

## National Practical Guidance for Skin Cancer Care

Published by the Royal Belgian Society for Dermatology and Venereology (KBVDV), 22 February 2026

*This document serves as a guidance for all dermatologists in Belgium. It has been drawn up on the basis of the most recent Dutch and European guidelines, AJCC8 and consensus documents. Individual studies, as well as more recently published meta-analyses or systematic review that were not included or considered in the underlying guidelines, have not been separately evaluated or incorporated into this document.*

The care of patients with skin cancer requires a tailored approach. The importance of **shared decision-making** and providing good **patient information** is emphasised in all of the recommendations below.

### 1. Basal cell carcinoma (BCC)

#### Diagnostics

##### Gold Standard and First-Line Diagnostics:

1. Diagnostics include visual inspection and **dermoscopy**. Dermoscopy is indispensable for diagnostic accuracy, especially for trained clinicians (through training as a dermatologist and/or a recognised dermoscopy course).
2. **Histopathological examination** (biopsy) remains the gold standard for diagnosis.
3. A **biopsy may be omitted** if the diagnosis of BCC is **confirmed by dermoscopy**, if the subtype is not essential for the choice of treatment, and the lesion is located **outside the H zone** (face). In all other cases, additional diagnostics are required.

##### Additional imaging:

- **CT or MRI** can be performed to visualise invasion into deeper structures in the case of **locally advanced BCC (laBCC)**. Consult a radiologist from a multidisciplinary team/tumor board (MDT) to determine the most appropriate imaging.

#### Classification and risk classification

BCCs are classified based on histopathological characteristics. The classification into low and high risk supports therapeutic decisions and the excision margin. Risk mainly reflects the chance of non-radicality/local recurrence.

Category	Histopathological Growth Patterns (Preferred Classification)	Implication
Differentiated/Non-aggressive Types	Superficial BCC, Nodular BCC	Low risk
Aggressive types	Micronodular, Morpheaphormic, Infiltrative BCC	High risk
Rare type	Basosquamous carcinoma	High risk

#### Complex BCC terminology:

- **Locally advanced BCC (laBCC):** Advanced disease with extensive destruction of surrounding tissue, where curative surgery and/or radiotherapy is **not** considered **feasible** or would result in unacceptable functional or cosmetic outcomes. Diagnosis should be discussed in a MDT.
- **Metastatic BCC (mBCC):** Disease with one or more metastases. Diagnosis should be discussed in a MDT.

## Treatment

<b>Surgery is the most effective treatment for BCC compared to all alternative treatments</b>	Treatment	Clinical Margin (Conventional Excision, CE)	Histological Margin
BCC Type			
Low-risk BCC	<b>CE</b> (first choice). Alternatives: Imiquimod 5% or 5-FU 5% or photodynamic therapy (for superficial growth), cryosurgery, radiotherapy	3–4 mm	It is generally accepted that <b>no minimum histological margin is necessary</b> .
High-risk BCC	<b>CE</b> or 3D micrographic surgery such as <b>Mohs' Micrographic Surgery (MMS)</b> , radiotherapy.	Minimum 5 mm.	It is generally accepted that <b>no minimum histological clearance margin is necessary</b> .
Complex/Selected BCCs	<b>MMS</b> (e.g. on the face, recurrence), radiotherapy.	N/A (MMC is margin-controlled).	N/A

**Local Non-Invasive Treatments (Low-risk BCC):** Local creams (Imiquimod, 5-FU) and photodynamic therapy (PDT) have lower cure rates than surgery (5-year tumour-free survival 70-85%). Patients should be well informed about the risk of recurrence and the importance of self-inspection.

### Systemic Therapy (laBCC or mBCC):

- Treatment with Hedgehog signalling pathway inhibitors (HHI: Vismodegib or Sonidegib) can be discussed in a MDT if curative surgery or radiotherapy is **not** considered **feasible**.
- HHIs must be prescribed in a **reference centre** with MDT. **Pregnancy prevention programmes** must be strictly applied due to the teratogenicity of HHIs in both women and men of childbearing age.
- **Checkpoint inhibitors** (such as Cemiplimab) may be effective; discussion in MDT is necessary and treatment is not reimbursed since 01-01-2025.

