The aim of this leaflet

This leaflet is designed to help you understand more about actinic keratosis, a type of non-melanoma skin cancer. It tells you what this condition is, what causes it, what it looks like, what can be done for treatment and prevention, and practical advice for managing this condition.
What is actinic keratosis?
Actinic keratosis (AK) (also known as “solar keratosis” or “senile keratosis”; plural: keratoses) is generally classified as a premalignant skin lesion. However, a few authors challenge this viewpoint, and believe that it represents an early variant of a squamous cell carcinoma (SCC) in situ (also known as Bowen’s disease).

Who is affected by actinic keratosis?
The main risk factors for AK are fair skin, advanced age, use of phototoxic drugs, and high cumulative UV exposure (over the course of a person’s life). Immunosuppressed patients have higher risk of progression of AK into invasive SCC (iSCC) and development of metastasis (spreading of the cancer).

What causes actinic keratosis?
AK is caused by chronic exposure to ultraviolet (UV) radiation. DNA mutations (genetic changes) associated with UVB (UV B-rays which cause burning) are found in all AKs. At a molecular level, the function of tumour-suppressive proteins such as p53 is usually abnormal, leading to increased tumour keratinocytes (epidermal cells that make keratin). Radiation with UVA (UV A-rays which cause aging) can cause, at a lower extent, the same genetic damages as well as oxidative damage that can contribute to the malignant transformation of keratinocytes.

Can it be inherited?
A few hereditary, phenotypic (characteristic) features, such as fair skin and red/blond hair, are relevant risk factors. Genetic syndromes associated with impaired DNA repair mechanisms or deficiency in melanin production have a higher risk as well.

What does actinic keratosis look like?
Clinically, AKs typically present as erythematous and scaly patches or plaques (elevated lesions). AKs are classified based on their level of thickness or dysplasia (abnormal growth): the clinical Olsen (I-III) score according to thickness or the histological keratinocyte intraepithelial neoplasia KIN (I-III) score according to the degree of dysplasia.

Sometimes, isolated AKs develop on apparently normal skin. Usually, multiple lesions develop on skin with other clinical signs of chronic sun damage, including “spider veins,” pigmented spots, skin with a yellowish hue, and wrinkles. Chronic sun-exposed areas such as the scalp, face, hands, and arms are the most involved. Photo-aged skin surrounding multiple AKs (the so-called “cancerization field”) has been shown to harbour the same molecular damage of AK and iSCC, and represents a risk factor for the development of additional AKs.

How is actinic keratosis diagnosed?
Clinical examination and dermoscopy (a non-invasive technique to examine the skin) are sufficient in almost all cases. However if the diagnosis is uncertain, or the progression to iSCC is suspected, a biopsy is recommended.
Why and how is actinic keratosis treated?

The biological behaviour of a single AK cannot be predicted: it may disappear spontaneously, remain unchanged for decades, or progress to an iSCC. The risk of cancerous progression of a single AK is low, but the cumulative risk becomes high in patients with multiple AKs.

Several different treatments are available. The choice of treatment modality depends on several factors: the clinical thickness, size, number and localization of lesions, the patient’s age and general health condition, and the patient’s ability to perform home treatments. Two types of treatment options exist: lesion-directed procedures that only aim to remove lesions, and field-directed chemical treatments that aim to remove lesions and treat the surrounding photodamaged skin as well.

**Lesion-directed procedures for isolated lesions (1-5 AK on a limited body area):**

- **Cryotherapy:** freezing lesions with liquid nitrogen is easy, effective, and cheap. The procedure is usually well tolerated although it may cause pain, redness, swelling, crusting, and blister formation, with healing over several weeks.
- **Curettage:** lesions are scraped with a surgical instrument called a curette. Curettage alone has a limited effectiveness, but it is often used to remove scales of thick lesions in order to improve the efficacy of other treatments.
- **Surgical excision:** surgery is highly effective but rarely used because it is invasive and expensive, and scars are a frequent complication.
- **CO2-laser, Erbium(Er):YAG-laser:** ablative lasers are expensive and less practical than cryotherapy, with similar or lower efficacy and safety.
ACTINIC KERATOSIS

Drugs approved for the treatment of multiple (≥6) AKs (clustered in a limited body area, with other clinical features of chronic actinic sun damage):

Topical treatments (containing Ingenol Mebutate 0.015/0.05%, 5-Fluorouracil (FU) 0.5/5%, 0.5% 5-FU + 10% Salicylic Acid (SA), Imiquimod 2.5% /3.75%/5%, or Diclofenac 3% in 2.5% Hyaluronic Acid) are applied to lesions and the surrounding skin. The resulting inflammatory and immunologic reactions lead to the clearance of lesions and improvement in the clinical, histologic, and molecular damage of the “cancerization field.” All treatments are performed by the patient him/herself at home. According to their approval status, drugs differ in terms of efficacy, tolerability, toxicity, size of the area that can be treated in a single treatment cycle, overall duration of treatment, and cost.

Creams containing 5-aminolaevulinic acid (ALA) or methylaminolevulinate (MAL) are also available. In this case (called photodynamic therapy), application of the drug (to make the affected areas sensitive to light) is followed by irradiation with artificial or natural light that is delivered by the clinician (doctor or nurse).

How can actinic keratosis be prevented?

It is important to reduce sun exposure. Patients should always use protective clothing, sunscreen (SPF 50+), and avoid tanning beds (especially for patients with fair skin).

What is practical advice regarding skin-care, and how can I notice any warning signs?

1. Careful sun protection can decrease the risk of developing AKs.
2. Consider AKs if you have one or more red scaling patches on sun-exposed skin.
3. If you have already been diagnosed with AKs, you are at risk of developing further lesions in the future.
4. Be alert to the development of a nodule or ulcer with bleeding; this may indicate an invasive skin cancer which requires urgent attention.
5. AK is a pre-cancerous lesion; seek medical advice to choose the best therapeutic option.