

## Drugs That Prolong the QT Interval and/or Induce Torsades de Pointes

### Introduction:

Prolongation of the QT interval can lead to a life threatening ventricular arrhythmia- torsades de pointes (TdP) - which can result in sudden cardiac death.

There are three mechanisms by which drugs can interact and increase the risk of QT prolongation:

- **Pharmacodynamic Interaction:** The concurrent use of more than one drug that prolongs the QT interval increases the risk of torsades de pointes and ventricular arrhythmia.
- **Pharmacokinetic Interaction:** Some drugs do not prolong the QT interval themselves but can increase the risk of QT prolongation by affecting the metabolism of drugs that do. Commonly used examples of this include drugs that inhibit the CYP3A4 enzyme.
- **Effects on Electrolytes:** Hypokalemia and hypomagnesemia can increase the risk of QT prolongation

### How to minimize the risk of Drug induced QT prolongation:

- Assess patient's risk factors for QT prolongation
- Avoid QT prolonging drugs in patients with congenital long QT syndrome
- Correct any modifiable risk factors such as electrolyte disturbance
- Where a patient has risk factors and / or is prescribed an interacting medicine, the first line option is to change to an alternative drug that is not known to prolong the QT interval whenever possible.
- Consider carrying out a baseline ECG prior to starting a QT prolonging drug in patients with risk factors then repeat when the medicine reaches steady state
- If there is no alternative to using two drugs in combination that are known to prolong the QT interval, especially in patients with additional risk factors, carry out an ECG at baseline and then repeat when the new medicine is likely to reach steady state
- If long term use of two medicines that can prolong the QT interval is deemed necessary the patient should be followed up and monitored

**QT prolonging drugs lists can fit these three criteria:**

- **Possible Risk of QT prolongation/TdP** Substantial evidence supports the conclusion that these drugs can cause QT prolongation BUT there is insufficient evidence at this time that these drugs, when used as directed in official labeling, are associated with a risk of causing TdP.
- **Conditional risk of QT prolongation/TdP:** Substantial evidence supports the conclusion that these drugs are associated with a risk of TdP BUT only under certain conditions (e.g. Overdose, hypokalemia, congenital long QT or by causing a drug-drug interaction that results in excessive QT interval prolongation concomitant drug with TdP risk)
- **Known risk of QT prolongation/TdP:** Substantial evidence supports the conclusion that these drugs prolong the QT interval AND are clearly associated with a risk of TdP, even when taken as directed in official labeling.

**TABLE 1. Drugs with POSSIBLE Torsades de Pointes risk<sup>1,2</sup>**

<b>Drug class</b>	<b>Generic name</b>	<b>Brand name(s)</b>
<b>Alpha1-blockers</b>	<b>Alfuzosin</b>	<b>Xatral</b>
<b>Antibiotics</b>	<b>Gemifloxacin</b>	<b>Factive</b>
	<b>Norfloxacin</b>	<b>Noroxin</b>
	<b>Ofloxacin</b>	<b>Floxin</b>
<b>Chemotherapeutic agents</b>	<b>Tamoxifen</b>	<b>Nolvadex</b>
	<b>Leuprolide</b>	<b>Lupron</b>
	<b>Degarelix</b>	<b>Firmagon</b>
	<b>Crizotinib</b>	<b>Xalkori</b>
	<b>Lapatinib</b>	<b>Tykerb</b>
	<b>Nilotinib</b>	<b>Tasigna</b>
	<b>Sunitinib</b>	<b>Sutent</b>
	<b>Eribulin mesylate</b>	<b>Halaven</b>
	<b>Bortezomib</b>	<b>Velcade</b>
	<b>Dasatinib</b>	<b>Sprycel</b>
	<b>Pazopanib</b>	<b>Votrient</b>
	<b>Sorafenib</b>	<b>Nexavar</b>
	<b>Antidepressants</b>	<b>Venlafaxine</b>
<b>Mirtazapine</b>		<b>Remeron</b>
<b>Clomipramine</b>		<b>Anafranil</b>
<b>Imipramine</b>		<b>Tofranil</b>
<b>Nortriptyline</b>		<b>Nortrilen</b>
<b>Antiemetics</b>	<b>Dolasetron</b>	<b>Anzemet</b>
	<b>Granisetron</b>	<b>Sancuso</b>
<b>Antimanic agents</b>	<b>Lithium</b>	<b>Comcolet</b>
<b>Antipsychotic/antiemetic</b>	<b>Promethazine</b>	<b>Phenergan</b>

