Keratinocyte Cancers
(Non-Melanoma Skin Cancers)

This pathway is about non-pigmented malignant lesions. See also:
- Benign and Premalignant Skin Lesions
- Suspected Melanoma

Disclaimer

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Background

About Keratinocyte Cancers (Non-Melanoma Skin Cancers)

➢ Keratinocyte cancers were formerly known as non-melanoma skin cancers.
➢ Keratinocyte cancers are mainly basal cell carcinomas or squamous cell carcinomas.
➢ Basal cell carcinoma (BCC):
  • Basal cell carcinoma (BCC) is the most common skin cancer, accounting for approximately two thirds of all skin cancers.
  • BCC can be a locally invasive skin cancer arising from the basal cells of the epidermis.
  • Patients with BCC are highly likely to develop more primary tumours over time.
➢ Squamous cell carcinoma (SCC):
  • Cutaneous squamous cell carcinoma (SCC) is the second most common skin cancer, accounting for approximately 28% of all skin cancers. It is derived from squamous cells within the epidermis that make keratin.
  • Cutaneous SCC is a risk for invasive disease, wherein cancer cells grow beyond the epidermis/dermis. SCC can metastasise (spread to distant tissues) and may prove fatal.

Assessment

1. Take a history to determine if any risk factors or suspicious symptoms are present.

➢ Risk factors
  • Work or leisure history associated with increased sun exposure or severe sunburn
  • Personal or family history of skin cancer, especially melanoma in first-degree relatives
  • Fair or red hair colour
  • History of blistering sunburn
  • Immunosuppression
  • Increasing age
  • Lesion noticed by another person
  • Multiple solar keratoses
  • Previous basal cell carcinoma (BCC) or squamous cell carcinoma (SCC)
  • Previous exposure to arsenic
  • Previous radiotherapy
  • Skin that burns and does not tan
  • Solarium use
  • Tendency to freckle

➢ Suspicious symptoms
  • Lesion persists, bleeds, or is not healing at 4 weeks
  • Lesion is changing or growing in size, colour, or shape
  • Thickened or indurated
  • Tender to touch
  • Symptoms the patient is concerned about

2. Perform examination, preferably including dermoscopy if confident with this instrument. There is a suggested framework for conducting skin checks.

➢ Examination
  • Ensure good lighting and privacy.
  • Ask the patient to nominate all spots that they (or their partner, friend, or family member) are concerned about.
• Examine:
  o all body parts, including non-sun exposed areas, e.g. feet, between toes, area covered by underwear.
  o every lesion in turn, paying particular attention to any new or patient-nominated lesions

➢ Suggested framework for conducting skin checks
  1. Have patient sit in the centre of the couch and examine hands, arms, and face.
  2. Ask patient to lie face down to examine their back, legs, and soles of feet.
  3. Ask patient to roll over to examine chest, abdomen, legs, and feet (including between toes).
  4. Ask about lesions of concern on the scalp or those concealed by underwear. Only examine these areas with verbal consent from the patient.

3. If there are any pigmented lesions of concern, follow the Melanoma pathway to determine likelihood of melanoma and whether excision biopsy is required.

4. Identify clinical features and characteristics of malignant skin lesions:
   ➢ Basal cell carcinoma (BCC) - characteristics can include:
     • non-healing ulcer.
     • slow-growing plaque or nodule.
     • usually pink or variably pigmented.
     • varies in size from a few millimetres to several centimetres in diameter.
     • easy bleeding.

