Actinic Keratosis prescribing guidelines for adults

Actinic Keratoses are by far the most common lesions with malignant potential to arise on the skin. NICE estimates that over 23% of the UK population aged 60 and above have AK. Predominantly seen on the face, head, neck, forearms, hands and ears, as a result of chronic sun exposure, AK are scaly, rough or crusted, reddish, brownish or skin-coloured, keratotic lesions. AKs may resolve, remain stable, or progress to invasive squamous cell carcinoma (SCC). The risk for progression to invasive SCC over a 10-year period for patients with multiple AKs has been estimated at 10%. **This pathway is for AK only.**

- AK can present as single lesions, as multiple lesions or in the context of field change. The lesions can be classified into 3 different clinical grades
  - **Grade I**: Single or a few flat, pink or grey lesions with slight scale or gritty to touch. Better felt than seen
  - **Grade II**: Moderately thick hyperkeratosis on background of erythema that are easily felt and seen
  - **Grade III**: Severe, hyperkeratotic, thick lesions

  Field Change: Confluent areas of several centimetres or more with multiple AK of any grade on a background of erythema, telangiectasia and other changes seen in sun-damaged skin.
- **AK should be managed within skills and competencies in primary care, except for "high risk" and "red flags" patients. The choice of treatment depends on the number, size, duration, and location of lesions, patient's compliance, and cosmetic outcome.**

Hyperkeratosis is thickening of the stratum corneum (the outermost layer of the epidermis). For further details on clinical findings and images see Primary Care Dermatology Society website

Red Flags

- Lesions that are rapidly growing, painful and /or bleeding
- An elevated lesion (papule / nodule) lesions that have a firm and fleshy base (Hypertrophic)
- Ulceration, induration, and tenderness
- Surrounding inflammation
- Lesions on lips where SCC can be very subtle

High Risk Patients

- Immunosuppressed patient
- History of skin cancer
- Extensive evidence of sun damage
- Previous history of phototherapy (UVB/PUVA)
- Young patients (<35 years)
- Xeroderma pigmentosium
- Periocular AK
- Diagnostic uncertainty
- **Previous failure to respond to first line therapies in primary care**

History/ examination suggestive of SCC

Priority Cancer referral to secondary care under 2-week wait

SCC is unlikely

Refer to specialist: accredited GPER or secondary care

Patient Education/Empowerment

- Patients should have a full understanding of their diagnosis, that AK is a marker of sun/UV damage and that they should examine risk areas such as scalp, ears, face, shoulders, and hands regularly.
- As AK is a precancerous condition patients should understand skin cancer and how to prevent it: covering skin with hats and clothes and using sunscreen.
- Encourage patients to report change e.g.: growth, discomfort, ulceration, bleeding and new lesions
- Links for patient information leaflets on AK, sun damage and skin cancer are listed in the next section
- Patients should have a full understanding of their treatment: how to apply and the duration of treatment: intermittent ongoing use may be needed, and a bad initial experience can limit further use.
- Patients should be warned at the outset of using active topical therapies to expect local skin reactions/inflammation, which can be severe and last for a few weeks. This should be seen as an effect of the treatment not an undesired side effect. Details are included in the relevant patient information leaflets

Patient leaflets

Skin cancer: https://patient.info/health/preventing-skin-cancer
British Association of Dermatologists: patient leaflet on AK :
Primary Care Dermatology Society (PCDS) patient leaflet on AK https://www.pcds.org.uk/patient-info-leaflets/actinic-solar-keratosis
Oxford University Hospital PIL on AK https://www.ouh.nhs.uk/patient-guide/leaflets/files/32059Psolar.pdf
Patient leaflets for each topical treatment are given in product information section page 4

Management of Actinic Keratosis

Solitary AK Lesions

- Few lesions or larger numbers that are widely distributed
- Treating individual lesions and not the surrounding area

Grade I and Grade II

- Cryotherapy (see PCDS for further information)
- Fluorouracil 0.5% & salicylic acid 10% cutaneous solution (salicylic acid acts as a keratolytic to enhance the efficacy of fluorouracil for more keratotic AKs)
- Fluorouracil 5% cream
  1. Initiated within primary care, prescribed within licence OR
  2. To treat new episodes in a patient who previously had it initiated by a specialist: GP to prescribe according to guidance from a specialist where treatment is modified to enable patient to tolerate treatment

NOTE: For any episode of AK, responsibility for monitoring and assessing the patient's treatment progress remains with the prescribing clinician.

