Association of British Neurologists (ABN) autoimmune myasthenia gravis management guidelines (2025 update)

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ABSTRACT

The 2025 update of the Association of British Neurologists guidelines for the management of autoimmune myasthenia gravis (MG) emphasises several points that are distinct from the 2015 guidelines based on recent research and publications. The main differences from the previous guidelines are: (1) The recommendation to prescribe daily steroids rather than the alternate day regimen is now standard practice. (2) There is a clear emphasis on the beneficial effects of early thymectomy. (3) Randomised controlled trial evidence now supports early use of rituximab (within 1 year of generalised disease onset), although the evidence is less robust, but still likely to be useful, in established treatment-refractory MG. (4) Finally, several clinical trials have been published for newer targeted therapies in MG, predominantly those that inhibit the complement and neonatal Fc gamma receptor pathways, the roles of which are being slowly established especially in patients unresponsive to conventional therapy.

INTRODUCTION

The previous Association of British Neurologists (ABN) myasthenia gravis (MG) guidelines, published in 2015,[1] were based on evidence where available, and expert opinion.[2] Several recent MG guidelines have been published by other national MG societies.[3–5] It is therefore appropriate to revise the ABN MG guidelines to reflect current practice and review future opportunities.[I, II] Therefore, where the evidence base is too limited, where there is a range of treatment options or when the disease is difficult to manage, the guidelines direct the managing neurologist to seek the advice of a neurologist with a specialist interest in MG. (See Acknowledgements and Author note for how the guidelines were developed).

MG symptoms are variable, so patients are best managed as far as possible by using a multidisciplinary team (MDT) approach. An MG specialist nurse or neuromuscular advisor/nurse, if available, can benefit patient care. All patients should be given contact details of the appropriate clinical team members in case of clinical deterioration and should be directed to literature (including drugs to avoid, driving licence regulations, etc), produced by reputable patient associations, for example, *Myaware* (www.myaware.org)[III] in the UK (superscripts (in roman numerals) correspond to the numbers in online supplemental table 1).

These guidelines can only offer suggestions on how to manage common clinical scenarios. This document is intended to offer guidance to general neurologists—it can be followed closely or used flexibly, depending on the level of clinical experience and the patient circumstances. It also gives brief information on newer therapies that are likely to be used in the specialist setting. Figure 1 shows a suggested algorithm.

The UK Medicines and Healthcare products Regulatory Agency (MHRA) regularly updates advice on the use of a range of medications. Please refer to contemporaneous advice on the uses and interactions of the medications discussed in these guidelines. This guideline does not cover related conditions such as

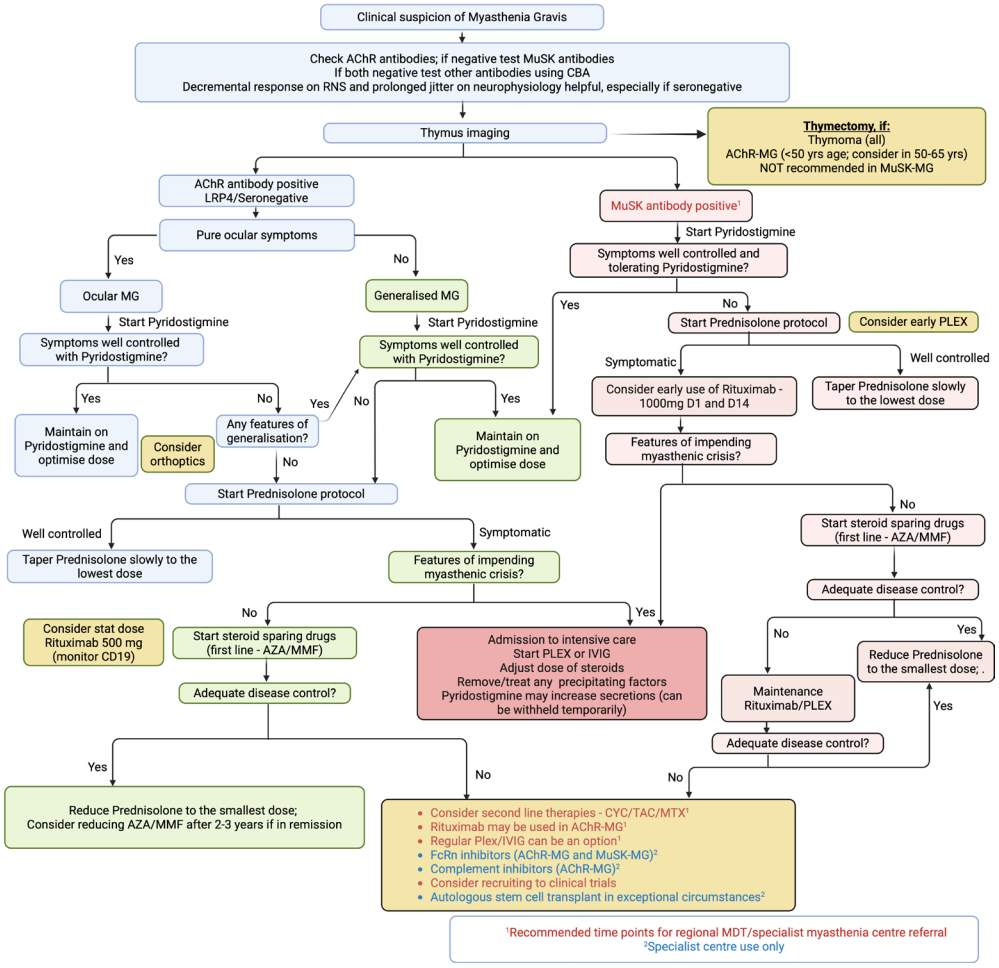

Figure 1 Suggested algorithm for management of myasthenia gravis. AChR, acetylcholine receptor; AZA, azathioprine; CBA, cell-based assay; CYC, ciclosporin; FcRn, neonatal Fc gamma receptor; IVIG, intravenous immunoglobulin; LRP4, lipoprotein receptor related protein 4; MDT, multidisciplinary team; MG, myasthenia gravis; MMF, mycophenolate mofetil; MTX, methotrexate; MuSK, muscle-specific tyrosine kinase; PLEX, plasma exchange; RNS, repetitive nerve stimulation; TAC, tacrolimus.

Lambert-Eaton myasthenic syndrome or congenital myasthenic syndromes.

INITIAL ASSESSMENT, INVESTIGATIONS AND DIAGNOSIS

The first presentation of myasthenia is often fatiguable weakness presenting usually with ptosis and diplopia. The symptoms may remain restricted to the ocular[IV] muscles or can involve other muscle groups including bulbar muscles. If MG is strongly suspected but antibodies are negative, please consider other possibilities like a congenital myasthenic syndrome caused by genetic mutations, or a muscle disorder (eg, mitochondrial disorders, oculopharyngeal muscular dystrophy). A detailed review of the clinical features and differential diagnoses is described in various other articles and is beyond the scope of these management guidelines.[6–8] Even though tests can help to make the diagnosis, they should complement clinical acumen rather than replace it.

Diagnostic tests

- Acetylcholine receptor (AChR) antibody testing: This is a first-line investigation for non-urgent patients. Radioimmunoassay and cell-based assays have better sensitivity and specificity than ELISA and should be used when practically possible.[9]
- If the AChR antibodies are negative, check for muscle-specific tyrosine kinase (MuSK) antibodies (many laboratories may test both simultaneously using a fixed cell-based assay).
- Thyroid function should be performed in all patients.[V]
- If standard antibody tests are negative and there is a high index of suspicion, or suspicion of false positivity, consider sending serum to a specialist neuroimmunology laboratory (eg, Oxford, UK), for testing using the high-sensitivity MG antibody cell-based assay panel. This includes clustered AChR, clustered MuSK and lipoprotein receptor-related protein 4.
- Various other antibodies such as striated muscle, titin, are unlikely to be diagnostically helpful.