   ➢ There are 4 main clinical presentations of BCC:
     • Nodular (shiny, translucent, telangiectatic papule or nodule – may be ulcerated)

![Nodular basal cell carcinoma](https://www.dermnetnz.org/assets/images/basalcellcarcinoma_nodular.jpg)

Nodular basal cell carcinoma
Copyright 2018 DermNet NZ
➢ **Superficial** (usually erythematous, slightly scaly, irregular, with or without an obvious margin or superficial ulceration)

![Basal cell carcinoma](image1)

Basal cell carcinoma
Copyright 2018 [DermNet NZ](https://www.dermnetnz.org)

➢ **Morphoeic** (pale, scar-like lesion – more visible when skin is stretched or presents as an indented scar without prior injury)

![Morphoeic basal cell carcinoma](image2)

Morphoeic basal cell carcinoma
Copyright 2018 [DermNet NZ](https://www.dermnetnz.org)
• **Basisquamous** (mixture of both SCC and BCC, and may have clinical features of both cancers i.e., scaly and nodular erythematous plaques)

![Basisquamous cell carcinoma](https://unsplash.com/photos/DQjA9YB3PFk)

Basisquamous cell carcinoma  
Copyright 2018 [DermNet NZ](https://www.dermnetnz.org)

• BCC is very rarely a threat to life. A tiny proportion of BCCs grow rapidly, invade deeply, or metastasise to local lymph nodes.
• See also DermNet NZ – [Basal Cell Carcinoma](https://www.dermnetnz.org)

➢ **Squamous cell carcinoma (SCC)**  
There are 3 main clinical presentations of SCC:
• Classic (variable appearance e.g., nodular, keratotic, scaly, indurated, tender, and ulcerated)

![Facial squamous cell carcinoma](https://unsplash.com/photos/6Y7A50OOG9k)

Facial squamous cell carcinoma  
Copyright 2018 [DermNet NZ](https://www.dermnetnz.org)
➢ **Keratoacanthoma** (tender, rapidly growing lesions, often with a smooth outer dome and central keratin core)

![Keratoacanthoma Image](https://dermnetnz.org/SkinCancer/SkinCancers-KeratinocyteCancers/SkinCancer-KeratinocyteCancers-Keratoacanthoma.png)

Facial squamous cell carcinoma
Copyright 2018 DermNet NZ

➢ **SCC in situ** (also known as intraepidermal SCC or Bowen's disease – slowly expanding, irregular, scaly, and erythematous patch; may also contain pigment)

![SCC in situ Image](https://dermnetnz.org/SkinCancer/SkinCancers-KeratinocyteCancers/SkinCancer-KeratinocyteCancers-SCCinSitu.png)

In situ squamous cell carcinoma
Copyright 2018 DermNet NZ

➢ See also DermNet NZ – [Cutaneous Squamous Cell Carcinoma (SCC)](https://dermnetnz.org/SkinCancer/SkinCancers-KeratinocyteCancers/SkinCancer-KeratinocyteCancers-SCC.html)
- **Amelanotic and hypomelanotic melanoma** – if any suspicion of this, follow the [Suspected Melanoma](#) pathway.

- **Amelanotic and hypomelanotic melanoma**
  - Often not recognised as melanoma because of the absence of pigmentation.
    - Up to 20% of all melanomas are only partially pigmented.
    - Over one third of nodular, desmoplastic, and acral melanomas are hypomelanotic.
    - This stresses the importance of obtaining a histological diagnosis for all suspicious lesions.
  - **EFG rule** – consider any lesion that is elevated, firm, and growing over a period of 4 to 6 weeks suspicious for melanoma, even if non-pigmented.
5. If malignant skin lesions have been confidently ruled out clinically, and the lesion/s are thought to be **benign** or **premalignant**, follow the [Benign and Premalignant Skin Lesions](#) pathway.

➢ **Benign skin lesions**

  **Seborrhoeic keratosis:**
  - Also known as senile warts or barnacles.
  - Appear as adherent warty plaque, usually pigmented and waxy.
  - More common with increasing age – occurring in sun exposed sites and elsewhere in people with genetic propensity.
  - Solar lentigines are similar but thinner than Seborrhoeic keratosis, and only occur in sun exposed sites especially the back of the hands.

