HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
30 MARCH 2022

The legally binding text is the original French opinion version

Clostridium Botulinum neurotoxin type A
XEOMIN 50 UNITS powder for solution for injection
XEOMIN 100 UNITS powder for solution for injection
XEOMIN 200 UNITS powder for solution for injection

New indication

Key points

Favourable opinion for reimbursement in the symptomatic treatment in adults of chronic sialorrhea due to neurological disorders associated with Parkinson's disease, traumatic brain injury or stroke only, in the event of intolerance to or failure of anticholinergic agents.

Unfavourable opinion for reimbursement in the other clinical situations of the MA.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

The management of chronic sialorrhea in patients with neurological disorders should be initiated in accordance with a multidisciplinary approach, including behavioural therapies and oral motor physiotherapy as first-line treatments.

If these treatments fail, pharmacological options exist. However, there is little robust data enabling recommendations to be established and to date, all the medicinal products are used off-label.

According to expert opinion, anticholinergic agents (atropine as sublingual drops, scopolamine patches) are used as first-line treatments (off-label). **However, this class of medicinal products requires monitoring in the elderly, in particular patients with Parkinson's disease, due to the risk of cognitive deterioration.**

Surgery for chronic sialorrhea (ablation of submaxillary and sublingual glands) and radiotherapy of the salivary glands are last-resort options.

Role of XEOMIN (botulinum toxin type A) in the care pathway:

The proprietary medicinal product XEOMIN is a second-line medicinal treatment for chronic sialorrhea in patients with neurological disorders associated with Parkinson's disease, traumatic brain injury or stroke, in the event of intolerance to or failure of anticholinergic agents.

The Committee highlights the fact that, in accordance with the SPC, XEOMIN should only be administered by an appropriately qualified healthcare practitioner with expertise in the use of botulinum toxin type A.

In the absence of data, XEOMIN has no role in the treatment of chronic sialorrhea associated with other neurological disorders, in particular, in patients with progressive neurodegenerative diseases, such as ALS, who are liable to present swallowing difficulties in the context of bulbar or pseudobulbar dysfunction as the condition worsens.

Special recommendations

The Committee highlights the fact that, in accordance with the SPC, the recommended dose per treatment session is 100 units and this maximum dose should not be exceeded (with treatment intervals of more than 16 weeks).

Therefore the vial of XEOMIN (botulinum toxin type A) 200 units powder for solution for injection is not suitable for the prescribing conditions in this indication.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Chronic sialorrhea is an incapacitating condition that can lead to a marked deterioration in quality of life and sometimes serious complications.

◗ XEOMIN (botulinum toxin type A) medicinal products are a symptomatic treatment.

◗ Considering the superiority of botulinum toxin type A compared to placebo, demonstrated only:
- in the short term (co-primary efficacy endpoints at 4 weeks) and with a moderate effect size on two co-primary endpoints of debatable relevance,
- in patients predominantly with Parkinson's disease, and a smaller proportion of patients with head injury or stroke,

the efficacy/adverse effects ratio of XEOMIN is:
- moderate in patients predominantly with Parkinson's disease, and a smaller proportion of patients with head injury or stroke,
- not established in the other clinical situations of the MA, in particular patients with ALS.

◗ There are no medicinal alternatives for the symptomatic treatment of chronic sialorrhea in adults due to neurological disorders, as second-line treatment, in the event of intolerance to or failure of anticholinergic agents.
In first-line treatment, there are alternatives, but these do not have an MA in this indication (see paragraph 05 "clinically relevant comparators").

◗ XEOMIN (botulinum toxin type A) is a second-line treatment for chronic sialorrhea in adult patients due to neurological disorders such as Parkinson's disease, traumatic brain injury or stroke, in the event of intolerance to or failure of anticholinergic agents.
In other clinical situations, XEOMIN has no role in the care pathway.

Public health impact

Considering:
- the seriousness of the disease and its prevalence,
- the medical need very partially met by medicinal products used off-label,
- the lack of additional response to the identified need, with the absence of any demonstrated additional impact on morbidity and mortality and quality of life,
- the lack of data on a potential additional impact on the organisation of care,

XEOMIN (botulinum toxin type A) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of XEOMIN is:
- **moderate in the indication for the symptomatic treatment in adults of chronic sialorrhea due to neurological disorders associated with Parkinson's disease, traumatic brain injury or stroke only, in the event of intolerance to or failure of anticholinergic agents.**
- **insufficient in the other clinical situations of the MA.**

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication for the symptomatic treatment in adults of chronic sialorrhea due to neurological disorders associated with Parkinson's disease, traumatic brain injury or stroke, in the event of intolerance to or failure of anticholinergic agents, and at the MA dosages.

The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the other clinical situations of the MA.

Clinical Added Value

In adults with chronic sialorrhea due to neurological disorders associated with Parkinson's disease, traumatic brain injury or stroke, in the event of intolerance to or failure of anticholinergic agents,

considering:

- demonstration of the superiority of botulinum toxin type A versus placebo in a randomised, double-blind study, in the symptomatic treatment of chronic sialorrhea in patients with neurological disorders due to Parkinson's disease, traumatic brain injury or stroke, in terms of change in unstimulated salivary flow rate and improvement in the global impression of change scale (co-primary endpoints), with a moderate effect size,
- the debatable clinical relevance of the co-primary endpoints, for which the reproducibility of measurement has not been verified,
- the absence of long-term safety data, in particular in patients liable to present dysphagia or swallowing difficulties as their condition worsens,
- and despite the need for authorised medicinal products having demonstrated their efficacy, in view of the current strategy based on anticholinergic drugs prescribed off-label as first-line treatment in adults,

the Committee considers that XEOMIN provides no clinical added value (CAV V) in the care pathway for the treatment of adult patients with chronic sialorrhea.