

S3 guideline „actinic keratosis and cutaneous squamous cell carcinoma”: update 2023, part 1: treatment of actinic keratosis, actinic cheilitis, cutaneous squamous cell carcinoma in situ (Bowen’s disease), occupational disease and structures of care

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GUIDELINE

S3 guideline „actinic keratosis and cutaneous squamous cell carcinoma“ – update 2023, part 1: treatment of actinic keratosis, actinic cheilitis, cutaneous squamous cell carcinoma in situ (Bowen’s disease), occupational disease and structures of care

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For involved societies see long version at www.awmf.org.

Summary

Actinic keratosis (AK) are common lesions in light-skinned individuals that can potentially progress to cutaneous squamous cell carcinoma (cSCC). Both conditions may be associated with significant morbidity and constitute a major disease burden, especially among the elderly. To establish an evidence-based framework for clinical decision making, the guideline “actinic keratosis and cutaneous squamous cell carcinoma” was updated and expanded by the topics cutaneous squamous cell carcinoma *in situ* (Bowen’s disease) and actinic cheilitis. The guideline is aimed at dermatologists, general practitioners, ear nose and throat specialists, surgeons, oncologists, radiologists and radiation oncologists in hospitals and office-based settings, as well as other medical specialties, policy makers and insurance funds involved in the diagnosis and treatment of patients with AK and cSCC. A separate guideline exists for patients and their relatives. In

†The first two authors and the last two have contributed equally to the manuscript.

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this part, we will address aspects relating to AK, actinic cheilitis, Bowen's disease, occupational disease and care structures.

INTRODUCTION

The guideline represents a short version of the complete guideline available at www.awmf.org. Information on epidemiology and etiology, diagnostics, surgical and systemic treatment of cutaneous squamous cell carcinoma (cSCC), surveillance and prevention can be found in part 2 of the short version – update 2023 of the guideline or in the long version. A full list of references and the analysis of evidence underlying the recommendations and statements, along with the conflicts of interest of the authors involved in the present guideline, are available in the long version and in the guideline report. The guideline is an update of the previous version published in 2020.^{1,2}

METHODOLOGY

See long version at www.awmf.org.

TREATMENT OF ACTINIC KERATOSIS

Indication for treatment and natural course of the disease

See long version at www.awmf.org.

General principles of treatment

See long version at www.awmf.org.

Treatment combinations

Evidence-based recommendation	Modified 2022
GoR B	Concurrent or sequential combinations of distinct field- or lesion-targeted treatments should be offered for actinic keratosis.
LoE 1	1: De-novo-research
Strong consensus	

Abbr.: GoR, Grade of Recommendation; LoE, Level of Evidence

Ablative and physical procedures

Cryosurgery

See long version at www.awmf.org.

Surgical procedures

See long version at www.awmf.org.

Chemoexfoliation

Evidence-based recommendation	Modified 2022
GoR 0	Chemoexfoliation by chemical peelings may be offered for single or multiple actinic keratoses and field cancerization.
LoE 3	3: De-novo-research
Strong consensus	

Potassium hydroxide

Evidence-based recommendation	New 2022
GoR 0	Potassium hydroxide 5% solution may be offered for single or multiple actinic keratoses.
LoE 3	3: De-novo-research
Strong consensus	

Laser treatment

See long version at www.awmf.org.

Topical drugs

Diclofenac

See long version at www.awmf.org.

5-Fluorouracil

See long version at www.awmf.org.

Evidence-based recommendation	New 2022
GoR B	5-Fluorouracil 4% cream should be offered for single or multiple actinic keratoses and field cancerization.
LoE 2	2: De-novo-research
Strong consensus	

5-Fluorouracil with salicylic acid

See long version at www.awmf.org.

Ingenol mebutate

Evidence-based recommendation	Modified 2022
GoR A	Ingenol mebutate shall not be offered for actinic keratosis.
LoE 2	2: De-novo-research
Strong consensus	

Imiquimod

See long version at www.awmf.org.

Tirbanibulin

Evidence-based recommendation	New 2022
GoR B	Tirbanibulin 1% ointment should be offered for single or multiple actinic keratoses and field cancerization.
LoE 2	2: De-novo-research
Strong consensus	

Photodynamic therapy

See long version at www.awmf.org.