- It is recommended to diagnose seronegative MG only after all the above tests have been completed (including cell-based assays).
- Neurophysiology can confirm the diagnosis and should always be done in patients suspected to have MG but with no detectable antibodies. Neurophysiology should be performed by a practitioner with experience of MG. Repetitive nerve stimulation is the initial test and single-fibre electromyogram (SFEMG) should be considered if appropriate expertise is available. To improve the sensitivity of the test, it is recommended to withhold pyridostigmine for at least 12 hours before testing. Neurophysiological tests for neuromuscular junction disorders can occasionally be abnormal in other conditions such as denervation and myopathies. Symptomatic muscles should be tested; *a normal single-fibre EMG in a weak muscle would be extremely unusual in a neuromuscular junction disorder*.[10]
- Patients with diplopia and ptosis but who have negative serology and neurophysiology should have a contrast-enhanced MR brain and orbits (and MR angiography where appropriate) to exclude structural intracranial or orbital disease.
- All patients with suspected MG, irrespective of distribution (ocular/generalised) or serology (seropositive/negative), should have imaging of the thymus to rule out a thymoma.[VI] The modality (CT or MRI) is best decided locally, based on radiologists' expertise. Chest X-ray alone is insufficient. (See section on "role of thymectomy".)
- If tests are negative and MG is still suspected, or if suspecting a congenital myasthenia syndrome, refer to a clinician with experience in managing myasthenia (often referred to in this document as an 'MG specialist').
- The edrophonium/Tensilon test is no longer recommended as it can have significant complications including bradycardia and vomiting. In cases of diagnostic doubt, refer to a specialist clinic or centre.
- The ice-pack test is a simple clinical test with high sensitivity and specificity for the diagnosis of MG. Furthermore, Cogan's eyelid twitch phenomenon may be present in the ptotic lid.[6]
- With the increasing use of immune checkpoint inhibitors, there is a small risk of developing a neuromuscular transmission defect or MG, often associated with myositis and myocarditis—the management approach is very similar to primary autoimmune MG. Although often more aggressive due to the high mortality, it is best to follow appropriate guidelines where available and ideally to discuss with a regional MG specialist. An MDT guideline is currently being developed.
- Various scores are useful in assessing disease severity (see box 1).[VII]

Box 1 Assessment of disease severity

- Antibody levels are not helpful in monitoring disease severity.
- Myasthenia gravis-activities of daily living (MG-ADL) and MG composite scores can help in objectively assessing disease severity and treatment response. In clinical trials, a 2-point change in MG-ADL and a 3-point change in MG composite scores are considered clinically significant.
- MG-ADL score of 0–1 is often referred to as minimal symptom expression and is considered a desirable goal in managing MG.
- There are other ocular MG-specific scores, but these are still not widely used in routine clinical practice.

TREATMENT SETTINGS

Choose inpatient care:

For patients with significant/early bulbar symptoms, low forced vital capacity (less than 30 mL/kg), low single breath count (less than 25 per minute) or symptoms of suspected respiratory insufficiency, significant limb weakness or rapidly progressive deterioration.[11 12]

Choose out-patient care:

For patients with ocular symptoms, mild-to-moderate limb weakness (not limiting independent function) or mild bulbar symptoms.

TREATMENT

If there is a strong clinical suspicion, treatment can be started before the antibody results are back.

Initial management

- Approximately 50% of patients with ocular MG develop generalised MG within 2 years and up to 75% within 3 years of disease onset, especially in the AChR seropositive group (AChR-MG).
- Start pyridostigmine following the protocol (see box 2 'pyridostigmine protocol'[VIII]) in ocular and mild-to-moderate generalised MG.
- In patients with AChR-MG and aged under 65 years: consider thymectomy at presentation[IX].
- In symptomatic patients with clear signs of extraocular muscle weakness despite taking maximal tolerated doses of pyridostigmine for 4–6 weeks (or earlier if there is significant peripheral weakness), then start prednisolone: see box 3: 'prednisolone protocol (outpatients)'. For severe bulbar weakness, see "emergency inpatient management".
- Titrate steroids down as per protocol. If a relapse occurs on a prednisolone dose of 7 mg/day or greater, consider non-steroidal immunosuppressive therapy.[X] This may also be used for patients with steroid-related side effects on low-dose prednisolone. See section on "Immunosuppression".

Box 2 Pyridostigmine protocol

Initiation:

- Start initially 30 mg (half tablet) three or four times a day (TDS-QDS); titrate slowly by 30 mg every 2-4 days to find the lowest effective dose.
- Then titrate if necessary up to 60 mg (one tablet) QDS over 5–10 days and experiment with timing.
- Increase to 360 mg/day in divided doses if required. Doses above 360 mg/day rarely produce additional benefit. The duration of action of each dose varies, and some patients require five or six divided daily doses. Requirements of pyridostigmine over 300 mg a day should prompt a quick review and introduction/escalation of additional treatment (typically prednisolone). Refer to or discuss with a myasthenia gravis (MG) specialist clinic rather than relying on escalating doses of pyridostigmine.

Take care in the elderly or those with significant cardiac history, asthma or patients who take beta-blockers (which should be cautiously used in MG), or when there is an electrolyte imbalance. Check ECG before starting pyridostigmine.

Management of cholinergic side effects (diarrhoea, muscle cramps): propantheline, mebeverine, loperamide.

Withdrawal:

- If pyridostigmine monotherapy: use lowest effective dose.
- If asymptomatic only after introducing prednisolone/other immunosuppression, taper slowly at 30–60 mg per week, until withdrawn, or until identifying the lowest effective dose. Some patients may choose to remain on pyridostigmine or use it as and when required.

Note: Patients with muscle-specific tyrosine kinase (MuSK) antibodies (MuSK-MG) may not respond as well to or tolerate pyridostigmine

Box 3 Prednisolone protocol (outpatients)

Initiation:

- Start 5–10 mg daily[XI] and increase by 5 mg every 3–5 days until symptoms improve with an initial target dose of 20 mg/day for ocular MG or 30 mg/day for generalised MG.
- Sometimes a further titration is required to a maximum dose of 0.5 mg/kg/day (not more than 30 mg/day) for ocular MG, and up to 1 mg/kg (not more than 60 mg/day) for generalised MG; such patients are best discussed with an MG specialist.
- Refer to local guidelines for bone and gastric protection and pneumocystis pneumonia prophylaxis.
- It is recommended to check HbA1c and lipid profile before starting, and periodically during treatment, instituting appropriate management as necessary.

Maintenance dosing:

Once a patient with MG has achieved remission, consider withdrawing pyridostigmine to ensure the patient is in remission. Prednisolone should be continued for 4 weeks at the dose that achieved remission and then titrated down slowly seeking the lowest effective dose. The optimal titration regimen has not been formally established but an example of a reasonable regimen is outlined below. This may need to be modified depending on comorbidities and steroid side effects. Patients should be advised that they should notify their neurology team as soon as they start to notice a recurrence in their MG symptoms as the dose is reduced.

- After 4 weeks of minimal effective dose of prednisolone, reduce the daily dose by 5 mg every 2–4 weeks down to 20 mg per day.
- Then reduce the daily dose by 2–2.5 mg every 2–4 weeks down to 10 mg per day.
- Once the dose is below 10 mg per day, reduce by 1 mg/month, aiming for a maintenance dose of 5 mg/day if possible.
- It is sometimes possible to wean prednisolone altogether, but this requires careful monitoring, and the patient should be counselled appropriately.
- A steroid dose requirement of 7 mg/day or more is an indication to introduce additional non-steroidal immunosuppression, and to consider steroid side effects and other comorbidities.
- Early introduction of steroid-sparing medication (eg, azathioprine, mycophenolate mofetil, methotrexate or calcineurin inhibitors) should be considered in patients with significant steroid side effects and/or those with significant comorbidities such as diabetes mellitus or obesity.
- Should myasthenic symptoms recur, follow guidance for myasthenic relapse (see section on 'Assessment and management of the relapsing patient with myasthenia').
- Non-specific fatigue is not an indication to increase steroid dose.