  ![Seborrhoeic keratoses](seborrheic-keratoses.png)  
  ![Seborrhoeic keratoses](seborrheic-keratoses.png)

  ![Epidermoid cyst](epidermoid-cyst.png)  
  ![Cyst](cyst.png)

  **Epidermoid (sebaceous) cysts:**
  - Present as a firm skin-coloured nodule with punctum.
  - Caused by blockage of follicular infundibulum, the epidermal cells of which break down and can rupture into surrounding tissue causing an inflammatory and granulomatous reaction.
• **Skin tags/acrochordons:**
  - Painless, skin-coloured, or pigmented non-cancerous pedunculated growths.
  - Vary in size from 1 mm to several millimetres.
  - Generally occur in flexural areas where there is increased skin-to-skin friction e.g., axilla, neck, groin.
  - More numerous in obesity.

![Skin tags](https://dermnetnz.org/skin-tag-skin-nerve-photograph.jpg)

**Premalignant skin lesions**

- **Actinic/solar keratosis:**
  - Caused by chronic and cumulative sun exposure.
  - Variably scaly, crusty, and spikey patches which vary from very tiny to 1 to 2 cm. Can be red and or pigmented.
  - Very common – developed by 40 to 50% of Caucasians aged over 40 years.
  - Considered a precursor lesion to developing skin cancer, with reported annual transformation rates to squamous cell carcinoma ranging from 0.025 to 20%.

- **Actinic cheilitis:**
  - Caused by sun exposure as above – usually lower lip.
  - Chronic scaling or white plaques of the vermilion border.
  - More common in males than females.
  - Histologically the same as actinic keratosis.
6. If SCC suspected, examine regional lymph nodes for metastatic disease, especially if head and neck lesions.

7. Arrange investigations as required:
   - Arrange a punch or shave biopsy to confirm pathology if:
     - uncertain of diagnosis, or
     - considering topical treatment.
   - If any suspicion of lymph node metastasis, request:
     - CT or ultrasound imaging of relevant lymph node basin, and
     - fine needle biopsy.

Management

**Practice Point**

**Excision is generally best practice**

Excision allows for histological assessment of tumour margins and generally provides better cure rates than topical therapies.

1. Most BCCs and SCCs do not require referral. Consider referral to a skin specialist (dermatologist, plastic surgeon, general surgeon, or Mohs surgeon) if the BCC or SCC has:

   - **High-risk clinical features of a BCC or SCC**
     - These features correlate with an increased likelihood of positive excision margins, loco-regional recurrence, and/or surgical complication rates.
       - Larger than:
         - 20 mm on trunks or extremities
         - 10 mm on cheek, forehead, or scalp
       - Rapid growth
       - Recurrent lesions – previously incomplete excision of lesion, and any previously treated area (cryotherapy, curette and cautery, excision)
       - Incompletely excised lesions – where surgical expertise is required for appropriate margins
       - Lesions fixed to underlying structures
       - Lesions involving or lying adjacent to significant nerves, e.g. facial or accessory nerve
       - Poorly defined lesions
       - Lesions with regional lymph node metastasis
       - Cosmetically sensitive sites, e.g. central face, nose, ears, lips, periocular
       - Functionally important sites, e.g. digits, genitalia, hands, feet
       - Immunosuppressed patients, e.g. those with solid organ transplant, chronic lymphocytic leukaemia, or HIV
       - Primary mucosal SCC

   - **High-risk histological features of a BCC or SCC**
     - These features correlate with an increased likelihood of positive excision margins, loco-regional recurrence, and/or surgical complication rates.
       - Depth of invasion more than 4 mm
       - Perineural or vascular invasion
       - Extension into subcutaneous fat
       - BCC
Micronodular
- Infiltrative
- Morphoeic (sclerosing)

- SCC
  - Poorly differentiated
  - High-risk histological variants of SCC:
    - Spindle cell carcinoma
      - Acantholytic SCC
      - Adenosquamous tumours

2. If lesion is small and low-risk, surgical excision is usually the best treatment option as it allows for assessment of tumour margins and provides better cure rates than topical therapies.