Evidence-based recommendation	Modified 2022
GoR B	Photodynamic therapy using natural or simulated daylight with 5-aminolevulinic acid (ALA) or its methyl ester (MAL) should be offered for single or multiple actinic keratoses and field cancerization.
LoE 1	1: De-novo-research
Strong consensus	

Treatment on chronic immunosuppression and in organ transplant recipients

See long version at www.awmf.org.

Other interventions

See long version at www.awmf.org.

Synopsis of interventions for actinic keratosis (balance sheet)

Intervention	TA	Type and application of the intervention	Anatomical location	Clearance rates ¹	Side-effects and tolerability ²	Cosmesis ³	Duration of the treatment ⁴	Practicability ⁶		Strength of recommendation and evidence base by subgroups ⁷			
								Physician	Patient	Single AK (1–5)	Multiple AK (≥ 6)	Field cancerization	Immune suppression
Cryosurgery	L	One to two freeze-thaw cycles with liquid nitrogen (–196° C)	Face, scalp	+++ Lesion-specific clearance rate: 41.9%–88%	+++	+/++	∞	++++	+++	↑	↑		
		Cold exposure of the target lesions for 15–60 seconds (whitening)	Neck Trunk Extremities	Patient-specific clearance rate: 25%–90.3%						2	2		
Surgical procedures ⁶	L	Open spray method											
		Contact method (cryo stamp, cryo probe)											
Surgical procedures ⁶	L	Curettage ± electrocautery	Face, Scalp	+++ (No data available from RCT) ⁸	++ (No data available from RCT) ⁸	+/++ (No data available from RCT) ⁸	∞	+++	++	↑ EC			↑ EC
		Shave excision Complete excision	Neck Trunk Extremities										
Chemo-exfoliation	L+F	Ablation of superficial skin layers using chemical agents (e.g., trichloroacetic acid, Jessner's solution, phenol)	Face, Scalp	++ Lesion-specific clearance rate: 31.9%	++/++++	+++	∞	++	++	↔	↔	↔	
			Neck Trunk Extremities	Patient-specific clearance rate: 11.8%–92%						3	3	3	
Dermabrasion ⁶	L+F	Mechanical removal of the uppermost skin layers up to the dermoepidermal junction zone	Face, Scalp	+	+	+	∞	+/++	+				
			Neck Trunk Extremities	(No data available from RCT) ⁸	(No data available from RCT) ⁸	(No data available from RCT) ⁸							
Potassium hydroxide 5% solution (Solcera [®])	L	Single and well-defined lesions < 2 cm in diameter	Face, Scalp	++ Lesion-specific clearance rate: 69.9%–83%	+++	++	∞	+++	++++	↔	↔		
		Max. 10 lesions 1 cycle: 2 x/day over 14 days, then 14 days treatment-free interval (max. 3 cycles = 12 weeks) Availability as a medical device	Neck Trunk Extremities	Patient-specific clearance rate: 54.9%						3	3		

(Continues)

Intervention	TA	Type and application of the intervention	Anatomical location	Clearance rates ¹	Side-effects and tolerability ²	Cosmesis ³	Duration of the treatment ⁴	Practicability ⁶		Strength of recommendation and evidence base by subgroups ⁷			
								Physician	Patient	Single AK (1–5)	Multiple AK (≥ 6)	Field cancerization	Immune suppression
Laser ⁶	L+F	Ablative laser treatment (e.g., CO ₂ laser, Er:YAG laser)	Face, Scalp	++	++	+++/++++	0–3	+++	++	⇔	⇔	⇔	
			Neck	Lesion-specific clearance rate: 72.4%–91.1%						2–3	2–3	2–3	
			Trunk										
			Extremities	Patient-specific clearance rate: 8%–65.3%									
L	L	Non-ablative laser procedures ⁶ (e.g., Nd:YAG laser, fractional 1540 nm laser)	Face, Scalp	++	+++	++	0–3	+++	+++	⇔	⇔		
			Neck	(No data available from RCT) ⁸	(No data available from RCT) ⁸	(No data available from RCT) ⁸				⇔	⇔		
			Trunk							EC	EC		
			Extremities										

Semiquantitative assessment taking into account lesion- and patient-related response rates: + little effective, ++ moderately effective, +++ effectively, ++++ very effective