Continued

Ocular myasthenia resistant to treatment

Some patients fail to respond to pyridostigmine and prednisolone. A small minority of patients may have milder symptoms and may not be suitable for long-term treatment with pyridostigmine or prednisolone, to minimise side effects. Serial monitoring with an orthoptist can be very helpful, since selected patients may do well with a prism, patch or a frosted lens to manage their diplopia. Ptosis props or Lundie loops may help some patients with ptosis. Squint surgery and botulinum toxin treatment should be avoided. If there is doubt, discuss these options with an MG specialist.

Patients who fail to achieve minimal symptom expression with prednisolone

There are several reasons why some MG symptoms do not respond to steroids:

Box 3 Continued

- Patients with MG who remain symptomatic at 3 months and need more than 30 mg/day of prednisolone (or who cannot bring down the maintenance steroid dose below 7 mg/day even with adequate dose and duration of non-steroidal immunosuppressants) should be discussed with the regional MG specialist clinic.
- Patients taking steroids should be given an alert card[XII] to indicate they are being prescribed steroids (or this information should be amalgamated with their myasthenia alert card). There should be dialogue with other specialties when other comorbidities require steroid dose changes in a different regimen format than that usually considered for MG.

- Slow treatment response: patients should continue steroids at an optimal dose (see section on steroids) for at least 2–3 months before concluding that steroids are not going to induce remission.
- Underdosing: ensure the patient has reached an appropriate target dose.
- Some patients find steroids are not effective treatment for their MG. When this is the case, the advice of an MG specialist should be sought.

ROLE OF THYMECTOMY IN MYASTHENIA GRAVIS

Summary of thymectomy in myasthenia gravis

- Thymectomy is recommended for all acetylcholine receptor (AChR) antibody-positive patients aged below 50 years.
- Thymectomy should be discussed in patients with AChR-myasthenia gravis (MG) aged 50–65 years.
- Thymectomy should be offered irrespective of the radiological appearance of the thymus, and as early in the disease course as possible in AChR-MG.
- Thymectomy should be done in all patients with thymoma (irrespective of antibody status).
- Thymectomy for non-thymoma is preferably done within 2 years of diagnosis, but can be considered later if there are high steroid requirements despite appropriate dose and duration of non-steroidal immunosuppressants.
- Minimally invasive surgery is preferable, with video or robot-assisted thoracoscopic thymectomy offered to all patients unless there are specific contraindications.
- Optimum control of MG should be achieved before elective thymectomy.
- Thymectomy (unless thymoma) is not indicated in muscle-specific tyrosine kinase MG.
- Anaesthetic guidelines can be accessed via www.orphananesthesia.eu

Thymectomy for thymoma

All patients with thymoma should be offered thymectomy. Refer to a thoracic surgeon experienced in this procedure, with the support of an appropriately skilled anaesthetist. Thymectomy is best done in a hospital with immediate access to a neurology team with experience in MG because of the risk of perioperative complications. Optimum control of MG should be achieved before thymectomy even at the expense of a delay in surgery. All MG medications should be continued as normal. There is no role for routine intravenous immunoglobulin (IVIg)/plasma exchange before thymectomy if there is no clinical indication for this. Oncology referral is also required for any thymoma, and surveillance should be arranged as per MDT outcomes.

Thymectomy for non-thymoma

There is class I evidence for thymectomy in patients with AChR antibody-positive generalised MG (including clustered AChR antibodies) or those with borderline titres of AChR antibodies combined with confirmatory neurophysiology.[13] The trial recruited patients within 5 years of diagnosis and showed clinical improvement over 3 years and also the need for lower doses of prednisolone. Since approximately 75% of those presenting with ocular myasthenia eventually develop generalised MG, thymectomy is worth considering for patients with AChR-MG with pure ocular disease (especially those needing immunosuppression), but only in the first 2–3 years, after which generalisation is much less likely, and efficacy of thymectomy is probably reduced.

Minimally invasive thymectomy has greatly improved the cosmetic outcome with reduced postoperative pain, duration of hospital stay and of complications. The less traumatic and scar-minimising video or robot-assisted thoracoscopic thymectomy is available in most centres and should be the first-line treatment in all patients unless there are surgical/anaesthetic contraindications. There are limited efficacy data for patients aged 50–65 years, but thymectomy should be offered unless there are significant comorbidities. There are no data to support thymectomy in patients with seronegative MG. Appropriate chest imaging as per local protocol (CT/MRI) should also be carried out in these patients and if thymectomy is being considered this should be discussed within an MDT/with MG specialists.

INTRODUCING NON-STEROIDAL IMMUNOSUPPRESSION

- It is recommended to introduce non-steroidal immunosuppressive therapy if a patient requires prednisolone more than 7 mg/day to maintain remission.[XIII]
- Intolerable steroid side effects are an indication to introduce non-steroidal immunosuppressive therapy to reduce steroid maintenance dose.

- Non-steroidal immunosuppressive therapy should be considered early in patients with diabetes, osteoporosis, ischaemic heart disease, psychiatric disorders or significant bulbar or respiratory weakness that does not respond rapidly to steroids. Please see other reviews on the use of steroids in neurology.[14 15]
- The risk of opportunistic infection is felt to be low when corticosteroids and immunosuppression monotherapy is used in MG. The use of co-trimoxazole should be discussed with the local infectious disease/immunology team in any patient with risk factors that increase their vulnerability for pneumocystis pneumonia infection (for example, if CD4 count is less than 200×10^6/L (normal 430–1690) or if required by local immunosuppression guidelines).[XIV]

Immunosuppression with first-line agents

- Tables 1–3 summarise the most commonly used medications.
- A common goal of treatment is stable remission or minimal manifestations on prednisolone 5 mg daily or less.
- Before starting any non-steroidal immunosuppressive therapy, local protocols should be followed regarding viral or other infection screening (eg, hepatitis B/C, tuberculosis, HIV).
- Azathioprine has been the traditional first-line steroid-sparing agent in myasthenia following a positive placebo-controlled randomised controlled trial (RCT) showing efficacy and a steroid-sparing effect that became evident after 18 months of treatment. Despite a lack of RCT evidence of efficacy, mycophenolate mofetil is frequently used as an alternative. Methotrexate is another alternative: there is no placebo-controlled trial evidence of efficacy but it appeared to have similar efficacy to azathioprine but with more rapid onset, in one randomised trial against azathioprine in MG. Mycophenolate and methotrexate must not be used where pregnancy is possible.
- Azathioprine remains the first-choice immunosuppression in women of childbearing potential, and in young men. It is possible to take azathioprine during pregnancy,[XV] and it is considered safe in breastfeeding mothers.[XVI]
- Thiopurine methyltransferase (TPMT) should be measured before starting azathioprine in view of the association between TPMT deficiency and myelosuppression with azathioprine.[XVII] Patients with very low TPMT activity should not be given azathioprine. Cautious use with close monitoring of the blood tests can be done in patients with limited options (eg, women of childbearing potential) if the TPMT activity is intermediate.
- 6-thioguanine nucleotides (6-TGN), which are incorporated into DNA, are the active metabolites of azathioprine. 6-TGN can be used to monitor adherence, dosing and toxicity, especially in inflammatory bowel disease[XVIII], but this may not always be sufficient to optimise the treatment. Moreover, this is not widely available or practised in myasthenia, but where available should be considered.
- Azathioprine should be increased over 1–2 months to a maintenance dose of 2.5 mg/kg/day. Blood tests should be monitored closely (full blood count, urea and electrolytes, liver function tests) as the dose is titrated upwards.[XIX] A drop in lymphocyte count and/or an elevation in mean corpuscular volume often occurs when patients are taking azathioprine and is often considered desirable.[XX] We recommend using local shared-care protocols or previous reviews.[2]
- There is an increased risk of skin malignancy, especially with long-term azathioprine use, and adequate ultraviolet light protection is advised on exposure to sunlight.
- Ciclosporin does not appear to be more harmful than azathioprine in pregnancy.
- Methotrexate is teratogenic in females (evidence is limited in males), and effective contraception is mandatory until at least 3 months after the drug is stopped.
- Mycophenolate mofetil is reported to produce congenital malformations and effective contraception should always be used and continued for at least 6 weeks after stopping. It should be used with caution when men take it without contraception.[XXI14]
- Clinicians should be aware of inadequate dosing of non-steroidal immunosuppressive therapies when patients do not respond to the medications, and this needs to be taken into account before switching medications.
- Steroid tapering may be attempted gradually on patients who have minimal symptom expression on non-steroidal immunosuppressive therapies.
- For steroid-sparing agents, once treatment goals have been achieved and maintained for 1–3 years, this can be tapered slowly to the minimal effective dose. Dosage adjustments should be made no more frequently than every 3–12 months. It is usually necessary to maintain low-dose immunosuppression for many years, sometimes for life. *Some patients may be in a position or may wish to attempt to wean completely; the risk of relapse is unknown in many cases and this uncertainty, balanced with the risk of long-term immunosuppression, should be carefully discussed with the patients regularly*.
- Ensure to exclude hypogammaglobulinaemia if there are recurrent infections.

