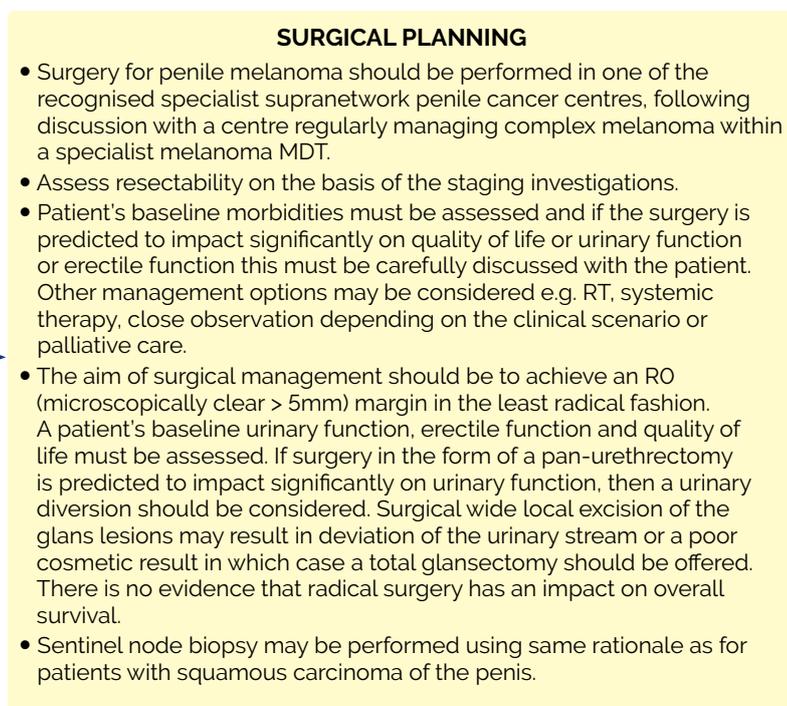
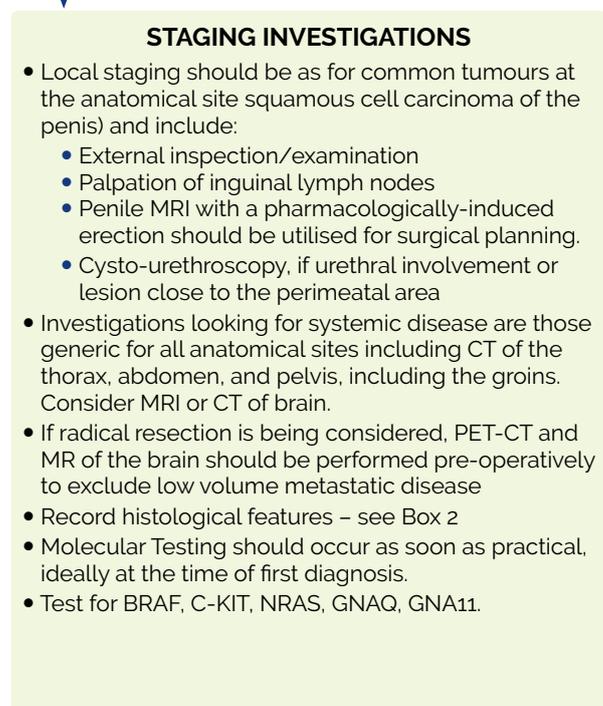
