HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
19 FEBRUARY 2020

volanesorsen
WAYLIVRA 285 mg solution for injection in pre-filled syringe

First assessment

Key points

Favourable opinion for reimbursement only in patients with genetically confirmed familial chylomicronemia syndrome (FCS), in whom response to diet and triglyceride lowering therapy has been inadequate, and with a history of pancreatitis.

What therapeutic improvement?

Slight therapeutic improvement in the current treatment of FCS.

Role in the care pathwayWhat role for the product ?

The treatment of familial chylomicronemia syndrome is currently based on a life-long low-fat diet with 15 to 20 g of fat per day. The aim of this diet is to maintain triglyceride levels < 1000 mg/dL, in particular to limit the risk of occurrence of acute pancreatitis.

The fibrates and omega-3 used in other dyslipidemias have a marginal efficacy in patients with familial chylomicronemia syndrome.

Role of the medicinal product in the care pathway

WAYLIVRA is a first-line treatment in patients with genetically confirmed familial chylomicronemia syndrome (FCS), with a history of acute pancreatitis.

In patients with no history of acute pancreatitis, WAYLIVRA has no place in the care pathway.

Special recommendations

The decision to initiate WAYLIVRA treatment should be taken during multidisciplinary review meetings within a rare pancreatic diseases reference centre (PaRaDis) or, otherwise, a multidisciplinary review meeting organised by the NSFA (New French Atherosclerosis Society) given the specific population likely to benefit from this treatment in view of the efficacy data and safety profile, particularly with respect to the risk of thrombocytopenia (the treatment is accompanied by regular platelet count monitoring).

COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Familial chylomicronemia syndrome (FCS) is a rare and serious disease, impairing quality of life and with consequences in terms of morbidity and mortality, primarily related to the frequency and severity of acute pancreatitis.

◗ WAYLIVRA (volanesorsen) is a symptomatic treatment.

◗ The efficacy/adverse effects ratio is:

- moderate in patients with genetically confirmed familial chylomicronemia syndrome (FCS), with a history of acute pancreatitis, given the efficacy results on hypertriglyceridemia, exploratory results for the occurrence of acute pancreatitis events in patients with a history of acute pancreatitis, taking into account the fact that in the natural course of the disease, patients having already had pancreatitis are at higher risk of a further episode of acute pancreatitis, and the correlation suggested between lowering triglyceride levels and a reduced frequency of pancreatitis;
- inadequately established, given the absence of usable data for the occurrence of acute pancreatitis episodes in patients with no history of acute pancreatitis (1 patient in the study), in the absence of data with no history of acute pancreatitis, WAYLIVRA has no role in the treatment of genetically confirmed familial chylomicronemia syndrome (FCS).

◗ There are no therapeutic alternatives. Treatment is based solely on a life-long low-fat diet (10 to 20% of calorie intake).

◗ On the basis of data obtained in the clinical trial, namely an efficacy on hypertriglyceridemia, exploratory results concerning for the occurrence of acute pancreatitis events in patients with a history of acute pancreatitis, taking into account the fact that in the natural course of the disease, patients having already had pancreatitis are at higher risk of a further episode of acute pancreatitis, and given the correlation suggested between lowering triglyceride levels and a reduced frequency of pancreatitis and the safety data, the Committee considers that:

- WAYLIVRA (volanesorsen) is a first-line treatment in patients with genetically confirmed familial chylomicronemia syndrome (FCS), with a history of acute pancreatitis.
- with no history of acute pancreatitis, WAYLIVRA has no role in the treatment of genetically confirmed familial chylomicronemia syndrome (FCS).

Public health impact:

Considering:

- the seriousness of the disease,
- the FCS prevalence of 1/100,000 people,
- the unmet medical need,
- the absence of robust demonstration of efficacy on a relevant clinical endpoint (reduction of pancreatitis or other comorbidities associated with this major hypertriglyceridemia),
- the absence of an expected impact on quality of life, in the absence of data,
- the lack of expected impact on the organisation of care,
- the partial response to the identified need,

WAYLIVRA is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of WAYLIVRA is:

- **substantial in patients with genetically confirmed familial chylomicronemia syndrome (FCS), with a history of acute pancreatitis, in whom response to diet and triglyceride lowering therapy has been inadequate.**
- **insufficient to justify its funding by the French national health insurance system in patients with genetically confirmed familial chylomicronemia syndrome (FCS), with no**

history of acute pancreatitis, in whom response to diet and triglyceride lowering therapy has been inadequate.

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 patients with genetically confirmed familial chylomicronemia syndrome (FCS), with a history of acute pancreatitis, in whom response to diet and triglyceride lowering therapy has been inadequate, and at the MA dosages.

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 patients with genetically confirmed familial chylomicronemia syndrome (FCS), with no history of acute pancreatitis, in whom response to diet and triglyceride lowering therapy has been inadequate, and at the MA dosages.

Clinical Added Value

Patients with genetically confirmed FCS and with a history of pancreatitis

Considering:

- **the performance of a phase III, multicentre, double-blind, randomised, placebo-controlled superiority study,**
- **the demonstration of the efficacy of volanesorsen on the basis of a 94.1% reduction in fasting triglyceride levels at 3 months (interim biological endpoint), compared to placebo, with a demonstration of efficacy that persists after 6 and 12 months despite the effect size being lower over time,**
- **only exploratory results in a small number of patients with a history of acute pancreatitis, for the occurrence of acute pancreatitis episodes, a more relevant criterion,**
- **the unmet medical need in this rare disease, and taking into account the fact that in the natural course of the disease, patients having already had pancreatitis are at higher risk of a further episode of acute pancreatitis,**

the Committee considers that WAYLIVRA (volanesorsen) provides a minor clinical added value (CAV IV) in the current treatment of FCS.

Patients with FCS with no history of pancreatitis

Not applicable.