Rituximab

- Since the last guideline was issued, the cost of rituximab has fallen considerably, worldwide experience has substantially increased and RCTs have been published that show evidence for efficacy in early generalised MG.[16]
- Rituximab as a 500 mg single dose is useful early in the disease course (greater probability of attaining minimal manifestations at week 16 without need for rescue therapies, as per RINOMAX trial)[16] and can be considered around the time of starting steroids in generalised

Table 1 Summary of the most commonly used medication in myasthenia gravis effective within days

Effective within days					
Medication	**Usual adult dose**	**Common side effects**	**Caution/monitoring**	**Notes**	**Level of evidence**
Pyridostigmine	Start at 30 mg TDS to QDS, slowly titrate up to 360 mg/day	Muscle/abdominal cramps, diarrhoea, increased salivation, bladder urgency	Bradycardia, asthma, heart disease	Propantheline 15 mg TDS to QDS may be used to counteract cholinergic side effects.	Clinical practice
Intravenous immunoglobulin	1 g/kg or 2 g/kg in divided doses over 2–5 days	Headache (aseptic meningitis) and raised blood pressure; rarely skin rash and transaminitis	Venous thromboembolism prophylaxis may be necessary.	May be repeated monthly. Use as maintenance therapy is exceptional.	Clinical practice; RCT
Plasma exchange	Four to five exchanges	Hypocalcaemia symptoms during infusion (due to EDTA use). Haemodynamic instability	Caution in anticoagulation, active sepsis or pregnancy	May be repeated monthly. Use as maintenance therapy is exceptional.	Clinical practice; Case series; RCT
Efgartigimod*	10 mg/kg once weekly if intravenously (max. per dose 1.2 g) for 4 weeks; subcutaneous dose is 1000 mg (for all patients) weekly for 4 weeks. Repeated if necessary as per MG-ADL scores (usually at least 3 weeks after the last dose of previous cycle).	Transient IgG depletion		Not routinely available – specialist initiation only	DBRCT
Zilucoplan*	Daily s/c dose adjusted for body weight. Range 16.6 mg to 32.4 mg daily	Injection site reactions	Need meningococcal vaccination	Not routinely available – specialist initiation only	DBRCT
Rozanolixizumab	280–840 mg (as per body weight) once weekly for 6 weeks, subsequent 6-week treatment cycles to be administered according to clinical evaluation	Angioedema, arthralgia, increased risk of infections		Not routinely available – specialist initiation only	DBRCT

*Some of the potentially effective therapies include calcineurin inhibitors (ciclosporin, tacrolimus), neonatal Fc gamma receptor blockers (eg, efgartigimod, rozanolixizumab), C5 complement inhibitors (eg, eculizumab, ravulizumab, zilucoplan) and alkylating chemotherapy agents (eg, cyclophosphamide). From the newer class of medications, only efgartigimod, rozanolixizumab and zilucoplan are mentioned above since these drugs are most familiar to the authors outside a clinical trial. This does not mean that these are the only drugs available or these are in any way superior to other drugs with similar mechanisms of action. We recommend discussion with an MG specialist in advance of starting these agents.

ADL, activities of daily living; DBRCT, double-blind RCT; MG, myasthenia gravis; OD, once daily; QDS, four times a day; RCT, randomised controlled trial; s/c, subcutaneous; TDS, three times a day.

Table 2 Summary of the most commonly used medication in MG effective within weeks to months

Effective within weeks to months (useful for induction of remission)					
Medication	**Usual adult dose**	**Common side effects**	**Caution/monitoring**	**Notes**	
Prednisolone	Start at 5 mg OD, increase by 5 mg every 3–5 days until on 20 mg OD (ocular MG) or 30 mg OD (generalised MG) or until significant improvement, whichever is earlier. (See prednisolone protocol for details)	Short term: heartburn, sleep disturbance, mood changes, acne, weight gain, blurred vision. Long-term: gastric ulcers, osteoporosis, proximal myopathy, fluid retention, weight gain, diabetes mellitus, hypertension, cataracts, glaucoma, thin skin, easy bruising and infection risk. Steroid-induced Addisonism with long-term use.	Steroid-induced exacerbation of weakness after 5–10 days. Greater risk with high doses and in weakest muscles. Avoid leaving patients at high doses for long periods. Refer to local guidelines for bone and gastric protection. Periodic bone density scans, regular HbA1c and blood pressure monitoring. Be aware of the risk of avascular necrosis of the hip.	Continue effective dose for 4 weeks; then reduce by 5 mg every 2–4 weeks until on 20 mg OD and thereafter by 2–2.5 mg every 2–4 weeks until on 10 mg OD. Further reductions in steps of 1 mg every 4 weeks until on 5 mg OD. Medium term goal is stable remission on prednisolone 5 mg OD alone or in combination with additional immunosuppression.	Clinical practice; RCT (ocular MG)
Rituximab	500–1000 mg – repeated if necessary (lower doses have been used). Recommended early in generalised MG requiring immunosuppression to induce remission. **Early use in all symptomatic patients with MuSK-MG**	Infections: reactivation of TB, hepatitis, VZV, etc. Rare but serious: PML. Immunoglobulin deficiency with repeated use (IgM common, symptomatic generalised IgG deficiency less common).	Check FBC, U&E, LFT, chest X-ray, hepatitis, HIV and varicella serology and immunoglobulin levels before initiation. Follow local guidelines. Monitor blood counts, immunoglobulins and CD19 levels during therapy. B cells may not recover if used with drugs which inhibit lymphocyte proliferation.	If CD19 levels rise to more than 1%, consider re-dosing (usually single dose – 500 mg/day), if relapsing symptoms. Early use may increase remission rates, reduce crisis frequency and reduce steroid requirements.	Case series; DBRCT
Ciclosporin*	Start at 25 mg BD increased by 50 mg every 3–7 days until on 2.5 mg/kg/day	Dose-dependent and reversible renal impairment and hypertension are common SEs usually settling with dose reduction. Nausea, vomiting, excessive body hair, renal failure, headache PRES. Additional irreversible risk of renal impairment with long-term use.	Regular monitoring of blood pressure and renal function.	Can monitor drug levels. Useful in steroid-resistant disease and in women of childbearing potential.	Clinical practice; RCT
Tacrolimus*	Maximum dose of 50 mcg/kg/day	Nausea, vomiting, myelosuppression, high blood pressure, diabetes, renal and hepatic dysfunction	Check FBC, U&E and LFT every 2–4 weeks for 3 months and 3 monthly thereafter. Regular BP monitoring.	Trough level to be maintained at 5–10 ng/mL. Useful in steroid-resistant disease.	Clinical practice
Cyclophosphamide*	Pulsed intravenously as per CYCLOPS vasculitis regimen	Nausea, vomiting, diarrhoea, fatigue, haemorrhagic cystitis (risk reduced by Mesna use), myelosuppression, ovarian failure. PJP pneumonia risk – use with prophylactic co-trimoxazole. Long-term TCC bladder and solid tumour risk.	Check FBC (severe neutropenia and lymphopenia risk), U&E and LFT every 1–2 weeks for 3 months and monthly thereafter. Adjust doses as per cyclops regimen.	Rarely used but of potential use in refractory disease.	Clinical practice; case series; RCT