### Basal cell nevus syndrome (BCNS)

Patients with BCNS (Gorlin-Goltz) often develop multiple BCCs, often at a young age. When selecting treatment options, particularly extensive surgery, the high risk of developing multiple additional BCCs over time and the cumulative treatment burden should be considered.

- Refer to the **clinical geneticist** for counselling and DNA diagnostics in cases of clinical suspicion of BCNS (based on major/minor criteria).
- Adequate **sun protection** should be discussed frequently.
- **Vitamin D supplementation** may be considered, given the risk of deficiency.
- Avoid (additional) **X-ray examinations** as much as possible due to the potentially increased risk of BCCs from low-dose radiation.

### BCC follow-up

**Routine follow-up for all BCC patients is not recommended.** The emphasis is on **self-monitoring** and proper instruction. Patients have an increased risk of subsequent BCC (up to 30%), cSCC (3x) and melanoma (2.5x).

### Indications and duration of monitoring by a dermatologist:

1. **One-time check-up (6–12 months):** After treatment **without histological check-up for radicality** (e.g. local creams, cryosurgery, PDT). If it was only one BCC that was surgically removed in toto, a check-up is not

necessary. However, all patients should receive appropriate education regarding regular self-examination and the importance of primary prevention measures.

2. **Minimum annual check-up (or more frequently):**

- For patients with **more than one low-risk BCC**, **annual check-ups** are **recommended** for a period of up to **3 years after the last BCC**. The frequency of check-ups can be increased if multiple BCCs are detected at each check-up.
  - Patients with BCC with a **high risk of local recurrence** (such as large and aggressively growing primary BCCs and **recurrent BCCs on the face** where a subsequent recurrence could cause high morbidity). These patients should **be monitored**. Once 5 years have passed without a recurrence or new skin cancer diagnosis, the monitoring period can be concluded.
  - **High-risk patients** (BCNS, long-term immunosuppressants, extensive actinic skin damage). In patients with proven BCNS, increased frequency of monitoring (every six months or every three months) is recommended from the development of the first BCC.
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## 2. Cutaneous squamous cell carcinoma (cSCC)

### *Diagnosis and Staging*

#### **Diagnosis:**

- If SCC is suspected, diagnostic excision should be performed. Large tumors or tumors on the head and neck can undergo a (punch) biopsy for histological confirmation.
- The pathology report should contain crucial information for AJCC8 staging and risk classification, including **degree of differentiation, depth of invasion, growth beyond subcutaneous fat, perineural invasion (PNI) and angioinvasion.**

#### **Staging system and risk classification:**

- Use the **8th edition of the AJCC** for staging cSCC of **all cutaneous locations.**
- The AJCC8 should be **supplemented** with additional clinical and pathological risk factors to correctly identify high-risk patients.
- **High-Risk Factors:**

Localisation on the temple, ear, lip

Diameter > 20 mm -> T2+

Depth > 6 mm or invasion beyond the subcutaneous fat -> T3+

Poor differentiation

Desmoplasia

Perineural invasion (microscopic, symptomatic, imaging) -> T3+

Bone erosion -> T3+

Immunosuppression\

Positive margins after excision

Presence of multiple risk factors further increase the risk of local recurrence and nodal metastases.

### *Staging examination*

#### **Regional lymph nodes:**

- **Routine screening of lymph nodes with imaging is not recommended** for low-risk cSCC.
- **Ultrasound** of the lymph node stations, combined with **fine needle aspiration cytology (FNAC)** of radiologically suspicious lymph nodes, is recommended for patients with **high-risk cSCC**. This should be performed by radiologists in an experienced centre.
- **PET/CT** should be performed in cases of **lymphogenous metastatic cSCC**.

#### **Local invasion:**

- In cases of clinical suspicion of soft tissue invasion (beyond subcutaneous fatty tissue and/or muscle tissue) and clinical suspicion of perineural growth, an **MRI** scan with gadolinium-containing contrast is preferred.
- If **bone involvement** is suspected, a **CT scan** is preferred.

