

## **CLINICAL GUIDELINE**

# Myasthenia Gravis or Lambert-Eaton Myasthenia Syndrome, Medicines that may affect patients

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Approval Group:	Medicines Utilisation Subcommittee of ADTC

#### Important Note:

The Intranet version of this document is the only version that is maintained.

Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.



Information for healthcare professionals

### Medicines that may affect patients with Myasthenia Gravis or Lambert-Eaton Myasthenic Syndrome

There are certain medicines that have been reported to worsen or induce myasthenia gravis (MG), often by increasing muscular weakness, and should be used with caution in patients with this condition. The list of medicines in table 1 has been compiled to assist prescribers in the decision making process when prescribing medicines for patients with myasthenia gravis.

The medicines in this list have been classed according to those which should be:

- Absolutely contraindicated
- Avoided
- Used with caution
- Probably safe with patient monitoring.

This list is not exhaustive, best attempts have been made to identify problematic medicines but it is acknowledged that information may not be complete. If a medicine is not on the list it is not guaranteed that it will be safe in myasthenia gravis, please be vigilant with new medicines where safety in myasthenia gravis may be lacking. It is important that patients and doctors be alert to the early signs of an exacerbation of myasthenia gravis (MG) when a new medicine is commenced, even if it is not on the list or is listed as probably safe.

If further advice is required this can be obtained from the neurology pharmacy team (Tel: 0141 201 2688 or email: neuro.pharmacy@ggc.scot.nhs.uk) or the on call neurology registrar who can be contacted via switchboard.

Avoid 🔺	Caution	Probably Safe
	Gastrointestinal	
Co-phenotrope ▲ Magnesium containing antacids/laxatives ▲ Antimuscarinics <sup>(a)</sup> ▲ Hyoscine (hydrobromide and	H2-receptor antagonists Anti-emetics Prochlorperazine, levomepromazine, droperidol	Antimuscarinics Propantheline ● (this is routinely used to counteract the side effects of pyridostigmine)
butylbromide), dicycloverine Anti-emetics Cinnarizine, promethazine		
	Cardiovascular	1
Anti-arrhythmics <sup>(b)</sup> A Procainamide, lidocaine, disopyramide, propafenone, quinidine	Anti-arrhythmics Flecainide, amiodarone, dronedarone Anti-platelets Dipyridamole (may counteract the effect of pyridostigmine) Beta-blockers <sup>(a)</sup> (class effect including ophthalmic preparations) Calcium Channel Blockers Amlodipine, diltiazem, felodipine, nifedipine, verapamil Diuretics (class effect, monitor electrolytes) Methyldopa Statins (class effect)	
	Respiratory	
Sedating antihistamines Alimemazine, clemastine, chlorphenamine, cyproheptadine, hydroxyzine, ketotifen, promethazine	Corticosteroids (inhaled) Caution if high dose, probably safe at lower doses	Antimuscarinics (inhaled) – probably safe due to minimal systemic absorption

- a) Do not stop if stable on treatment discuss with neurology
- b) If this medicine is clinically indicated and no alternative exists, seek specialist advice
- c) Discuss with neurology if considering use
- d) New onset or exacerbation of myasthenia gravis has been identified as a rare side effect of immune checkpoint inhibitors. See <u>Cautionary Drugs (myasthenia.org)</u> for more details
- e) Use may be considered on a case by case basis discuss with neurology
- f) Small number of case reports of myasthenia gravis in association with hepatitis B vaccination but more evidence needed to determine if causative effect

Avoid 🔺	Caution 💻	Probably Safe 🔍
	Nervous System	·
Epilepsy and other seizure disor	ders	
	Anti-epileptics	Anti-epileptics  Levetiracetam, Lamotrigine, Sodium Valproate
Mental health disorders		
<b>Benzodiazepines</b> (class effect)	Antipsychotics (class effect, includes first and second generation) Buspirone	
	Lithium 📕	
	Monoamine-Oxidase Inhibitors Isocarboxacid, phenelzine, tranylcypromine	
	Tricyclic antidepressants (class effect)	
Movement disorders		1
Orphenadrine 🔺	Amantadine	
Procyclidine 🔺		
Trihexyphenidyl		
Botulinum Toxin Nausea and labyrinth disorders		
Anti-emetics	Anti-emetics	
Cinnarizine, promethazine	Prochlorperazine, levomepromazine, droperidol	
Pain		ł
Strong opioids <b>(</b> class effect)	Weak opioids <a>(class effect, includes tramadol)</a>	Paracetamol
Migraine		1
	Pizotifen 🧧	
	Eletriptan 📕	
Sleep disorders		
<b>Benzodiazepines</b> (class effect)	Chloral hydrate 📕	
Zopiclone, Zolpidem 🔺	Clomethiazole	
Diphenhydramine (Nytol®)	Melatonin 🗕	
Nicotine dependence	Nicotine replacement	