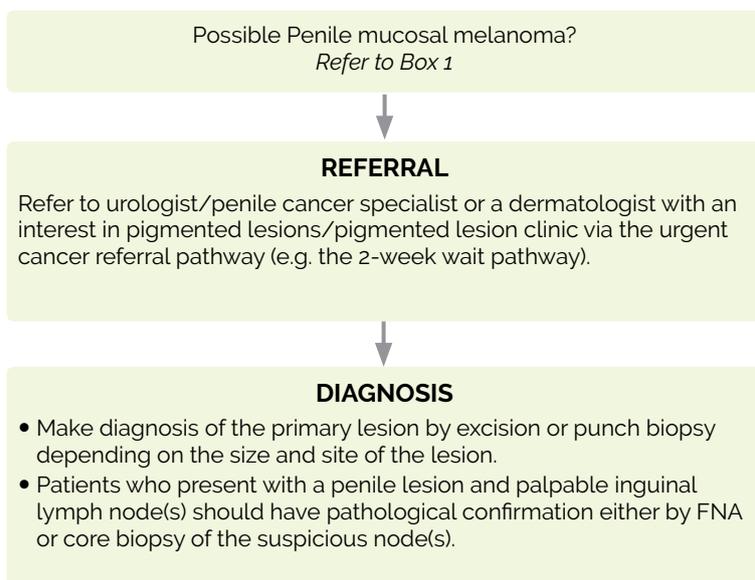
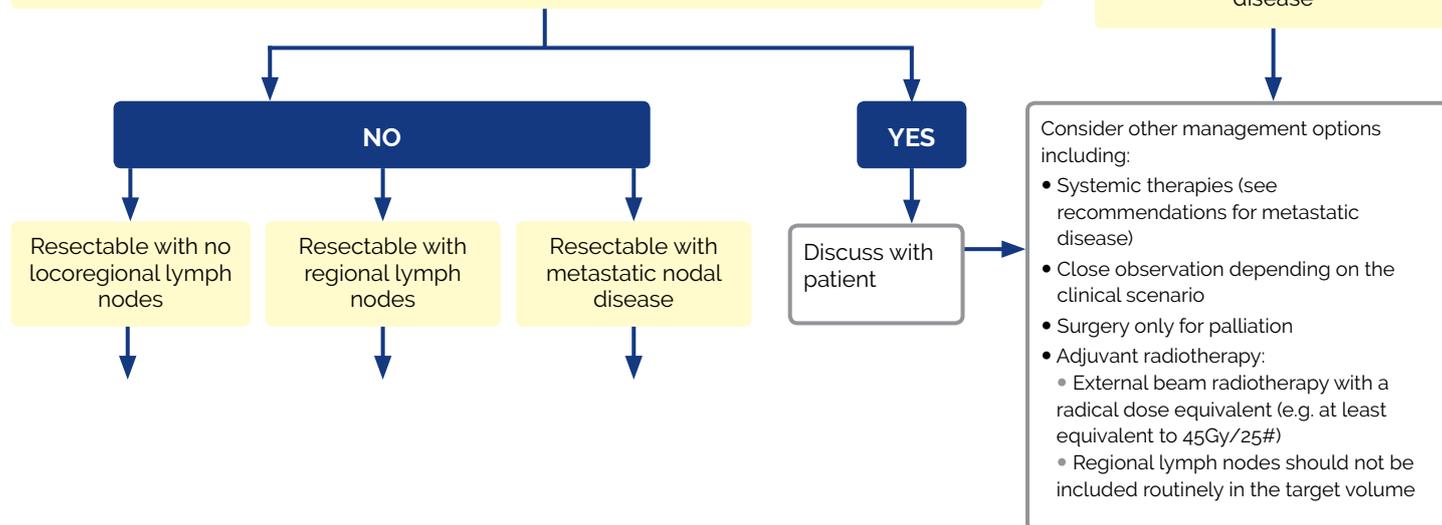


