HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
09 SEPTEMBER 2020

The legally binding text is the original French opinion version

budesonide
JORVEZA 0.5 mg orodispersible tablets
JORVEZA 1 mg orodispersible tablets

First assessment

Key points

Favourable opinion for reimbursement in the treatment of eosinophilic oesophagitis (EoE) in adults, only in patients not responding to PPIs.

Unfavourable opinion for reimbursement in patients responding to PPIs.

What therapeutic improvement?

Therapeutic improvement in the treatment of adult patients with eosinophilic oesophagitis (EoE), only in patients not responding to PPIs.

Role in the care pathway?

The management of patients may be medicinal and/or dietary. No medicinal product currently has an MA in EoE. When a medicinal treatment is proposed, the drugs recommended and used off-label are PPIs and topical corticosteroids as a spray or viscous solution to be swallowed (primarily fluticasone and budesonide). These treatments have a suspensive effect only, with the condition systematically recurring when they are stopped. Only an avoidance/reintroduction protocol for foods potentially implicated, which is complex and difficult to implement, may represent a long-term curative treatment.

Role of the medicinal product in the care pathway

JORVEZA (budesonide orodispersible tablets) is a second-line treatment that should be reserved for adult patients not having responded to PPIs used off-label, the only population for which its efficacy and safety have been documented *versus* placebo. In fact, JORVEZA (budesonide) has been assessed in studies that exclusively included patients in whom a clinical and histological response to PPIs had been excluded following treatment for at least 4 weeks with a dose that had to be at least the standard dose in accordance with the SPC.

JORVEZA (budesonide) is currently the only medicinal product and, in particular, the only corticosteroid, to have an MA in France in the treatment of EoE and it is consequently the corticosteroid of choice in this indication.

The role of JORVEZA (budesonide) compared to the medicinal products currently prescribed off-label - PPIs and swallowed corticosteroid sprays - cannot be defined in the absence of direct comparative data. In comparison with the other corticosteroids used off-label, JORVEZA (budesonide) presents the advantage of having a more appropriate delivery form.

To date, only comparative data versus placebo after 48 weeks are available, a duration that is too short in this chronic disease that generally progresses slowly over several years. Consequently, the benefit of maintaining JORVEZA (budesonide) as long-term treatment to prevent progression to oesophageal fibrosis or stenosis has not been demonstrated. Furthermore, there are uncertainties with respect to the benefit of this type of maintenance treatment taken continuously compared to intermittent treatment. A study that aims to document this aspect is ongoing.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Eosinophilic oesophagitis (EoE) is a chronic allergic and immune system disease characterised by a local inflammatory reaction in which eosinophils predominate. Most of the allergens responsible come from food.
The disease is not life-threatening and does not affect life expectancy but it can impair patients' quality of life and cause long-term complications, such as oesophageal fibrosis, food impaction or the need for instrument-assisted oesophageal dilation, potentially leading to repeated hospitalisations. In adolescents and adults, dysphagia is the main symptom in the very great majority of cases. Patients are accustomed to living with moderate dysphagia, adapt their diets and usually only consult a doctor if the symptoms worsen or in an emergency in the event of oesophageal food impaction.

◗ JORVEZA (budesonide) is a symptomatic treatment.

◗ The efficacy/adverse effects ratio is high only in patients not responding to PPIs. It is not established outside this population due to a lack of data.

◗ There are medicinal alternatives used off-label (PPIs and some ingested topical corticosteroids). A food exclusion diet is a non-medicinal alternative. (see paragraph 5 "clinically relevant comparators").

◗ JORVEZA (budesonide) is a second-line treatment, only in patients not responding to PPIs. It has no role in the treatment of eosinophilic oesophagitis outside this population in the absence of data (see paragraph 8).

Public health impact
Considering:
- the lack of seriousness of eosinophilic oesophagitis in the great majority of cases,
- its low prevalence,
- the medical need partially met by medicinal products used off-label and a food avoidance diet,
- the lack of demonstrated impact on quality of life,
- the partial response provided to the identified need in the absence of a demonstrated impact to date on progression towards oesophageal fibrosis or stenosis,

JORVEZA (budesonide) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of JORVEZA (budesonide) orodispersible tablets is:
- **substantial in the treatment of eosinophilic oesophagitis in adults, only in patients not responding to PPIs.,**
- **insufficient to justify public funding cover in patients responding to PPIs, in view of the available alternatives.**

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 eosinophilic oesophagitis (EoE) in adults (older than 18 years of age) and at the MA dosages, only in patients not responding to PPIs.

In patients responding to PPIs, 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.

Clinical Added Value

Treatment of eosinophilic oesophagitis in adults not responding to PPIs

Considering :
- **demonstration of the superiority of JORVEZA (budesonide orodispersible tablets) compared to placebo on histological and clinical remission rates (primary endpoint) after 6 weeks, and maintenance of this remission after 48 weeks, in phase III randomised, controlled studies having only included patients not responding to PPIs,**
- **the satisfactory safety profile,**
- **the fact that JORVEZA (budesonide) has a better level of evidence, with the other corticosteroids currently used as second-line therapy not having an MA,**

and despite :
- **the absence of long-term efficacy and safety data (in particular, the absence of a demonstrated impact on the progression towards oesophageal stenosis and fibrosis, the main complications of the disease),**

the Transparency Committee considers that JORVEZA (budesonide) provides a minor clinical added value (CAV IV) in the treatment of adult patients with eosinophilic oesophagitis (EoE) not responding to PPIs.

Treatment of eosinophilic oesophagitis in adults responding to PPIs

Not applicable.