**SUMMARY**

zilucoplan

# ZILBRYSQ 16.6 mg, 23 mg and 32.4 mg

**solution for injection in pre-filled syringe**

Initial inclusion

**Original French opinion adopted by the Transparency Committee on 27 March 2024**

**The legally binding text is the original French opinion version**

## Summary of opinion

Favourable opinion for reimbursement only “as an add-on to standard therapy, including first-line immunosuppressants, for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive, who remain symptomatic.”

Unfavourable opinion for reimbursement in the other situations included in the MA indication.

# Transparency Committee’s conclusions

## Clinical Benefit

- Myasthenia is an incapacitating, rare, serious autoimmune disease causing fluctuating muscle weakness and excessive fatigability, which can impair patients’ quality of life and autonomy. Severe forms may progress towards life-threatening myasthenic crises.
- The proprietary medicinal product ZILBRYSQ (zilucoplan) as an add-on to standard therapy, including first-line immunosuppressants, is a curative disease-modifying treatment.
- Considering:
  - evidence of the superiority of zilucoplan compared to placebo for the primary endpoint of change from baseline to week 12 in MG-ADL score (primary endpoint), with a mean difference (SD) of -2.09 (0.58) points),
  - in a context in which the majority of patients were receiving antimyasthenic treatments at baseline and then concomitantly with zilucoplan (anticholinesterases (96.6%), prednisone (85.6%), IgIV or EP (69.0%), azathioprine (40.2%), mycophenolate (32.8%), ciclosporin (12.1%) and tacrolimus (11.5%)), without the median number of previous treatments being specified,

- the safety profile reported in the studies, consistent with that of other C5 complement inhibitors, and with uncertainties in the long term,

the efficacy/adverse effects ratio is:

- high as an add-on to standard therapy, including first-line immunosuppressants, for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive, who remain symptomatic.
- not established in the other clinical situations of the MA due to a lack of data.

➔ This is a first-line treatment as an add-on to standard therapy, including first-line immunosuppressants, for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive, who remain symptomatic despite well managed treatment.

However, within the scope included in the MA but not selected for reimbursement, ZILBRYSQ (zilucoplan) has no role in such a situation.

### ➔ Public health benefit

Considering:

- the seriousness of the disease and its low prevalence,
- the partially met medical need,
- the partial response to the identified need, with:
  - evidence of an additional impact on morbidity and quality of life only in the short term versus placebo,
  - the lack of evidence of an additional impact on long-term morbidity and mortality in view of the limited data available,
- the lack of evidence of an additional impact on the organisation of care and the patient's care and life pathway,

ZILBRYSQ (zilucoplan) is unlikely to have an additional impact on public health.

**Considering all these elements, the Committee deems that the clinical benefit of ZILBRYSQ (zilucoplan) is:**

- **substantial only as an add-on to standard therapy, including first-line immunosuppressants, for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive, who remain symptomatic,**
- **insufficient to justify public funding in the other clinical situations of the MA.**

**The Committee issues the following opinions:**

- **favourable opinion for inclusion of ZILBRYSQ (zilucoplan) in both the list of covered drugs for inpatients and the list of covered drugs for outpatients approved for use only within the scope retained and at the MA dosages.**
- **unfavourable opinion for inclusion of ZILBRYSQ (zilucoplan) in both the list of covered drugs for inpatients and the list of covered drugs for outpatients approved for use in the other clinical situations of the MA.**

### ➔ Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%

## Clinical Added Value

**Considering:**

- **evidence of the superiority of zilucoplan compared to placebo:**
  - **in terms of the change from baseline to week 12 in MG-ADL score (primary end-point), with a mean change (SD) of -2.09 (0.58) points (95% CI [-3.24; -0.95]); (p<0.001),**
  - **on the clinical ranked secondary endpoints of disease severity assessed at week 12 (QMG and MGC scores and percentage of clinical responders),**
  - **in terms of quality of life measured using the specific MG-QOL15r scale, with a difference in mean change of -2.5 points (95% CI [-4.45; -0.54], p=0.013) out of 30 points,**

**but in view of:**

- **comparative efficacy data limited to the short term (12 weeks),**
- **the safety profile reported in the studies, consistent with that of other C5 complement inhibitors, and with uncertainties in the long term,**
- **the lack of comparison versus rituximab or eculizumab despite the fact that this would have been possible; as well as the absence of comparison versus efgartigimod alfa or ravulizumab due to their concomitant development,**

**the Committee deems that, like ULTOMIRIS (ravulizumab) and VYVGART (efgartigimod alfa), ZILBRYSQ 40 mg/mL (zilucoplan) solution for injection in pre-filled syringe, as an add-on to standard therapy, including first-line immunosuppressants, provides a minor clinical added value (CAV IV) in the care pathway for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive, who remain symptomatic, excluding rituximab and SOLIRIS [eculizumab].**