Semiquantitative assessment taking into account frequency and severity of treatment-related side effects: + poorly tolerated/ many side effects, ++ moderately tolerated, +++ well tolerated, ++++ very well tolerated

Semiquantitative assessment taking into account investigator- and patient-assessed endpoints such as dyspigmentation, improvement of hyperkeratosis, global assessment: + poor, ++ moderate, +++ good, ++++ excellent

Short (< 1 week), Medium (1–6 weeks), Long (> 6 weeks)

€ 100–500 Euro, € 500–1000 Euro, > € 1000 Euro; only direct treatment costs per cycle performed were considered; topical drugs were based on the public pharmacy dispensing prices in Germany (as of August 2021); procedural procedures were based on the assessments of the Gebührenordnung für Ärzte (GOÄ, as of August 2021).

Taking into account expert assessments

Strength of recommendation: Can ⇔ Should ↑, Shall ↑↑; indication of evidence levels according to Oxford 2011.

When applying the mentioned search strategy and inclusion and exclusion criteria

Abbrev.: L, lesion-directed; F, field-directed; AK, actinic keratosis; EC, expert consensus; FK, field cancerization; RCT, randomized controlled trial; TA, therapeutic approach

Strength of recommendation and evidence base by subgroups ⁷															
Practicability ⁶															
Immediate treatment costs per cycle ⁵															
Side-effects and tolerability ²															
Cosmesis ³															
Duration of treatment ⁴															
Doctor															
Patient															
Single AK (1–5)															
Multiple AK (≥ 6)															
Field cancerization															
Immune suppression															
Intervention	TA	Mechanism of action	Recommended max. area of the treatment field	Approval for anatomical location	Efficacy ¹	Side-effects and tolerability ²	Cosmesis ³	Duration of treatment ⁴	Immediate treatment costs per cycle ⁵	Doctor	Patient	Single AK (1–5)	Multiple AK (≥ 6)	Field cancerization	Immune suppression
Diclofenac sodium 3% gel (Solaraze [®]) (Solacutan [®]) (Diclofenac acis [®]) (Diclofenac AbZ [®]) (Diclofenac-ratiopharm [®])	F	Cyclooxygenase-2 inhibitors 2 x daily for 60–90 days	8 g/d or max. 200 cm ²	Face and scalp	++ Lesion-specific clearance rate: 51.8%–81.0% Patient-specific clearance rate: 27%–50%	+++ / +++++ +++ / +++++	+ / +++	2222	€–€€	+++++	++	↑ 1	↑ 1	↑ 2	↑ 3
5-Fluorouracil 5% cream (Efudix [®])	F	Cytostatic agent 2 x daily until erosion stage (usually 2–4 weeks) Application with finger cloth or glove No nucleoside analogues (e.g., brivudine, sorivudine) for at least 4 weeks	500 cm ² (approx. 23 × 23 cm)	Face and scalp Neck Trunk Extremities	+++ / +++++ Lesion-specific clearance rate: 47%–94% Patient-specific clearance rate: 38%–96%	++	++ / +++++	22	€	+++	+++	↑ 1	↑ 1	↑ 2	
5-Fluorouracil 4% cream (Tolak [®])	F	Cytostatic agent 1 x daily for 4 weeks No nucleoside analogues (e.g., brivudine, sorivudine) for at least 4 weeks	None (in studies 240–961 cm ²)	Face and scalp	+++ Patient-specific clearance rate: 80.5%	+++	+++	22	€	+++	+++	↑ 2	↑ 2	↑ 2	
5-Fluorouracil 0.5% with salicylic acid 10% in solution (Actikeral [®])	F+L	Cytostatic and keratolytic agent 1 x daily until the lesions have cleared completely (max. 12 weeks) No nucleoside analogues (e.g., brivudine, sorivudine) for at least 4 weeks	25 cm ²	Face and scalp Neck Trunk Extremities	+++ Lesion-specific clearance rate: 39.4%–98.7% Patient-specific clearance rate: 55.4%	+++	+++	2222	€	+++	++	↑ 2	↑ 2	↑ 2	
Ingarden mebutate gel (Picato [®])	F	Garden spurge extract (cytotoxic) 0.015% (face and scalp): 1 x daily for 3 consecutive days 0.050% (trunk, extremities): 1 x daily for 2 consecutive days	25 cm ²	Face and scalp Neck Trunk Extremities	+++ Face/scalp: Lesion-specific clearance rate: 62.9%–87.2% Patient-specific clearance rate: 36.4%–61.6% Extremities/trunk: Lesion-specific clearance rate: 73%–100% Patient-specific clearance rate: 22%–54.4%	+ (increased incidence of skin tumors in treatment fields)	++	2	€	+++	+++	↑↓ 2	↑↓ 2	↑↓ 2	↑↓ 2

