytosis □  HPV-associated features □
CIN (cervical intra-epithelial neoplasia) Absent □  Epithelial changes of uncertain significance □
Endocervical edge           Clear □  Involved □
                          CIN 1 □  CIN 2 □  CIN 3 □
Ectocervical edge          Clear □  Involved □
Deep lateral edge          Clear □  Involved □
Endocervical epithelium     Normal □  Low grade CGIN □  High Grade CGIN □
Endocervical epithelium at end of canal     Yes □  No □
Invasive malignancy: Absent □  Microinvasive □  Squamous cell carcinoma □
                          Adenocarcinoma □  Adenosquamous carcinoma □
Microinvasive carcinoma, early stromal invasion □
Microinvasive carcinoma, small confluent tumour □  Maximum horizontal dimension
………………..mm
                          Maximum depth of invasion ………………..mm

N.B.: If invasive foci are seen in three or more blocks of tissue, the third dimension of the lesion
(which is not routinely measured) may exceed 7 mm (i.e. more than Stage IA2).

Is there lymphovascular space involvement?  Yes □  No □

Provisional pathological FIGO stage:.............................................................

Comments

SNOMED codes
T83000 (Cervix) E3345 (HPV) / M74001 (Koilocytosis) / M74005 (Epithelial changes, uncertain significance)
*M74008 (CIN 3) / *M74007 (CIN 2) / *M74006 (CIN 1) M80715 (Microinvasive squamous cell carcinoma)
M80703 (Squamous cell carcinoma) M74009 (CGIN, low or high grade)
M81402 (Adenocarcinoma in situ) / M81403 (Adenocarcinoma)

Signature ...............................................................  Date ................../........../..........
National Minimum Dataset modified for SWCIS
Cervical Cancer Histopathology Report

Surname ..................................  Forenames ..................................  Date of birth ......................
Hospital ..................................  Hospital No .............................  NHS No .............................
Date of request ..........................  Date of reporting .....................  Report No..........................
Pathologist .................................  Surgeon ..................................

**Gross description**
Dimensions of uterus:  Length ..........mm  Transverse ......mm  Anteroposterior.......mm
Vaginal cuff:  Present □  Absent □  Length ......mm (anterior); ..........mm (posterior).
Maximum dimensions of tumour: ........mm

**Histology**
Type:  squamous carcinoma □  adenocarcinoma □  adenosquamous □
Other (please specify).................................................................
Histological differentiation:  Well □  Moderate □  Poor □
Tumour size:  maximum horizontal dimension .......mm  depth of invasion .........mm
distance from closest resection margin (minimum tumour-free rim) .......mm;
position of this .................................
Paracervical involvement:  Yes □  No □
Parametrial involvement:  Yes □  No □
Vaginal involvement:  Yes □  No □  Distance from closest vaginal margin ......mm;
position of this..........................
Lymphovascular invasion:  Present □  Absent □
CIN:  Absent □  Present □  Grade (please circle) 1  2  3
CGIN:  Absent □  Present □  Grade (please circle) High  Low

**Pelvic nodes**
(including obturator, internal & external iliac)
total number of nodes retrieved  ...........  ...........
total number of lymph nodes with tumour deposits  ...........  ...........
Extranodal spread:  Yes □  No □  Yes □  No □

**Para-aortic nodes:**
not sampled □  positive □  negative □
Extranodal spread:  Yes □  No □

Endometrium:  Normal □  Abnormal (please specify)
Myometrium:  Normal □  Abnormal (please specify)
Right ovary/tube:  Normal □  Abnormal (please specify)
Left ovary/tube:  Normal □  Abnormal (please specify)

**Pathological FIGO stage:**

**Comments**

SNOMED codes
T83000 (Cervix)  M80703 (Squamous cell carcinoma)  M81403 (Adenocarcinoma)
M85603 (Adenosquamous carcinoma)  T08000 (Lymph node)  M80706 (Metastatic squamous carcinoma)  M81406 (Metastatic Adenocarcinoma)

Signature ........................................  Date.........../........./..........
NATIONAL MINIMUM DATASET MODIFIED FOR SWCIS
ENDOMETRIAL CANCER HISTOPATHOLOGY REPORT

Surname ........................................... Forenames .................................. Date of birth......................

Hospital ........................................ Hospital No ...................... NHS No..................

Date of request ..................Date of reporting.................. Report No..................

Pathologist ........................................ Surgeon ..........................................

Gross description
Dimensions of uterus: Length ..........mm Transverse ......mm Anteroposterior........mm

Maximum dimensions of tumour: ........x.................mm

Is there obvious macroscopic myometrial invasion: Yes ☐ No ☐

Histology
Type: Endometrioid ☐ Serous ☐ Clear cell ☐

MMMT ☐ other (please specify) ........................................

