SUMMARY

5-aminolevulinic acid

AMELUZ 78 mg/g,

gel

First listing

Adopted by the Transparency Committee on 23 October 2024

Summary of opinion

Favourable opinion for reimbursement in the "treatment of actinic keratosis of mild to moderate severity (Olsen grade 1 to 2) and of field cancerization in adults."

Transparency Committee's conclusions

Clinical Benefit

- Actinic keratoses are skin lesions occurring in sun-exposed zones, usually in the elderly. They frequently occur as multiple lesions, which may develop into skin carcinomas in the absence of treatment.
- AMELUZ 78 mg/g (5-aminolevulinic acid) gel is a curative medicinal product.
- The efficacy/adverse effects ratio is moderate.
- This is a first-line treatment, as an alternative to cryotherapy, for multiple actinic keratosis lesions of mild to moderate severity (Olsen grade 1 to 2) and of field cancerization in adults. Cryotherapy remains the reference treatment when lesions are not numerous (≤ 5 lesions).

Public health benefit

Considering:

- the seriousness of the disease, insofar as it develop into a skin carcinoma in the absence of effective treatment,
- its prevalence, which increases with age,
- the partially met medical need,
- the partial response to the identified need given:
  - the demonstrated additional impact versus placebo in the treatment of actinic keratoses of the trunk, neck or extremities and localised field cancerization of the face or scalp in adults,
  - the lack of evidence of an additional impact versus methyl aminolevulinate (METVIXIA) when natural daylight photodynamic therapy is used to treat actinic keratosis of the face or scalp,

- the absence of data on quality of life, but a demonstrated additional impact versus placebo in terms of overall cosmetic outcome,
- the lack of evidence of an additional impact of the organisation of care or on the patient's care or life pathway,

AMELUZ (5-aminolevulinic acid) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of AMELUZ (5-aminolevulinic acid) 78 mg/g gel is moderate in the MA indication.

The Committee issues a favourable opinion for inclusion of AMELUZ (5-aminolevulinic acid) 78 mg/g gel in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the MA indication and at the MA dosages.

Clinical Added Value

Considering:

- demonstration in three phase 3 clinical studies of:
  - the superiority of 5-aminolevulinic acid versus placebo for the percentage of patients with complete clearance of lesions 12 weeks after the last red-light photodynamic therapy (PDT) (primary endpoint), with a clinically relevant effect size (86.0% versus 32.9%, $p < 0.0001$), in adults with mild to severe actinic keratosis (AK) of the extremities, trunk or neck (ALA-AK-CT010 study),
  - the superiority of 5-aminolevulinic acid versus placebo for the percentage of completely cleared lesions 12 weeks after the last red-light PDT (primary endpoint), with a clinically relevant effect size (90.9% versus 21.9%, $p < 0.0001$), in adults with mild to moderate AK of the face or scalp located in a field cancerization (ALA-AK-CT007 study),
  - the superiority of 5-aminolevulinic acid versus placebo for all the ranked secondary efficacy endpoints in both studies versus placebo, particularly on the percentage of patients with complete clearance of lesions confirmed by histological examination, although the effect size is lower than in the absence of histological confirmation,
  - the non-inferiority of 5-aminolevulinic acid versus METVIXIA (methyl aminolevulinate), for the percentage of completely cleared lesions 12 weeks after natural-light PDT (primary endpoint), in adults with mild to moderate AK of the face or scalp (ALA-AK-CT009 study), with no evidence of a superiority of 5-aminolevulinic acid compared to methyl aminolevulinate,
- a better overall cosmetic outcome with 5-aminolevulinic acid in the studies versus placebo,
- recurrences after 6 or 12 months of follow-up after the last PDT for lesions having had a complete response at week 12 (at 12 months of follow-up: 9.1% and 14.1% with red-light PDT [1 to 2 sessions of PDT] and 19.5% with natural daylight PDT [1 session of PDT] versus 31.2% for methyl aminolevulinate),
- the absence of any comparison with cryotherapy, which remains the reference treatment when lesions are not numerous (≤ 5 lesions),
- the similar safety profile to that of METVIXIA (methyl aminolevulinate), primarily including local reactions, such as irritation, erythema and pain,

the Committee deems that AMELUZ 78 mg/g (5-aminolevulinic acid) gel provides no clinical added value (CAV V) in the treatment of actinic keratosis of mild to moderate severity (Olsen grade 1 to 2) and of field cancerization in adults.