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Avoid 🔺	Caution	Probably Safe
	Infection	-
🔺 🔺 Teli	thromycin is Absolutely Contr	aindicated
Aminoglycosides <sup>(b)</sup> ▲ Gentamicin, amikacin, tobramycin, streptomycin, neomycin Antimalarials ▲ Chloroquine, mefloquine, quinine Clindamycin ▲ Polymyxins ▲ Colistimethate sodium Ribavirin ▲	Macrolides Clarithromycin, erythromycin, azithromycin Penicillins Ampicillin Quinolones Ciprofloxacin, delafloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin Tetracyclines Doxycycline, lymecycline, minocycline, oxytetracycline, tetracycline, demeclocycline Cefoxitin Co-trimoxazole (sulphonamides) Daptomycin Imipenem-cilastin Nitrofurantoin Rifampicin Vancomycin I	Aztreonam • Ceftriaxone • Meropenem • Metronidazole • Penicillins (except ampicillin) • Trimethoprim • Aciclovir •
	Ritonavir	
	Endocrine	1
Levothyroxine A Avoid over replacement	Corticosteroids (commonly used to treat MG. Sudden increases in dose could exacerbate symptoms – please consult neurology) Bisphosphonates Hormonal changes may affect MG symptoms	
	Genito-urinary	1
Antimuscarinics Darifenacin, fesoterodine, flavoxate, oxybutynin, propiverine solifenacin, tolterodine, trospium (solifenacin may be safest of drug class, please discuss with neurology)	Apha-adrenoceptor blockers Alfuzosin, doxazosin, indoramin, prazosin, tamsulosin, terazosin Oestrogens/Progestogens Hormonal changes may affect MG symptoms	

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Avoid 🔺	Caution	Probably Safe
	mune system and malignant dise	
	vised prior to commencing chemoth Aldesleukin, busulfan, cisplatin, doxorubicin, etoposide, fludarabine, mitotane Monoclonal antibodies <sup>: (d)</sup> atezolizumab, avelumab, cemiplimab, durvalumab, ipilimumab, nivolumab, pembrolizumab Oestrogens/Progestogens Hormonal changes may affect MG symptoms Interferon (alpha and beta)	
	Blood and Nutrition	
Magnesium supplements (unless treating hypomagnesaemia)	Desferrioxamine Eltrombopag Miglustat Sodium lactate Trientene	
	Musculoskeletal	
Rheumatology Penicillamine ▲ Hydroxychloroquine ▲ Colchicine ▲ Muscle Relaxants – dantrolene, methocarbamol ▲ Quinine ▲	Collagenase Etanercept Febuxostat Muscle Relaxants <sup>(c)</sup> Baclofen, tizanidine Riluzole	lbuprofen ● Naproxen ●

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Avoid 🔺	Caution	Probably Safe
	Eye	
Polymyxin or bacitracin containing preparations	Antimuscarinic eye drops atropine, cyclopentolate, tropicamide	
Aminoglycoside eye drops 🔺	Beta-blocker eye drops	
	Carbonic anhydrase inhibitors (oral and ophthalmic) Acetazolomide, brinzolomide, dorzolamide	
	Corticosteroid eye drops	
	Ear, nose and oropharynx	
Polymyxin or bacitracin containing preparations	Corticosteroids (ear, nose and oropharynx)	
Aminoglycosides (ear and nose) 🔺	Lidocaine (oropharynx) 📕	
	Skin	
Polymyxin or bacitracin containing preparations Aminoglycosides (topical)	Clindamycin (topical) Corticosteroids (topical) Imiquimod Macrolides (topical)	Antimuscarinics (topical)
	Vaccines	
Yellow fever vaccine ▲ <sup>(e)</sup> Avoid live vaccines if on immunosuppression ▲	Hepatitis B vaccine <sup>(f)</sup>	

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Avoid 🔺	Caution 📕	Probably Safe	
	Anaesthesia		
Discussion with neurology ac	lvised prior to myasthenic patient un	dergoing anaesthesia	
Muscle Relaxants – dantrolene	Inhalational agents myasthenic patients require smaller amounts of these agents Depolarising drugs variable response in myasthenia gravis Non-depolarising drugs myasthenic patients are particularly sensitive to these agents Local anaesthetics myasthenic patients require smaller amounts of these agents Antimuscarincs Atropine, glycopyrronium	Propofol <sup>(c)</sup>	
	Emergency treatment of poisonin	g	
	Pralidoxime chloride 📕		
Miscellaneous			
	Iodinated Contrast Media 📕		

#### References

The following references have been used to compile this list in conjunction with local expert opinion:

- Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press. Accessed at <u>www.medicinescomplete.com</u> Dec 2021
- Various Manufacturers. Summaries of Product Characteristics. Accessed at <u>www.medicines.org.uk</u> Dec 2021
- Drug Consult: Drug-Induced Myasthenia Gravis. In: DRUGDEX<sup>®</sup> System (Internet database). Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed at <u>www.micromedexsolutions.com</u> Dec 2021
- Baxter K, Preston CL (eds), Stockley's Drug Interactions (online). London: Pharmaceutical Press (electronic version). Accessed at <u>www.medicinescomplete.com</u> Dec 2021
- Myaware.org. Drugs to Avoid. Accessed at Drugs to Avoid | myaware Dec 2021
- Myasthenia Gravis Foundation of America. Cautionary Drugs. Accessed via <u>Cautionary Drugs</u> (<u>myasthenia.org</u>)
- Mehrizi M, Fontem RF, Gearhart TR, Pascuzzi RM. Medications and Myasthenia Gravis (A reference guide for healthcare professionals) Myasthenia Gravis Foundation of America Inc. August 2012. Accessed via:

https://myasthenia.org/portals/0/draft medications and myasthenia gravis for MGFA website 8%2 010%2012.pdf

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