Grade (FIGO): (only applies to endometrioid carcinoma) I II III N/A

Myometrial invasion: None ☐ <50% ☐ >50% ☐

Is there microscopic involvement of
the cervical surface Yes ☐ No ☐
the cervical stroma Yes ☐ No ☐
the parametria Yes ☐ No ☐
the adnexa Yes ☐ No ☐
the uterine serosa Yes ☐ No ☐

Is there lymphovascular invasion: Yes ☐ No ☐

Is there associated endometrial hyperplasia: No ☐ Yes ☐ Simple ☐ Complex☑ Atypical ☐

Normal: right ovary ☐ left ovary ☐ right tube ☐ left tube ☐

Abnormal: (please specify) ...................................................................................

Pelvic Nodes
(including obturator, internal & external iliac)

<table>
<thead>
<tr>
<th></th>
<th>right</th>
<th>left</th>
</tr>
</thead>
<tbody>
<tr>
<td>total number of nodes retrieved</td>
<td>......</td>
<td>......</td>
</tr>
<tr>
<td>lymph nodes with tumour deposits</td>
<td>......</td>
<td>......</td>
</tr>
</tbody>
</table>

Extranodal spread: Yes ☐ No ☐

Para-aortic nodes: not sampled ☐ positive ☐ Extranodal spread Yes ☐ No ☐ negative ☐

Peritoneal washings: negative ☐

Pathological FIGO stage:.................................

Comments

SNOMED Codes
T82000 Uterus (T84000 endometrium) M81403 (Adenocarcinoma) M84413(Serous adenocarcinoma) M83103 (Clear cell carcinoma) M89503 (Mixed Müllerian tumour)
T08000 Lymph node M81406 (Metastatic carcinoma)

Signature ........................................... Date............./........./.........
NATIONAL MINIMUM DATASET MODIFIED FOR SWCIS
VULVAL CANCER HISTOPATHOLOGY

Surname............................ Forenames............................... Date of birth............
Hospital......................... Hospital No ......................... NHS No ......................
Date of request................... Date of reporting............... Report No...................
Pathologist........................ Surgeon.................................

Nature of Specimen:......................................................................................

**Gross description**

Size of specimen:    Length ..........mm    Width .......mm    Depth ........mm

No macroscopic residual tumour: ☐

Site(s) of tumour: ........................................................................................

Dimensions of tumour:    Length ..........mm    Width .......mm    Depth ........mm

**Histology**

Histological type:    squamous (usual) ☐    basaloid ☐    other (please specify) ☐..............................

Histological differentiation:    well ☐    moderate ☐    poor ☐

Histological size:    maximum horizontal dimension ..........(mm)

   depth of invasion..................(mm)

Minimum tumour-free skin margin .......... (mm)
Minimum tumour-free vaginal margin .......... (mm) N/A ☐
Minimum tumour-free anal margin .......... (mm) N/A ☐
Minimum deep soft tissue margin .......... (mm)

VIN:    absent ☐    present ☐    Grade: VIN 1  2  3 (circle as appropriate)

Nature of adjacent non-neoplastic skin:    lichen sclerosus ☐    Squamous hyperplasia ☐

HPV-associated features ☐

Lymphovascular invasion:    present ☐    absent ☐

Groin nodes:    total number of nodes (right) .......    total number of nodes (left) .......

Total number of positive nodes (right) .......    total number of positive nodes (left) .......

Extranodal extension:    yes ☐    no ☐

Pathological FIGO stage:..............................................................................

**Comments**

..............................................................................................................................

**SMOMED Codes**

T80100 Vulva
T08000 Lymph node

**SMOMED Codes**

M80703 Squamous cell carcinoma
M80416 Metastatic squamous carcinoma

Signature ........................................... Date ........../........../.........
NATIONAL MINIMUM DATASET

FALLOPIAN TUBE CARCINOMA HISTOPATHOLOGY REPORT

Surname............................ Forenames............................... Date of birth....................
Hospital........................ Hospital No ............................. NHS No ..........................
Date of request............... Date of reporting............... Report No..........................
Pathologist............................ Surgeon..............................

MACROSCOPIC FEATURES

Nature of specimen: ..........................................................

**Fallopian tubes**

Right: Normal □ Abnormal □
Size of tumour ................. Serosal involvement Yes □ No □

Left: Normal □ Abnormal □
Size of tumour ................. Serosal involvement Yes □ No □

**Ovaries**

Right: Dimensions ...... x ...... x ...... mm
Tumour involvement: Yes □ No □

Left: Dimensions ...... x ...... x ...... mm
Tumour involvement: Yes □ No □

**Uterus and cervix:**

Normal □ Abnormal □ Comment ......................

**Omentum:**

Biopsy □ Omentectomy □
Normal □ Abnormal □ Comment ......................

**Peritoneal biopsies:**

Not received □ Normal □ Abnormal □ Comment ......................

MICROSCOPIC FEATURES – FALLOPIAN TUBES

**Right**

**Borderline epithelial changes:**

None □ Serous □ Mucinous □ Other □ ...