- **Excise in general practice** if:
  - the patient consents,
  - Low risk lesion and the wound can be directly closed within **appropriate margins**.
  - **Lesions that can be excised by a general practitioner** with experience and confidence in surgical procedures include:
    - Well-defined primary lesions of:
      - trunk and extremities that are less than 15 mm diameter – 15 to 20 mm is a grey zone and these need referral depending on circumstances
      - the face and scalp that are less than 10 mm diameter
    - Less than 4 mm thick
    - Favourable histology – well differentiated, no high-risk features

- **Lesions with the following characteristics should be referred for specialist care:**
  - Located on:
    - scalp
    - peri-ocular
    - ears
    - lips
    - nose
    - genitalia
  - Recurrence, or near a previously treated area
  - Rapidly growing
  - Extending beyond subcutaneous tissue

- **Appropriate margin**

<table>
<thead>
<tr>
<th>Type of lesion</th>
<th>Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected melanoma (excisional biopsy)</td>
<td>2 mm</td>
</tr>
<tr>
<td>Benign lesions</td>
<td>2 mm</td>
</tr>
<tr>
<td>BCC with well-defined border</td>
<td>3 mm</td>
</tr>
<tr>
<td>Aggressive BCC or BCC with unclear border</td>
<td>4 to 5 mm</td>
</tr>
<tr>
<td>SCC in situ (Bowen’s disease)</td>
<td>2 mm</td>
</tr>
<tr>
<td>SCC (&lt; 2 cm)</td>
<td>4 to 5 mm</td>
</tr>
<tr>
<td>SCC (&gt; 2 cm)</td>
<td>May require margins of up to 10 mm – consider referral</td>
</tr>
<tr>
<td>Benign lesion</td>
<td>Generally 2 mm, less if clearly benign, e.g. sebaceous cyst</td>
</tr>
</tbody>
</table>

- If the excision is beyond your expertise, consider referring to an experienced general practitioner colleague, skin cancer clinic, dermatologist, general surgeon, plastic surgeon, or Mohs surgeon.
3. If excision is unsuitable or not desired by the patient, consider alternative therapies:

- **Superficial BCC (biopsy proven)**
  - Curettage and cautery or **shave excision**
    - Can be used if:
      - experienced in this technique, and
      - lesion is on trunk or limbs. Use with caution in lower legs of elderly patients due to poor healing and risk of chronic ulceration.
  - **Liquid nitrogen (cryotherapy)**
    - Requires a 30 second freeze followed by thawing and another 30 second freeze (not a short freeze as used for solar keratoses).
    - For more information, see DermNet NZ – **Cryotherapy**.
  - **Photodynamic therapy (PDT)** – if required, refer to dermatologist.
  - **Imiquimod (Aldara)**
    - With superficial BCC (biopsy proven)
    - Cosmetically sensitive area
    - Efficacy – it has a lower cure rate than excision (84% clearance at 3 years, compared with 98%).
    - Requires **PBS Authority**.
    - Patient selection:
      - Patient selection is important as treatment efficacy is based on the inflammatory reaction that is induced.
      - May be useful in patients:
        - who are prone to scarring
        - on anticoagulants
        - unable to access surgery
        - with multiple lesions
      - Contraindications:
        - Any BCC other than superficial, i.e. recurrent, invasive, infiltrating, or nodular BCC.
        - Lesion within 1 cm of hairline, eyes, ears, nose, or lips
        - Patients who are immunosuppressed, e.g. HIV positive, abnormal blood count, on immunosuppressive medications
        - Lesions treated with Imiquimod previously
        - Pregnancy and breastfeeding
    - Common side-effects include:
      - local skin reactions
      - flu-like symptoms
      - post-inflammatory hypopigmentation
  - **Instructions for use**:
    1. Advise patient to:
      - apply to lesion/s (tumour/s) and a 5 mm margin of surrounding normal skin in the evening, not at bedtime, 5 times a week for 6 weeks.
      - wash the treated area the morning after with mild soap and water
      - use sun protection on the treated areas.
    2. Ensure patient is aware that the normal clinical response includes early and severe inflammation (often worse in the second week), followed by skin erosion and then finally healing. It may take up to 6 weeks before skin returns to normal.
    3. Give the patient a printed copy of the **TGA consumer medicine information (CMI)**.
    4. Assess response:
      - 2 weeks into course – consider dose interruption if intense reaction develops.
• Approximately 1 to 2 months after course completion.
5. If lesion/s persist at 3 months, arrange surgical excision. Repeat treatment is contraindicated.
6. For full prescribing details, see TGA Product Information – Imiquimod (Aldara).
   See also DermNet NZ – Imiquimod (Aldara).