#### **Treatment**

- **Surgical excision**, either conventional or Mohs micrographic surgery in selected cases, is the first-line treatment.
- **Histopathological Margins (Radicality):** The clinical margin should be 5mm, and minimum histopathologically free margin is **≥ 1 mm for low-risk cSCCs**. For **high-risk cSCCs**, clinical margin should be 6-10mm and re-excision is recommended when the histopathological margin is narrowly radical (margin > 0 but < 2 mm).

- **Micrographically Controlled Surgery (MMC):** Consider for tumours that are difficult to delineate and/or where tissue preservation is crucial (e.g. face). Discuss internally with the responsible pathologist whether MMS for cSCC should be performed on frozen sections or paraffin sections. In the case of paraffin sections, a 'slow Mohs' procedure should be performed.
- **Adjuvant Radiotherapy:** Should be discussed in the MDT after surgery in cases of multiple risk factors or insufficient surgical margins. The decision to use adjuvant RT is a carefully considered choice and not a standard treatment for every high-risk cSCC.
- **MDT:** Complicated high-risk and metastatic cSCCs should be discussed in an **MDT at a reference centre** with dermatologists, radiotherapists, oncologists and surgeons skilled in oncology and reconstruction.

### Prevention

- **Chemoprevention:** Consider **systemic retinoids (Acitretin) and nicotinamide** as chemopreventive agents in patients with **multiple cSCCs** (including transplant patients).
- **Sun advice/smoking:** Advise the patient to avoid excessive sun exposure and sunbeds, to use protective clothing and sunscreen (SPF 50+), and to **stop smoking** (increased risk of cSCC of more than 50%).
- **Hydrochlorothiazide (HCTZ):** HCTZ has previously been associated with a dose-dependent risk of cSCC. However, there is **insufficient scientific evidence** to advise against the use of HCTZ.
- **Immunosuppression:** Patients who are being prepared for **organ transplantation** should be referred to a dermatologist at an early stage for information. Patients with a haematological malignancy such as chronic lymphocytic leukaemia (CLL) or who are being treated with hydroxyurea or Jakavi have an increased risk of squamous cell carcinoma.

### Follow-up cSCC

Follow-up should be based on risk classification. Most recurrences and metastases occur within the first two years.

### Follow-up schedule for cutaneous squamous cell carcinoma (cSCC)

Type SCC	Margins	Staging	Follow-up	Notes
<b>Lowrisk T1</b>	Surgical excision with clinical margin 5mm and histopathological margin of >1mm	Lymphnode palpation, ultrasound only in case of suspicion	6-monthly during first 2 years. No ultrasounds unless suspicion after palpation.	
<b>Highrisk T1</b>	Surgical excision with clinical margin of 6-10mm and histopathological margin of >2mm	Ultrasound of draining lymphnodes	6-monthly during first 2 years, yearly until 5 years after diagnosis. No ultrasounds unless suspicion after palpation.	

<b>&gt;T1</b>	Surgical excision with clinical margin of 6-10mm and histopathological margin of >2mm	Ultrasound of draining lymphnodes, CT if bone involvement suspected, MRI if perineural invasion suspected, PET-CT if metastases suspected	3-monthly for first 2 years, 6-monthly in third year, yearly until 5 years after diagnosis. Ultrasound lymphnodes 3-6-monthly during first 2 years.	Risk factors add up: personalize follow-up interval and ultrasound frequency based on risk factors.
<b>OTR/hematological malignancy</b>	According to T-stage: immunosuppression is a high risk factor	According to T-stage	According to T-stage, at least 6-monthly examination for life after first SCC.	Personalize based on SCC frequency.

### 3. Melanoma

#### Diagnosis and Treatment of Localised Disease (Staging)

##### Diagnosis and excision:

- Dermoscopy is indispensable and improves diagnostic accuracy for trained users.
- If melanoma is suspected, a diagnostic excision with a clinical margin of 2 mm should be performed. New melanoma diagnoses and complex cases with regard to staging, follow-up and treatment may be discussed in the MDT.

##### Therapeutic Re-excision Margins:

- In situ melanoma: **0.5 cm.**
- Breslow thickness up to and including 2 mm: **1 cm.**
- Breslow thickness greater than 2 mm: **2 cm.**
- The re-excision should extend to the underlying fascia in case of invasive melanoma and the deep subcutaneous fat for melanoma in situ.

