



## Important Statement

Many different drugs have been associated with worsening myasthenia gravis (MG). However, these drug associations do *not* necessarily mean that a patient with MG should not be prescribed these medications because in many instances the reports are very rare and in some instances they might only be a “chance” association (i.e. not causal). Also some of these drugs may be necessary for a patient’s treatment. Therefore, some of these drugs should not necessarily be considered “off limits” for MG patients. **Careful thought** needs to go into decisions about prescription. It is advisable that patients and physicians *recognize and discuss* the possibility that a particular drug might worsen the patient’s MG. They should also consider, when appropriate, the pros and cons of an alternate treatment, if available. It is important that the patient notify his or her physicians if the symptoms of MG worsen after starting any new medication. We are only listing the *more common* prescription drugs with the *strongest* evidence suggesting an association with worsening MG.

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### Some of the more common prescription drugs associated with worsening MG.

(See “read this first” for more information. Also see [myasthenia.org](http://myasthenia.org) for more information.)

- **Telithromycin (Ketek)** – inpatient drug for serious pneumonia. Should not be used in patients with MG. FDA has designated a “black box” warning (see below for explanation) on this drug in MG patients.
- The **fluoroquinolones**, including **Ciprofloxacin** and **Levofloxacin** – commonly prescribed antibiotics that are rarely associated with worsening MG. The US FDA has designated a “black box warning” on **Ciprofloxacin/Avelox** and **Levofloxacin**. Use cautiously, if at all.
- **Zithromax** (e.g. “Z-pak”) – commonly prescribed but potentially dangerous in MG. Use cautiously, if at all.
- **Gentamycin, neomycin** (aminoglycoside antibiotics; tobramycin may be least offensive) – use cautiously if no alternative treatment available.
  - Other antibiotics have been rarely reported with worsening MG. Please discuss with physician.
- **Botulinum toxin** (e.g. “Botox”) – avoid.
- **Steroids** (e.g. prednisone) – steroids are a common treatment *for* MG but patients who start steroids may have transient worsening of their MG during the first two weeks prior to an improvement in their MG. Thus, patients need to monitor carefully for this possibility.
- **Quinine** - sometimes used for leg cramps.
- **Procainamide** - cardiac drug used for irregular heart rhythm.

- **Magnesium** in patients with kidney disease; potentially dangerous if given intravenous, for example, for eclampsia treatment during late pregnancy. (Many multivitamins contain small amounts of magnesium, which is okay.)
- **D-penicillamine** - drug rarely used these days but strongly associated with causing MG.
- **Beta-blockers** – commonly prescribed for hypertension, heart disease and migraine but potentially dangerous in MG. Use cautiously, if necessary.

## What is a “black box warning”?

In the US, a “black box warning” (also known as boxed warning) is an alert that appears on the package insert for certain prescription drugs. A black box warning signifies that studies have shown the drug carries a significant risk of a serious or life-threatening adverse event. The black box warning is the strongest warning by the US FDA. For MG patients, some of the drugs that carry black box warnings include the **fluoroquinolones** (e.g. **Ciprofloxacin, Levofloxacin**; see above) and **Teletromycin** (i.e. **Ketek**); these particular antibiotics have been associated with worsening of MG in some patients. **Mycophenolate mofetil** (CellCept) also carries a black box warning for an increased risk of teratogenicity (e.g. malformation of fetus in utero) for pregnant mothers. MG patients should discuss potential risks of these drugs (and others on the provided list above) with their doctors.

## Comments about vaccinations

- **Vaccinations:** It is generally believed that vaccinations (e.g. influenza) are safe in patients with MG (with a major caveat below). The evidence suggests that vaccine-related worsening of MG is rare and thus most MG specialists believe the benefits of immunization outweigh any small risk related to possible transient worsening of MG symptoms.
  - **Exception/caveat:** If you are taking immunosuppressive medication, such as Prednisone, Azathioprine or Mycophenolate, it is usually recommended that you avoid *live, attenuated* vaccines. Examples of live, attenuated vaccines include the shingles vaccine and the nasal spray form of the influenza vaccine (the influenza injection is inactivated and thus not alive, so it is much safer in immunosuppressed patients). You need to discuss this with any doctor when considering a vaccine. If you are not sure, you should ask your doctor if you are taking immunosuppressive drugs and, if so, if the vaccine is safe in that setting. It’s worth noting that most vaccines are inactivated (e.g. dead), but because there are a few vaccines that are alive and attenuated (i.e. the pathogen is alive but not very virulent and thus immunizes the patient without causing the disease) and because the live, attenuated vaccines carry higher risk for those who are immunosuppressed, this technicality about vaccines is important and is always worth consideration.

**Checkpoint inhibitors:**

Immunotherapy for cancer is an exciting treatment advance for many types of cancers. However, one newly recognized rare side effect of some of these treatments is myasthenia gravis (MG). MG has become recognized as a rare complication of immune checkpoint inhibitors (ICIs) for cancer (immunotherapy). People who did not have MG before beginning immunotherapy have a higher likelihood of developing the disease, although worsening of myasthenic weakness has been reported in people with existing, previously-diagnosed MG. The average onset of MG symptoms is within 6 weeks (range 2–12 weeks) of starting immunotherapy. To date, development or exacerbation of MG has been reported for pembrolizumab, although it has been seen with nivolumab, ipilimumab and other ICIs. Risk may be increased with administration of combinations of ICIs. Patients with MG and cancer considering cancer immunotherapy should talk to their oncologist and neurologist about this possible side effect. Likewise, doctors evaluating new-onset weakness in cancer patients on immunotherapy should consider MG. Additionally MG with ICIs can be accompanied by inflammation of skeletal and/or heart muscle. MG patients who experience worsening weakness following ICI treatment should contact their Neurologist and Oncologist immediately.

Examples of immune checkpoint inhibitors (ICIs):

- Pembrolizumab (Keytruda)
- Nivolumab (Opdivo)
- Atezolizumab (Tecentriq)
- Avelumab (Bavencio)
- Durvalumab (Imfinzi)
- Ipilimumab (Yervoy)