AMELUZ (5-aminolaevulinic acid), photodynamic therapy

No clinical benefit demonstrated over METVIXIA in the treatment of actinic keratosis on the face and scalp.

Main points

- AMELUZ has Marketing Authorisation in the treatment of mild to moderate actinic keratosis on the face and scalp (Olsen grade 1 to 2).
- The clinical data have not demonstrated any advantage, in terms of efficacy or safety, over a cream containing 160 mg/g methyl aminolevulinate (similar composition to METVIXIA).
- No comparisons between AMELUZ and cryotherapy are available.

Therapeutic use

- Actinic keratoses can develop into skin cancers (squamous cell carcinoma). If squamous cell carcinoma of the skin is suspected, histological diagnosis of the lesions is necessary before they are treated.
- Cryotherapy is the standard treatment if there are few lesions. Photodynamic therapy using a sensitising agent is an alternative to cryotherapy, particularly if there are multiple lesions located on the face and/or alopetic scalp. METVIXIA cream (methyl aminolevulinate hydrochloride) is a first-line therapy for multiple, thin or non-hyperkeratotic and non-pigmented lesions on the face and scalp. For EFFALA (5-aminolaevulinic acid plaster), treated lesions should not exceed 1.8 cm in diameter. Under these conditions, EFFALA has been shown to be superior to cryotherapy.
- When the lesions are large, surgery is sometimes used, occasionally followed by a graft if the area to be treated is extensive. When there are multiple lesions, topical 5-FU (EFUDIX), imiquimod (ALDARA), ingenol mebutate (PICATO) and mechanical dermabrasion are used. CO2 laser therapy and electrocoagulation and curettage may also be treatment options.
- **Role of the medicinal product in the therapeutic strategy**
  - AMELUZ is a first-line therapy, as an alternative to cryotherapy, in the treatment of mild to moderate actinic keratoses on the face and scalp.

Clinical data

- A single-blind (observer-blind) study compared AMELUZ with placebo and to a 160 mg/g methyl aminolevulinate cream (METVIX) that has a similar strength to METVIXIA 168 mg/g. In this study, the intensity of the lesions was primarily moderate (83.3%) rather than mild (16.5%). The phototypes of patients were not comparable, with phototypes IV and V over-represented in the AMELUZ group (14.9%) versus placebo (5.3%) and METVIX (10.1%). Phototype is actually an important factor in the technique of photodynamic therapy. The groups’ characteristics in terms of surface area to be treated or method of irradiation were not specified, meaning that it is not possible to judge their comparability. In addition, the method of irradiation was not standardised, and this may influence the results. On inclusion, the lesions were small in size (between 0.5 and 1.5 cm in diameter), which is not typical for photodynamic therapy. The superiority of AMELUZ to METVIX was demonstrated in the per-protocol population. At 6 months of follow-up, 19.1% of patients in the AMELUZ group (14.9%) versus placebo (5.3%) and METVIX (10.1%). Phototype is actually an important factor in the technique of photodynamic therapy. The superiority of AMELUZ to METVIX was demonstrated in the per-protocol population. At 6 months of follow-up, 19.1% of patients in the AMELUZ group with a complete response 12 weeks after the last photodynamic therapy treatment had recurrent lesions; this figure was 18.2% in the METVIX group and 15.4% in the placebo group.
  - The mean numbers of recurrent lesions per patient were 0.4, 0.4 and 0.2 respectively.
  - At 6 and/or 12 months of follow-up, 41.6% of patients in the AMELUZ group versus 44.8% in the METVIX group had had recurrent lesions. The mean numbers of recurrent lesions per patient were 0.9 and 1.1.

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Adverse events with AMELUZ were more common than with placebo and were similar to METVIX. These were primarily local reactions such as irritation, erythema and pain.

Special prescribing conditions

- Prescription restricted to dermatology specialists and departments.

Benefit of the medicinal product

- The actual benefit* of AMELUZ is moderate.
- AMELUZ does not provide clinical added value** (CAV V).
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.

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