- Imiquimod 5% Cream
- Photodynamic Therapy (PDT) – Hospital Only

Grade III

Non-Hypertrophic lesions if grade III or unclear if grade II or III start treatment with fluorouracil 5% cream and refer for cryotherapy/curettage

Grade III

Hypertrophic Lesions refer to GPER or secondary care

Field Change

- Multiple AKs with background erythema
- Treating the whole area of field change and not just the individual lesions
- Possibly higher risk of developing SCC so apply to whole area

Small Areas (up to 25cm^2, an area the size of a palm or most of the forehead)

Grade I and Grade II

- Fluorouracil 5% cream
  1. Initiated within primary care, prescribed within licence OR
  2. To treat new episodes in a patient who previously had it initiated by a specialist: GP to prescribe according to guidance from a specialist where treatment is modified to enable patient to tolerate treatment
- Tirbanibulin 1% cream ***for Grade I of face or scalp only****, if 5-fluorouracil 5% cream is not tolerated, contraindicated or not clinically appropriate.* A single 5-day treatment for one area. If recurrence occurs or if new lesions develop within the treatment area, other treatment options should be considered.
- Diclofenac sodium 3% in a sodium hyaluronate gel

NOTE: For any episode of AK, responsibility for monitoring and assessing the patient's treatment progress remains with the prescribing clinician.

- Imiquimod 5% Cream: Use on area up to 25 cm^2
- Photodynamic Therapy (PDT) – Hospital Only

Large Areas

see additional note 2.

- Diclofenac sodium 3% in a sodium hyaluronate gel
- Fluorouracil 5% Cream: **up to 23cm x 23cm (500cm^2)**
- Photodynamic Therapy (PDT) – Hospital Only

Choice of treatment should be made on an individual basis after discussion between the responsible clinician and the patient about the advantages and disadvantages of the treatments available.

RAG rating: Green: Drugs for which primary care prescribers would normally take full responsibility for prescribing and monitoring.

RAG rating: Red: Drugs which should only be prescribed in secondary care

Additional notes
1. Patient should be provided with advice on how to manage side effects: break in treatment, altering the frequency of application, use of emollient and in some instances applying hydrocortisone 1% cream to settle the inflammation ○ Cryotherapy: Loss of pigmentation and scarring. Blistering, oedema, and soreness are also common ○ Diclofenac sodium 3%: well tolerated. May cause slight pruritus, dryness, erythema, or rash ○ Fluorouracil 5% Cream: inflammation of the skin is expected, but if the skin becomes very sore or uncomfortable stop using allow the reaction to settle ○ Fluorouracil 0.5%, salicylic acid 10%: Early and severe inflammatory reaction is normal, typically peaking in the second week. ○ Imiquimod 5% cream: Flu like symptoms are usually reported **2. For treatment of large areas of field change: it may be preferable to divide into smaller ones and treat sequentially. The size of the field needs to be defined with the patient to ensure anticipation and tolerance of side effects. Patient remains under specialist.** 3. Complete clearance can be delayed for up to several weeks following completion of topical therapies. 4. Patient should be aware that sun protection should be applied twice daily (SPF at least 30) 5. Actinic Keratosis patient information leaflet should be provided to all patients

Notes on treatment regime for fluorouracil 5% cream	
Initiated within primary care, prescribed within licence by GPs	To treat new episodes in a patient who previously had fluorouracil 5% cream initiated by a specialist or GP
Do not put on repeat	**Do not put on repeat**
Prescribe in line with license and consider using the regime suggested by Primary Care Dermatology Society guidance of once a day for 4 weeks https://www.pcds.org.uk/clinical-guidance/actinic-keratosis-syn-solar-keratosis **Solitary AK lesions**: treat the individual lesion and not the normal surrounding skin apply every night for four weeks. Wash hands thoroughly after application. Leave treated areas uncovered and wash the following morning. 1 x 40g tube **Field change:** Only treat an area up to 25cm^2 (the size of palm or most of forehead) at any time. Use once a day for four weeks. Apply thinly in an evening with a gloved finger, alternatively wash the finger after application. The treated area should be washed the following morning. After four weeks stop the treatment and consider the use of a mild topical steroid eg 1% Hydrocortisone twice daily for two to four weeks to help settle down any inflammation. Follow up three months after the treatment was started. 1 x 40g tube Once the cream has been opened, it will only keep for three months and should not be used after this time	**For both solitary AK lesions and SMALL * area field change:** • Specialist details the treatment plan, instructions for use and advice given to patient about off-licence regime in letter to GP • GP should add instructions from specialist to patient record so all clinicians can see rationale for prescribing outside licence. • Once the cream has been opened, it will only keep for three months and should not be used after this time *For large area field change patient should remain under specialist care. ▪ NOTE: For any episode of AK, responsibility for monitoring and assessing the patient's treatment progress remains with the clinician prescribing for that episode.

