HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
9 MARCH 2022

The legally binding text is the original French opinion version

abrocitinib
CIBINQO 50 mg film-coated tablets
CIBINQO 100 mg film-coated tablets
CIBINQO 200 mg film-coated tablets

First assessment

Key points

Favourable opinion for reimbursement in the treatment of moderate to severe atopic dermatitis in adults who are candidates for systemic therapy **in the event of failure, intolerance or contraindication to ciclosporin.**

Unfavourable opinion for reimbursement in the treatment of moderate to severe atopic dermatitis in adults in whom topical therapies have failed and who are **ciclosporin-naïve, in the absence of comparative data.**

What therapeutic improvement?

Therapeutic improvement compared to DUPIXENT (dupilumab) in the treatment of moderate to severe atopic dermatitis in adults who are candidates for systemic therapy, **in the event of failure, intolerance or contraindication to ciclosporin.**

Role in the care pathway?

The overall objective of atopic dermatitis (AD) treatment is to improve patients' quality of life by treating their skin lesions and preventing the risk of secondary infections in the event of flare-ups, early relapses and xeroderma. Outside inflammatory flare-ups, all patients should be treated using adjuvant measures (hygiene, emollients) and relapses should be treated at an early stage.

The treatment of acute flare-ups is initially based on the use of topical treatments: topical corticosteroids or, in the event of failure/contraindication, a calcineurin inhibitor (tacrolimus). The wet wrapping technique may be used in the event of an inadequate response.

Phototherapy is mainly recommended in the management of the chronic phase but can be used as second-line treatment in acute flare-ups in the event of failure of topical treatments, although its use is limited by its accessibility.

Systemic treatments are reserved for severe chronic atopic dermatitis resistant to topical corticosteroids or phototherapy. The choice of systemic treatment depends on various factors, in particular comorbidities, age, clinical experience or potential pregnancy plans.

Non-biologic systemic treatments are currently available, including ciclosporin used as first-line treatment and immunosuppressive therapies used off-label (methotrexate, mycophenolate mofetil and azathioprine). Their use should be time-limited due to the unfavourable long-term safety profile.

Other treatment options have also become available recently: two biologic interleukin inhibitors administered subcutaneously, dupilumab (anti-IL4 and anti-IL13, in 2017) and tralokinumab (anti-IL-13, in 2021), and two janus kinase inhibitors administered orally, baricitinib (anti-JAK 1 and 2, in 2020) and upadacitinib (anti JAK1 and JAK1/3, in 2021). These treatments are recommended by the Transparency Committee in the event of failure, intolerance or contraindication to ciclosporin.

Alitretinoin, a systemic retinoid, has an MA exclusively for the treatment of severe chronic eczema of the hands, following the failure of potent topical corticosteroids.

Role of CIBINQO (abrocitinib) in the care pathway:

As knowledge currently stands, in the absence of a direct comparison of abrocitinib (JAK1 inhibitor) with oral ciclosporin following the failure of topical treatments, its role compared to ciclosporin cannot be determined in first-line systemic therapy (following the failure of topical corticosteroids).

Consequently, CIBINQO 50 mg, 100 mg and 200 mg (abrocitinib) is a second-line systemic treatment to be reserved for adults with moderate to severe atopic dermatitis, who are candidates for systemic therapy, in the event of failure, intolerance or contraindication to ciclosporin.

The Transparency Committee specifies that the choice of second-line systemic therapy should be made on a case-by-case basis depending on the severity of the disease, patients' characteristics, their treatment history, the risks of intolerance and contraindications to the various treatments available.

As regards abrocitinib, it is necessary to take into account its less favourable safety profile than that of dupilumab (see the respective SPCs of these medicinal products), the need to monitor various laboratory parameters (haematological and lipid), its contraindication in the event of pregnancy, as with other JAK inhibitors, as well as uncertainties in terms of safety, in particular relative to the risks of major cardiovascular and thromboembolic events and the carcinogenic risk indicated in the RMP for abrocitinib and shared by other JAK inhibitors.

The superiority of abrocitinib compared to dupilumab has been demonstrated only at the dose of 200 mg, which corresponds to the maximum daily dose according to the SPC.

Special recommendations

The Committee wishes to highlight the fact that abrocitinib is contraindicated during pregnancy, due to the teratogenic effects demonstrated in animals, and that for women of childbearing potential effective contraception should be used during treatment and for 1 month following the final dose of abrocitinib (see the SPC for more details).

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Atopic dermatitis is not usually a serious disease but in its moderate to severe forms, it has a significant impact on the quality of life of patients and marked social repercussions.

◗ The proprietary medicinal products CIBINQO 50 mg, 100 mg and 200 mg (abrocitinib) film-coated tablets have a suspensive effect on symptoms.

