19 January 2026
EMA/9533/2026
Committee for Medicinal Products for Human Use (CHMP)

Concept paper on the need of a guideline on clinical investigation of medicinal products in the treatment of Myasthenia Gravis

Agreed by CNS Working Party	25 September 2025
Adopted by CHMP for release for consultation	19 January 2026
Start of public consultation	13 February 2026
End of consultation (deadline for comments)	30 August 2026

Comments should be provided using this EUsurvey form. For any technical issues, please contact the EUSurvey Support.

Keywords	Myasthenia Gravis, acetylcholine receptor (AChR), muscle-specific tyrosine kinase (MuSK), low-density lipoprotein receptor-related protein 4 (LRP4), Guideline, Confirmatory trials

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

1. Introduction

Neuromuscular junction (NMJ) disorders represent a heterogeneous group of acquired or congenital disorders characterized by an impaired signal transmission between motor neurons and skeletal muscle fibers, leading to muscle weakness and fatigability as the main clinical characteristics.

The most common NMJ disorder is myasthenia gravis (MG), a chronic disorder characterized by fluctuating weakness and fatigability of skeletal muscles due to a humoral immune response targeting key components of the post-synaptic membrane. Myasthenia gravis is an uncommon disorder, with a prevalence range of 150 to 200 per million in general population (Dresser L et al, J Clin Med 2021;10(11):2235. The exact prevalence of juvenile MG (i.e. MG with onset before age 18) is unknown but it may represent approximately 10-15% of all MG cases in Europe (Orphanet). In the majority of the patients, antibodies targeting the nicotinic acetylcholine receptor (AChR), resulting in decreased number of available AChR, are identified. In a subset of patients, antibodies target muscle-specific tyrosine kinase (MuSK) or low-density lipoprotein receptor-related protein 4 (LRP4), which are involved in the maintenance and clustering of AChRs. For a minority of the patients, none of the three antibodies are identified. The therapeutic management of MG includes symptomatic treatments (i.e. acetylcholinesterase (AChE) inhibitors) and immunotherapy aiming to prevent new exacerbations or to rapidly abolish severe myasthenic crisis.

2. Problem statement

There is no guidance on clinical investigation of medicinal products in the treatment of Myasthenia Gravis. Although a few medicinal products have been authorised for the treatment of MG, drug development in this area continues actively and represents a rapidly evolving field. This dynamic landscape justifies the need for an up-to-date and comprehensive regulatory guidance.

Furthermore, the currently authorised medicinal products are primarily indicated for the treatment of generalized MG (i.e. MG with weakness affecting muscles other than the extraocular muscles) in adult patients with antibodies targeting AChR. The challenges in the development of medicinal products for paediatric patients and for those who are seronegative for AChR antibodies are recognised. The future guidance will specifically address the drug development in these underrepresented populations as well.

Guidance on the clinical investigation of medicinal products in the treatment of other NMJ disorders such as Lambert-Eaton Myasthenic Syndrome and congenital myasthenic syndromes are not in the scope of the guidance.

Guidance on the clinical investigation of body plasma exchange, thymectomy and immunoglobulins as therapeutic strategies for MG are also not in scope.

3. Discussion (on the problem statement)

The following aspects will be discussed in the guidance document:

- Specific considerations when developing products for the treatment of Myasthenia gravis: general strategy including main goals of treatment of myasthenia gravis, symptomatic treatments and disease-modifying therapies.
- Patient characteristics and selection of population: ocular myasthenia gravis (i.e. MG limited to extraocular muscles), generalized myasthenia gravis, disease subtypes based on serostatus (i.e. myasthenia gravis with antibodies targeting the AChR; myasthenia gravis with antibodies

targeting MuSK; myasthenia gravis with antibodies targeting LRP4; seronegative MG (i.e. MG without antibodies targeting AChR, MuSK or LRP4).

- Design of exploratory and confirmatory trials:
    - Tools for the outcome assessment: general issues and specific aspects in connection to tools for evaluating clinical severity, functional impact and quality of life. Role of anti-AChR / anti-MuSK / anti-LRP4 titers.
    - Exploratory trials: general aspects and objectives.
    - Confirmatory trials: trial design features for symptomatic treatments and for medicinal products targeting the underlying disease pathophysiological mechanism(s). including efficacy endpoints, duration and aligment to the estimand framework
    - Requirements for monotherapy and add-on trials.
- Studies in special populations: juvenile myasthenia gravis, refractory generalized myasthenia gravis, myasthenia gravis in the elderly.
- Safety evaluation.

4. Recommendation

The Central Nervous System Working Party (CNSWP) recommends drafting a guideline on clinical investigation of medicinal products in the treatment of Myasthenia Gravis taking into account the issues identified above.

5. Proposed timetable

It is planned to release for consultation a draft Committee for Medicinal products for Human Use (CHMP) guidance document not later than Q4 2026.

6. Resource requirements for preparation

The preparation of this guideline will involve the CNSWP. Drafts of the document will be discussed as needed with the CHMP, the Scientific Advice Working Party (SAWP), the Paediatric Committee (PDCO) the Methodology Working Party (MWP), and other relevant working parties and committees.

7. Impact assessment (anticipated)

It is aimed that this guideline will be helpful to attain high-level standardisation of the clinical development plan for medicinal products for the treatment of myasthenia gravis and encourage and guide developments for medicinal products for subpopulations with fewer therapeutic options.

8. Interested parties

The interested parties in the guidance document include learned societies and academia – The European Reference Network for Rare Neuromuscular Disorders (ERN EURO-NMD), European Academy of Neurology (EAN), European Paediatric Neurology Society (EPNS), The International Society for CNS Clinical Trials and Methodology (ISCTM), The European College of Neuropsychopharmacology (ECNP), pharmaceutical industry (e.g. EFPIA and others) and other regulatory agencies.

9. References to literature, guidelines, etc.

Procedure for European Union guidelines and related documents within the pharmaceutical legislative framework (EMEA/P/24143/2004): https://www.ema.europa.eu/en/documents/scientific-guideline/procedure-european-union-guidelines-and-related-documents-within-pharmaceutical-legislative-framework_en.pdf

[See http://publications.europa.eu/code/en/en-250304.htm for guidance on referencing published information.]