*Some of the potentially effective therapies include calcineurin inhibitors (ciclosporin, tacrolimus), neonatal Fc gamma receptor blockers (eg, efgartigimod, rozanolixizumab), C5 complement inhibitors (eg, eculizumab, ravalizumab, zilucoplan) and alkylating chemotherapy agents (eg, cyclophosphamide). From the newer class of medications, only efgartigimod, rozanolixizumab and zilucoplan are mentioned above since these drugs are most familiar to the authors outside a clinical trial. This does not mean that these are the only drugs available or these are in any way superior to other drugs with similar mechanisms of action.
BD, two times a day; CD19, cluster of differentiation 19 cells (B lymphocytes); DBRCT, double-blind RCT; FBC, full blood count; LFT, liver function tests; MG, myasthenia gravis; MuSK, muscle-specific tyrosine kinase; OD, once daily; PJP, Pneumocystis Jirovecii Pneumonia; PML, Progressive Multifocal Leukoencephalopathy; PRES, Posterior Reversible Encephalopathy Syndrome; RCT, randomised controlled trial; SEs, Side Effects; TB, tuberculosis; U&E, urea and electrolytes; VZV, Varicella Zoster Virus.

Table 3 Summary of the most commonly used medication in MG effective within months to years

Effective within months to years: long term maintenance of remission on minimal steroid dose, sometimes termed 'steroid-sparing' agents.					
Medication	**Usual adult dose**	**Common side effects**	**Caution/monitoring**	**Notes**	
Azathioprine	Start at 50–75 mg OD (1 mg/kg) and titrate over 1–2 months to reach 2.5 mg/kg/day.	Nausea, vomiting, myelosuppression, liver dysfunction, risk of skin cancer	Always check and ensure TPMT levels are normal before initiation. Check FBC, U&E and LFT every 2–4 weeks for 3 months and 3 monthly thereafter.	Lymphopenia and macrocytosis are common and often desirable. Drug of choice in women of childbearing age.	Clinical practice; RCT
Mycophenolate mofetil	Start at 500 mg BD, increased within 2–4 weeks to 1000 mg BD (can go up to 1500 mg BD)	Dyspepsia, gastrointestinal upset and myelosuppression	Check FBC, U&E and LFT every 2–4 weeks for 3 months and 3 monthly thereafter.	Avoid, if risk of pregnancy.	Clinical practice;
Methotrexate	Start at 5–7.5 mg/week, maximum dose usually 15–25 mg/week as per response and tolerance	Nausea, vomiting, mouth ulcers, myelosuppression, respiratory and hepatic dysfunction.	Chest X-ray prior to starting. Check FBC, U&E and LFT every 2–4 weeks for 3 months and 3 monthly thereafter.	Folic acid to be given 5 mg/6 days a week except on the day of methotrexate or follow local guidance (eg, 10 mg weekly avoiding the MTX day). Some patients may need subcutaneous therapy if not well absorbed orally.	Clinical practice; RCT
Thymectomy	Required for thymoma if patient fitness allows. Recommended early in generalised non-thymoma AChR-MG<50 years. Consider in AChR-Ab positive ocular MG requiring immunosuppression to achieve remission and in 50–65 year olds generalised AChR-MG.	Scarring (prominent with open technique). Minimally invasive techniques recommended. Rare phrenic/recurrent laryngeal nerve injury. Worsening of respiratory failure in the short term.	Ensure adequate symptom control (esp. respiratory function) preoperatively. Consider anaesthetic issues – orphanesthesia.eu	Early use may increase remission rates, reduce crisis frequency and reduce steroid requirements in AChR-MG.	Clinical practice; DBRCT

A common goal of treatment is stable remission or minimal manifestations on prednisolone 5 mg daily or less. Induction of remission often requires high-dose prednisolone. Medium-term steroid and immunosuppression requirements are reduced by early thymectomy or rituximab (see indications) in AChR-Ab generalised MG. Long-term maintenance of remission on low-dose prednisolone often requires combination therapy with a 'steroid-sparing' immunosuppressant.
AChR-Ab, acetylcholine receptor antibody; BD, two times a day; DBRCT, double-blind RCT; FBC, full blood count; LFT, liver function tests; MG, myasthenia gravis; MTX, methotrexate; OD, once daily; RCT, randomised controlled trial; TPMT, thiopurine methyltransferase; U&E, urea and electrolytes.

AChR-MG with moderate-to-severe disease (Myasthenia Gravis Foundation of America (MGFA) class III or above).

- RCTs have not tested whether rituximab should be used in conjunction with thymectomy. Thymoma was specifically excluded from the RINOMAX RCT. The efficacy of rituximab in thymoma-associated MG is therefore unclear.
- Early referral to an MG specialist is recommended and regional guidelines[XXII] should be followed where appropriate, especially if there is a need to assess the role for chronic treatment-refractory MG. The role and dose of rituximab beyond 12 months is unclear but currently not supported by trial evidence.
- MuSK-MG is often refractory to most conventional MG treatments but highly responsive to rituximab. Early rituximab is recommended in patients with bulbar symptoms. The dose used in MuSK-MG studies is more conventional—that is, 1000 mg at day 1 and repeated at day 14. However, relapse is common and hence it is recommended that all patients with MuSK-MG should be referred to an MG specialist.

Novel immunomodulatory treatments

A range of new treatments have been developed that can help to manage MG symptoms by acting on the complement system (AChR-MG only) or by reducing plasma antibody concentrations through inhibiting neonatal Fc receptors (FcRn). These agents should be considered in treatment-resistant MG (sometimes referred to as refractory MG); such cases include those with highly active disease that has not responded to standard treatment with at least two steroid-sparing agents, or those ineligible/intolerant to these agents,

those with frequent acute severe exacerbations and those who depend on regular IVIg/plasma exchange.

These agents are only currently available through specialist clinics after discussion via an MG MDT, usually through an early access programme or within a clinical trial setting. A detailed discussion of these medications is beyond the scope of this guideline but can be found in other reviews.[17–19] All patients considered for newer immunomodulatory therapies should be referred to a specialist MG clinic (see Myaware website for suggestions, but please be aware that this is often an incomplete list, https://www.myaware.org/specialists-in-myasthenia) and it is anticipated that when these drugs are approved, their use will be based on discussion at a regional or national MDT.

Complement inhibitors

Autoantibodies to the acetylcholine receptors in MG have been shown to activate the complement cascade leading to structural damage to the postsynaptic membrane at the neuromuscular junction resulting in impaired transmission. Complement activation results in cleavage of complement component 5 (C5) which initiates the terminal complement pathway to form the membrane attack complex.

- Complement inhibitors typically bring about rapid improvement in generalised AChR-MG symptoms within days to weeks and have had only mild side effects, including injection site reactions, headache and diarrhoea.
- C5 inhibitors can be used as intravenous infusion (eg, eculizumab and ravulizumab) or as a daily subcutaneous injection (zilucoplan, which is licensed by the MHRA) and all patients must receive a quadrivalent (serotype ACWY, one dose) and serotype B meningococcal vaccine, two doses 4 weeks apart, at least 4 weeks before starting treatment. In addition, patients needing to start complement inhibitors within 2 weeks of vaccination MUST receive oral antibiotic prophylaxis

FcRn blockers

The FcRn plays a pivotal role in recycling of endogenous IgG. Recently, monoclonal antibodies targeting the FcRn have been developed, which significantly reduce recycling of endogenous IgG, thereby leading to a reduction in circulating autoantibodies in patients with both AChR-MG and MuSK-MG. Several anti-FcRn agents have been studied to date. Efgartigimod, rozanolixizumab, batoclimab and nipocalimab have all been studied in Phase 3 RCTs comparing treatment to standard care.