◗ In the absence of direct comparative data versus ciclosporin (first-line systemic therapy), the efficacy/adverse effects ratio of abrocitinib has not been established in adults with moderate to severe atopic dermatitis in whom topical treatments have failed and who are ciclosporin-naive.
Consequently, its efficacy/adverse effects ratio is considered to be high only in patients in whom ciclosporin treatment has failed.

◗ There are medicinal alternatives.

◗ This medicinal product is a second-line systemic treatment to be reserved for adults with moderate to severe atopic dermatitis, in the event of failure, intolerance, or contraindication to ciclosporin (see 08 **Erreur ! Source du renvoi introuvable.**).

Public health impact

Considering:

- the seriousness of the disease in its severe forms requiring systemic treatment and its significant impact on patients' quality of life,
- the high prevalence of the disease (between 2 and 5% of the population),
- the medical need that is partially met in adults with moderate to severe atopic dermatitis who are candidates for systemic therapy,
- the partial response to the identified need, due to:
    - a demonstrated impact in terms of morbidity (in particular on IGA 0 or 1, EASI-75, EASI-90 responses and pruritus) according to placebo-controlled studies or versus dupilumab, as monotherapy or in combination with a topical background therapy in adults,
    - a safety profile including important identified risks (thrombotic events, herpes zoster), uncertainties, in particular with respect to important potential risks of major cardiovascular events, serious and opportunistic infections and tumours, indicated in the RMP, and a contraindication during pregnancy,
    - the expected impact for this medicinal product administered orally on the organisation of care and the patient's life pathway (reduction in need for nursing care, hospitalisations required to administer biologic therapies and use of medical transport), but considering:
        - the need to monitor haematological and lipid parameters during treatment,
        - the need for women of childbearing potential to use effective contraception,

CIBINQO (abrocitinib) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of the proprietary medicinal products CIBINQO 50 mg, 100 mg and 200 mg (abrocitinib) film-coated tablets is:

- **Substantial in the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy, in the event of failure, intolerance or contraindication to ciclosporin;**

- **insufficient to justify public funding cover in view of the available alternatives in the treatment of moderate to severe atopic dermatitis in adults in whom topical therapies have failed and who are ciclosporin-naïve, in the absence of comparative data.**

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy in the event of failure, intolerance or contraindication to ciclosporin and at the MA dosages.

- **Recommended reimbursement rate: 65%**

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the treatment of moderate to severe atopic dermatitis in adults in whom topical therapies have failed and who are ciclosporin-naïve, in the absence of comparative data.

Clinical Added Value

In the indication retained for reimbursement

Considering:

- demonstration in studies having included patients with moderate to severe atopic dermatitis requiring systemic treatment:
  - of the superiority of abrocitinib 100 mg and 200 mg compared to placebo, with a substantial effect size, in terms of IGA 0 or 1, EASI-75 responses, and pruritus after 12 weeks of treatment (ranked endpoints), as monotherapy (JADE MONO-1 and 2 studies) or in combination with a topical background treatment (JADE COMPARE study) in adult or adolescent patients;
  - the superiority of abrocitinib 200 mg compared to dupilumab, in terms of EASI-75 response at week 16 (54.3% versus 41.9%, $p < 0.0008$), EASI-90 response at week 4 (28.5% versus 14.6%, $p < 0.0001$) and the percentage of PP-NRS4 responders at week 2 (48.2% versus 25.5%, $p < 0.0001$), in the JADE DARE study;
  - the probability of the absence of flare-ups during the maintenance period in patients responding to induction therapy, which was lower in the placebo group (19.1%) compared to the abrocitinib 200 mg group (81.1%, $p < 0.0001$) and the abrocitinib 100 mg group (57.4%, $p < 0.0001$) in the JADE REGIMEN study;

And despite:

- the absence of a demonstrated benefit on patients' quality of life, despite this being particularly impacted in this condition,
- uncertainties with respect to maintenance of efficacy beyond 26 weeks of treatment for endpoints assessing the severity of the disease and the intensity of pruritus, and beyond 52 weeks for the probability of the absence of flare-ups during the maintenance phase in patients responding to induction therapy;
- a comparable safety to that observed with the other janus kinase inhibitors, including:
  - important identified risks (such as thrombotic events, including pulmonary embolism, and the risk of herpes zoster),
  - uncertainties with respect to major cardiovascular risks, risks of serious infections, gastrointestinal perforations, myopathies, impaired growth and carcinogenic risks, in particular,
  - the need to monitor various laboratory parameters (haematological and lipid), and
  - a contraindication during pregnancy.

The Committee considers that CIBINQO (abrocitinib) 50 mg, 100 mg and 200 mg film-coated tablets provide a minor clinical added value (CAV IV) compared to DUPIXENT (dupilumab) in adults with atopic dermatitis who are candidates for systemic therapy in the event of failure, intolerance or contraindication to ciclosporin.