HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

16 SEPTEMBER 2020

The legally binding text is the original French opinion version

fremanezumab

AJOVY 225 mg solution for injection in pre-filled syringe

AJOVY 225 mg solution for injection in pre-filled pen

First assessment

Key points

Favourable opinion for reimbursement in adult patients with severe migraine who have at least 8 migraine days per month, with previous failure to at least two prophylactic treatments and without cardiovascular disease (patients having had clinically significant cardiovascular disease or vascular ischaemia, or thromboembolic event).

Unfavourable opinion for reimbursement in the rest of the MA indication.

What therapeutic improvement?

No clinical added value in the management of migraine.

Role in the care pathway?

The management of migraine is based on both the treatment of attacks and, if necessary, the initiation of long-term prophylactic treatment to reduce their frequency.

The medicinal products used in the treatment of attacks are non-specific migraine treatments (analgesics and nonsteroidal anti-inflammatories) and specific treatments (triptans, mainly and ergot derivatives).

The prevention of the onset of attacks will, first and foremost, take into consideration the identification and avoidance of trigger factors. Thereafter, the initiation of long-term treatment will depend, in particular, on the frequency and intensity of attacks and the resulting disability in terms of quality of life, as well as the prevention of any risk of acute medication overuse.

In the absence of contraindications, beta-blockers (propranolol and metoprolol), are the first-line treatments to be favoured. Treatment should be initiated as monotherapy, at low doses that are progressively increased. In the event of contraindication or intolerance to beta-blockers, topiramate is an alternative with a demonstrated efficacy. Another three drugs also have an MA for the prophylactic treatment of migraine (pizotifen, oxetorone, flunarizine) but are used as salvage therapies only due to their safety profile, in particular. Other drugs without a marketing authorisation for the prophylactic treatment of migraine are also cited in the national recommendations with a lower level of evidence of efficacy (grade B or C): anti-epileptic drugs (sodium valproate and divalproate, gabapentin), antidepressants (amitriptyline, venlafaxine), other beta-blockers (atenolol, nadolol, nebivolol, timolol), candesartan, naproxen sodium.

Erenumab (AIMOVIG), the first anti-CGRP monoclonal antibody assessed by the Committee in 2019, and galcanezumab (EMGALITY), the second anti-CGRP monoclonal antibody assessed in 2020, represent alternatives in patients with severe migraine who have at least 8 migraine days per month, with previous failure to at least two prophylactic treatments and without cardiovascular disease.

Alternative therapies, such as relaxation and cognitive and behavioural stress management therapies can also be used in some patients.

Role of the medicinal product in the care pathway

AJOVY (fremanezumab) is the third anti-CGRP monoclonal antibody to be assessed by the Committee and is a medicinal option in adult patients with severe migraine who have at least 8 migraine days per month, with previous failure to at least two prophylactic treatments and without cardiovascular disease (patients having had clinically significant cardiovascular disease or vascular ischaemia, or thromboembolic events). In other clinical situations, including patients with fewer than 8 migraine days per month, previously untreated or with previous failure to only one alternative, as well as patients with severe cardiovascular disease, AJOVY (fremanezumab) has no role in the care pathway.

As a reminder, of the three anti-CGRP antibodies, EMGALITY (galcanezumab) currently has the most robust quality of life data (ranked secondary endpoint) in the population concerned (patients with severe migraine who have at least 8 migraine days per month, with previous failure to at least two prophylactic treatments and without cardiovascular disease).