- Currently, efgartigimod is licensed by the MHRA, the European Medicines Agency (EMA) and US Food and Drug Administration as an add-on to standard therapy for adult patients with generalised AChR-MG.
- Rozanolixizumab is approved by the MHRA and EMA as an add-on to standard therapy for adults with generalised disease in both AChR-MG and MuSK-MG.
- There are no data directly comparing the different anti-FcRn treatments to each other, nor are there data comparing the anti-FcRn treatment to other targeted therapies.
- IgG concentrations must be checked before starting anti-FcRn therapy and treatment should not be started if the IgG concentration is <6 g/L. As both IVIg and FcRn monoclonal antibodies bind to the FcRn receptor, they cannot be given concurrently; a washout period of 4 weeks is required before starting an anti-FcRn following IVIg treatment.
- Anti-FcRn therapies work quickly with a response to treatment generally occurring in the first cycle (usually 3–4 weeks). A small proportion of patients who do not respond in the first cycle may respond to a second or occasionally third cycle, but if there is no clear response at this point, the patient should be considered a non-responder and treatment should be stopped.

Other newer therapies

There are several newer trials using molecules targeting B-cell/plasma cells or cytokines/chemokines or using chimeric antigen receptor-T cell therapies which are in various phases of clinical trials but there is no evidence to suggest using any of these in routine clinical practice at present. Autologous haematopoietic stem cell transplantation can attenuate, or even completely terminate, disease activity in many autoimmune neurological diseases including MG, but should only be considered under specialist recommendation and MDT discussion.

Criteria for IVIg use and plasma exchange

IVIg and plasma exchange should only be used for severe generalised MG in the inpatient or ambulatory care setting, when there is a risk of impending or established myasthenic crisis (see section on “emergency inpatient managament” for details). It should not generally be used as a maintenance therapy. If MG symptoms cannot be controlled even after one course of IVIg/plasma exchange, a specialist opinion should be sought for consideration of alternate treatments, if available.

ASSESSMENT AND MANAGEMENT OF THE RELAPSING PATIENT WITH MG

It is important to determine whether the patient’s deterioration is a myasthenic relapse, a side effect of treatment or secondary to another condition.[XXIII] MG relapses can be triggered by intercurrent infection, reduction/stopping steroids and/or immunosuppressant medication or a patient starting a treatment known to exacerbate MG.

Consider repeating mediastinal imaging (using MRI or CT scan of the thorax) in patients with thymoma and without thymoma to exclude the development/recurrence of thymic pathology where there is no obvious precipitant.

- If a cause for MG deterioration can be found, it should be managed.
- Reintroduce pyridostigmine for symptom control if it has been withdrawn.
- Patients with MG deterioration should return to the steroid protocol. Patients often achieve remission at a lower dose of prednisolone than that required at disease onset. Once stabilised, the prednisolone should then be titrated down to the lowest effective dose. If this is more than 7 mg per day, a non-steroidal immunosuppressive therapy should be introduced (if not already on it) or a specialist MG opinion should be sought.
- If the MG deterioration was a result of steroid withdrawal in a patient receiving non-steroidal immunosuppression, the relapse may have been a result of too short a duration of immunosuppressant treatment or too low a dose, which should prompt review.
- If MG relapses are recurrent and unrelated to the above factors, please refer to an MG specialist.

EMERGENCY INPATIENT MANAGEMENT OF MYASTHENIA GRAVIS

General principles

- A patient should be managed in hospital for significant bulbar or respiratory symptoms, especially with progressive deterioration or those with highly active disease.
- Assessment by a speech and language therapist to advise on swallowing is recommended.
- Regular assessment of forced vital capacity (FVC) is essential (single breath count and respiratory rate can occasionally be used as surrogate markers, but do not replace FVC). More than 30% drop in baseline FVC or less than 20 mL/kg should prompt intensive care unit (ICU) referral (normal FVC is approximately 50 mL/kg; approximate calculation of FVC (in mL) is single breath count × 100).[12]
- Sequential FVC measurements are key, with the rate of decline guiding early intervention.
- Pulse oximetry is not a reliable marker for neuromuscular respiratory failure and should not be used to exclude respiratory compromise, since oxygen desaturation often occur very late.
- Caution should be applied to using oxygen in a non-intensive care setting and the presence of hypoxia should prompt immediate critical care referral for neuromuscular respiratory support.
- The critical care/ICU team should be notified about the presence and status of the patient (when making critical care decisions, please bear in mind that patients with MG have normal life expectancy and have excellent response to treatment).
- Be aware of drug interactions with concomitant medications (see Myaware website for details).
- Optimise pyridostigmine dose (see Pyridostigmine Protocol).
- Any patient needing hospital admission for MG should be promptly reviewed in the neurology outpatients soon after discharge, to ensure there is a clear steroid tapering plan and review of any non-steroidal immunosuppressive therapies.

Intravenous immunoglobulin

- If there are significant bulbar symptoms, but the patient is not requiring mechanical ventilation, the current guideline is to give 1 g/kg IVIg over 2–3 days and repeat within 5–7 days if there is no significant response or discussed with a specialist.
- If the patient is in (impending) ventilatory failure, the recommendation is to give 2 g/kg IVIg over 5 days.[XXIV]
- If symptoms persist despite IVIg, request a specialist opinion on whether to use a second course of IVIg, or preferably use plasma exchange (if IVIg non-responder).
- Please note that the duration of efficacy of IVIg is 3–4 weeks, after which a stable patient may deteriorate if effective steroid dosing or alternate immunosuppression has not been established.
- Ensure to check hepatitis B/C serology and serum immunoglobulin concentration before starting IVIg, though it is not necessary to wait for the results in an emergency scenario.
- IVIg should be used with caution in renal failure, hypersensitivity to immunoglobulins and hypercoagulable states.

Plasma exchange

- Plasma exchange is now considered as effective and safe as IVIg if the facilities are available. Where possible, plasma exchange should be performed via peripheral vein access with centrifugal machines which minimises the requirement for central venous access and significantly reduces the morbidity of the procedure. Each session should aim to exchange up to 1.5 plasma volumes and a typical schedule is five sessions over 5–10 days, as per local guidelines.
- Plasma exchange is best avoided in sepsis.

Prednisolone (inpatients)

If rescue treatment (plasma exchange/IVIg) has not been administered, start prednisolone 5–10 mg/day and increase by 5 mg every other day, until target dose achieved. Patients should be monitored closely for deterioration, which can occasionally happen with steroid therapy.

If the patient has been or is being treated with IVIg/plasma exchange during the admission, steroids can be introduced more rapidly (eg, starting at 10 mg/day increasing 5–10 mg every second day until on 30 mg/day). There is no trial evidence to guide the speed of titration and where there is uncertainty, advice should be sought from an MG specialist. Again, the dose must be tapered down following the Prednisolone protocol detailed above.

MANAGEMENT OF MYASTHENIA IN THE INTENSIVE CARE UNIT SETTING

Patients may require intensive care or high dependency care to monitor bulbar and respiratory function or to

provide assisted ventilation or airway support. The critical care team should be informed when patients with acute severe exacerbations of MG are admitted to the hospital so they can be regularly reviewed, progress monitored and care escalated before acute deteriorations. Patients who are slow to recover from elective or emergency surgery may also require ICU admission. Factors predicting impending myasthenic crisis and general management principles are outlined in figure 2.

