CLINICAL GUIDELINE

Pyridostigmine for Myasthenia Gravis Q&A

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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Important Note:

The online 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.

PYRIDOSTIGMINE FOR MYASTHENIA GRAVIS

Q&A

This guideline aims to raise awareness and educate practitioners on the important issues to consider when a patient is prescribed pyridostigmine

Key messages

- **Missed dose of pyridostigmine can cause myasthenic crisis which is a medical emergency**
- **Contact pharmacy urgently to obtain stock of pyridostigmine**
- **Contact the on-call neurology registrar for acute clinical advice for patients with myasthenia gravis who are NBM**
- **Contact pharmacy for advice on dosage and administration of alternative formulations in patients who are NBM**

Background Information

What is pyridostigmine?

Pyridostigmine bromide is an anticholinesterase drug used for the symptomatic treatment of myasthenia gravis. It is used to enhance neuromuscular transmission in voluntary and involuntary muscles in myasthenia gravis.

How does it work?

It prolongs the action of acetylcholine in the neuromuscular junction by inhibiting the action of the enzyme acetylcholinesterase. More acetylcholine in the neuromuscular junction results in stronger muscle contractions and less muscle weakness/increased strength of muscles involved in eye movements, limb strength, swallowing and breathing.

What is the usual dosage?

No single fixed dose schedule will suit all patients with myasthenia gravis, whose medication requirements vary from time to time, day to day, and in response to stress or infection. The usual starting oral dose is 15-30mg three to four times daily. The 60mg tablet can be halved to produce a 30mg dose or quartered to produce a 15mg dose.

The usual maximum daily dose of pyridostigmine is 360mg; higher doses are unlikely to give additional benefit. Most patients require around 180mg/day. It is inadvisable to

exceed a total daily dose of 450mg in order to avoid acetylcholine receptor down regulation.

Pyridostigmine usually takes 30-60 minutes to start working so patients should take their first dose of the day when they get up and other doses about 30-60 minutes before a meal. The usual duration of action is 3 to 4 hours in the daytime but a longer effect (6 hours) is often obtained with a dose taken on retiring for bed.

Pyridostigmine is excreted renally therefore lower doses may be required in renal impairment. Reducing pyridostigmine doses may increase the risk of myasthenic crisis; please contact pharmacy or neurology for advice if a patient has new renal impairment or acute kidney injury.

What are the cautions and side effects?

Pyridostigmine should be used with caution in the elderly, those with cardiac history, asthma, patients on beta-blockers (which may themselves aggravate MG) and in electrolyte disturbances. Carry out an ECG prior to starting pyridostigmine in elderly or frail patients and those with cardiac history.

Gastrointestinal side effects are common, especially if just started on pyridostigmine or recently increased dose. Cholinergic side effects such as abdominal cramps, diarrhoea, increased salivation and sweating are counteracted by giving oral propantheline (15mg usually 15-30 minutes before the pyridostigmine dose is due) or loperamide. Increased bronchial and oral secretions may be a problem in patients presenting with swallowing difficulties or respiratory insufficiency.

Safety Issues

What are the most important things to consider when someone is taking pyridostigmine?

Missed Doses

Pyridostigmine MUST be given on time, at the same times the patient takes at home, and exactly as it has been prescribed. Medication administered too late may result in excessive weakness and even the inability to swallow. It is important to maintain the prescribed dosing schedule because a missed or late dose can precipitate *myasthenic crisis*, which can be fatal.

If a dose is missed within an hour of the prescribed time, the patient should take the missed dose and continue with the other doses as scheduled. If the dose is missed by more than one hour, the patient should take the dose immediately and then wait 3 to 4 hours before taking the next dose. Subsequent doses should be taken as scheduled. Never double up a dose to make up for a missed one.