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Migraine is a chronic, disabling disease that, due to the frequency and severity of attacks, can cause a severe deterioration in quality of life.
◗ This is a preventive treatment for migraine attacks.
◗ Considering:
- the demonstrated efficacy with a moderate effect size and only versus placebo in episodic migraine and in chronic migraine, whereas studies versus active comparators could have been performed, particularly in the patients included with previous failure to less than two prophylactic treatments,
- the efficacy data observed in patients with previous failure to 2 to 4 prophylactic treatment classes, and,
- only short-term safety data and uncertainties with respect to long-term safety, in particular cardiological and immunological safety,
- exploratory quality of life data in patients with previous failure to 2 to 4 prophylactic treatment classes,

the efficacy/adverse effects ratio of AJOVY (fremanezumab) is moderate in adult patients with at least 8 migraine days per month, with previous failure to at least two prophylactic treatments and without cardiovascular disease.
In other clinical situations, including patients with fewer than 8 migraine days per month, previously untreated or with previous failure to only one alternative, as well as patients with severe cardiovascular disease, the efficacy/adverse effects ratio of AJOVY (fremanezumab) cannot be determined, due to a lack of data.
◗ There are alternatives indicated in the long-term prophylactic treatment of episodic migraine and chronic migraine.
◗ AJOVY (fremanezumab) is a medicinal option in adult patients with severe migraine who have at least 8 migraine days per month, with previous failure to at least two prophylactic treatments and without cardiovascular disease (patients having had clinically significant cardiovascular disease or vascular ischaemia, or thromboembolic events). In other clinical situations, including patients with fewer than 8 migraine days per month, previously untreated or with previous failure to only one alternative, as well as patients with severe cardiovascular disease, AJOVY (fremanezumab) has no role in the care pathway.

Public health impact

Considering:
- the seriousness of the disease,
- its prevalence,
- the identified partially met medical need,
- the superiority in terms of efficacy demonstrated only versus placebo as prophylactic treatment in episodic migraine and in chronic migraine, particularly in patients with more than 8 migraine days per month with previous failure to at least 2 prophylactic treatments, with a nonetheless moderate effect size,
- the lack of an impact on the patient's care and/or life pathway, in the absence of robust quality of life data or data relative to the organisation of care in patients with previous failure to 2 to 4 prophylactic treatments, for whom a specific need exists,
- the lack of additional response to the identified need,

AJOVY (fremanezumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of AJOVY (fremanezumab) is:

- **moderate only in adult patients with severe migraine who have at least 8 migraine days per month, with previous failure to at least two prophylactic treatments and without cardiovascular disease (patients having had clinically significant cardiovascular disease or vascular ischaemia, or thromboembolic event).**
- **insufficient to justify coverage through public funding in the other MA situations.**

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 only in patients with severe migraine who have at least 8 migraine days per month, with previous failure to at least two prophylactic treatments and without cardiovascular disease (patients having had clinically significant cardiovascular disease or vascular ischaemia, or thromboembolic events).

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 other patients falling within the scope of the MA indication.

- **Recommended reimbursement rate: 30%**

Clinical Added Value

Considering:
- **demonstration of the superiority of fremanezumab compared to placebo:**
  - **in episodic migraine with a moderate effect size on the primary outcome measure of variation in monthly migraine days (-1.3 to -1.5 days in patients with 9 migraine days per month at baseline),**
  - **in chronic migraine with a moderate effect size on the primary outcome measure of variation in monthly migraine days (-1.8 to -2.1 days in patients with 16 migraine days per month at baseline),**
  - **in episodic and chronic migraine in patients with previous failure to 2 to 4 prophylactic treatment classes with a moderate effect size on the primary outcome measure of variation in monthly migraine days (-3.1 to -3.5 days in patients with 14 migraine days per month at baseline),**
- **the availability of short-term safety data (maximum follow-up of 1 year) with uncertainties with respect to long-term safety, in particular in terms of cardiological and immunogenicity risks,**
- **only exploratory quality of life data in patients with previous failure to 2 to 4 prophylactic treatment classes in this condition that has a significant impact on quality of life,**

the Committee considers that AJOVY (fremanezumab) provides no clinical added value (CAV V) in adult patients with severe migraine who have at least 8 migraine days per month, with previous failure to at least two prophylactic treatments and without cardiovascular disease (patients having had clinically significant cardiovascular disease or vascular ischaemia, or thromboembolic event).