Toxic Neuropathy

for the CMT Patient

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This fact sheet is intended to alert patients with Charcot-Marie-Tooth about medications that might worsen their neuropathy and be harmful to their strength, sensation, and function. Of the thousands of recognized medications, only a small number are known to damage nerves or cause neuropathy. Most of these drugs fall into two broad categories: **chemotherapies or antibiotics**, most notably, fluoroquinolones (oral and injectible), but numerous other treatments are also known to cause nerve injury. While there are notable exceptions, most examples of toxic neuropathy produce damage to sensation or pain nerves and have lesser effects on motor or strength nerves.

The nerves of individuals with neuropathy from any cause, including CMT, may be more vulnerable to certain conditions and stresses such as toxins and certain medications than other people's nerve. The list of potentially toxic medications can be divided by the relative likelihood or risk of causing a problem. Some medications are well known to cause toxicity, while others have been found to cause neuropathy only rarely. For a handful of medications, evidence of toxicity is controversial, doubtful, or extremely rare.

Other factors may further influence whether a treatment is tolerated or not, including other medical conditions, especially diabetes, kidney failure, or alcohol abuse. Establishing a clear causative link between medication use and increased symptoms or nerve loss is not always simple. Worsening nerve function very soon after starting a new drug is very suspicious, especially if the medication is of high concern. However, some agents may cause problems only after extended use, for example the antibiotics metronidazole and linezolid. Toxicity of this type after years of use is very rare.

When problems appear immediately after starting a new treatment or medication, it is important to see your doctor as soon as possible. One would expect symptoms or function to improve after the drug is stopped; however, improvement may be delayed by weeks or months depending on the degree of injury and how long the agent stays in the body.

For example, the heart drug amiodarone may take several months to clear one's system. Alternatively, some medications may carry excessive concern only because they are used so widely, such as statins and certain stomach acid blockers. The decision to stop a treatment to see if improvement occurs must be weighed against the benefits of treatment.

For most drugs listed, the risk of exposure must be weighed against the benefit of use, including the severity of the treated condition, available alternative treatments, and drug effectiveness. There is only one example of a treatment that must be avoided in all circumstances. This exception is the chemotherapy treatment **vincristine** that may cause severe weakness and nerve injury after only 1 or 2 doses in patients with minimal or unknown CMT1A, the most common form. This medication carries a "black box" warning by the Food and Drug Administration (FDA) against use in CMT patients or in patients that might have CMT (e.g., relatives of individuals with CMT). Virtually all other treatments carry a relative but not absolute risk of use. There is no proven link between worsening neuropathy and anesthesia or vaccinations, although some claim increased symptoms following these events. In most but not all instances the condition prevented by a vaccination is much worse than the consequences of the injection. It is important, however, to always discuss any known family history of CMT with your health care provider, particularly your anesthesiologist.

Generic Name (Common brand name/s)

Definite High Risk (including asymptomatic CMT)	**Moderate to Significant Risk**	**Uncertain or Minor Risk**	**Negligible or Doubtful Risk**
Vinca alkaloids (Vincristine) (1)	Amiodarone (Cordarone)	5-Fluoracil (Adrucil)	Allopurinol (Zyloprim, Aloprim)
Taxols (paclitaxel, docetaxel, cabazitaxel)	Arsenic Trioxide	Adriamycin	Amitriptyline (Elavil)
	Auranofin (Ridaura)	Almitrine (not in U.S.)	Chloramphenicol
	Aurothioglucose (Solganal)	Atorvastatin (Lipitor)	Chlorprothixene (Taractan)
	Bortezomib (Velcade)	Chloroquine	Cimetidine (Tagamet)
	Brentuximab Vedotin	Cytarabine (high dose)	Clioquinil
	Cetuximab	Ethambutol	Clofibrate (Atromid)
	Ciprofloxacin (Cipro)	Etoposide (VP-16)	Cyclosporin A (Sandimmune, Neoral)
	Cisplatin & Oxaliplatin	Fluvastatin (Lescol)	Enalapril (Vasotec)
	Colchicine (extended use)	Gemcitabine (Gemzar)	Gluthethimide
	Dapsone	Griseofulvin (Grifulvin, Fulvicin)	Phenelzine (Nardil)
	Didanosine (ddI, Videx)	Hexamethylmelamine (Hexalen)	Propafenone (Rythmol)
	Dichloroacetate	Hydralazine (Apresoline, Apresazide, Marpres)	Sulfonamides
	Disulfiram (Antabuse)	Ifosphamide (Ifex)	Sulphasalzine (Azulfidine)
	Eribulin Mesylate (Halaven)	Infliximab (Remicade)	Sulfathiazole
	Fluoroquinolones (oral and injectable antibiotics) (2)	Interferon Alfa	Sulphamethoxazole
	Gemifloxacin (Factive)	Isoniazid (INH)	Sulfisoxazole
	Gold salts	Lansoprazole (Prevacid)	
	Ipilmumab	Lithium (Lithobid, Eskalith)	
	Ixabepilone (Ixempra)	Lovastatin (Mevacor, Altocor)	
	Leflunomide (Arava)	Omeprazole (Prilosec)	
	Lenolidomide	Penicillamine (Cuprimine, Depen)	
	Levofloxacin (Levaquin)	Phenytoin (Dilantin)	
	Lomefloxacin (Maxaquin)	Podophyllin resin	
	Mefloquine (Lariam)	Sertraline (Zoloft)	
	Metronidazole/Misonidazole (extended use) (Flagyl)	Statins	
	Moxifloxacin (Avelox)	Tacrolimus (FK506, ProGraf)	
	Nitrofurantoin (Macrodantin, Furadantin, Macrobid)	Zimeldine (not in U.S.)	
	Nitrous oxide (inhalation abuse or Vitamin B12 deficiency)		
	Nivolumab		
	Norfloxacin (Noroxin)		
	Ofloxacin (Floxin)		
	Pembrolizumab		
	Perhexiline (not used in U.S.)		
	Pertuzumab		
	Pomalidomide		
	Pyridoxine (mega dose of Vitamin B6) (see NIH Fact Sheet)		
	Sparfloxacin (Zagam)		
	Stavudine (d4T, Zerit)		
	Suramin		
	Thalidomide		
	Trovafloxacin (Trovan)		
	Zalcitabine (ddC, Hivid)		

1. Beutler et al (2014)
2. FDA Announcement July 26, 2016

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