(Continues)

(Continues)

Strength of recommendation and evidence base by subgroups ⁷										
Intervention	TA	Mechanism of action	Recommended max. area of the treatment field	Approval for anatomical location	Efficacy ¹	Side-effects and tolerability ²	Cosmesis ³	Duration of treatment ⁴	Immediate treatment costs per cycle ⁵	Practicability ⁶
		Application								
						</				

(Continues)

Strength of recommendation and evidence base by subgroups ⁷														
Practicability ⁶														
Immediate treatment costs per cycle ⁵														
Intervention	TA	Mechanism of action	Recommended max. area of the treatment field	Approval for anatomical location	Efficacy ¹	Side-effects and tolerability ²	Cosmesis ³	Duration of treatment ⁴	Doctor	Patient	Single AK (1–5)	Multiple AK (≥ 6)	Field cancerization	Immune suppression
ALA daylight PDT (Ameluz [®])	F	Precursor of protoporphyrin (photosensitizer) Application of chemical light protection filter, after 15 min pre-treatment, application of ALA without occlusion, within 30 min exposure to natural daylight for 2 h, second cycle after 12 weeks if necessary	None (apply thin layer) Lesion or entire cancerized fields	Face and scalp	+++ Patient-specific clearance rate: 27.5%–42.9% Lesion-specific clearance rate: 79.7%–79.8%	+++ +/+/+/+/+	+++	∞	++	++++	↑	↑	↑	
MAL daylight PDT (Metvix [®]) (Luxerm [®])	F	Precursor of protoporphyrin (photosensitizer) Application of chemical light protection filter, after pre-treatment drying, application of MAL without occlusion, within 30 min exposure to natural or simulated daylight (Metvix [®] only) for 2 h, second cycle after 12 weeks if necessary	None (apply thin layer) Lesion and/or field cancerization	Face and scalp	+++ Patient-specific clearance rate: 27.5%–38.8% Lesion-specific clearance rate: 77.2%–89.2%	+++ +/+/+/+/+	+++	∞	++	++++	↑	↑	↑	
Tirbanitulin (Klisyri [®])	F	Topical microtubule inhibitor 1 x/d over 5 consecutive days	25 cm ²	Face and scalp	+++/+++ Patient-specific clearance rate: 44%–54% Lesion-specific clearance rate: 76%–82%	+++ +/+/+/+/+	+++	∞	+++	+++	↑	↑	↑	

¹ Semiquantitative assessment taking into account lesion- and patient-related response rates: + little effective, ++ moderately effective, +++ effective, ++++ very effective

² Semiquantitative assessment taking into account frequency and severity of therapy-mediated side effects: + poorly tolerated/ many side effects, ++ moderately tolerated, +++ well tolerated, ++++ very well tolerated

³ Semiquantitative assessment considering investigator- and patient-assessed endpoints such as dyspigmentation, improvement of hyperkeratosis, global assessment: + poor, ++ moderate, +++ good, ++++ excellent

⁴ ≈ short (< 1 week), ≈ medium (1–6 weeks), ≈ long (> 6 weeks)

⁵ € < 100 Euro, € 100–500 Euros, € 500–1000 Euros; only direct treatment costs per cycle performed were considered; topical drugs were based on the public pharmacy dispensing prices in Germany (as of August 2021); procedural procedures were based on the assessments of the Gebührenordnung für Ärzte (GOÄ, as of August 2021).