• SCC in situ (biopsy proven), Bowen’s disease, intraepidermal carcinoma (IEC), and severe dysplasia
  • For localised lesions, treatment options include:
    o Curettage and cautery can be used if:
      ▪ experienced in this technique, and
      ▪ lesion is on trunk or limbs. Use with caution in lower legs of elderly patients due to poor healing and risk of chronic ulceration.
    o Liquid nitrogen (cryotherapy)
      ▪ Requires a 30 second freeze followed by thawing and another 30 second freeze (not a short freeze as used for solar keratoses).
      ▪ For more information, see DermNet NZ – Cryotherapy
    o Photodynamic therapy (PDT) or laser therapy – if required, refer to dermatologist
  
• If multiple or widespread lesions, treatment options include:
  o Photodynamic therapy (PDT) or laser therapy – if required, refer to dermatologist
  o Fluorouracil (Efudix 5-FU)
    Efficacy – cure rates of Bowen’s disease with 5-FU are 67% to 92%, as opposed to 95% with excision.
    Patient selection:
    ▪ Contraindications:
      • DPD enzyme deficiency.
      • Pregnancy and breastfeeding.
    ▪ Precautions:
      • Avoid in patients who have outdoor occupations as UV exposure can produce a diffuse phototoxic response.
      • Thickened lesions are more likely to contain an invasive component and excision may be required. If in doubt, a punch biopsy is useful.
    ▪ Common side-effects – inflammation and skin erosion.
  o Instructions for use:
    1. Advise patient to:
      ▪ apply once to twice daily for 3 weeks, and
      ▪ protect treated areas from UV exposure with appropriate sun protection.
    2. Advise patient that the normal clinical response includes early and severe inflammation (often worse in the second week), followed by skin erosion and then healing. It may take up to 6 weeks before skin returns to normal.
    4. Review patient:
      ▪ at 2 weeks to ensure adequate reaction and
      ▪ 2 to 3 months after course completed to check for clearance of lesion/s.
    5. If lesion/s persist at 3 months, arrange surgical excision. Repeat treatment is contraindicated.
    6. For full prescribing details, see:
      ▪ TGA Product Information – Fluorouracil (Efudix).
    7. PBS – Imiquimod (PBS authority required).
   See also Dermnet – Fluorouracil.
• Consider referral to radiation oncology to arrange radiotherapy for BCCs and SCCs that are not suitable for surgery:
  • if the patient is elderly and frail.
  • the lesion is very large or awkwardly placed.
  • as an adjunctive treatment when margins are incomplete.
  • if persistent, recurrent, or advanced BCC and SCC.

4. After managing the initial skin cancer, ongoing monitoring is crucial to detect new lesions, recurrent lesions, or metastatic disease. Counsel patient regarding recurrence rates and risk.
   • **Recurrence rates and risk**
     Risk of further primary tumours:
     • 44% of people will develop a second BCC within 3 years of BCC excision
     • 18% risk of subsequent SCC within 3 years after index SCC
     Risk of local persistence of the previous primary tumour or metastatic disease:
     • BCC – 66% of recurrences will arise within 3 years of initial treatment. Metastasis is rare.
     • SCC – recurrence is highly dependent on tumour size, anatomic site, and histological features.
     High-risk features include:
     o Larger than 2 cm diameter
     o Lesions on lip and ear
     o Poorly differentiated SCC
     o More than 4 mm thick
     o Recurrent SCC
     o Perineural invasion (most serious risk factor) up to 50% risk of regional recurrence

