HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
21 SEPTEMBER 2022

The legally binding text is the original French opinion version

isotretinoin
ISOTRETINOIN ACNETRAIT 5 mg, 10 mg, 20 mg and 40 mg, softgel

Reassessment

Key points

Re-evaluation of all oral isotretinoin-based proprietary medicinal products indicated for the treatment of severe acne:

Retention of approval for reimbursement for the marketing authorisation indication.

Role in therapeutic strategy?

The medication arsenal includes topical and systemic treatments, combined with appropriate hygiene care. The choice of treatment will depend on the severity of the acne.

According to the SFD, an initial treatment is prescribed as a first-line treatment for a period of three months, with the aim of obtaining a significant reduction or disappearance of the lesions and preventing the occurrence of scarring. After three months, the effectiveness of the treatment is reassessed, and if it fails, a second-line treatment is implemented. Local treatments, whether creams or gels, based on benzoyl peroxide and retinoids are preferable, alone or in combination, as a first-line treatment for very mild (GEA grade 1) to moderate (grade 3) acne. In the event of failure after three months, the recommended second-line treatments are:

- Grade 1 acne: a combination of benzoyl peroxide and local retinoids;
- Grade 2 acne: intensification of local treatment, or a combination of first-line treatment with oral antibiotics (cyclin), or a combination of local retinoids or azelaic acid with local antibiotic therapy;
- Grade 3 acne: oral isotretinoin;
- Grade 4 acne: oral isotretinoin (treatment can be initiated prior to three months if there is a high risk of scarring or in the event of recurrence).

For highly inflammatory grade 5 acne with nodules covering the face, oral isotretinoin is prescribed as the first-line treatment.

After remission, local maintenance treatment (adapalene or adapalene + benzoyl peroxide, or even tretinoin instead of adapalene) should be prolonged as long as necessary to prevent relapse.

An oestrogen-progestin therapy for contraceptive purposes may be administered to women with acne, regardless of its severity.

Role of proprietary medicinal products assessed in the therapeutic strategy

Oral isotretinoin-based proprietary medicinal products (ACNETRAIT, CONTRACNE, CURACNE and PROCUTA) continue to play a role in the treatment of severe acne (such as nodular acne, acne conglobata or acne likely to lead to permanent scarring) that is resistant to appropriate courses of conventional therapy (for three months, with good compliance) involving systemic antibiotics and topical treatment.

Due to the adverse effects observed with isotretinoin, and because of the risk of teratogenicity in particular, it is essential for the recommendations associated with its prescription to be followed [see SPC, Pregnancy Prevention Programme (PPG) and Risk Management Plan (RMP)].

The use of this medicine is contraindicated in pregnant or breastfeeding women (see SPC).

COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Acne is not a serious disease, but in its severe forms it can have a significant impact, both psychological and on quality of life, and often leads to permanent scarring.

◗ Oral isotretinoin-based proprietary medicinal products (ACNETRAIT, CONTRACNE, CURACNE and PROCUTA) are used for curative treatment.

◗ The efficacy of isotretinoin is significant. There are many common adverse effects, the most severe being a teratogenic effect and a suicide risk requiring numerous risk-minimisation measures, including a pregnancy prevention plan. Despite the reinforcement of these measures over the years, the number of pregnancies on isotretinoin remains stable and not negligible, and the number of pregnancies initiated during treatment has increased since the previous survey (see opinion of the Transparency Committee of 8 February 2017).
The efficacy/adverse reaction ratio of these proprietary medicinal products for severe acne is moderate.
◗ There are several alternatives to oral isotretinoin.

◗ Isotretinoin-based proprietary medicinal products continue to play a role in the treatment of severe forms of severe acne (such as nodular acne, acne conglobata or acne likely to lead to permanent scarring) that are resistant to appropriate courses of conventional therapy (for three months, with good compliance) involving systemic antibiotics and topical treatment.

Public health benefit

Considering:
- the severity of the disease due to its significant impact on quality of life and its high prevalence,
- the identified, partially met medical need,
- the partial response to the identified need, given:
    - the high efficacy but substantial risks associated with tolerance, including teratogenicity, and a plausible suicide risk,
    - the lack of a demonstrated impact in terms of quality of life,
    - a negative impact on the patient's care or life pathway given the numerous prevention and monitoring measures mentioned in the Pregnancy Prevention Plan, including monthly visits for all patients (prescription limited to 30 days), and – specifically for women of childbearing age – monthly pregnancy tests, and the need for reinforced contraception,

the oral isotretinoin-based proprietary medicinal products (ACNETRAIT, CONTRACNE, CURACNE and PROCUTA) are not likely to have an additional impact on public health. A negative impact of these proprietary medicinal products on public health cannot be excluded.

Considering all of these elements, the Committee deems that the actual clinical benefit of oral isotretinoin-based proprietary medicinal products (ACNETRAIT, CONTRACNE, CURACNE and PROCUTA) is substantial in the marketing authorisation indication.

The Committee approves continued inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary medicinal products approved for community use in the indication and at the dosages of the marketing authorisation.

◗ **Recommended reimbursement rate: 65%**