##### Sentinel lymph node biopsy (SLNB):

- SLNB is a **staging** procedure for prognosis determination and selection for adjuvant therapy.
- SLNB is recommended from **pT1b** onwards [Table A].

**Table A: Staging of Primary Melanoma (pT status) and Initial Imaging**

NB Systemic staging is not routinely indicated based on pT status alone [Table A].

T Stage (AJCC 8)	Breslow thickness (mm) and ulceration	Sentinel Lymph Node Biopsy (SLNB) Recommendation	Initial Systemic Staging
Tis	In situ	Do not perform	Not routinely recommended.
pT1a	<0.8 mm, without ulceration	Do not perform	Not routinely recommended.
pT1b	0.8–1.0 mm, with or without ulceration, or <0.8 mm with ulceration	Perform	Perform ultrasound of lymph nodes.
pT2a to pT4b	>1.0 mm, with/without ulceration	Perform	Perform ultrasound of lymph nodes. PET-CT and MRI/CT brain from pT3b+*

\*Systemic imaging based on AJCC 8: PET-CT and MRI/CT brain for stage IIB+.

##### Follow-up (frequency, duration and staging)

Follow-up focuses on clinical examination (CE: scar, entire skin, palpation of glands) for the detection of second primary melanoma (multiple melanomas are observed in 5-8% of melanoma patients) and relapse/metastatic disease. The use of imaging depends on the risk of systemic disease.

**Table B: Follow-up, Imaging and Laboratory Tests per AJCC Stage**

AJCC Stage	Risk group	Follow-up Frequency (CI)	Regional Monitoring (Ultrasound lymph nodes)	Systemic Staging / Follow-up Imaging	Lab (LDH / S100B)
Stage 0	Very Low/Low	Additional visit for instruction.	Not applicable.	None.	No routine test.
Stage IA	Low-Intermediate	<b>Once a year</b> (5 years).	N/A	No routine imaging.	No routine testing.
Stage IB and IIA	Intermediate	Y 1-2: Every <b>6 months</b> . Y 3-5: Every <b>12 months</b> .	N/A	No routine imaging.	No routine testing.
Stage IIB and IIC	High risk (e candidates for adjuvant therapy)	Y 1-2: Every <b>3-4 months</b> . Y 3: Every 6 months. Y 4-5: Every 12 months.	<b>Recommended</b> (3-6 months monthly).	PET-CT twice a year during Y1-2, once a year during Y3-5.	No routine test.
Stage III (A-D)	Locoregional Very High	Y 1-3: Every <b>3 months</b> . Y 4-5: Every 6 months.	<b>Recommended</b> (every 3-6 months).	<b>Recommended</b> PET-CT at least twice a year during Y1-2, twice a year during Y3-5.	No routine testing.
Stage IV (Metastatic)	Systemically active / Resected	Every <b>3 months</b> (depending on systemic therapy).	On indication.	<b>PET-CT and CT/MRI brain (frequency personalised)</b> .	<b>Serum LDH</b> should be determined. No S-100B.

**Important Notes on Imaging:**

- Routine screening of the brain with CT or MRI in **asymptomatic patients** is **not recommended** [Table B].
- Brain metastases are better detected with **MRI brain with intravenous contrast** than with a CT scan.

## 4. Indications for Periodic Naevi Monitoring and Prevention

Periodic checks are indicated in patients with an increased risk of melanoma.

### Indications for Periodic Dermatological Naevi Monitoring

**A. Phenotype and History:** Individuals with the following characteristics are eligible for annual periodic monitoring:

- Patients with a **history of melanoma**.
- Patients with **more than 100 naevi**.
- Patients with **5 or more clinically atypical naevi or high-grade dysplastic naevi**.

### Criteria for Clinically Atypical Naevi

For the clinical diagnosis of a single atypical naevus, at least 3 of the following criteria must be met:

- $\geq 5$  mm in diameter
- blurred borders
- irregular shape
- irregular pigmentation
- erythema

### Periodic checks for dysplastic naevi:

- If there are fewer than five high-grade dysplastic naevi and no personal or family history of melanoma, periodic check-ups are not necessary.
- Five or more high-grade dysplastic naevi is a relative indication for periodic check-ups (annually).

