HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
23 SEPTEMBER 2020

The legally binding text is the original French opinion version

tafamidis
VYNDAQEL 61 mg, soft capsule

Inclusion in list

Key points

Favourable opinion for reimbursement in adult patients with wild-type or hereditary transthyretin amyloid cardiomyopathy (ATTR-CM).

What therapeutic improvement?

Therapeutic improvement in the management of wild-type or hereditary transthyretin amyloid cardiomyopathy.

Role in the care pathway?

The care pathway for transthyretin amyloid cardiomyopathy is currently based on conventional symptomatic treatments for heart failure.

In the treatment of cardiac amyloidosis, three mechanisms of action are targeted:

- the elimination of abnormal transthyretin and/or its main synthesis source: a heart and/or liver transplant may be envisaged.
- stabilisation of transthyretin: tafamidis in the form of VYNDAQEL 20 mg, has a temporary recommendation for use (RTU) in hereditary or senile transthyretin amyloid cardiomyopathy and now has a marketing authorisation in France in the form of VYNDAQEL 61 mg.
- the resorption of toxic amyloid fibrils of transthyretin.

In addition, another two medicinal products have a marketing authorisation in ATTR, but only in the neurological form: ONPATTRO (patisiran) and TEGSEDI (inotersen).

Role of VYNDAQEL in the care pathway:

VYNDAQEL (tafamidis) is a first-line treatment for transthyretin amyloid cardiomyopathy. It is the only medicinal product with a MA in this indication. The Committee highlights that:

- class NYHA IV patients had been excluded from the study and very few class NYHA I patients (8.4%) were included in the study,
- it questions the dose selected by the MA - 80 mg and not 20 mg - in the absence of robust data reported to the Transparency Committee making it possible to differentiate between the two dosages in terms of efficacy and safety.

For ATTR patients with both cardiac and neurological involvement, the Committee cannot currently reach a decision concerning the strategy of joint or sequential use of the various existing treatments - ONPATTRO (patisiran), TEGSEDI (inotersen) and VYNDAQEL 20 mg or now VYNDAQEL 61 mg (tafamidis) - in the care pathway for transthyretin amyloidosis with associated cardiomyopathy, in the absence of data.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Wild-type or hereditary transthyretin amyloid cardiomyopathy is a rare, serious disease with fatal outcome.
◗ VYNDAQEL 61 mg soft capsules (tafamidis) is a preventive treatment to stop the formation of new amyloid deposits.
◗ Its efficacy/adverse effects ratio is high.
◗ There are no therapeutic alternatives to VYNDAQEL in this indication.
◗ This proprietary medicinal product is a first-line treatment.

Public health impact

Considering:
- the seriousness of the disease,
- its prevalence
- the identified major medical need,
- the demonstrated impact on the organisation of care, in particular in terms of reduction in the frequency of hospitalisation,
- the partial response to the identified need (demonstrated superiority in terms of all-cause mortality and quality of life),

VYNDAQEL (tafamidis) is likely to have an additional impact on public health.

Given all these elements, the Committee deems that the clinical benefit of VYNDAQEL (tafamidis) is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion of VYNDAQEL (tafamidis) in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the marketing authorisation indication and dosages.

◗ **Recommended reimbursement rate : 65%**

Clinical Added Value

Considering:

- **the demonstration in a clinical study of good methodological quality (phase III, randomised, double-blind study) of the superiority of tafamidis (20 mg and 80 mg) compared to placebo, in patients with transthyretin amyloid cardiomyopathy in terms of:**
  - **all-cause mortality after 30 months with HR = 0.70 95% CI [0.51; 0.96] p=0.0259 and frequency of cardiovascular-related hospitalisations over 30 months RR = 0.68 95% CI [0.56; 0.81] p<0.0001 (primary endpoint),**
  - **6-minute walk test and quality of life assessed by the Kansas City cardiomyopathy questionnaire (ranked secondary endpoints).**
- **the satisfactory safety profile of tafamidis,**
- **the major medical need in this serious disease,**

the Committee considers that VYNDAQEL provides an important clinical added value (CAV II) in the management of adult patients with wild-type or hereditary transthyretin amyloid cardiomyopathy.