5. Recommended follow-up:
   • All patients with a previous skin cancer:
     • Annual skin examinations for life.
     • Education about prevention and risk reduction for other cancers.
     o **Prevention and risk reduction**
       Advise patient about general sun safety, e.g:
       ▪ Stay in the shade.
       ▪ Cover up with SPF rated clothing and hat.
       ▪ Use a 50+ broad spectrum (UVA/UVB) sunscreen to exposed skin and reapply frequently, e.g. every 2 to 3 hours.
       ▪ Avoid tanning and solariums.
       Recommend patient commences a Nicotinamide (Vitamin B3) supplement, 500 mg twice daily. This has been shown to reduce rates of new BCC and SCC in high-risk patients by 23% after 1 year compared with placebo.
   • Prompt self-reporting of new or changing skin lesions to treating clinician.

➢ After non-surgical skin cancer treatment, arrange follow-up at 3 to 6 months to check for clearance, then 6- to 12-monthly.
➢ If poorly differentiated SCC, SCC of the lip, or in immunosuppressed patients, arrange follow-up at 3 months, then every 6 months. Include examination of the relevant lymph node drainage region.
➢ For patients with **chronic immunosuppression**, consider referral to a specialist dermatology service for closer monitoring.
  • **Patients with chronic immunosuppression**
    o Organ transplant recipients
    o Chronic lymphocytic leukaemia (CLL)
Referral

- Most **low-risk** BCCs or SCCs can be managed in general practice and do not require referral.

- If the skin lesion is unable to be managed in general practice, consider referring to an experienced general practitioner colleague, skin cancer clinic, dermatologist, plastic surgeon, or general surgeon.

- Consider referral to a skin specialist (dermatologist, plastic surgeon, general surgeon, or Mohs surgeon) if the BCC or SCC has:
  - high-risk clinical features, or
  - high-risk histological features.

- For patients with **chronic immunosuppression**, consider referral to a dermatologist for closer monitoring and possible adjunctive treatment, e.g. with oral acitretin.

- Consider referral to **radiation oncology** to arrange radiotherapy for BCCs and SCCs that are not suitable for surgery:
  - if the patient is elderly and frail.
  - the lesion is very large or awkwardly placed.
  - as an adjunctive treatment when margins are incomplete.
  - For cases of persistent, recurrent, or advanced BCC and SCC.

Information

For health professionals

- Australian Family Physician:
  - Non-melanoma Skin Cancers: Treatment Options
  - Skin Checks
- Australian Journal of General Practice – Improving Diagnostic Accuracy of Skin Biopsies
- Cancer Council Australia:
  - Clinical Practice Guidelines for Keratinocyte Cancer
  - Optimal Care Pathway for People with Basal Cell Carcinoma or Squamous Cell Carcinoma
  - Optimal Care Pathway for People with Basal Cell Carcinoma or Squamous Cell Carcinoma: Quick Reference Guide
  - Aboriginal Communities
  - Aboriginal Resources
- DermNet New Zealand:
  - 5-Fluorouracil Cream
  - Basal Cell Carcinoma
  - Cutaneous Squamous Cell Carcinoma
  - Imiquimod
- SunSmart – Melanoma and Other Skin Cancers: A Guide for Medical Practitioners

For patients

- Better Health Channel – Skin Cancer
- Cancer Council:
  - Checking for Cancer: What to Expect

South Eastern Melbourne PHN Keratinocyte Cancers (Non-Melanoma Skin Cancers) pathway
Skin Cancer

Cancer Council Victoria – Aboriginal Communities: Information

DermNet NZ:

- 5-Fluorouracil cream
- Imiquimod
- Melanoma
- Skin Cancer

National Indigenous Cancer Network – About Cancer

Patient:

- Non-Melanoma Skin Cancer
- Melanoma

TGA:

- Imiquimod (Aldara)
- Fluorouracil (Efudix)

References


Last Reviewed: December 2019

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