⁶ Taking into account expert opinions

⁷ Strength of recommendation: May ⇌ Should ↑ Shall ↑↑; indication of evidence levels according to Oxford 2011

Abb.: L, lesion-directed; F, field-directed; AK, actinic keratosis; OLU, off-label use; TA, treatment approach

Treatment of actinic cheilitis

Indication for treatment and natural course of the disease

Consensus-based recommendation	New 2022
EC	The indication for the treatment of actinic cheilitis should be made based on the clinical presentation, risk factors (e.g., immunosuppression, cumulative UV exposure, involvement of the entire lower lip, involvement also of the upper lip), comorbidities, life expectancy, and patient desire.
	Strong consensus
Consensus-based recommendation	New 2022
EC	Prior to treatment, a biopsy should be obtained for diagnostic confirmation and to exclude invasive squamous cell carcinoma of the lip.
	Consensus
Consensus-based recommendation	New 2022
EC	A biopsy should be obtained if there is clinical evidence of a lack of response or incomplete response to treatment.
	Strong consensus

Abbr.:EC, expert consensus.

General principles of treatment

See long version at www.awmf.org.

Surgical procedures

Evidence-based recommendation	New 2022
GoR A	Surgical treatment of actinic cheilitis (e.g., by vermilionectomy or lip shave with histologic assessment and analysis of resection margins) shall be offered for extensive involvement of the lip.
LoE 1	1: De-novo-research
	Consensus

Ablative procedures

Laser treatment

Evidence-based recommendation	New 2022
GoR 0	Ablative laser treatment (e.g., CO ₂ , Er:YAG) may be offered for actinic cheilitis.
LoE 1	1: De-novo-research
	Strong consensus

Consensus-based statement New 2022

- EC** No recommendation for non-ablative laser treatment of actinic cheilitis can be made due to insufficient data.
- Strong consensus

Cryosurgery

Consensus-based statement New 2022

- EC** The data available on cryosurgery do not allow a conclusive recommendation for the treatment of actinic cheilitis.
- Strong consensus

Chemoexfoliation

Consensus-based recommendation New 2022

- EC** Chemical peelings should not be used for the treatment of actinic cheilitis due to a lack of evidence for clinical benefit.
- Strong consensus

Topical drugs

Diclofenac

Evidence-based recommendation New 2022

- GoR 0** Diclofenac sodium 3% gel may be offered for the treatment of actinic cheilitis.
- LoE 2** 2: De-novo-research
- Strong consensus

5-Fluorouracil

Consensus-based statement New 2022

- EC** No evidence-based recommendation for the treatment of actinic cheilitis with 5-fluorouracil can be made due to insufficient data.
- Strong consensus

Imiquimod

Consensus-based statement new 2022

- EC** No evidence-based recommendation for the treatment of actinic cheilitis with imiquimod 5% and 3.75% cream can be made due to insufficient data.
- Strong consensus

Photodynamic therapy

Evidence-bases recommendation		New 2022
GoR B	Photodynamic therapy with illumination by red light and 5-aminolevulinic acid (ALA) or its methyl ester (MAL) should be offered for the treatment of actinic cheilitis.	
LoE 1	1: De-novo-research	
Strong consensus		

Evidence-based recommendation		New 2022
GoR B	Methyl aminolevulinate (MAL) in combination with illumination by natural or simulated daylight (MAL daylight PDT) should be offered for the treatment of actinic cheilitis.	
LoE 3	3: De-novo-research	
Strong consensus		

Treatment combinations

See long version at www.awmf.org.

Synopsis of interventions for actinic cheilitis (balance sheet)