General principles

- Monitoring is key. Initially, treat patients with non-invasive ventilation (NIV) in the ICU, not outside. If they do not tolerate NIV, high-frequency oscillatory ventilation is an option, but it may not be as effective as NIV.
- If patients need ventilatory support, a semi-elective intubation is preferable to an emergency intubation. Signs that ventilatory support may be required include falling vital capacity, inability to complete a sentence in one breath, use of accessory muscle of respiration, tachycardia and difficulty managing secretions.
- NIV can be used to provide respiratory support, but as diaphragmatic weakness is generally accompanied by bulbar failure, it is often not tolerated. It may, however, be used to provide additional ventilatory support following extubation. High flow nasal oxygen can also be a useful non-invasive adjunct in the ICU (but is not recommended outside the ICU).
- The mainstay of management is to treat the precipitant cause, chest physiotherapy, monitoring ventilatory parameters while instituting medical treatment. Magnesium supplements should be used cautiously and only to replace very low levels.
- A nasogastric tube should be inserted to allow nutrition, hydration and administration of medication.
- If the patient is intubated, pyridostigmine should be used with caution due to increased secretions burden. It may be held during this time, if necessary, but should be restarted before extubation, if the patient previously responded to it.
- Treatment with IVIg or plasma exchange should be initiated promptly depending on what is available locally. For patients with a crisis, the IVIg dose is 2 g/kg of ideal body weight, usually over 5 days. If plasma exchange is available, it is often preferable to use it first.
- If first-line rescue therapy is not effective, recommend discussing with an MG specialist.

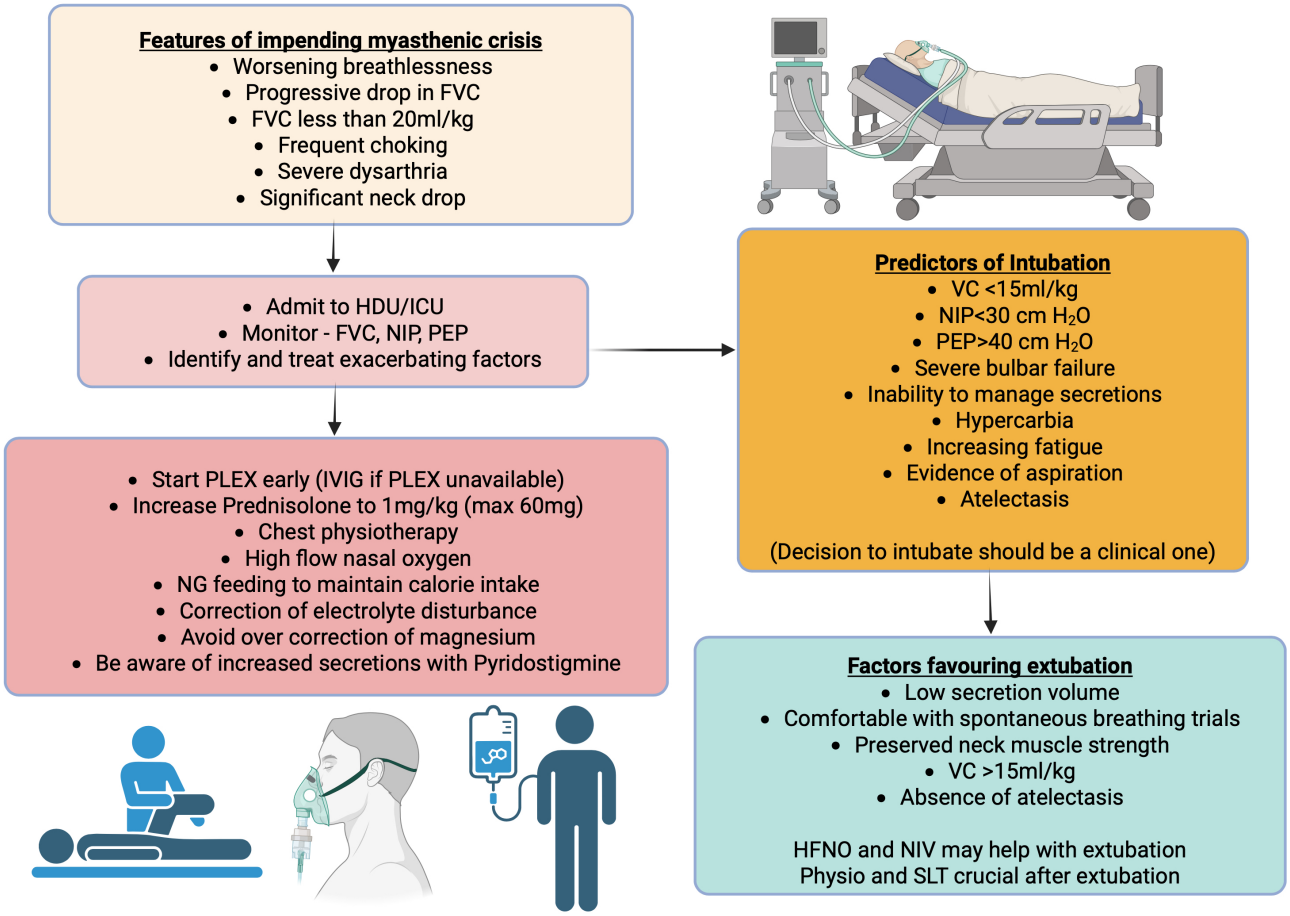

Figure 2 Myasthenic crisis predictors and treatment. FVC, forced vital capacity; HDU, high dependency unit; HFNO, high flow nasal oxygen; ICU, intensive care unit; IVIG, intravenous immunoglobulin; NG, nasogastric; NIP, negative inspiratory pressure; NIV, non-invasive ventilation; PEP, positive expiratory pressure; PLEX, plasma exchange; SLT, speech and language therapy; VC, vital capacity.

- The prednisolone dose may be increased up to 60 mg per day or 1 mg /kg/day (whichever is lower).
- Starting a non-steroidal immunosuppressive therapy can generally be delayed until the myasthenic crisis has resolved.
- Likewise, thymectomy is rarely indicated in the acute setting of myasthenic crisis. There are rare occurrences when thymoma removal has been performed while the patient still requires ventilation. This is the exception rather than the rule, and it is recommended to discuss the case in an MDT with a specialist myasthenia centre and thymectomy expertise.
- Intercurrent infections are not infrequently encountered during ICU admissions and should be treated promptly, bearing in mind the range of medications including antibiotics that can exacerbate myasthenic symptoms.[XXV]
- It is important to recognise the importance and clinical relevance of fatiguability. Assessments over several days may be needed to assess the suitability and timing of extubation.
- Tracheostomy is not infrequently required—this can allow respiratory weaning, secretion management with suctioning, the possibility of oral nutrition and speech (assuming adequate bulbar function) and is more comfortable—allowing weaning of sedative medication. Consider mucolytics such as carbocisteine to thin secretions and aid clearance.
- Even if patients require prolonged intubation and ventilatory support, they generally do well in the longer term, including those with older onset MG. It is rare to require long-term ventilatory support.
- Consider transfer to a specialist neuroscience centre for those who require prolonged intubation.
- A specialist neuroscience centre will also have the input of physiotherapists who are experienced in dealing with the slow ventilatory wean of the patients with MG as well as communication. The involvement of a respiratory physician who has expertise with domiciliary ventilation is helpful in planning the need for NIV. The MDT usually includes a clinical psychologist and speech/language therapists who can help with discussions around communication when intubated.

MYASTHENIA IN PREGNANCY AND BREASTFEEDING

- Planning for breastfeeding should ideally be instituted well in advance of any potential pregnancy to allow time for myasthenic status and drug optimisation.[20]
- Those with generalised myasthenic weakness need early planning and careful multidisciplinary management throughout, with prompt access to specialist advice and facilities.
- Most women with well-controlled MG should be able to go through pregnancy without difficulty.
- Multidisciplinary liaison should occur throughout pregnancy, delivery and in the neonatal period.
- Unless there are obstetric or personal reasons, spontaneous vaginal delivery in hospital should be safe in most patients with MG.
- Babies born to mothers with myasthenia have a 10% risk of transient neonatal myasthenia with potential onset of myasthenic weakness until a few days post partum, even if the mother's MG is well-controlled, and should have access to neonatal high-dependency support.[XXVI]
- Arthrogryposis multiplex congenita in the fetus is a rare but recognised complication of maternal MG. Specialist advice should be sought in managing subsequent pregnancies.
- Fetal acetylcholine receptor antibody-related disorders comprise both the more severe arthrogryposis multiplex congenita and the milder fetal acetylcholine receptor inactivation syndrome.[21]
- Pyridostigmine is not expected to cross the placenta, and there have been no reports of fetal malformations. It is compatible with breastfeeding.
- Abrupt reductions or withdrawal of immunosuppressant agents should be avoided as this may destabilise myasthenic control.
- Prednisolone has not been shown to increase fetal malformations. It may reduce fetal growth, but this need not limit its use.
- Azathioprine is considered safe in pregnancy and breastfeeding, as is ciclosporin.
- Rescue treatment with IVIg or plasma exchange is considered safe and is preferably given after discussion with specialist colleagues.
- Mycophenolate mofetil and methotrexate should be avoided in pregnancy and breastfeeding.
- Other drugs such as rituximab may be justified early in the pregnancy (especially until the end of the first trimester) and if being considered, should be discussed with an MG specialist. Information on novel therapies, such as FcRn inhibitors and complement inhibitors, is not available at present and patients taking these treatments should be counselled to avoid pregnancy.
- Clinicians and patients should be alert to the possibility of puerperal or postpartum exacerbation of myasthenia.