Treatment information for topical preparations for Actinic keratosis						
Successful treatment results in a smooth red area of skin. If the treated area is still rough at time of assessment, consider further treatment options.						
Drug Name	Brand Name	Licensed Indication	Dose Direction	Area	Treatment duration	Review treatment
0.5% Fluorouracil and 10% Salicylic Acid	Actikerall®	Topical treatment of slightly palpable and/or moderately thick hyperkeratotic actinic keratosis (grade I/II) in immunocompetent adults.	Apply to affected area once daily to the affected area until the lesions have completely cleared or for up to a maximum of 12 weeks Actikerall PIL	Maximum area of skin treated at one time 25cm^2	Up to 12 weeks	4 to 8 weeks after treatment
Diclofenac sodium 3% Gel	Solaraze®	Actinic keratosis	Apply thinly twice daily for 60 to 90 days: maximum 8g daily. Solaraze PIL	0.5g of the gel is used on a 5cm x 5cm	60 to 90 days	Up to 30 days after treatment
Fluorouracil 5% Cream	Efudix®	Topical treatment of superficial pre-malignant skin lesions *Specialist use for malignant skin lesions is outside the scope of this guidance.	Apply thinly to the affected area once or twice daily for 3 to 4 weeks. PCDS recommendation for primary care is *Apply thinly to the affected area once daily for 4 weeks* For widespread sun-damage, it is advisable to divide the affected area into smaller areas and to complete treatment in one area before moving on to the next. This will help make the treatment more tolerable Efudix BAD PIL	Maximum area of skin treated at one time 25cm^2 For specialist only: Maximum area of skin treated at one time, 500 cm^2 larger areas should be treated a section at a time.	3 to 4 weeks	Follow up 3 months after therapy is complete
Tirbanibulin ointment	Klisyri®	Topical field treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis (Olsen grade 1) of the face or scalp in adults.	Ointment should be applied to the affected field on the face or scalp once daily for one treatment cycle of 5 consecutive days. Klisyri PIL	A thin layer of ointment should be applied to cover the treatment field of up to 25cm^2	5 consecutive days	Follow up to 3 months after therapy is complete
Imiquimod 5% Cream	Aldara®	AKs on the face or scalp when other treatment options are contraindicated or less appropriate	Apply to lesion 3 times a week at night for 4 weeks and leave on skin for 8 hours; repeat 4-week course if lesions persist after 4 weeks interval; maximum 2 courses. Aldara PIL	Treatment area of 25cm^2 (5cm x 5cm) One sachet a day	4 weeks can be repeated	8 weeks after the last 4-week course of treatment

References. All accessed February 2023

1. Primary Care Dermatology Society (PCDS) . Actinic keratosis (syn. solar keratosis) guidelines: http://www.pcds.org.uk/clinical-guidance/actinic-keratosis-syn.-solar-keratosis
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3. D. de Berker, J.M. McGregor, M.F. Mohd Mustapa, L.S. Exton and B.R. Hughes, British Association of Dermatologists' guidelines for the care of patients with actinic keratosis 2017, British Journal of Dermatology (2017) 176, pp20–43 https://onlinelibrary.wiley.com/doi/10.1111/bjd.15107
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6. SPC for Efudix

Document history

Version	1.0
Approved by	Hertfordshire & West Essex Area Prescribing Committee
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Developed by:	Developed by pharmacy and medicines optimisation team Hertfordshire and West Essex (HWE) ICB with relevant HWE ICS stakeholders.
Review Date	This HWE APC recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available.
Superseded version	WEMOPB Actinic Keratosis Primary Care Treatment Pathway April 2022, amended as follows 1.Removed Zyclara from formulary and guidelines 2.Simplified Efudix guidance based on local agreement 3.Addition of tirbanibulin 4.Addition of definition for hyperkeratosis and when 5FU & salicylic acid should be used 5.Treat and refer for grade III solitary lesions