There is a known risk of adverse clinical incidents because of repeated missed doses of

pyridostigmine. Pyridostigmine may not be readily available in all ward areas but can be obtained urgently from pharmacy. Out of hours it can be obtained from the neurology ward at the Queen Elizabeth University Hospital, from your local emergency cupboard or via the on call pharmacist.

Nil by Mouth Status

Patients who are unable to take tablets orally or who are "nil by mouth" should be assessed for suitability of a nasogastric tube, and should receive pyridostigmine via this route of administration. Administration of pyridostigmine via nasogastric feeding tube is the preferred option in patients who are nil by mouth.

Pyridostigmine bromide is available as tablets or as an oral solution both of which can be administered via enteral tubes.

- The oral solution is licensed for administration via NG and PEG tubes (except those made of latex).
- The tablets can be crushed to a fine powder (and mixed with at least 10ml of water) which suspends in water to give an even dispersion which flushes via a nasogastric tube without blockage.

If the patient is unable to swallow and nasogastric administration is not possible, parenteral neostigmine may be given as a short term measure instead following **specialist neurology advice**.

Oral pyridostigmine 60mg is equivalent to 1mg to 1.5mg of intramuscular or subcutaneous neostigmine

- Contact pharmacy for advice on HOW to convert pyridostigmine to neostigmine if required.
- If the patient is dysphagic and passage of nasogastric tube is difficult, parenteral neostigmine could be used to facilitate tube passage.
- The half-life of neostigmine is short (~1-2 hours) compared to pyridostigmine (~3-4 hours). Due to this, myasthenia symptoms may be controlled for a shorter period of time when using neostigmine. Contact neurology for advice.
- Prescribers should be cautious not to overdose neostigmine when managing symptoms (see below for further details); patients should be monitored closely to ensure that the neostigmine is adequately controlling myasthenia gravis symptoms, and is not causing untoward cholinergic side effects. Doses should be adjusted accordingly.

Overdose

Acetylcholinesterase inhibitors in overdose can cause a life-threatening cholinergic crisis. Cholinergic crisis is a medical emergency, requiring urgent medical attention. It is important to identify the difference between Cholinergic Crisis and Myasthenic Crisis; see *Table 1* for related symptoms.

Table 1: Symptoms of Cholinergic Crisis and Myasthenic Crisis

Cholinergic Crisis	**Myasthenic Crisis**
Abdominal cramps	*Respiratory distress*
Diarrhoea	*Respiratory arrest*
Nausea and vomiting	*Cyanosis*
Excessive secretions	*Increased pulse and blood pressure*
Miosis	*Diaphoresis*
Fasciculations	*Poor cough*
Diaphoresis	*Inability to handle oral secretions*
Weakness	*Dysphagia*
Weakness worse with acetylcholinesterase inhibitors	*Weakness improves with acetylcholinesterase inhibitors*

Toxicity be can hard to evaluate since the symptoms of muscle-weakness could also be due to a worsening of myasthenia or under medication. In such cases the time of the pyridostigmine/neostigmine dose administration could provide crucial information.

- If the acute worsening of strength is 3-4 hours after dose, then it could be due to under dosing and indicate the next dose is due.
- If symptoms occur soon after (15-60 minutes) a dose, this might indicate signs of cholinergic toxicity.

If a patient with myasthenia gravis has a suspected acetylcholinesterase inhibitor overdose, refer to the on-call neurology registrar for further advice. For acute management of suspected toxicity please refer to TOXBASE.

If unsure, **CHECK** the dosage with the prescriber before administration of any cholinesterase inhibitor.

If in doubt, consult neurology on-call registrar.

General Information

Medicines which may aggravate myasthenia gravis

There are certain medicines (or classes of medicines) that have been reported to worsen or induce myasthenia gravis, often by increasing muscular weakness, and should be avoided or used with caution in patients with this condition. The following guideline has

further information on medicines that may affect myasthenia gravis: Myasthenia Gravis or Lambert-Eaton Myasthenia Syndrome, medicines that may affect patients (642) Right Decisions

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