ROLE OF SPECIALIST MULTIDISCIPLINARY TEAM

- The role of the MG clinical nurse specialist (CNS), where available, has transformed the holistic care of patients with MG. Rather than being constrained by the consultant clinic capacity, the CNS can provide timely and more frequent responses to enquiries from patients. The CNS may be able to identify early indicators of myasthenic deterioration enabling prompt adjustments to treatment and potentially avoiding hospital admission.
- CNS may be the primary point of contact for other healthcare professionals such as surgeons, anaesthetists, pre-assessment staff, obstetricians, general practitioners and dentists.
- Liaison with a neurosciences pharmacist familiar with MG can be helpful for many enquiries, particularly availability of MG drugs, potential interactions of drugs and

vaccines (see also box 4 on vaccinations). For monitoring of possible complications from immunosuppressant drugs, different centres will have their own practice, but generally either the CNS or neurosciences pharmacist may run a drug monitoring clinic. A structured approach allows reliable checks at set intervals to be put in place, with the potential to pick up emerging problems early.

- Referral to a neuro-specialist occupational therapist may be helpful for fatigue management.
- Patient support organisations like *Myaware* provide peer support to patients in addition to being a source of information.

FATIGUE MANAGEMENT IN MYASTHENIA

- Up to 80% of patients with MG experience fatigue. The prevalence is higher in patients with symptomatic MG but can also be experienced when in pharmacological remission. Escalating MG therapies in patients with prominent or isolated symptoms of fatigue should be avoided. Patients should be educated in managing their fatigue by planning accordingly, prioritising activities during the day and pacing their lives in negotiation with their MG status. Advice on adopting healthier lifestyles may also be relevant.
- Various studies support the importance of exercise, including low-impact exercise such as walking, swimming, balance strategies and protocols that include aerobic training as well as resistance/stretch training. Patients with mild and moderate MG may be able to exercise in a gym setting. Patients with moderate MG who are older should be advised on low-impact exercise including balance exercises and stretch training such as yoga. Onward referral to the local physiotherapy team for guidance on a suitable exercise protocol is mostly relevant for patients who are older, those with moderate MG or who may be extremely deconditioned.[22]
- Isolated breathlessness does not always indicate respiratory muscle weakness and can be from weight gain, deconditioning, an altered breathing pattern or an alternative underlying medical condition. This can still be limiting to the individual and aggravate fatigue. Respiratory muscle training has a role in MG and is beneficial also in patients undergoing thymectomy when implemented preoperatively. A discussion with the local respiratory team and physiotherapist is recommended.

Box 4 Vaccinations and immunosuppression

- Vaccines are less effective in immunosuppressed patients.
- Live vaccines are absolutely contraindicated if there is any ongoing immunosuppression including steroids.
- Corticosteroids in high doses and other immunosuppression can reduce immune response to vaccines and live virus vaccinations should be delayed for at least 1 month after stopping high-dose corticosteroids. When practically possible, patients requiring immunosuppression may be advised to have their vaccinations updated before starting treatment, including pneumococcus, influenza, *Haemophilus influenzae,* COVID-19 and varicella zoster (in patients aged 50 and over). Where feasible, clinicians should consider completing any necessary vaccinations ideally 4 weeks before starting immunosuppression including rituximab.
- Patients on immunosuppression should also minimise contact with other people (especially children) who have had recent live vaccinations; close contacts of immunosuppressed individuals should also be fully immunised as per the UK schedule. (see - Live attenuated vaccines: avoid use in those who are clinically immunosuppressed - GOV.UK).
- Vaccines are likely to be less effective after rituximab; for full efficiency, it is best to vaccinate once B-cells have repopulated.
- Where a patient has been counselled to be fully vaccinated before starting immunosuppression, but they elect not to have some or all the available vaccinations, this should be clearly documented.
- Meningococcal vaccinations should be given before starting complement inhibitor therapies.

When to consider referral to (or discussion with) the MG specialist

- Repeated hospital admissions with need for rescue therapy.
- Patients in myasthenic crisis (especially if not responding to first-line rescue therapy).
- Persistently high myasthenia gravis (MG) activities of daily living score of >5 after adequate immunosuppression.
- Inability to tolerate first-line non-steroidal immunosuppression.
- Patients with MG who remain symptomatic at 3 months and need more than 30 mg/day of prednisolone.
- Patients unable to bring down the maintenance prednisolone dose below 7 mg/day despite adequate dose and duration of non-steroidal immunosuppressants.
- Patients needing consideration of rituximab.
- Pregnancy and preconception.
- Patients with complex comorbid disease, which can confound MG assessment and treatment.
- Recommend early referral/discussion in patients with seronegative/muscle-specific tyrosine kinase-MG.
- Suspected or confirmed congenital myasthenic syndrome.
- Lambert-Eaton myasthenic syndrome.

SUMMARY

The management of MG has evolved over the last few years with slightly different approaches to AChR-MG and MuSK-MG. The emphasis is now on lower doses of long-term corticosteroids, and ideally these are given once daily. In AChR-MG, early thymectomy is recommended in patients younger than 50 years of age and can be considered between the ages of 50 and 65. There is reasonable evidence to use a single dose of rituximab early on at diagnosis in patients with generalised AChR-MG but only limited evidence for long-term maintenance therapy, unlike in MuSK-MG, which traditionally responds less to conventional treatments and is usually rituximab-responsive (see online supplemental figure). Newer therapies are in the process of being approved to use in the UK, and their potential role in the treatment algorithm (figure 1) is slowly being established.

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Author note Methodology: The ABN special interest group (SIG) met at the ABN Annual Meeting in Belfast (May 2023) and a proposal for updating the MG guidelines was recommended based on several lines of emerging novel therapies, new evidence and change in practice since the last ABN guidelines in MG was published. Our approach was that of a modified Delphi process. At the annual Myasthenia Day in Birmingham (Feb 2024) expression of interest to revise the guidelines was invited from all the members of the SIG to join the guidelines coordinating group. Coordinating group consisted of representatives from each of the devolved nations and within England, regional spread of experts who possess relevant experience, who have contributed to the MG field and represented NHSE selected regional MG centres. All

needed to be willing to contribute their opinions (and review evidence). A topic guide was developed through open-ended questions. Where there was disagreement, matter was resolved through discussion and finally by the chair to avoid any dominant opinions. There were no significant disagreements, as such consensus was reached for all topics, although there were some areas where further research and data are needed. The coordinating group met weekly since April 2024 and each member was assigned topics based on their subspecialist interests. Other stake holders like intensivists and obstetricians were consulted for review of specific subset of topics. This was then put through consensus voting and agreement was reached based on the evidence available. Each coordinating member would participate in a series of discussion-based meetings. Where there was disagreement, discussion continued until a statement could be generated that met a consensus position. Extensive document was first generated which was then reviewed by each coordinating member for accuracy and relevance. The first draft of the guideline has been circulated to all other members of the Myasthenia SIG, patient organisations (Myaware and MDUK), general neurologists, specialist nurses as well as trainee neurologists for their feedback and the comments, which were reviewed and incorporated into the final guidelines document by the coordinating group.

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