**Invasive carcinoma:**

Not present □ Serous □ Mucinous □ Endometrioid □
Clear cell □ Transitional □ Mixed epithelial types □ (tick all that apply)
Malignant mixed Mullerian tumour □ ......... Other □ ...................... (please specify)
Differentiation (if appropriate) Well/Grade 1 □ Moderate/Grade 2 □ Poor/Grade 3 □

**Left**

**Borderline epithelial changes:**

None □ Serous □ Mucinous □ Other □

**Invasive carcinoma:**

Not present □ Serous □ Mucinous □ Endometrioid □
Clear cell □ Transitional □ Mixed epithelial types □ (tick all that apply)
Malignant mixed Mullerian tumour □ ......... Other □ ............... (please specify)
Differentiation (if appropriate) Well/Grade 1 □ Moderate/Grade 2 □ Poor/Grade 3 □
**MICROSCOPIC FEATURES: OTHER TISSUES**

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Right: Not involved</th>
<th>Involved</th>
<th>(see Notes)</th>
<th>Left: Not involved</th>
<th>Involved</th>
<th>(see Notes)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ovaries</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Endometrium</strong></td>
<td>Normal</td>
<td>Abnormal</td>
<td>Comment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Myometrium</strong></td>
<td>Normal</td>
<td>Abnormal</td>
<td>Comment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Uterine serosa</strong></td>
<td>Not involved</td>
<td></td>
<td>Borderline changes (non-invasive implants)</td>
<td>Invasive carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Omentum</strong></td>
<td>Not involved</td>
<td></td>
<td>Borderline changes (non-invasive implants)</td>
<td>Invasive carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Peritoneal biopsies (if received):</strong></td>
<td></td>
<td>Site(s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not involved</td>
<td></td>
<td>Borderline changes (non-invasive implants)</td>
<td>Invasive carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Peritoneal washings (if received):</strong></td>
<td></td>
<td>Not involved</td>
<td>Involved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Appendix (if received):</strong></td>
<td>Not involved</td>
<td>Involved</td>
<td>Comment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lymph nodes (if received):</strong></td>
<td>Site(s)</td>
<td>Total number</td>
<td>Number involved</td>
<td>(see Notes)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comments/additional information:

__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________

Signature: __________________________ Date: __________/____/____ SNOMED codes: ______/_______
### NATIONAL MINIMUM DATASET

**PRIMARY PERITONEAL CARCINOMA HISTOPATHOLOGY REPORT**

Surname ..........................  Forenames ..........................  Date of birth ..........  Sex ......

Hospital ..........................  Hospital no ..........................  NHS no ..........................

Date of receipt ..................  Date of report ..................  Report no ..........................

Pathologist ..........................  Surgeon ..........................

---

### MACROSCOPIC FEATURES

Nature and site of specimen (s):  

**Peritoneal biopsies:** Normal □  Abnormal □  Comment ........................................

**Omentum:**  

<table>
<thead>
<tr>
<th>Biopsy</th>
<th>Omentectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal □  Abnormal □</td>
<td>Comment</td>
</tr>
</tbody>
</table>

**Ovaries:**

<table>
<thead>
<tr>
<th>Dimensions ...... x ..... x ..... mm</th>
<th>Tumour involvement: Yes □ No □</th>
</tr>
</thead>
</table>

**Fallopian tubes:**

| Right: Normal □ Abnormal □ | Comment ........................................ |
| Left: Normal □ Abnormal □ | Comment ........................................ |

| Uterus and cervix: Normal □ Abnormal □ | Comment ........................................ |

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### MICROSCOPIC FEATURES – PERITONEUM AND OMENTUM

**Peritoneum**

| Borderline epithelial changes: None □  Serous □  Mucinous □  Other □ .......... |
| Invasive carcinoma: Not present □  Serous □  Mucinous □  Endometrioid □ |

| Clear cell □  Transitional □  Mixed epithelial types □ (tick all that apply) |

| Malignant mixed Mullerian tumour □ .................  Other □ ................. (please specify) |

| Differentiation (if appropriate) Well/Grade 1 □  Moderate/Grade 2 □  Poor/Grade 3 □ |

**Omentum**

| Borderline epithelial changes: None □  Serous □  Mucinous □  Other □ .......... |
| Invasive carcinoma: Not present □  Serous □  Mucinous □  Endometrioid □ |

| Clear cell □  Transitional □  Mixed epithelial types □ (tick all that apply) |

| Malignant mixed Mullerian tumour □ .................  Other □ ................. (please specify) |

| Differentiation (if appropriate) Well/Grade 1 □  Moderate/Grade 2 □  Poor/Grade 3 □ |
### MICROSCOPIC FEATURES – OTHER TISSUES

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</tr>
<tr>
<td><strong>Fallopian tubes</strong></td>
<td>Not involved □</td>
<td>Not involved □</td>
</tr>
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<td>Abnormal □</td>
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<tr>
<td><strong>Peritoneal washings (if received):</strong></td>
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<td>Involved □</td>
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<td><strong>Appendix (if received):</strong></td>
<td>Not involved □</td>
<td>Involved □</td>
</tr>
<tr>
<td><strong>Lymph nodes (if received):</strong></td>
<td>Site(s)..............</td>
<td>Total number......</td>
</tr>
</tbody>
</table>

**Comments/additional information:**

- ........................................................................................................
- ........................................................................................................
- ........................................................................................................
- ........................................................................................................
- ........................................................................................................
- ........................................................................................................

**Signature**............................................. **Date**....../....../......  **SNOMED codes** ....../........