Intervention	TA	Mechanism of action & application	Efficacy ¹	Side effects and tolerability ²	Cosmesis ³	Duration of the treatment ⁴	Direct treatment costs per cycle ⁵	Practicability ⁶			Strength of recommendations and evidence base ⁷
								Physician	Patient		
Ablative procedures											
Cryosurgery	L	1 to 2 freeze-thaw cycles with liquid nitrogen (−196°C) Cold exposure of the target lesions for 15–60 seconds "whitening" Open spray method Contact method (cryo stamp, cryo probe)	+++/+++ (No data available from RCT) ⁸	++	+	0–3	€	++++	+++		~ EC
Surgical procedures with histological assessment ⁶	F	Complete excision, vermillionectomy, lip shave	++++ (No data available from RCT) ⁸	++ (No data available from RCT) ⁸	++ (No data available from RCT) ⁸	0–3	€–€€	+++	++		↑↑ 1–3
Surgical procedures without histological assessment ⁶	F	Electrodesiccation, dermabrasion	+ (No data available from RCT) ⁸	+ (No data available from RCT) ⁸	+/+++ (No data available from RCT) ⁸	0–3	€–€€	+/++	+		~ EC
Chemoexfoliation	F	Ablation of superficial skin layers using chemical agents (e.g., 50% trichloroacetic acid)	+ Clearance rate: 30%	+/+++	++	0–3	€–€€	++	++		~ 1–4
Laser treatment ⁶	F	Ablative laser treatment (e.g., CO ₂ -, Erbium YAG laser) Non-ablative laser treatments ⁶ (e.g., Nd:YAG laser, fractional 1540 nm laser)	+++ Clearance rate: 93.4% + (No data available from RCT) ⁸	++ ++ (No data available from RCT) ⁸	+++/+++ ++ (No data available from RCT) ⁸	0–3	€€€ €€€	+++	++		↔ 2–3 ~ EC
Topical drugs and drug-based procedures											
Diclofenac sodium 3% gel (Solaraze [®]), (Solacutan [®]), (diclofenac acis [®]), (Diclofenac AbZ [®]), (Diclofenac-ratiopharm [®]) Off-label use	F	Cyclooxygenase-2 inhibitor 2 x daily for 60–90 days; max. 8 g/d for up to 200 cm ²	++ Clearance rate: 45.2%	+++/ ++++	+/+++	0–3 0–3 0–3	€–€€	++++	++		↔ 2–3
5-Fluorouracil 5% cream (Efudix [®]) Off-label use	F	Cytostatic drug 2 x daily for max. 4 weeks; max. 500 cm ² (approx. 23 × 23 cm)	+++/++++ Clearance rate: 50%–68.2%	++	+++/+++	0–3	€–€€	+++	+++		~ EC
Imiquimod 3.75% cream (Zyclara [®]) Off-label use	F	Toll-like receptor 7 agonist 1 x daily for 2 weeks, 2 weeks treatment-free interval, 1x daily for 2 weeks (interval therapy) per application up to 2 sachets of 250 mg imiquimod cream per sachet	+	++	+++	0–3	€€	+++	+++		~ EC

(Continues)

Intervention	TA	Mechanism of action & application	Efficacy ¹	Side effects and tolerability ²	Cosmesis ³	Duration of the treatment ⁴	Direct treatment costs per cycle ⁵	Practicability ⁶		Strength of recommendations and evidence base ⁷
								Physician	Patient	
Imiquimod 5% cream (Aldara [®]) Off-label use	F	Toll-like receptor 7 agonist 3 x weekly for 4 weeks Recommended maximum dose is the contents of one sachet	++ Clearance rate: 40%–73.3%	++	+++	3–6 w	€€	+++	+++	~ EC
ALA red light PDT (Alacare [®])	F, L	Prodru of protoporphyrin (photosensitizer) Application of ALA-containing patch for 4 h, illumination with red light for approx. 10–20 min, if necessary, repeat after 4–12 weeks Alacare [®] 4 cm ² (max. 6 patches)	+++ / +++++ Clearance rate: 66.6%–84.2%	++	+++ / +++++	3–6 w	€€–€€€	++ / +++++	++	↑ 2–3
ALA red light PDT (Ameluz [®]) Off-label use	F	Prodru of protoporphyrin (photosensitizer) Application of ALA, light-protective bandage for 3 h, illumination with red light for approx. 10–20 min, if necessary repeat after 4–12 weeks	+++ / +++++ Clearance rate: 58.0%–80%	++	+++ / +++++	3–6 w	€€–€€€	++ / +++++	++	↑ 2–3
MAL red light PDT (Metvix [®])	F	Prodru of protoporphyrin (photosensitizer) Application of MAL, light protection and occlusive dressing for 3 h, illumination with red light for approx. 10–20 min, repeat after 4–12 weeks if necessary	+++ / +++++ Clearance rate: 47%–62.5%	++	+++ / +++++	3–6 w	€€–€€€	++ / +++++	++	↑ 2–3
MAL daylight-PDT (Luxerm [®]), (Metvix [®])	F	Prodru of protoporphyrin (photosensitizer) Application of chemical photoprotective filter and MAL. Daylight exposure for 2 h Conditions: > 10°C outdoor temperature, cloudless to overcast sky, no rain	+++ Clearance rate: 80%–91%	++++	+++	3–6 w	33	++	++++	↑ 3

