Corona Virus Disease 2019 (COVID-19) is a new illness caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Symptoms are variable but typically include fever, cough, respiratory symptoms, diarrhea, reduction of smell and taste sensation. Severity ranges from mild to severe and the virus may lead to pneumonia, acute respiratory distress syndrome and death, in some patients. Nearly every country in the world has been affected by this virus and is currently defined as a pandemic, by the World Health Organization. There are no known proven therapies for treating this virus and no vaccine to prevent the infection at this time.

No data currently exist on how COVID-19 affects people with myasthenia gravis (MG)/LEMS or patients with other diseases on immunosuppressive therapies. However, because most patients with MG are on immunosuppressive or immunomodulatory therapies and may also have respiratory muscle weakness, there is a theoretical concern that MG/LEMS patients may be at higher risk of contracting the infection or experiencing severe manifestations of COVID-19.

Individuals with MG and LEMS have asked for guidance on the use of therapies during the COVID-19 pandemic. There are numerous recommendations circulating that attempt to provide clarity and guidance, however, differences among the recommendations have created confusion. Immunotherapy decision making varies significantly from country to country, ranging from highly provider-directed to a collaborative decision-making model. The advice below was developed by a panel of MG experts. We recognize that peer reviewed published literature regarding COVID-19 in MG or in immunocompromised patients to date is lacking.

The MG expert panel* suggests that therapy decisions should be individualized and made collaboratively between the person with MG and his/her healthcare provider. Based on their expert advice, it is suggested that:

1. People with MG should follow the corresponding national guidelines and any additional recommendations for people at risk for serious illnesses from COVID-19.

Patients on existing therapies for MG/LEMS

2. MG/LEMS patients should continue their current treatment and are advised not to stop any existing medications, unless specifically discussed and approved by their healthcare provider.

3. There is no scientific evidence to suggest that symptomatic therapies like Pyridostigmine or 3,4 Diaminopyridine increases the risk of infection and should not be discontinued unless there are other clinical reasons to do so.
4. Even though strong evidence is lacking, it is recommended that MG patients already on immunosuppressive medications\textsuperscript{2,3} should practice extra-vigilant social distancing, including avoiding public gatherings/crowds, avoiding crowded public transport and where possible use alternatives to face-to-face consultations (eg: telemedicine), if clinically appropriate.

5. When altering or stopping an existing immunosuppressive therapy\textsuperscript{3} that carries a potential for increased disease activity and/or MG exacerbation or crisis, people with MG and their MG healthcare providers should consider specific risks (e.g., age, comorbid health conditions, location) and benefits.

**Infusion therapies, intravenous immunoglobulins and plasma exchange**

6. Certain infusion therapies in MG may require travel to hospitals or infusion centers and we strongly recommend that this decision be made based on regional incidence of COVID-19 and risk/benefit of the therapy for the individual patient. The healthcare provider should be able to give region-specific advice, and where possible consider switching to home infusion.

7. There is currently no evidence to suggest that intravenous immunoglobulin (IVIG\textsuperscript{4}) or therapeutic plasma exchange (PLEX or TPE) carry any additional risk in catching COVID-19. However, the use of IVIG has to be based on individual patient need and indiscriminate use should be avoided. In general, PLEX and IVIG should be reserved for patients with acute exacerbations. However the panel recognize that there are some patients receiving these as maintenance therapy, who should continue these, but extra precautions may need to be taken because of the need for travel to and from a healthcare facility.

8. There is currently no evidence to support that inhibition of complement using the monoclonal antibody (mAb), eculizumab increases susceptibility to COVID infection or its outcome.

**Blood tests for existing therapies**

9. Weigh risk and benefits of routine blood monitoring at this time. Some of the MG therapies require frequent blood work monitoring and decisions regarding the ongoing need for testing, which requires patient to leave their home, should be individualized and based on regional COVID-19 incidence.

**What to consider when starting an immune therapy in patients with MG/LEMS now?**

10. Before starting a B-cell depleting therapy\textsuperscript{2} (e.g., rituximab), healthcare providers should consider the risk of worsening myasthenia or crisis and the risk of catching the viral infection. It may be advisable to delay initiation of cell depleting therapies, until the peak of the outbreak is over in their region. However, the risk of not starting the cell depleting therapy in occasional patients may outweigh the risk of severe COVID-19 infection and this has to be discussed with the patient in detail.
Advice for patients in ongoing clinical trials

11. Currently there are many clinical trials in progress for MG and we strongly recommend that any decision regarding ongoing need for in-person evaluations and treatments under the clinical trial be based with consideration for patients’ best interest. At present, there is no scientific evidence to suggest that complement inhibitors or neonatal Fc Receptor blockers (FcRn) may increase the risk of catching the viral infection, but the panel recommends extra precautions (as in point 4 above), to minimize the risk. In clinical trials this also has to be discussed and approved by the trial sponsor, institutional review board and medical monitor.

Is there reasonable evidence for medications treating COVID-19?

12. Various medications have been mentioned in the news and social media as being useful to treat COVID-19 (e.g., choloroquin, azithromycin, anti-virals etc), however, these are not proven to be effective or studied systematically at this time. Patients should be aware that some of these medications can potentially worsen MG and should avoid using these without specific medical approval. If the evidence changes and suggests there is benefit for treating COVID-19, these treatments should be used under strict medical supervision weighing the risks and benefits in an individual patient.

Should MG or LEMS patients go for vaccinations?

13. Vaccinations can protect for a variety of infections/pathogens. However, in the current situation it is recommended to only use dead vaccines in this patient group. For COVID-19, there is no vaccine available currently.

What if patients have already contracted COVID-19?

14. Most patients who develop COVID-19 have mild disease and should continue the current best practice standard of care for MG/LEMS. There might be a need to increase the dose of corticosteroids as in standard infection/stress protocol. However, if the symptoms are severe (requiring hospitalization) it may be worthwhile considering pausing current strong immunosuppression temporarily, especially if there is additional super added infections/sepsis. Immune depleting agents should not be given under such condition, milder immune-suppressive agents (azathioprine, mycophenolate) should probably be continued, since effects of dosing are longer lasting, wash out takes longer and rebuilding of effects take several months.

15. Most decisions for treatment escalation have to be individualized based on the relative severity of COVID-19 and MG.
*These recommendations have been prepared and endorsed by an international working group of MG experts in response to COVID-19 pandemic.

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Decisions regarding immunotherapy use should be individualized and made by the person with MG and his/her healthcare provider. For additional questions, we encourage that patients contact their MG provider.

**We are continuing to monitor this quickly evolving situation and these recommendations may be modified as data becomes available.**

1. This list is not exhaustive, but only representative – please check for up to date guidance in each country/region:
   
   a. [CDC guidelines](#)
   b. [European CDC guidelines](#)
   c. [UK guidelines](#)
   d. [Australia](#)
   e. [Japan](#)

2. B-cell depleting therapies include: rituximab, ocrelizumab

3. Immunotherapies which on withdrawal carries potentially severe increase in disease activity, relapse, and exacerbation/crisis include: corticosteroids, azathioprine, mycophenolate mofetil, methotrexate, cyclosporine, tacrolimus and others.

4. Immunodulatory therapies: IVIG/SCIG (intravenous immunoglobulin, subcutaneous immunoglobulin)