<b>Antipsychotics</b>	<b>Aripiprazole</b>	<b>Abilify</b>
	<b>Clozapine</b>	<b>Leponex</b>
	<b>Olanzapine</b>	<b>Zyprexa</b>
	<b>Paliperidone</b>	<b>Invega</b>
	<b>Risperidone</b>	<b>Risperdal</b>
	<b>Sertindole</b>	<b>Serdolect</b>
<b>Antivirals</b>	<b>Atazanavir</b>	<b>Reyataz</b>
	<b>Foscarnet</b>	<b>Foscavir</b>
	<b>Rilpivirine</b>	<b>Edurant</b>
<b>Immunosuppressants</b>	<b>Tacrolimus</b>	<b>Prograf</b>
<b>Muscle relaxants</b>	<b>Tizanidine</b>	<b>Sirdalud</b>
	<b>Tolterodine</b>	<b>Detrusitol</b>
<b>ADHD agents</b>	<b>Atomoxetine</b>	<b>Strattera</b>
<b>Oxytocics</b>	<b>Oxytocin</b>	<b>Syntocinon</b>
<b>Sedatives</b>	<b>Dexmedetomidine</b>	<b>Precedex</b>
<b>Somatostatin analogues</b>	<b>Pasireotide</b>	<b>Signifor</b>
<b>Multiple sclerosis medications</b>	<b>Fingolimod</b>	<b>Gilenya</b>

**TABLE 2. Drugs with **KNOWN** Torsades de Pointes risk**

<b>Drug class</b>	<b>Generic name</b>	<b>Brand name(s)</b>
<b>Anesthetics</b>	<b>Propofol</b>	<b>Diprivan</b>
	<b>Sevoflurane</b>	<b>Ulane, Sojourn</b>
<b>Antiarrhythmics</b>	<b>Amiodarone</b>	<b>Cordarone</b>
	<b>Disopyramide</b>	<b>Norpace</b>
	<b>Dronedarone</b>	<b>Multaq</b>
	<b>Flecainide</b>	<b>Tambocor</b>
	<b>Procainamide</b>	<b>Pronestyl</b>
	<b>Quinidine</b>	<b>Kinidin</b>
	<b>Sotalol</b>	
<b>Antibiotics</b>	<b>Azithromycin</b>	<b>Zithromax</b>
	<b>clarithromycin</b>	<b>Klacid</b>
	<b>Erythromycin</b>	
	<b>Ciprofloxacin</b>	<b>Cipro</b>
	<b>Levofloxacin</b>	<b>Tavanic</b>
	<b>Moxifloxacin</b>	<b>Avalox</b>
<b>Antidepressants</b>	<b>Citalopram</b>	<b>Cipram</b>
	<b>Escitalopram</b>	<b>Cipralext</b>
<b>Antiemetics</b>	<b>Ondansetron</b>	<b>Zofran</b>
<b>Antifungals</b>	<b>Fluconazole</b>	<b>Diflucan</b>
<b>Antimalarials</b>	<b>Chloroquine</b>	<b>Aralen</b>
<b>Anti-nausea agents</b>	<b>Domperidone</b>	<b>Motilium</b>
<b>Antipsychotics</b>	<b>Haloperidol</b>	<b>Haldol, Serenace</b>
	<b>Pimozide</b>	<b>Orap</b>
	<b>Sulpiride</b>	<b>Dogmatil</b>
	<b>Thioridazine</b>	<b>Mellaril</b>
<b>Antipsychotics/antiemetics</b>	<b>Chlorpromazine</b>	<b>Largactil</b>
<b>Antidementia agents</b>	<b>Donepezil</b>	<b>Aricept</b>
<b>GI stimulants</b>	<b>Cisapride</b>	<b>Propulsid</b>
<b>Opioid agonists</b>	<b>Methadone</b>	<b>Physeptone</b>