¹Semiquantitative assessment taking into account lesion- and patient-related response rates (+ = little effective, ++ = moderately effective, +++ = effective, ++++ = very effective)

²Semiquantitative assessment taking into account frequency and severity of treatment-mediated side effects (+ = poorly tolerated/moderately side effects, ++ = moderately tolerated, +++ = well tolerated, ++++ = very well tolerated)

³Semiquantitative assessment considering investigator- and patient-assessed outcomes such as dyspigmentation, improvement of hyperkeratosis, global assessment (+ = predominantly poor, ++ = predominantly moderate, +++ = predominantly good, ++++ = predominantly excellent)

⁴Short (< 1 week), 3–6 w = medium (1–6 weeks), 3–6 w = long (> 6 weeks)

⁵Costs per cycle performed were considered; public pharmacy dispensing prices in Germany (as of August 2021) were used as the basis for topical drug procedures; procedural procedures were based on the valuations of the Gebührenordnung für Ärzte (GOÄ, as of August 2021)

⁶Taking into account expert opinions

⁷Strengths of recommendation: May = ⇌, Should = ↑, Shall = ↑↑; ~ no recommendation if data / evidence base is unclear; indication of evidence levels according to Oxford 2011

⁸When applying the mentioned search strategy and inclusion and exclusion criteria

⁹Abbri.: L, lesion-directed; F, field-directed; AK, actinic keratosis; EC, expert consensus; RCT, randomized controlled trial; TA, treatment approach

TREATMENT OF CUTANEOUS SQUAMOUS CELL CARCINOMA IN SITU (BOWEN'S DISEASE)

Clinical presentation and natural course of the disease

See long version at www.awmf.org.

Indication for treatment and treatment approaches

Consensus-based recommendation	New 2022
EC	Prior to treatment of Bowen's disease, a biopsy should be obtained to exclude invasive squamous cell carcinoma of the skin, other skin neoplasms, or inflammatory conditions. If there is clinical evidence of a lack of response or incomplete response to treatment, a biopsy with histologic assessment should be performed.
Strong consensus	

Surgical procedures

Consensus-based recommendation	New 2022
EC	Surgical removal of Bowen's disease (e.g., by shave excision or complete excision) should be offered for single lesions.
Strong consensus	

Ablative procedures

Cryosurgery

Consensus-based recommendation	New 2022
EC	Cryosurgery may be offered for the treatment of Bowen's disease.
Consensus	

Ablative laser treatment

Evidence-based recommendation	New 2022
GoR 0	Ablative laser treatment may be offered for the treatment of Bowen's disease.
LoE 2	2: De-novo-research
Consensus	

Topical drugs

5-Fluorouracil

Evidence-based recommendation	New 2022
GoR B	5-Fluorouracil 5% cream should be offered for the treatment of Bowen's disease.
LoE 2	2: De-novo-research
Consensus	

Imiquimod

Evidence-based recommendation	New 2022
GoR 0	Imiquimod 5% cream may be offered for the treatment of Bowen's disease in immunocompetent patients. The lack of approval for this indication should be considered.
LoE 2	2: De-novo-Recherche
Consensus	

Photodynamic therapy

Evidence-based recommendation	New 2022
GoR B	Photodynamic therapy with illumination by red light should be offered for the treatment of Bowen's disease, performed as two treatment cycles within 4 weeks.
LoE 1	1: De-novo-research
Strong consensus	

Evidence-based recommendation	New 2022
GoR 0	Pretreatment (e.g., with ablative fractional laser, microneedling) may be offered prior to photodynamic therapy with illumination by red light to enhance drug penetration.
LoE 2	2: De-novo-research
Strong consensus	

OCCUPATIONAL DISEASES OF ACTINIC KERATOSIS AND CUTANEOUS SQUAMOUS CELL CARCINOMA

See long version at www.awmf.org.

Structures of care

Certified skin cancer centers

See long version at www.awmf.org.

Quality indicators

See long version at www.awmf.org.

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