**B. Hereditary and familial melanoma:** Take a **family history** for every patient with melanoma.

### Diagnostic Criteria for Familial Melanoma:

**Familial melanoma is defined as:**

- A family with three relatives with invasive melanoma, at least two of whom are first-degree relatives, and where the affected individuals are first- or second-degree relatives.  
or
- A family with two first-degree relatives with invasive melanoma, one of whom has multiple melanomas.

### Recommended policy

Refer patients who meet the above criteria to a clinical geneticist for genetic counselling. In consultation with the clinical geneticist, DNA testing for pathogenic variants in known melanoma predisposition genes may be considered. A causative genetic variant is found in approximately 20–30% of patients. If no pathogenic variant is found, the genetic basis of melanoma susceptibility is unknown; the risk for unaffected family members is then determined by age at diagnosis, number of melanomas, and degree of familial burden.

In patients in whom a germline mutation is confirmed, screening frequency should be adapted accordingly; this is irrespective of prior melanoma diagnosis.

### Suspicion of hereditary predisposition outside the above criteria

Even if the formal criteria for familial melanoma are not met, a hereditary predisposition may be suspected. Referral to a clinical geneticist is also recommended in the following cases:

- Two first-degree relatives with invasive melanoma, at least one of whom was diagnosed before the age of 40.
- Two first-degree relatives with invasive melanoma and a relative with pancreatic carcinoma on the same side of the family.
- A family in which, in addition to cutaneous melanoma, ocular melanoma, mesothelioma, renal cell carcinoma or BAP1-inactivated melanocytic naevi occur (suspicion of *BAP1-associated hereditary tumour syndrome*).
- A person with three or more melanomas, or a combination of melanoma and pancreatic carcinoma.

- A person diagnosed with melanoma at a young age (< 18 years).

**Point of attention:** If relatives have **not** inherited the known predisposition based on DNA testing, the indication for periodic skin checks lapses, unless there are other risk factors (e.g. 5 or more clinically atypical naevi, more than 100 naevi).

#### **Periodic checks for patients without high-risk characteristics**

There are **no known absolute risk differences** within the group of people with fewer than 100 nevi and without 5 or more clinically atypical nevi. The threshold for high phenotypic burden is **5 or more atypical nevi, or more than 100 common nevi**. Individuals who do not meet the criteria for familial/hereditary predisposition or an abnormal phenotype are likely to have a risk closer to that of the general population.

Patients without an increased risk of melanoma are defined as individuals without a personal or family history of melanoma or other skin cancers, without genetic predisposition, without a pronounced naevus pattern (more than 100 naevi or >5 atypical naevi) and without long-term immunosuppression.

There is no scientific basis for routine, systematic skin checks in individuals without an increased risk of melanoma. Opportunistic evaluation on indication is most appropriate, in combination with self-inspection.

A **lesion-directed screening approach** is recommended: patients are assessed on the basis of a specific skin lesion that they themselves consider suspicious or changed. This approach is efficient, patient-centred and has a similar yield of skin cancer diagnoses per consultation as a full skin examination, but is considerably less time-consuming. If the index lesion is a cutaneous malignancy, the entire skin should be inspected.

**Serial Dermoscopy/Total Body Photography (Mole Mapping):** Recommended for patients at increased risk of melanoma, particularly those with multiple atypical naevi, more than 100 naevi and a personal history of multiple melanomas, in order to monitor changes.

Automatic analysis by Artificial Intelligence (AI) on Total Body Photography (TBF) or other digital diagnostic software **is currently not suitable for independent and unsupervised use for skin diagnostics, and images must always be assessed by a dermatologist before medical advice can be given.**

**Sun advice and smoking:** Adequate **sun protection** from an early age is crucial. **Avoid sunbeds.** CDKN2A mutation carriers should be strongly advised against **smoking** due to an increased risk of pancreatic and lung cancer.

**Smartphone apps for patient use:** Commercial smartphone apps that assess the risk of skin cancer (including melanoma) based on photographs show varying and often insufficient sensitivity and specificity, with both a real risk of missed melanomas and over-detection. These apps are therefore unsuitable for people with an increased risk of melanoma, and their place in the general population remains uncertain given the limited and conflicting data on diagnostic performance and effects on healthcare consumption.