**TABLE 3. Drugs with **CONDITIONAL** Torsades de Pointes risk**

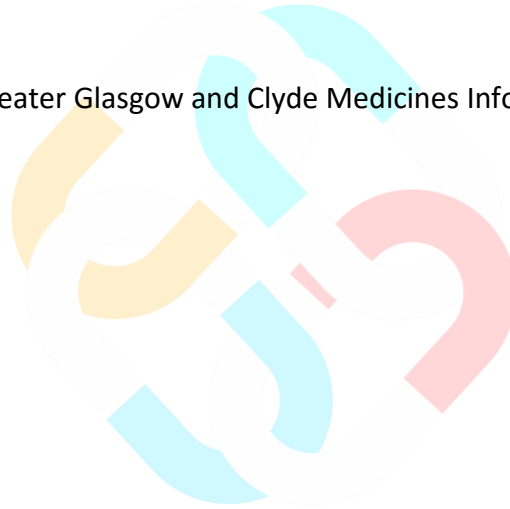
<b>Drug class</b>	<b>Generic name</b>	<b>Brand name(s)</b>
<b>Anti-anginal agents</b>	<b>Ivabradine</b>	<b>Procoralan</b>
<b>Antibiotics</b>	<b>Metronidazole</b>	<b>Flagyl</b>
<b>Antidepressants</b>	<b>Fluoxetine</b>	<b>Prozac</b>
	<b>Paroxetine</b>	<b>Seroxat</b>
	<b>Sertraline</b>	<b>Zoloft</b>
	<b>Amitriptyline</b>	<b>Tryptizol</b>
	<b>Doxepin</b>	<b>Sinequan</b>
<b>Antiemetics</b>	<b>Metoclopramide</b>	<b>Primperan</b>
<b>Antifungals</b>	<b>Itraconazole</b>	<b>Sporanox</b>
	<b>Ketoconazole</b>	<b>Nizoral</b>
	<b>Posaconazole</b>	<b>Noxafil</b>
	<b>Voriconazole</b>	<b>Vfend</b>
<b>Antihistamines</b>	<b>Hydroxyzine</b>	<b>Atarax</b>
<b>Antimalarials</b>	<b>Quinine sulfate</b>	<b>Qualaquin</b>
<b>Antimalarials/anti-inflammatory</b>	<b>Hydroxychloroquine</b>	<b>Plaquenil</b>
<b>Antipsychotics</b>	<b>Quetiapine</b>	<b>Seroquel</b>
	<b>Ziprasidone</b>	<b>Zeldox</b>
<b>Antivirals</b>	<b>Amantadine</b>	<b>Symmetrel</b>
	<b>Nelfinavir</b>	<b>Viracept</b>
	<b>Ritonavir</b>	<b>Norvir</b>
	<b>Telaprevir</b>	<b>Incivo</b>
<b>Antidementia agents</b>	<b>Galantamine</b>	<b>Reminyl</b>
<b>Diuretics</b>	<b>Furosemide</b>	<b>Lasix</b>
	<b>Hydrochlorothiazide</b>	<b>Esidrex</b>
	<b>Indapamide</b>	<b>Natrilix</b>
	<b>Torsemide</b>	<b>Demadex</b>
<b>Muscle relaxants</b>	<b>Solifenacin</b>	<b>VESIcare</b>
<b>Proton pump inhibitors</b>	<b>Pantoprazole</b>	<b>Proton</b>
<b>Sedatives</b>	<b>Chloral hydrate</b>	

NB. The list is not exhaustive and includes **only** locally encountered drugs. Most drugs have various other brand names which are not listed

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<sup>1</sup> Woosley, RL and Romero, KA, [www.Crediblemeds.org](http://www.Crediblemeds.org), QT drugs List, Accession Date, AZCERT, Inc. 1822 Innovation Park Dr., Oro Valley, AZ 85755

<sup>2</sup> Drug Induced QT Prolongation. Produced by NHS Greater Glasgow and Clyde Medicines Information Service Issue 21, December 2012



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