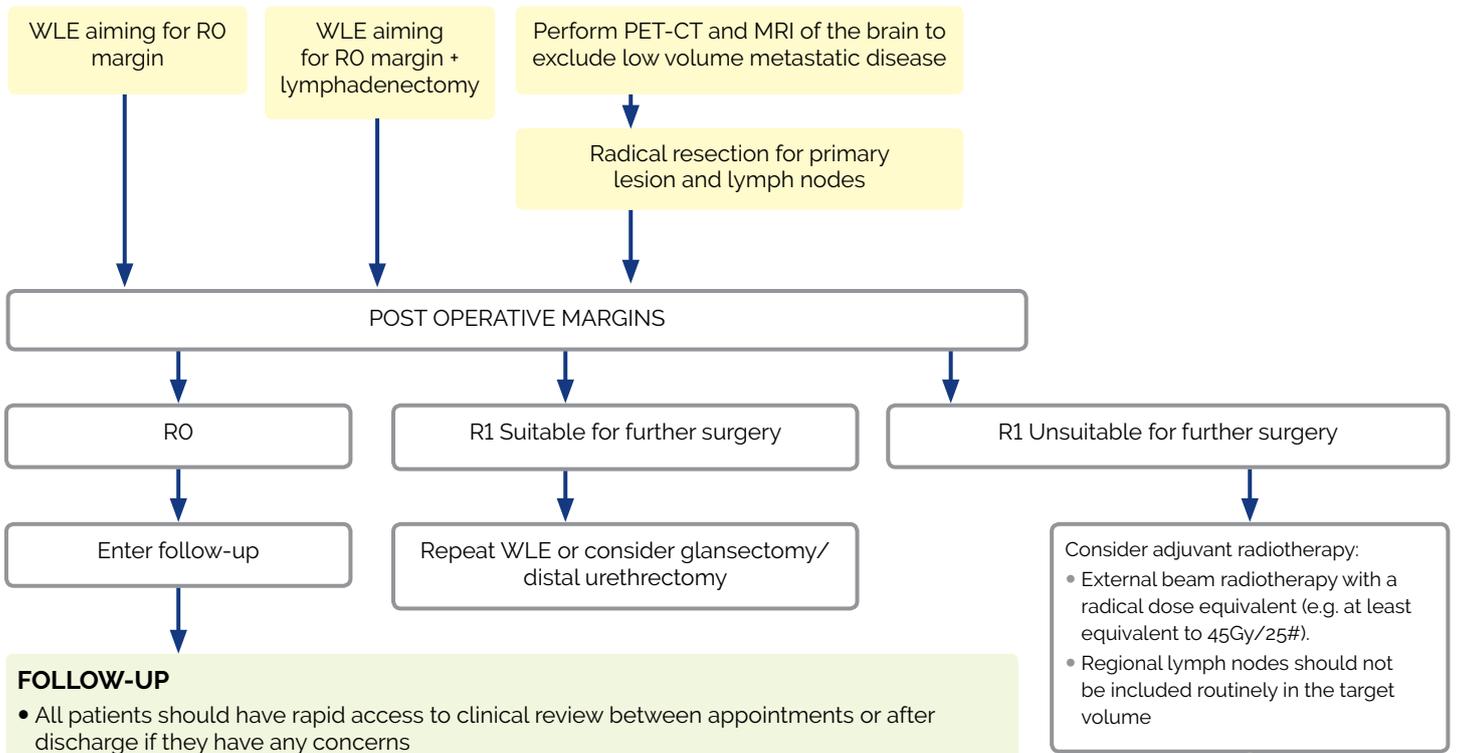
Care pathway: Penile mucosal melanoma



Surgery predicted to impact significantly on quality of life or urinary function or erectile function

Irresectable or metastatic disease





FOLLOW-UP

- All patients should have rapid access to clinical review between appointments or after discharge if they have any concerns
- If appropriate, discuss the advantages and disadvantages of surveillance imaging as set out in NG14 1.9.16 http://optiongrid.org/option-grids/pdf/63/en_gb
- All patients following potentially curative treatment or treatment for relapse should be followed up as follows:

Site of relapse	First three years	Years 3-5
Loco-regional relapse	3-monthly clinical examination including: <ul style="list-style-type: none"> • External inspection/examination • Palpation of inguinal lymph nodes • Cystourethroscopy, if urethral involvement or lesion close to the perimeatal area 	6-monthly clinical examination including: <ul style="list-style-type: none"> • External inspection/examination • Palpation of inguinal lymph nodes • Cystourethroscopy, if urethral involvement or lesion close to the perimeatal area
Systemic	<ul style="list-style-type: none"> • 3-monthly clinical examination according to that used for other malignant tumours at the primary site • Baseline CT thorax, abdomen, pelvis including groins 2-3 months post-surgery • 6-monthly CT thorax, abdomen, and pelvis including groins • 6-monthly CT or MRI of brain (to be discussed with the patient) 	<ul style="list-style-type: none"> • 6-monthly clinical examination according to that used for other malignant tumours at the primary site • 12-monthly CT thorax, abdomen and pelvis including groins • 12-monthly CT or MRI of brain (to be discussed with the patient)

- From years 6-10 patients should be given an annual appointment for clinical examination or open rapid access if available
- Patients should be discharged at year 10

ADJUVANT SYSTEMIC TREATMENT

- Choice guided by the most contemporary data.
- Emerging data in cutaneous melanoma supports the use of immunotherapy agents and BRAF targeted treatments in the adjuvant setting and consideration should be given for its use in AUG melanoma.

BOX 1

SIGNS AND SYMPTOMS OF POSSIBLE PENILE MELANOMA

- Bleeding from penile lesion
- Urethral discharge/bleeding
- Irregularly outlined pigmented or non-pigmented macule, papule, patch or nodule with or without ulceration on penis or foreskin
- Non-pigmented nodular lesion
- Nodular mass on glans penis
- Ulcerated lesion on glans or prepuce
- Intra-urethral mass (papillary or nodular)
- Palpable urethral lump
- Palpable inguinal lymphadenopathy

Other possible symptoms

- Irritation
- Pruritus
- Dyspareunia
- Lower urinary tract symptoms

BOX 2

The following histological features of the primary should be included in all reports:

- macroscopic size of the tumour;
- vertical tumour depth;
- presence/absence of ulceration;
- cytomorphological subtype (i.e. spindle, epithelioid, mixed);
- presence/absence of perineural and/or lymphovascular invasion;
- involvement of surrounding structures;
- confirmation of the diagnosis of melanoma with immunostaining with a melanocytic marker;
- involvement (or not) of surgical resection margins with either invasive melanoma or melanoma in situ: this may often require immunostaining with a melanocytic marker where there are surgery-induced artefacts.

Additional features such as presence/absence of pigmentation, presence/absence of necrosis, presence/absence and the composition of an accompanying inflammatory infiltrate could also be noted.

The presence/absence of lymph node/distant metastases should be recorded according to the anatomical site using the "N" and "M" components of the AJCC/TNM system, as if the melanoma were a carcinoma.

METASTATIC DISEASE

Treatment

1. The choice of systemic treatment should be guided by the most contemporary data.
2. Use single agent anti- PD1 antibodies in patients with unresectable Stage III or Stage IV tumours, taking into account any contraindications to this therapy.
3. Consider combination immunotherapy, e.g. anti-CTLA and anti-PD(L)1 monoclonal antibodies in selected fit patients.
4. The data demonstrates lower response rates from immunotherapy in mucosal melanoma compared to cutaneous melanoma therefore the significant toxicity of combination immunotherapy needs to be carefully discussed with the patient.
5. Consider BRAF + MEK inhibitors as a treatment option for the small number of patients with BRAF mutated unresectable Stage III or Stage IV AUG melanoma.
6. In patients with targetable mutations, consider immunotherapy as the preferred first line option unless the patient has a poor performance status and/or symptomatic bulky disease. However, this is a grey area and the correct sequence of immunotherapy/targeted therapy is yet to be robustly defined by clinical trials.
7. Not all C-KIT mutations are successfully targeted. Therefore if one is identified, the patient needs to be carefully counselled that testing for a C-KIT mutation may not change their management. Funding for a C-KIT inhibitor would have to be sought and might not be obtained. This also needs to be discussed with the patient. However, the presence of a C-KIT mutation may facilitate entry into clinical trials.
8. There is insufficient evidence to recommend the routine use of chemotherapy or bio-chemotherapy in the treatment of metastatic disease. Such evidence as there is suggests low response rates.
9. Palliative radiotherapy can be considered alongside immunotherapy without interruption of the immunotherapy. Patients receiving BRAF inhibitors and palliative radiotherapy should have their systemic therapy withheld during RT. There is currently no data to suggest increased rates of toxicity. This is a consensus view which is the subject of ongoing research.
10. Other palliative options for skin metastases that could be considered include
 - Electrochemotherapy for metastases in the skin from tumours of non-skin origin and melanoma (IPG446) <https://www.nice.org.uk/guidance/ipg446>
 - Talimogene laherparepvec for treating unresectable metastatic melanoma (TA410) <https://www.nice.org.uk/guidance/ta410>
11. For management of supportive care refer to NICE guidance CSG4 <https://www.nice.org.uk/guidance/csg4>

Follow-up

If there is/has been loco-regional or metastatic disease, follow-up should include CT thorax, abdomen and pelvis including groins, and MRI or CT of brain should usually be at 3-monthly intervals for patients treated with immunotherapy, and 2-monthly intervals for those treated with targeted agents. In patients who have responded or whose disease has not progressed, after 2-3 years the interval between scans can be extended to 6 months up to year 5, and then annually up to year 10.